

Review of Access to New Medicines

Responses

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Respondents

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Response to Independent Review by Dr Brian Montgomery

Review of Access to New Medicines: Establishing more flexible approaches in evaluating medicines for rare conditions, including Duchenne Muscular Dystrophy.

Prepared by Action Duchenne

April 2016

Please find enclosed Action Duchenne’s feedback to the Review of Access to New Medicines, intending to realise more flexible approaches in the evaluation of orphan, ultra orphan and end of life conditions. In this response we have attempted to address the specific questions contained within the scope of the review as requested by Dr Brian Montgomery upon its launch. However, in this forward we are additionally eager to emphasise the disparity in standards, and divergence in outcomes, between the Scottish Medicines Consortium’s (SMC) process for evaluating orphan and ultra orphan medicine, and the National Institute for Health & Care Excellence’s (NICE) Highly Specialised Technology (HST) appraisal process.

Our recommendations for this review are predominantly yielded from our experience of engaging with the SMC on the evaluation of ataluren for the treatment of nonsense mutation Duchenne muscular dystrophy (nmDMD). The detailed advice document (DAD) for this therapy was published on April 11 not recommending ataluren for use within NHS Scotland owing to insufficient “justification of the treatment’s cost in relation to health benefits”. This advice was contradicted by NICE just four days later, who concluded that they’d; “been presented with sufficient evidence to show that the cost of ataluren was not materially greater than that for other treatments for small populations in relation to the benefits it offered [and that, moreover] the cost of ataluren per patient could be considered reasonable in the context of recouping manufacturing, research and development costs from sales to a small population”¹. NICE consequently recommended ataluren for treating nmDMD.

The cost of treatment presented to each appraisal body was consistent. These conflicting conclusions are therefore attributable to the prominence and gravity afforded to clinical and patient experts in each respective process. NICE fastidiously factored these views into their analysis, allowing parents to proactively participate in each evaluation committee meeting alongside the manufacturer and prominent clinicians. Conversely, the SMC systematically marginalised the patient and clinical voice, with key arguments from patient group submissions and the cursory PACE meeting offered terse and tokenistic acknowledgement within the determinative SMC committee meeting. That patient and clinical experts were moreover prevented from participating in this forum, leaving pressing and pertinent questions from committee members unanswered, further evidences the processes’ inability to engender equitable and robust decision making rooted in a comprehensive understanding of all available evidence.

Rare Diseases are commonly complex, heterogeneous and multi systemic in nature, often with a lack of experts and established treatment pathways. Patients, families, clinicians and patient groups therefore have a vital role to play in articulating levels of unmet clinical need and the impact potential treatments will have upon the lives of everyone concerned. Until the SMC accepts these truths as axiomatic and reflects this reality in the composition of their process for evaluating orphan and ultra orphan medicine, deferring responsibility for making these decisions, to NICE, needs seriously considering. Indeed, in a recent letter from Prof Jonathan Fox, we were reminded that, “The purpose of the Scottish Medicines Consortium (SMC) is to accept for use those newly licensed medicines that clearly represent good value for money”. It is clear from NICE’s recommendations on ataluren that the SMC is not fulfilling its purpose.

¹ NICE Final Evaluation Determination- ataluren for treating DMD with a nonsense mutation in the dystrophin gene, p.32.

It is therefore vital that you take stock of our points below and do all you can to ensure that drugs for rare and end of life conditions can be evaluated in the most expeditious, transparent and patient-focussed manner possible.

1. Background

1.1 Action Duchenne was the first organisation in the UK dedicated exclusively to Duchenne and Becker Muscular Dystrophy. We now fund cutting edge research into the condition whilst campaigning to improve the lives of everyone affected. We also oversee the UK DMD Registry, linking patients to clinical trials, and have published the only Duchenne research strategy of its kind in the UK.

1.2 This response has been composed by Aaron Revel (Campaigns Officer), Diana Ribeiro (Director of Research) & Paul Lenihan MBE (Chief Executive Officer) at Action Duchenne.

2. Summary of Key Points.

2.1 The Scottish Medicines Consortium (SMC) process for evaluating orphan and ultra orphan treatments is not fit for purpose. It requires monumental improvements in its ability to engender equitable and robust decision making rooted in a comprehensive understanding of all available evidence.

2.2 There is no transparency as to the role and impact of patient/patient group contributions in the development of funding recommendations on orphan or ultra orphan medicine from the SMC.

2.3 The patient and clinical voice needs better representation at each stage of this process, with appropriate significance attributed to the statements of patient groups, clinical experts and families.

2.4 The prevailing predominance of a QALY based analysis undermines the SMCs purported objectives to ascertain added benefits that may not be captured within the conventional clinical and economic assessment.

2.5 The likelihood that future treatments in clinical trial development will combine with current therapies to have an incremental impact makes QALY based analyses increasingly problematic.

2.6 UK national commissioning decisions need to be consistent, coherent, and understood within the context of UK Life Sciences Policy, and its express intention to boost innovation, health and wealth through the rapid development and adoption of innovative medicine.

Recommendations on specific areas highlighted within the review

3. How is the new approach to assessment orphan and ultra-orphan medicines working in practice?

3.1 The SMCs commitment to considering 6 to 8 medicines in one day is contributing towards committee members being ill-equipped to make fair and fully informed decisions in consideration of all available evidence.

3.1.2 Please acknowledge it is not our intention to criticise members of the SMC committee for lacking the requisite understanding and information to provide sound judgement and advice. The existing format makes adequate preparation, comprehensive understanding and an exhaustive evaluation undeniably and unnecessarily difficult and will require reviewing.

3.1.3 This is reflected in the inaccuracies and misunderstandings contained within the SMCs detailed advice document (DAD) on ataluren for the treatment of Duchenne muscular dystrophy DMD. For example, despite patient groups, parents and clinical experts outlining that treatment negates the onset of scoliosis through delaying loss of ambulation until after puberty, the committee still express a desire for “time to scoliosis [being] directly measured for ataluren”², an impossibility.

3.2 The SMC has proved itself susceptible to attributing analytical importance to irrelevancies in committee meetings, with specious and inaccurate theorising being permitted to continue by the chair, a dereliction of duty.

3.3 There is no evidence of what impact the contribution of patient groups is having at any stage of this process. For example, the impact of patient group submissions is not communicated back after being presented to the SMC by public partners when the former meet to consider the provisional recommendations of the New Drugs Committee, nor indeed, are patient group submissions read out thoroughly at the final SMC committee meeting.

3.3.2 Claims by the SMC that patient group engagement through the ‘new approach’ is translating into higher rates of approval for drugs for rare conditions are moreover fallacious. Indeed, when comparing the fifteen months preceding the reforms with the fifteen months following, we see a decline in the percentage of orphan and ultra- orphan medicines being approved.

3.4 Whilst the SMC does not have a formal threshold, the lack of positive recommendations for orphan and ultra-orphan medicines is owed to the fact that treatments with a cost per QALY of under £20,000 are being generally considered to have acceptable value for money³. Whilst QALYs can provide a useful indicator of an individuals anticipated health gain following a medical intervention, they do not fully capture the benefit a treatment can offer to patients and families affected by rare conditions which are often complex and multi-systemic.

² SMC Detailed Advice Document on ataluren Translarna for use within NHS Scotland, 11 April 2016, p.9.

³ Genetic Alliance UK, Patient Charter, *Patient Perspectives and priorities on access to medicines for rare conditions in Scotland*, March 2016, p.12.

3.4.2 This narrow focus and inflexibility towards orphan and ultra-orphan conditions is evidenced in the absence of carer dis-utilities from the SMCs base case assumptions: “these assumptions would not normally be considered as part of the SMCs base case”⁴. If the SMCs model is unable to accommodate the case being considered and the burden encumbered by caregivers in its analysis then this model is not fit for purpose.

3.5 The existing methodology of appraising orphan and ultra-orphan medicine is further problematized by the nature of rare diseases like Duchenne and the likelihood that a cocktail approach to treatment will be needed. That existing therapies will combine with treatments in clinical development to have an incremental effect invalidates a simplistic QUALY based analysis.

3.6 The contribution and insights of clinical experts within rare and ultra-rare conditions are being overlooked and marginalised within the SMCs existing process. This is reflected, not only in an overreliance upon Scottish health professionals (even when there’s an absence of expertise in the disease in question), but also in the frighteningly brief summation given to the views of clinical experts in the DAD. In the case of ataluren this extended to only two sentences⁵.

4. How are the views from the Patient and Clinician Engagement process taken into account in decision making?

4.1 Despite reassurances that, “the output from the PACE meeting will be a major factor in the SMC decision”, it is unclear how these considerations are taken into account and what actual weight they are given.

4.2 That patients are not allowed to convey the summation of these findings to the SMC committee directly, whilst responding to questions arising from the committee members in turn, is a major barrier denying the patient voice adequate significance. In our experience committee members raised questions that parents in the public gallery, and who were present at PACE, could’ve addressed. Instead these queries went unanswered.

4.3 Limiting each PACE meeting to one hour serves to circumscribe the committee’s ability to adequately ascertain the added benefits of a medicine that may not be fully captured within the conventional clinical and economic assessment. This is exacerbated by the heavily redacted account contained within the PACE statement which is included in the committee papers of the SMC.

4.3.2 As a consequence, salient points raised during the PACE meeting on ataluren concerning the significance of falls, the psychological impact of Duchenne, and the financial burden accompanying Duchenne were not reflected within the SMCs subsequent discussions and are absent from the DAD.

4.4 Relevant clinical expertise is afforded a shocking level of consideration at PACE and is subsequently unable to inform the SMCs conclusions as apposite. Indeed, in our experience, the clinical expert on Duchenne was offered only 10 minutes via video link to help support

⁴ SMC Detailed Advice Document on ataluren Translarna for use within NHS Scotland, 11 April 2016, p.8.

⁵ SMC Detailed Advice Document on ataluren Translarna for use within NHS Scotland, 11 April 2016, p.6.

the case for approval, and her contribution was relegated to a mere two sentences within the detailed advice document. In rare diseases that are complex, heterogeneous and multi systemic in nature, often with a lack of experts and established treatment pathways, this is wholly unacceptable.

4.4.2 The lack of significance afforded to the input of clinical experts moreover, in our experience, contributed to inaccurate conclusions within the DAD, with the SMC incorrectly believing that patients would remain on treatment indefinitely rather than discontinue treatment 6 months after loss of ambulation⁶.

4.5 The overview of the contribution made by patient groups within the DAD is an insult to the time they invest in proactively working to inform the committee and the totality of information they offer. The statement, “the following information reflects the views of the specified patient group”⁷ is particularly objectionable when the details contained are in no way reflective of, or commensurate to, the contribution made.

5. How must the transparency of the SMC be improved and what further opportunities are there for patient and clinician engagement?

5.1 If the SMC is serious about its so-called ‘new approach’ then the patient voice requires better representation and increased significance on all decision making panels. Most importantly, those who attended the PACE meeting need to be in the following SMC meeting to answer questions and support the conclusions of PACE.

5.2 The use and impact of patient group submissions must be communicated back to patient groups and given an adequate hearing at both the NDC and SMC committee meetings. Whilst these are inserted into the SMC committee papers, questions raised by members during this meeting, in our experience, suggested they’d been overlooked, under-considered, or misunderstood.

5.3 Whilst we would principally support demands for patient and public partners to be given parity within pharmaceutical industry representatives in being allowed to inform NDC conclusions, the bifurcated approach being pursued, in which the input of manufacturers and patient experts are sought and surmised in isolation is undesirable and ineffective.

5.5 More should be done to enable the input of patient experts, including reimbursement for attending meetings and the cost of developing evidence. Action Duchenne are a small organisation with limited capacity. To have invested so much time and resources in engaging and informing the SMC, only for the impact of our contribution to be left marginalised and un-communicated is extremely disheartening and will eventually dissuade patient groups from engaging in this process.

5.6 It is unacceptable that clinicians and patient experts have no recourse to directly challenge the conclusions of the SMC or their methodology. The manufacturing company cannot be the only party that can request any appeal or review of SMC guidance.

⁶ SMC Detailed Advice Document on ataluren Translarna for use within NHS Scotland, 11 April 2016, p.10.

⁷ *Ibid.* p.11.

5.7 Patients preferences should be accounted for in all the processes which lead the development of new medicines in Scotland, ensuring that the levels of risk patients are willing to tolerate, and the benefits which they prioritise, are taken into account.

6. How should NHS Boards be implementing SMC decisions under the new approach, and how can the New Medicines fund be best utilised?

6.1 Whilst we are pleased that money recouped under the Pharmaceutical Price Regulation Scheme is being appropriately utilised to ameliorate issues of affordability surrounding innovative and emerging treatments for rare diseases, it is disappointing that the New Medicines Fund isn't translating into positive national commissioning decisions for the said conditions in Scotland.

6.2 Owing to the inadequate, inequitable and opaque nature of SMCs process for evaluating orphan and ultra-orphan medicine , we would currently advise against the centralisation of decision making and the forced adoption of decisions into health board's local formularies.

6.2.1 Indeed, that SMCs advice, "does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient"⁸ has been a saving grace for many rare disease patients with high levels of unmet clinical need. Until the SMC have proved they are able to evaluate orphan and ultra orphan medicines in a fair, robust and timely manner this should remain unchanged.

7. How can the new approach accommodate advances in new medicines?

7.1 National commissioning decisions must be understood within the context of UK Life Sciences Policy⁹ and its express intention to boost innovation, health and wealth through the rapid development and adoption of new innovative medicine. UK processes have consistently proved themselves unsuitable and unresponsive to innovative treatments for orphan, rare and ultra rare conditions. If this continues, companies will be forced to seek out alternative and more auspicious environments for investment, thereby undermining this agenda.

8. How should the new approach be impacting on access to medicines on an individual patient basis?

8.1 Whilst the replacement of the IPTR process with the PACS was a positive step and acknowledged that the exceptionality criteria unfairly disadvantaged rare disease patients, we are concerned that formal guidance on PACS has yet to be issued publicly and there are no defined timescales for its introduction.

⁸ *Ibid.* p.14.

⁹ <http://www.actionduchenne.org/interim-report-on-the-accelerated-access-review-published/>

8.2 No health board should be using criteria based on exceptionality. “Whatever the reason for the apparent retention by some health boards of criteria based on exceptionality, this is in breach of the law”¹⁰.

8.3 The SMCs recommendation on the use of ataluren, made on the basis of cost, is divergent to other commissioning bodies within the UK. The National Institute for Health & Care Excellence (NICE) has recently published its Final Evaluation Determination on ataluren recommending the therapy for funding approval within NHS England, and subsequently, the devolved nations of Wales and Northern Ireland. The ‘new approach’ within Scotland needs to be consistent with willingness of NICE to consider the patient and clinical voice in its evaluations and fund medicines that meet areas of high unmet clinical need, and make a clinically meaningful difference. Whilst requests for funding on an individual basis are currently being assured through the New Medicines Fund, we are concerned about the potential for a postcode lottery, and that conflicting funding priorities across the border may lead to disparity in patient access across the UK.

8. How should the process be adapted to include commercial negotiation with the aim of 1. ensuring best value for the NHSS and 2. getting to a pharmaceutical companies best offering on price earlier?

8.4 Value for money in reality is benefit of treatment versus the risk of no intervention and there are many key caveats to this complex issue. Natural history data is very important in orphan diseases as these are often your control group, rather than n=1 cohorts in placebo-controlled trials. There needs to be an agreement on the endpoints used in the trials, whether the data can be extrapolated beyond the treatment period and its benefit. These can be mapped against the disease trajectory in the natural history data set, including the health-related quality of life questionnaire and patient reported outcome data, which are now increasingly being used as secondary outcomes in clinical trials. Value for money is an important, but there needs to be a reasonable and flexible approach in considering natural history and wider health economic burden data.

8.5 Commercial discussions should take place at the start of late clinical development (in planning the registration trial) and these should involve the EMA and HTA authorities and key opinion leaders as key stakeholders. We know this can be done with companies requesting formal and joint scientific advice, but this has been a recent precedent led by the companies. Within the NICE appraisal process, for example, there was the significant drawback of unnecessary duplication of effort. Manufacturers and the academic groups in some instances have worked in isolation, so difficulties may ensue if conflicts surrounding the available evidence are resolved late in the appraisal process. The time frame permits new information to be incorporated towards the end of the process without necessarily allowing time for review and critical appraisal. It is important that any HTA body balances transparency and collective participation with efficiency.

¹⁰ Genetic Alliance UK, Patient Charter, *Patient Perspectives and priorities on access to medicines for rare conditions in Scotland, March 2016, p.12.*

9. How should the new approach accommodate advances in new medicines and a developing regulatory framework?

9.1 Parent Project Muscular Dystrophy recently released a landmark qualitative study measuring Benefit Risk Assessment's in Rare Disorders. This surveyed parents and patients affected by Duchenne, and proposed that, "new approaches for regulatory benefit risk assessments are considered for [...] rare progressive, fatal disease(s) for which no current therapy is approved"¹¹. We further believe that this should be applied to the assessment processes which go beyond the regulatory framework. As such, we ask the SMC to heed this advice and afford patients views on benefit expectations and risk tolerance urgent consideration.

9.2 There needs to be a significant understanding that the type of approval and designation given by the EMA, the requirements for conditional approval and full marketing authorisation and even marketing exclusivity are different. It is evolving with the early access to medicines scheme, significant benefit designation; this is to provide an incentive for smaller companies to rapidly develop their pipeline and also for those who have a robust clinical data profile to apply for significant benefit. The CHMP process is also evolving to prioritise patient reported outcome measures and this has been recognised in the final guidelines¹¹ published by the EMA on Duchenne Muscular Dystrophy.

9.3 Lastly, it is widely recognised that polytherapy¹² will confer the most benefit, with different treatment strategies to tackle complex rare conditions. The pipeline is rich and diverse in this condition and companies are developing first-in class and best in-class compounds for the same target and also different manufacturers with different chemistries. Reimbursement mechanisms will need to consider the horizon of translational research in Duchenne Muscular Dystrophy.

¹¹ Franson, Paey: *PPMD Benefit Risk Assessments in Rare Disorders. The case for Therapeutic Development in Duchenne Muscular Dystrophy as the Prototype for new approaches*, 2015.

¹¹ Guideline on the clinical investigation of medicinal products for the treatment of Duchenne and Becker muscular dystrophy http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/12/WC500199239.pdf

¹² Valeria Ricotti: Challenges of clinical trial design for DMD Neuromuscul Disord. 2015 Dec;25(12):932-5

Review of Access to New Medicines – independent review by Dr Brian Montgomery

The following response is on behalf of Novartis Pharmaceuticals.

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Novartis in the UK

Novartis UK is the UK affiliate of Swiss-based Novartis AG – one of the largest healthcare companies in the world. In the UK Novartis operates across a number of sites. These sites are responsible for research, development, sales, marketing and manufacturing of products used in the UK and worldwide.

Novartis is one of the global healthcare industry's biggest investors in research and development (R&D). Novartis has one of the strongest and most productive pharmaceutical pipelines in the industry, with projects in development for cancer, rare diseases, precision medicine and immunotherapy.

Novartis welcomes the opportunity to provide a submission to the 'Montgomery Review' on the changes to access to medicines policy following the Health & Sport Committee's report¹ and the Scottish Government's response² in 2013.

This submission responds to some of the key questions outlined in the scope of the review.

How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice

Novartis supports the definitions for end of life (EoL), orphan and ultra-orphan medicines under the new approach. We believe that the definitions capture the intent of the Health & Sport Committee inquiry, Scottish Government response and the subsequent recommendations of the Task & Finish Group³ that the SMC should introduce new, more flexible approaches for the assessment of EoL medicines, orphan medicines and ultra-orphan medicines and adopt methodologies, which will substantially improve access to these new medicines. Novartis therefore believes that the definitions are working in practice to meet this intent and we support the Task & Finish Group's definitions as follows:

EoL medicine: "A medicine used to treat a condition at a stage that usually leads to death within 3 years with currently available treatments."

Orphan medicine: "A medicine with EMA designated orphan status (i.e. conditions affecting fewer than 2,500 people in a population of 5 million) or a medicine to treat an equivalent size of population irrespective of whether it has designated orphan status."

Ultra-orphan medicine: "A medicine used to treat a condition with a prevalence of 1 in 50,000 or less (or around 100 people in Scotland)".

¹ [Health and Sport Committee 8th Report, 2013 Access to New Medicines](#)

² [Scottish Government response to the Health and Sport Committee inquiry into access to new medicines](#)

³ [Assessment of medicines for end of life care and very rare conditions in Scotland: Task & Finish Group Report](#)

Whilst there has been some criticism assigned to the definition for EoL medicines, we agree with the Task & Finish Group's (T&FG) statement *"The criteria currently used by NICE to define end of life were considered, as they are one of the few HTA agencies to use this categorisation. The T&FG agreed that these criteria do not adequately reflect a medicine's benefits in terms of quality of life (as well as extension to life) and also that the requirement around 24 months of life expectancy was too specific and restrictive."*

We therefore believe the SMC definition is relevant and applicable to clinical practice given that terminal patients may be living longer with their condition.

One area that could be improved is the decision making process to confirm the categorisation of a medicine as EoL, orphan or ultra-orphan. Novartis are happy that we are able to present the evidence base to justify the categorisation. We also seek Scottish data where available, for example from ISD and where possible we also refer to Scottish clinical experts to validate the evidence. However, where SMC feel that the categorisation has not been justified the SMC could share the decision-making framework they have used to make their decision on categorisation. It would be helpful if the Company is then allowed to respond before a decision is finally taken, as it may help answer any issues of uncertainty and improve the overall decision making.

Recommendation: SMC should share the decision-making framework they have used to make their decision regarding categorisation of a medicine as EoL, orphan or ultra-orphan and allow the submitting Company to respond before the decision is finalised, as it may help answer any issues of uncertainty and improve the overall decision making.

How the views from the Patient and Clinician Engagement process are taken into account in decision making

The greater involvement of both patient groups and relevant expert clinicians through a PACE meeting has added a great deal to the appraisal process and provides the opportunity for SMC to take a wider more flexible view in their decision making. However, it is often not clear what the impact has been and how the PACE input has been taken into account. We suggest this could be specifically covered as part of the SMC discussion and/or included in the Detailed Advice Document.

An important improvement to ensure PACE input is taken into account should be to have PACE representation at the SMC Committee meeting to be able to answer queries and contribute to the discussion. At present the meeting of the PACE group results in a report, which is read out at the SMC meeting, but neither the clinical specialist nor the patient representative are invited to attend. The SMC members may not have the clinical expertise in the therapy area or experience of the disease and so any discussion would be enhanced by patient and clinical expert input. We have seen examples where there was discussion by SMC members raising concerns about one of our medicines under review, which would have benefited from expert clinical and patient contributions.

There may be other medicines, other than those for EoL and rare diseases, that may benefit from a PACE meeting. This may include medicines with limited data or high levels of uncertainty, or those that have a significant wider social impact, which may be increasingly important with the integration of health and social care. We suggest therefore that the option of a PACE meeting be extended to other appraisals.

Recommendation: There should be PACE representation at the SMC Committee meeting and the option of a PACE meeting be extended to other categories of medicine appraisal.

How the new approach to assessment of ultra-orphan medicines is operating in practice?

The new approach to assess ultra-orphan medicines and indications for very small patient numbers has been welcome. The introduction of this process has helped to address the difficulties of appraising such medicines by standard cost-utility analyses, whilst also incorporating a broader framework of decision-making criteria.

However, there is an expectation that companies are still required to provide a cost-effectiveness ratio and cost/QALY analysis. Therefore there is still an over reliance on this aspect and this is compounded when the assessors request detailed sensitivity analysis. There is still a great deal of scrutiny of the economic case in ultra-orphan appraisals and that the analyses are much the same as for 'standard' medicines. This seems at odds with the introduction of the framework for ultra-orphan appraisals, which recognises the *inability* to present robust and complex analyses in these indications.

The SMC T&FG report noted the following - "*Recognising that under current SMC processes ultra-orphan medicines are unlikely to be accepted for use, SMC should introduce a decision-making framework that is not based on the cost per QALY for these medicines.*" The report also noted that the SMC would pursue an approach consistent with the NICE Highly Specialised Technologies (HST) interim framework, which does not require cost/QALY analysis. This recommendation appears not to have been included in the new approach. Whilst health economists may wish to have a figure for reference, there is a concern that the SMC committee decision may be influenced by completely spurious and flawed cost/QALY figures.

Recommendation – The requirement for cost/QALY analysis be removed and the New Drugs Committee consider ultra-orphan medicines under a specific section of the agenda, which focuses on ultra-orphan medicines and decision making framework.

How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach?

In general Novartis has welcomed the changes to the SMC process for reviewing medicines for end of life and rare diseases. In particular we support the increased patient and clinician input to the review process through Patient and Clinician Engagement (PACE) meetings, as well as the SMC's willingness to apply greater flexibility to their appraisal of these medicines. The three factors that the SMC have introduced, or utilised to a greater extent; modifiers, PAS and PACE, have been shown to be associated with an increasing share of positive SMC decisions over time. There has been an increase in the rate of approval of medicines for end of life and rare diseases from around 50% to around 70%, which is similar to the rate of approval for other medicines.

Novartis recognises that SMC should not accept everything and anything. There is an onus on companies to ensure submissions provide a clear case for a medicine's value. If the process is working then the acceptance rate should be relatively high. Novartis has been positive in engaging with SMC and has made 10 full submissions and 2 resubmissions since the changes to the SMC process were introduced in May 2014. Of these, 7 medicines were for end of life or

rare disease. Only one, which was for advanced breast cancer, was not accepted for use in NHS Scotland and this has since been resubmitted and accepted.

How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement?

We believe that holding SMC meetings in public has helped to increase transparency by allowing attendees to witness the review process and committee discussion. This was one of the recommendations in the Health and Sport Committee's report, which was accepted by the Scottish Government. However as a consequence the SMC has introduced a new system for the way in which members reach the decision whether or not to approve a medicine. Previously the SMC Chair would summarise the discussion and moderate a committee consensus having resolved any outstanding concerns or misunderstanding. Because the meetings are now held in public, and there is a need to keep the decision confidential, a new system has been introduced that involves each committee member recording a written vote on whether or not to accept each medicine. The votes are counted and the decision announced to the SMC committee in a closed session following the meeting. How the committee members vote is secret and so decisions being made under the new voting system does not allow any reasoning for the decision to be apparent. This may be detrimental to the decision making process, as the Chair is no longer able to resolve any outstanding issues or misunderstandings. It also makes it more difficult for the SMC to give feedback on the reason for the decision either to the submitting company or to other stakeholders.

Recommendation: Novartis believes that SMC meetings and discussion should be held in public, but the SMC could return to a system of consensus decision making moderated by the Chair and have this under closed session at the end of the meeting.

How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund?

The Health and Sport Committee report supported the recommendation that NHS Board Area Drug and Therapeutics Committees (ADTCs) should publish their local response on the Board's website within 30 days of SMC's published advice. The recommendation indicated that where further work is required, this should be made clear and final arrangements published within 90 days.

The recommendation further indicated that formulary decisions should be easily accessed by both public and patients in "user friendly" language. It was also noted that NHS Board ADTCs should publish their formulary decisions and the reason for these in relation to SMC advice to comply with the national guidance set out under guidance SGHD/CMO (2012)⁴.

Novartis is not aware that any updated guidance has been issued to NHS Boards or any audit published. Variation between NHS Boards should be minimised and there should be greater transparency in tracking access and uptake of new medicines across health boards.

⁴ [CMO \(2012\) 1: Guidance to further strengthen the safe and effective use of new medicines across the NHS in Scotland](#)

Recommendation: Following the recommendations made by the Health & Sport Committee, it would be useful for Scottish Government to issue updated guidance to NHS Boards on the implementation of SMC advice. Health Improvement Scotland, as part of their 2015-18 Strategic Delivery Plan for Medicines⁵, should regularly audit and publish how NHS Boards are meeting recommendations on the implementation of SMC advice. The uptake of new medicines across health boards should also be published.

In 2014 the Scottish Government announced the New Medicines Fund⁶ to support funding for the increased access to medicines resulting from more SMC and IPTR approvals. The fund is very welcome and has been established by utilising the rebate to the Scottish Government made by the pharmaceutical industry under the UK-wide branded drug pricing scheme, the Pharmaceutical Price Regulation Scheme (PPRS).

For the year 2014-2015 the rebate amounted to £40 million. In evidence to the Health & Sport Committee⁷, the Cabinet secretary confirmed that “In 2014-15, NHS boards required £1.1 million to support SMC decisions and £20.5 million to support individual and group patient treatment requests from the new medicines fund. Any funding that was not required by NHS boards for that purpose in 2014-15 remains available in 2015-16 on top of the new allocation that was made for 2015-16.” The expected rebate for the year 2015-2016 is estimated to be around £90 million. It therefore appears that the amount of rebate available for the New Medicines Fund far exceeds the amount being allocated.

In addition, whilst some of the funding is being allocated to NHS Boards by the Scottish Government, this does not seem to be passed through to directorate budgets where the expenditure is being made. There appears to be a lack of awareness of the New Medicines Fund at directorate level, which may mean that Clinical Directors have a concern in signing off directorate budget for new medicines and IPTR applications when funding is not being passed through from the New Medicines Fund.

Recommendation: Scottish Government should issue guidance to NHS Boards through to directorate level staff on how to access funding from the New Medicines Fund. For each financial year Scottish Government should publish allocation of the fund to each NHS Board and the total allocated compared to the amount available to the New Medicines Fund through PPRS rebate.

How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system)?

It is difficult to say exactly how the new approach has had an impact on reliance on access to medicines on an individual patient basis. There has been no reporting of the number of IPTR applications and approvals for different medicines. In a letter to the Convener of the Health & Sport Committee⁸, the Cabinet Secretary for Health outlined allocation from the New Medicines Fund for a number of medicines. One was a Novartis medicine, which has subsequently been approved by SMC under the new approach and so the reliance on IPTRs will be diminished.

⁵ [Health Improvement Scotland 2015-18 Strategic Delivery Plan for Medicines](#)

⁶ [Scottish Government Press Release October 2014: Funding will give patients access to new treatments](#)

⁷ [Official Report Health & Sport Committee Tuesday 1 March 2016](#)

⁸ [Cabinet Secretary for Health Letter to the Convener of the Health & Sport Committee 18 March 2016](#)

However for some medicines which are awaiting SMC review, or where there has been difficulty in gaining approval, individual patients may need to rely on IPTRs.

In line with parliamentary expectations, there was initially an increase in the number of IPTR approvals following Chief Medical Officer (CMO) guidance in November 2013⁹ and where the clinicians felt that patients would benefit from a new medicine not yet approved by SMC. This guidance emphasised “*that the concept of exceptionality should not be a factor in any IPTR under consideration in your Board but should be primarily about the individual clinical case.*”

The increase in approvals may have given the impression that the problems with the IPTR process highlighted by the Health & Sport Committee inquiry had been addressed. However, in the absence of further guidance or the introduction of the Peer Approved Clinical System, NHS Boards have put in place their own processes, which have led to inequity of access between different NHS Boards.

Anecdotally, there appears to be an increasing difficulty in obtaining approvals for IPTRs. As mentioned, there is a lack of reporting of the number of applications and approvals, which was a commitment following the Health & Sport Committee inquiry.

The new PACS process was due to be introduced in May 2014 and although there is word that this is being piloted, there is no indication of how the new system is being developed. The PACS process was proposed to be focused on making decisions based primarily on the individual clinical case. It is not clear how decision making might now be varying between NHS Boards.

Recommendation: Regular reports should be published to track applications and approvals by each NHS Board under the IPTR/PACS process. The new PACS process should be consulted upon with key stakeholders and national guidance issued to NHS Boards as soon as possible within a definite timescale.

Whether there are further opportunities to take a ‘once for Scotland’ approach in any aspect of access to newly licensed medicines?

It is increasingly recognised that ‘one size will not fit all’ when it comes to the introduction and appraisal of new medicines. To be able to get it right first time there should be some degree of flexibility and alternative options available depending on the nature of the treatment being introduced, with discussions on the managed entry of a new medicine occurring at a much earlier stage. This could be at Horizon Scanning stage and include input from lead clinical experts, patient groups, NHS Board Area Drug & Therapeutic Committees and SMC to agree on areas of unmet need, health outcomes, position in therapy, eligible patients and areas of uncertainty. This would help with planning, data collection and evidence development ahead of Health Technology Appraisal (HTA).

The opportunity for early engagement will also help to identify issues relating to limited evidence. Many medicines, often in the oncology setting, come to market with limited evidence and a lack of the data required for a robust cost-utility analysis. At present, the process does not seem to make any allowance for such cases. Of course, in the event that the medicine treats an orphan/ultra-orphan disease, then there is a potential for other factors to be taken in to account.

⁹ [CMO \(2013\) 20: Access to new medicines – Transitional arrangements for processing individual patient treatment requests](#)

However, whereas orphan/ultra-orphan cases often lack data due to the low numbers of patients, in other non-orphan diseases, it may be the case that the limited evidence relates to the available duration of follow-up. There are no obvious concessions for such a situation and we believe this should be addressed.

A further item which could assist in situations of limited evidence would be the introduction of a system for conditional reimbursement. This could be in the form of a scheme which allows reimbursement whilst further data are collected and/or existing datasets are allowed to mature. A follow-up appraisal would be required to assess the extent to which the full data addressed the uncertainty and allow a decision to be made on full reimbursement. Alternatively, it could involve Managed Entry Agreement (MEA) providing reimbursement contingent on patients achieving certain outcomes or avoiding certain events. In this latter case, the risk for NHS Scotland is minimised since reimbursement will not be given in cases where the medicine is ineffective.

This early horizon scanning review could also act as a triage process to determine the most appropriate route for any subsequent assessment for example

- Rapid (expedited) Review e.g. for abbreviated and cost minimisation submissions
- Full Review
- Preliminary Review with conditional reimbursement to support early access whilst gathering further data on a new medicine, where there is high unmet need, uncertainty, immature/incomplete data



Recommendation: SMC, Health Improvement Scotland (through the ADTC collaborative), patient, clinician and industry stakeholders are convened for a Task & Finish Group to develop a process and methodology for early horizon scanning review. This would include the process to determine the most appropriate route for any subsequent assessment by SMC.

The possibility of a formal engagement at an earlier stage ahead of HTA would also help to smooth translation into clinical practice, as there would be greater agreement on uptake and impact on resource. After HTA this in turn could help to ensure delivery of value and address some of the affordability pressures, which would support a once for Scotland approach.

A once for Scotland approach should also mean that there is no need for further review by 14 NHS Board ADTCs. The possibility of a single national formulary has been proposed and if this is progressed there would need to be mandatory funding and adoption by NHS Boards, so that patients can be assured that medicines accepted for use within NHS Scotland are made

available. As mentioned, variation between NHS Boards should be minimised and there should be greater transparency in tracking access and uptake to new medicines across health boards.

How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier?

Firstly it is worth clarifying that the remit and role of SMC should not include commercial negotiation. The SMC has a clear role in assessing clinical and cost effectiveness. If it were to incorporate commercial negotiation it would provide a conflict. There needs to be clear separation and the proposal to introduce a pause for negotiation into the SMC decision making process would compromise the SMC's role.

However, as mentioned previously Novartis does believe there should be alternative options available depending on the nature of the treatment being introduced, with discussions on the managed entry of a new medicine occurring at a much earlier stage. The Patient Access Scheme Assessment Group (PASAG) would also need to be involved at an early stage to agree the best way to introduce a new medicine, including the most appropriate option for MEA where conditional reimbursement is being considered. Novartis believes that PASAG could develop their role from gatekeeper to enabler and to widen the scope to beyond simple discounts and consider alternative finance-based and outcomes-based schemes. In this way the process could be adapted to ensure best value for NHS Scotland and that pharmaceutical companies' best commercial offering is discussed earlier.

At present PASAG approves very few alternative schemes and favours Patient Access Schemes (PAS) with a simple discount. The main reason given is the administrative burden that alternative schemes might bring. The accessibility and availability of data can mitigate administrative burden and will be crucial to support alternative options, such as coverage with evidence development, multi-indication pricing and risk-share or outcomes based reimbursement. Indeed outcome data will be important to show whether a medicine's expected value is being delivered. Much is made of Scotland's health record data, but it is not readily available to use to assess value or to support MEAs. Novartis has extensive experience of different schemes both in the UK and internationally. We would welcome the opportunity to work in collaboration with PASAG and NHS Boards to develop workable schemes in Scotland.

Recommendation: PASAG could develop their role beyond simple discounts and consider alternative finance-based and outcomes-based schemes. Industry should have the opportunity to work in collaboration with PASAG and NHS Boards to develop workable commercial agreements in Scotland. The accessibility and availability of data should be improved to support alternative schemes.

Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report?

There have been clear resource implications for the new approach. Novartis has experienced several instances where medicines submitted for review have been delayed, including during the review process after the appraisal was scheduled. There remains a problem where a particular month is over-subscribed, with more submissions than SMC has capacity to deal with. In these instances, submissions are 'bumped' to the next month, or beyond. The criteria by which

submissions are prioritised seem reasonable, but the process could be made more transparent. The situation suggests that SMC require more resource in order to carry out their workload.

Recommendation: SMC resource is reviewed to ensure that this is sufficient to carry out their workload.

The SMC T&FG³ noted that “Concerns were raised about unintended consequences of the new approaches, for example that they might reduce the incentive for pharmaceutical companies to propose a PAS.” Novartis is not aware that this has happened in reality. Of the 7 submissions we have made for medicines for EoL and rare disease, 6 have come with a PAS.

How the new approach will accommodate advances in new medicines and a developing regulatory framework?

The new approach introduced a wider assessment of value for medicines at the EoL and for rare diseases. It has incorporated increased input from clinicians and patients and in this respect SMC has been leading the way. These reforms have been welcomed, however further system-wide evolution and change is needed to ensure that the system will accommodate advances in new medicines and a developing regulatory framework. There will need to be frequent reviews and a willingness to take on board continuous change in line with scientific advances for Scotland to stay at the cutting edge of new medicines introduction, rather than falling behind.

The pharmaceutical pipeline is becoming more specialised and advances in new medicines includes precision medicines with companion diagnostics, immunotherapies and regenerative medicine. Some of these innovative medicines will receive market authorisation with data that is too limited or immature for a robust cost-utility analysis. They may also be targeted to small numbers or provide wider benefits related to societal value, unmet clinical need and the potential impact on the standard of care in Scotland compared to the other nations of the UK and the rest of Europe.

As mentioned, the opportunity for early horizon scanning review should be made available and there should be some degree of flexibility and alternative options available depending on the nature of the treatment being introduced. This would also help to take account of policy drivers such as the Medicines Adaptive Pathway for Patients (MAPPs)¹⁰ and Early Access to Medicines Scheme (EAMS)¹¹. Providing a formal early stage review would allow discussion and agreement on the best and most appropriate way to introduce and manage the entry of a new medicine. It could focus on those medicines with likely significant impact, in areas of high unmet need, those with a Promising Innovative Medicine (PIM) designation, those with limited evidence and medicines for EoL or rare diseases. As well as looking at alternative options such as conditional reimbursement and MEAs, early review would also allow engagement with other parts of the system. For example, the introduction of new molecular tests is also very important for the introduction of precision medicines. Scotland already has a framework supported by the Molecular Pathology Consortium, but the approaches could be better aligned at an earlier stage.

¹⁰ [Medicines adaptive pathways for patients \(MAPPs\): report, by the Centre for the Advancement of Sustainable Medical Innovation](#)

¹¹ <https://www.gov.uk/guidance/apply-for-the-early-access-to-medicines-scheme-eams>

By driving this evolution Scotland will be able to build on existing health system structures and develop an end-to-end innovation pathway which can, and should be more responsive to increasing medicines innovation, particularly where its introduction will contribute to better outcomes for patients and more productive and efficient ways of delivering care. This would mean Scotland could take a lead in relation to UK policy initiative being developed under the Accelerated Access Review¹², which for example recommends “*Getting Ahead of the Curve*” to accelerate and manage entry into the NHS emerging products promising the most significant, potentially transformative impact in terms of patient benefit and overall value.

Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value?

In 2013 the Scottish Government told the Health & Sport Committee the review of SMC was: “...the first step in a wider process to determine Scotland’s requirement to a Value-Based Approach to Assessment. The question of how innovation should, or could, be considered in the new medicines assessment system in Scotland will be taken forward in the Scottish Model of Value.”

There is a continued need to consider wider decision making frameworks to support a Value-Based Approach to Assessment and to move away from the current focus on cost-effectiveness, QALY and opportunity cost methodology.

In a recent letter to the Cabinet Secretary for Health the Convener of the Health & Sport Committee noted “*We are pleased that the review will give consideration to the further development of a Scottish model of value. We hope that Dr Montgomery will propose steps that can be taken to encourage the development of the model as we are supportive of a broader assessment of value that goes beyond the ‘cost per QALY’*”.¹³

In line with the recommendations mentioned earlier, the further development of a Scottish Model of Value needs therefore to introduce flexibility and it needs to reflect what is important to the Scottish population in being able to access new medicines.

Recommendation: A SMC User Group Forum short-life working group could investigate the use of wider decision making frameworks to support a Value-Based Approach to Assessment.

¹² [Department of Health Accelerated Access Review](#)

¹³ [Access to new medicines — progress update: Letter to the Cabinet Secretary](#)

Alexion Pharma UK
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April 26, 2016

Re: Alexion's response to the Scottish Government's review of the Scottish Medicines Consortium (SMC) new process for appraising rare and ultra-rare medicines in Scotland

Dear Dr. Montgomery

We are writing to you in regards to the independent review of the new process put in place to evaluate medicines used to treat end-of-life and very rare conditions. Alexion is a biopharmaceutical company focused on the research and development of ultra-rare medicines. Our first medicine, eculizumab (Soliris®) has recently been evaluated via the new Scottish Medicines Consortium (SMC) process for two different ultra-rare conditions. We welcome the opportunity to provide feedback based on our direct experience.

Alexion is pleased that the Scottish Government recognised the flaws in the previous SMC process regarding patient access to medicines used to treat very rare conditions. We also appreciate efforts made to reform the old process and were encouraged by some of the changes put in place, particularly the patients and clinicians engagement (PACE) meeting. However, we are concerned that significant access barriers still exist for ultra-rare medicines and that the process has not altered sufficiently to take into account the wider criteria of severity of the condition, societal burden and opportunity cost, and therapeutic advances offered by such medicines in the context of extremely small patient numbers and lack of effective treatment options. These have been disregarded for both indications for eculizumab where we have robust long-term experience with the efficacy and safety of the medicine in treating the conditions.

Please find below four key concerns we have with the current SMC process and proposed ways in which these could be addressed to improve the process for ultra-rare diseases and drugs.

1. SMC's remit to make recommendations on behalf of the entire Scottish population does not sufficiently account for the needs of patients with rare/ultra-rare diseases

Alexion is concerned that the new process remains inadequate when it comes to appraising medicines to treat very rare conditions because SMC's remit is still focused on making recommendations from an overall Scottish population perspective, without sufficient regard to small patient populations with ultra-rare diseases. Specifically, within its remit, SMC does not consider the cost of funding "true" ultra-rare medicines for extremely small patient populations at the expense of other cheaper medicines for which the perception seems to be that they are "better value" to the Scottish healthcare system.

Regarding eculizumab, SMC did not recommend treatment in either indication, despite robust clinical data and extremely supportive statements made through the PACE process. Even though no treatment alternatives exist for these patients, and both patient populations are extremely limited, Alexion was told by SMC that they were unable to recommend eculizumab because the cost of treatment was not perceived to be justified in the context of its current remit.

In short, we believe that the new framework (i.e., the PACE process and wider decision criteria) is not working in the way it was intended, and as a result, ultra-rare medicines, where no treatment alternatives exist for these conditions, are still not being recommended by SMC (i.e., eculizumab [Soliris[®]], elosulfase alfa [Vimizim[®]], ataluren [Translarna[®]]). Instead, SMC's focus still appears to be on the absolute cost per patient rather than opportunity cost and value in the context of rarity, disease severity, and unmet need. One of the biggest problems in our opinion is that the assessment and appraisal of ultra-orphan medicines is still performed alongside all other non-ultra-orphan medicines, with the PACE process merely an "add-on" that seems to be given low weight in the final SMC decision-making (see point 2 below). On this basis, we recommend that a fully separate process within the SMC be created with distinct separate assessment criteria, where ultra-rare medicines are appraised on behalf of small patient populations within NHS Scotland (see point 4 below).

2. Transparency needed of SMC's weighting of the new criteria in their decision-making

A lack of transparency exists regarding SMC's weighting of the new criteria when it comes to recommending ultra-rare medicines for reimbursement. Specifically, for products that have received a positive PACE statement, and provided additional robust analyses within Appendix A of the New Product Assessment Form (NPAF), SMC still has not recommended ultra-rare medicines for funding. Only the following generic statement has been included as justification for such negative recommendations, which is not sufficient to explain the negative recommendation:

"The submitting company's justification of the treatment's cost in relation to its health benefits was not sufficient and in addition the company did not present a sufficiently robust economic analysis to gain acceptance by SMC.

This advice takes account of the views from a Patient and Clinician and Engagement (PACE) meeting."

Given the commitment required of stakeholders, including patient organisations and clinicians, to provide input to support access to medicines used to treat ultra-rare diseases, it is essential for the stakeholders to know how much weight is given to the new criteria in SMC's decision-making.

3. Transparency needed regarding SMC's willingness to pay for ultra-rare medicines

We are also concerned by the lack of transparency regarding SMC's willingness to pay for ultra-rare medicines, and request that SMC be more transparent in what they consider a "justification of treatment cost" for these medicines. Namely, there is no clear indication from the SMC on

how it has changed its decision-making to accommodate/incorporate the new PACE changes when it comes to the willingness to pay for such medicines.

As you likely are aware, completing comprehensive pricing and reimbursement dossier submissions requires a considerable amount of effort and resources. Therefore, if manufacturers, patient organisations, and clinicians know upfront that medicines costing in excess of a certain threshold will not be accepted, then a more informed decision can be made on whether to file or support the filing of a national reimbursement submission in Scotland. We recommend a separate process is established that uses the wider criteria framework (i.e., PACE meeting and added clinical and health benefits that are not captured within conventional clinical and economic assessments) and does not make use of implicit or explicit cost per QALY thresholds.

4. A separate process for the assessment of ultra-rare medicines for small populations


Alexion strongly believes that cost per QALY ratios should be taken out of SMC's decision-making when it comes to appraising ultra-rare medicines. It is widely accepted that conventional utility maximising frameworks such as cost per QALY do not provide a robust methodological rationale that is applicable to the assessment of treatments for ultra-rare diseases.

As discussed, greater weighting needs to be placed on the clinical value of the medicines and propose that the clinical value assessment considers specific and relevant elements of ultra-rare medicines like; rarity/prevalence, unmet need/lack of alternative treatments, severity of the disease, impact on survival, impact on QoL, societal impact, and disease modifying effect of the treatment. Once a process focused on the clinical value assessment is in place, a rating system of the clinical added benefit assessment could help set the expectations for funding/pricing decisions that manufacturers can expect to receive.

As always, Alexion remains committed to working closely with both the Scottish Government and SMC to ensure that all patients with ultra-rare conditions have timely access to these life-saving and transformative medicines throughout Scotland.

Please do not hesitate to contact me directly with any questions about our comments.

Kind regards,



Sara Trafford Jones
VP & General Manager, UK and Ireland
Alexion Pharma UK

Vertex submission to Review of Access to New Medicines

Vertex Pharmaceuticals – context of submission:

Vertex is a global biotechnology company that aims to discover, develop and commercialise innovative medicines so people with serious diseases can lead better lives.

Vertex launched its first medicine, Kalydeco[®], in 2012 for the treatment of cystic fibrosis (CF). Kalydeco is a ‘precision medicine’ that treats the underlying cause of the disease according to the genetic profile of the patient. Kalydeco is indicated for CF patients with the G551D genetic mutation (around 4% of the CF population, accounting to approximately 80 patients in Scotland).

Kalydeco was assessed by the SMC in late 2012, prior to the recent changes in the SMC processes, and was not recommended for use in NHS Scotland. However, the then Health Secretary Alex Neil MSP intervened and Kalydeco was made available to all eligible patients via the establishment of the then Rare Conditions Medicines Fund (now New Medicines Fund).

Vertex is currently subject to SMC orphan appraisal process for Orkambi[®], a precision medicine that treats around 40% of CF patients, and the SMC ultra-orphan process for the assessment of a Kalydeco license extension for children aged 2-5.

Observations

- The SMC orphan and ultra-orphan appraisal processes are primarily reliant on cost effectiveness analysis and are therefore not suitable for assessing highly innovative medicines with small patient numbers. Cost effectiveness thresholds are very hard for orphan and ultra-orphan drugs to meet due to small patient groups mean higher than average prices for medicines. For Cystic Fibrosis (CF), demonstrating gains in QALYs is extremely challenging because, as a genetic disease with manifestations from birth, patients score very high in terms of their quality of life on standard of care, meaning that it is not possible to significantly improve these scores with the addition of new therapies.
- Within CF, the key data used to assess the impact of medicines (increase in lung function and inflammation) does not adequately reflect the potential benefits of medicines in protecting future health deterioration.
- Ethical, holistic and societal benefits are not considered by the orphan appraisal and how the modifiers for the process are applied or weighted is unknown.
- The flexibility that the New Medicines Fund (NMF) provides is welcome, and the fund’s predecessor, the Rare Conditions Medicines Fund, was applied successfully to Kalydeco to ensure that all patients received access to the medicine on an ongoing basis. More however needs to be done to develop the NMF to provide clarity and certainty of how the policy is applied (see recommendations).
- The introduction of the PACE process has provided important insight to the SMC on patient experience, demand for new medicines, current standards of care and unmet medical need. However, the impact that this additional insight has had on the SMC’s final decisions is unclear as the weight allocated to the PACE report as part of the assessment process is unknown.
- Although the PACE process has increased access to orphan and ultra-orphan medicines, those with a higher QALY (circa £60k plus) are still difficult to access, suggesting that this measure remains the

dominant factor in decision-making. Given that a large proportion of orphan and ultra-orphan medicines have higher 'costs per QALY' (NICE's highly specialised technology evaluations allow for a higher QALY threshold), the focus on this measure makes securing access to medicines for rare diseases particularly challenging.

- Prior to the 2014 reforms to the SMC, after the publication of the Detailed Advice Document, the SMC would inform the manufacturer of their rationale for their decision, but under the current process SMC members can vote confidentially, thereby reducing the opportunity for manufacturers to discuss with the SMC the rationale for their decision. It has also made it unclear what impact the PACE report has on SMC members.

Recommendations

- Scotland should consider how to secure early access to transformative medicines that target unmet medical need, such as those included in the European Medicines Agency's PRIME initiative. One way this could be achieved would be for the SMC's Horizon Scanning function to plan for potential early or abbreviated assessment of promising medicines on or shortly after licence.
- Reforms to the SMC process must take into account the changing nature of licensing by regulatory agencies (i.e. faster licensing that increasingly takes into account real world evidence), to avoid a growing gap between the data required by regulatory agencies and that required by the SMC.
- The SMC's processes should more easily allow for commercial negotiations to take place, perhaps between the manufacturer and an external body such as NHS Scotland. In the SMC's final assessment of a medicine, they should be open to considering complex managed access agreements, for example conditional approval whilst real world evidence is gathered.
- Assessment of value for orphan medicines should not focus on 'cost per QALY' but should take into account other factors such as wider benefits to society and impact of medicines on disease deterioration over the medium to long-term.
- There is often limited availability of clinical data for rare diseases, and as such the SMC should be clear as to how much weight this data is given in the assessment process in relation to other elements, for example the PACE report.
- Consideration should also be given to involving the Scottish Government in or adjunct to the PACE process to ensure the affordability of medicines is considered as part of the discussions and decision-making process of the SMC.
- Clarity should be given on what funding mechanisms will be available in the future given the importance of stability and predictability to industry. For example, there ought to be planning for what will happen following the new UK-wide PPRS agreement in 2019, as the rebates from this currently contribute to the New Medicines Fund.
- Consideration should be given to link the NMF to the SMC process so that there is a clear qualifying criterion for a medicine to be considered under the NMF before a final decision by the SMC. Greater transparency of Ministerial decisions on the use of the NMF and how manufacturers can apply to access the NMF is strongly recommended. A lack of guidance on the NMF means that patient groups and clinicians are unsure of how it operates and can be accessed, creating anxiety, and manufacturers are

forced to engage with Ministers and MSPs to seek solutions.

- The model of distributing the NMF funding directly to health boards via IPTRs is unsuitable for medicines designed for rare conditions with higher patient numbers and / or for treatment within the accepted indication of the medicine.

Our recommendations regarding the PACE process as part of SMC assessments are as follows:

- To maximise the value that can be gained from patient group input, these groups should be given guidance on how to write PACE statements.
- Representatives from the PACE group should be able to attend the final SMC meeting so that they can elaborate and answer questions on the PACE report.
- PACE is only implemented late in the process following a Detailed Advice Document (DAD) not recommending a treatment. The PACE group should instead be involved before this point so that their input can inform the DAD.
- The PACE meeting should be chaired in such a way that discussion with clinicians is not diverted onto price and affordability but focuses on unmet need and clinical benefit.

COMMENTS FOR THE INDEPENDENT REVIEW OF ACCESS TO NEW MEDICINES

April 2016

Dear Dr Montgomery

aHUSUK was formed in 2011 in response to the need to campaign for effective treatment for people affected by aHUS. Our small charity is run by volunteers, and also aims to support affected patients and families and improve knowledge and awareness of aHUS.

We are pleased to have the opportunity to make some comments for this review, largely based on our recent experience of the ultra-orphan evaluation process, which resulted in a decision by SMC not to recommend the medicine. This decision was at odds with that taken for the rest of the UK, where the medicine was accepted in 2015, having received broader consideration, and where there was greater inclusion of the patient voice and more flexibility in decision-making.

Currently, the need for a patient voice is acknowledged and we are grateful to have been able to participate in the evaluation process. However, the patient voice is limited at the moment by a restrictive format and we lacked sufficient opportunity to raise all the issues we felt needed consideration in order to meet the complexities and challenges of evaluating orphan and ultra-orphan medicines robustly.

In our case, there was no opportunity for proper consideration of the likely budget impact from the potential for reducing the dose of the drug or stopping treatment. Had the format allowed, we could have provided evidence from various trials which are already taking place in a number of countries to demonstrate the progress being made into the understanding of treatment options, thereby benefitting patients as well as budgets. We believe that this should have been an important real life consideration in a robust evaluation of an innovative, but expensive, new medicine, particularly as it provides the first and only clinically effective treatment and can transform people's lives.

A more flexible PACE process and the participation of PACE representatives at the Committee meeting could have provided this opportunity. In fact, we were only able to briefly allude to the existence of trials in PACE, and we had to observe the lack of any reference to this important consideration during the course of the Committee meeting without being able to rectify this omission. As there was no reference within the DAD either, we are not aware that SMC members saw any evidence from these trials.

It is unclear what the real impact patient group submissions and PACE have had on decision making, even though this is supposed to be a major factor in the process. The current constraints of the Committee meeting do not permit adequate representation of their views and we do not feel that the brief summary of patient group input provided in the DAD "reflects the views of the group." Time and effort

had been spent trying to write as comprehensive an overview as possible within the confines of the format, and this was not properly reflected.

The right to appeal decisions should be extended to patient groups and clinicians if they have concerns about decisions. We have not been able to do this despite believing that more evidence should have been taken into consideration.

At the moment it is not possible for the SMC to be seen to deliver fair and equitable decisions because the current process is inadequate, overstretched and under-resourced. With such a workload, members cannot be expected to be able to give full consideration to all the available evidence.

The ability to make conditional recommendations could help improve access to orphan and ultra-orphan medicines in a timely manner. Account could then be taken of factors such as ongoing developments in knowledge and understanding of rare diseases and new medicines, and the likelihood of further new treatment alternatives in the future, with their associated potential for cost reduction. It could also facilitate ongoing reviews and dialogue with pharmaceutical companies. We believe that this is another reason why opposing decisions were reached within the UK in the two recent evaluations of the same medicine, for the same price.

Finally, under the current system, it would appear that there is a price threshold above which no medicine can be recommended, regardless of any other factors or the time and effort put in by the participants into the process. If there is no chance of justifying the treatment's cost in relation to its health benefits, even when these are immense, there seems to be little point in evaluating the medicine in the first place. Orphan and ultra-orphan medicines need a more relevant evaluation process if the unlucky few with rare diseases are to have any chance of equitable access to effective treatments. In contrast, the general population can access "cheaper" medicines, at great overall expense, even when they lack evidence of clinical effectiveness, and offer poor value for money.

Dear Dr. Montgomery,
Please find below feedback from Gilead Sciences regarding the review of access to medicines in Scotland:

How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical company's best offering on price earlier

Gilead do not consider the SMC processes needs to be adapted. Gilead offer the best price for medicines at the first opportunity, based on the value of the clinical benefit and at a level that offers value for money to the NHS in Scotland. Introducing a negotiation component could unnecessarily lengthen and complicate the SMC process.

Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report

Gilead believe the SMC have a strong record of providing timely advice on new medicines in a transparent manner. However, additional processes relating to orphan, ultra-orphan and end of life medicines, combined with a recent increase in volume of new submissions, seems to have had unintended consequences on SMC capacity and ability to schedule new assessments in a timely manner. This can have the effect of introducing uncertainty, and potentially delaying access to non-orphan medicines.

Gilead believe there would be benefit to introducing an abbreviated review mechanism for novel medicines proven to provide cost savings to the NHS in Scotland – this would provide a mechanism to support innovation and timely adoption of these new technologies.

Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value

Gilead would welcome further clarification around the definition of a Scottish Model of Value. Gilead consider the existing SMC evaluation process to be robust and accurately captures the value of medicines.

Best wishes,

Laurence

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Review of access to new medicines 2016

Response on scope from Kidney Research UK; 26th April 2016

General Remarks

The PACE process has allowed patient groups to have a positive voice, which was previously missing, and enables them to contribute beyond that of a written submission. The meetings allow patient groups to share views based on 'real' patient experiences, alongside other patient groups and invited Scottish patients. As a patient group, Kidney Research UK feels its contribution is valued.

Specific remarks on the scope

We have numbered the scope paragraphs below for ease of reference. The numbering in the following comments refer to the respective paragraphs below.

- The heavy reliance of the QALY analysis in the decision-making process can overshadow the real yet less tangible patient benefits that may not be captured in the clinical and economic assessment. (2)
- The patient and clinical voice needs to be heard much more and at each stage of the process, with more dialogue afforded to the statements of patient groups, clinical experts and families. (2)
- In the case of ultra-orphan drugs for very small numbers of Scottish patients we feel more flexibility is needed. This is to ensure that the true impact of a negative decision on whole families is understood. This is the case in rare genetic conditions where the inherited condition passes down generations. If a drug exists that could bring hope to future generations, the psychological impact of a refusal on the elder generation reaches far beyond the physical manifestation of the disease. A case in point is the decision not to recommend eculizumab to treat aHUS. This condition destroys the kidneys of those affected yet the drug offers the prospect of enabling kidney transplants to be successful in those already affected, and to protect the kidneys of their children. (3)
- In Patient Access Schemes, it would be helpful to a patient group to understand if such a scheme has been submitted to the Patient Access Scheme Assessment Group (PASAG). We appreciate that the details remain commercially confidential. However, the fact that a submission has been made would be useful in understanding the value a company places on access to a new medicine for Scottish Patients. (3 & 9)
- Where NICE has recommended a treatment, and SMC reject, we believe it essential that SMC communicates why the Scottish situation is different i.e. why Scottish patients are different to those in England and then subject to post code prescribing. The reverse of this situation is of course equally valid. (5 & 10)
- There needs to be an emphasis on public information about how the new system, and this review, will offer improved patient benefit. (5)
- The approach needs an effective method of environmental scanning to surface emerging technologies (11)

Numbered scope paragraphs

1. How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice;
2. How the views from the Patient and Clinician Engagement process are taken into account in decision making;
3. How the new approach to assessment of ultra-orphan medicines is operating in practice;
4. How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach;
5. How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement;
6. How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund;
7. How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system);
8. Whether there are further opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines;
9. How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier;
10. Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report;
11. How the new approach will accommodate advances in new medicines and a developing regulatory framework;
12. Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value.

Publishing preference

Publish response with name.

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Dear Sir

I am writing to provide information to the current review of access to medicines in Scotland under the call for evidence issued by Dr Brian Montgomery.

PTC Therapeutics (PTC) is a small US based bio-pharmaceutical company focused on the discovery and development of orally administered, proprietary small molecule drugs that target post-transcriptional control processes. Post-transcriptional control processes regulate the rate and timing of protein production and are essential to proper cellular function. PTC's internally discovered pipeline addresses multiple therapeutic areas, including rare disorders, oncology and infectious diseases.

We warmly welcome the Cabinet Secretary for Health, Wellbeing and Sport's decision to proactively review access to medicines in Scotland and are encouraged by Dr Montgomery's decision to open this to a public call for evidence.

In our response we have drawn on our experience of the review of our product Translarna, an ultra-orphan product, by SMC in March 2016. Translarna was approved by the EMEA in 2014 for the treatment of Duchenne muscular dystrophy for patients with a nonsense mutation in patients aged 5 years and above and ambulant. There are six patients in Scotland meeting the criteria.

Our feedback includes our experience and suggestions for how the process might be improved:

- How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice: *PTC Therapeutics' current area of focus is Duchenne muscular dystrophy in patients with a nonsense mutation (nmDMD). For this condition, the definition process, decision making and confirmation by SMC was relatively smooth and quick. In practical terms for nmDMD where there is only 6 patients in Scotland eligible for treatment it worked well.*
- How the views from the Patient and Clinician Engagement process are taken into account in decision making; - *Contribution to this process, from a clinician and/or patient organisation perspective, requires a significant amount of time and effort in order to produce and compile the responses. The subsequent contribution to the PACE meetings whilst welcomed, places an extra burden on patients, parents, patient organizations and clinicians in terms of time dedicated to preparing for and attending the meetings. For nmDMD those involved in the PACE process spent a significant amount of time and resources in contributing to the process and ultimately felt their views were not taken into account during the decision making process. It appears clear from the process and from post-review discussions with SMC that the ICER continues to be the main factor by which the decisions are made. If the SMC do not have the remit to recommend a drug with an ICER above £100,000 then they need to specify this before the process commences. The expectations of the nmDMD community was that the credence given to their input and evidence would be much greater than it was in reality. This has led to a huge amount of disappointment and disillusionment with the whole PACE process from those providing their input.*

- How the new approach to assessment of ultra-orphan medicines is operating in practice; *From PTC's perspective, this process does not seem to be functioning as intended. The ICER continues to be the main focus for the SMC's decision making. Clinical trials for ultra-orphan drugs are challenging to recruit for and the nature of many of these conditions means that it becomes unethical to continue a placebo controlled study beyond 48 weeks, as to do so may adversely affect the life of patients on placebo. The lack of long term efficacy data, and quality of life data, combined with the cost of the technology, almost inevitably leads to a high ICER. The current SMC decision making process for assessing technologies to treat very rare conditions focuses almost exclusively on the ICER even though budget impact may be low; for instance, the ICER for Translarna is £793.498 whereas the total annual budget impact is less than one million pounds. Guidance given to PTC during our assessment process suggested we should use the results from our 48 week clinical trial and then extrapolate the expected outcome over time. However, during the review this approach was questioned by SMC and the decision was taken that the extrapolation was too uncertain. Therefore, in order to enable patients with these very rare genetic conditions to gain access to ultra-orphan drugs a different approach to assessment by SMC is needed. Such an approach would need to take into account all the elements of developing treatments for these very rare conditions i.e. high risk, expensive developments programmes, a relatively limited package of clinical trial data and very small patient populations. It would also need to accept that ICERs for such treatments will usually be in excess of £500,000 but annual budget impact is likely to be less than £5 million. In the Netherlands health technology appraisals are not conducted for drugs where total budget impact is less than 2.5 million euro. To address the lack of long-term data, a managed access approach could be utilized whereby the pharmaceutical company works with other stakeholders including NHS Scotland, relevant clinical specialists and the patient organisations to collect data that could be resubmitted after an agreed period of time relevant to the condition being treated.*
- How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach; *Acceptance rates appear to have improved for end of life drugs but not treatments for rare and very rare long-term conditions. Treatments for orphan and ultra-orphan conditions appear to be considered more uncertain in terms of long-term outcomes than end of life drugs, where the patient will ultimately die so costs are contained. This can disadvantage patients with an ultra-orphan condition where treatment could offer considerable advantage in improving prognosis and quality of life for patients and their families. In rare genetic disorders patients have no influence on their condition. In contrast, many common conditions that can be the result of life style choices are currently placing a huge financial burden on NHS Scotland. SPICe briefing Obesity in Scotland January 2015 notes a total annual NHS cost of obesity to the NHS of 600 million with total economic costs estimated between 0.9 to 4.6 billion pounds. .*
- How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement; *PTC welcomed the improved transparency and working with the SMC. PTC found SMC to be helpful and engaging both prior to, during and after the submission was reviewed and not approved. However we are a very small organization (5 of us in total in the UK) and continued requests for information from the SMC placed a heavy burden on our internal resources. Also, given that it seemed clear that the SMC could not approve our technology due to the ICER this was not helpful. Small organisations do not have the resources, human or financial, to continually deal with re-analyses that will still result in the non-approval of a technology. We would urge SMC to consider their approach to asking for continued re-analysis of the information in the context of 'will it make a difference to the outcome?'*

- How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund; *PTC is aware of health boards approving individual funding requests (for our technology) whilst others are rejecting them. It is not clear why the rejections are taking place as the cohort of boys in Scotland applicable for treatment have similar disease states. This leads one to suspect the review process differs by board suggesting inequalities in accessing treatment. In terms of the New Medicines Fund across Scotland doctors do not know how this fund can be accessed, clarity is definitely needed.*
- How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system); *The new approach is still not geared up to review ultra-orphan drugs with a high ICER and limited data sets, hence reliance on individual requests remains significant in this group. The risk share scheme which Scotland previously used to fund high cost drugs to treat ultra-orphan conditions left less reliance on the individual funding requests and in our opinion should be restored.*
- Whether there are further opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines; *Ultra-orphan review of drugs is costly and time-consuming denying access to treatments for some groups of patients for significant periods of time. Scotland could lead the way with their approach in that when newly licensed drugs come to market they work with clinicians, patients and industry to put in place a managed access program. This would allow for collection of data over a longer period of time. In turn this would free up time for SMC to evaluate drugs for larger populations of people, which is their true area of expertise.*
- How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier. *There is clearly scope to improve the current system in Scotland where no dialogue between SMC and the submitting company about cost/value exists. SMC comprises a panel of experts with some members having very clear roles and responsibilities. Commercial negotiation roles should be put in place for future in order that there is ongoing dialogue with industry and the sealed bid approach ceases, it is clearly not beneficial for Scotland, Scottish patients or industry to use an approach to price which does not involve communication or negotiation.*
- Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report; *Nothing to add*
- How the new approach will accommodate advances in new medicines and a developing regulatory framework: *We do not believe that this approach will allow patients with rare diseases to access technologies in Scotland. Companies whose technologies may cost the same to develop as medicines for common conditions, but are able to treat a much smaller numbers of patients, will be reluctant to submit through SMC knowing that the process does not take rarity into account and that their technology will be rejected based on cost. Companies in this kind of situation may instead not submit to SMC at all as a rejection based on cost is perceived as more negative than a rejection based on non-submittal.*
- Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value. – *Nothing to add*

I look forward to following the review committee's deliberations and reading their recommendations in due course. In the meantime if I can provide you with further information, please do not hesitate to contact me.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Jo-anna Allen'. The signature is fluid and cursive, with a large initial 'J' and 'A'.

Jo-anna Allen
Area Business Manager PTC Therapeutics

Review of Access to New Medicines

Thank you for the opportunity to contribute views to this review, which is concerned with progress made in improving access to orphan, ultra-orphan and end-of-life medicines rather than new medicines generally; in particular, since the Scottish Medicines Consortium (SMC) was asked to deliver the more flexible approaches in evaluating medicines for treatment at end of life and for very rare conditions.

As a pharmacist working for NHS Highland and as a member of the Board's Formulary Subgroup and Area Drug and Therapeutics Committee, my impression that more medicines in these categories are being accepted by the SMC for use in the NHS in Scotland was confirmed by the data presented at the launch meeting in Edinburgh on 21st March.

I must express my concern that the exercise of a judicious balance between safety and effectiveness has been tipped inappropriately and that safety is being sacrificed to expediency. A notable feature of some recent SMC assessments is that medicines are being presented for use by the NHS on the basis of limited data, often citing phase 1 and phase 2 clinical trials. I appreciate that this is product licensing, the remit of the Medicines and Healthcare products Regulatory Agency, but a crucial role of the SMC and Health Board Formularies must be to provide a sense check to the proposed use of medicines presented to us. It can seem that the new processes have inhibited the SMC's critical faculties and that Boards are expected to automatically follow. Formulary Subgroups thus become little more than rubber stamps for expensive new medicines for rare indications that are supported by a limited evidence base and about which our misgivings must be suspended.

One of the features of the new process is PACE (Patient and Clinician Engagement). Engagement of interested parties is vital to a robust assessment process that we, as a society, can feel confident in and is to be welcomed. That said, it is inappropriate that the PACE process does not seem to be subject to the same level of disclosure that we expect of participants in the SMC or Board committees. The review should address this and require that links to the pharmaceutical industry are fully disclosed by all participants in the PACE process and available for inspection.

At the meeting in Edinburgh, there was discussion on "the problem with QALYs". There is no problem with QALYs *per se*, rather, some are dissatisfied with results that are presented by this methodology. The review needs to be careful that it does not ditch an established methodology that is supported by an extensive research base. We are now presented with the vagueness of cost-consequence modelling. I am concerned that some conditions may be considered more worthy than others: a prejudice that the use of the common unit, the QALY, protects us from. If we are to proceed down the route of cost-consequence modelling, then we must be assured of a consistency of approach in the application of societal values and views.

Lastly, a word about the elephant in the room. In a health economic analysis, the sensitivity analysis will test assumptions and identify those factors which influence the intervention's cost-effectiveness to a greater or lesser extent. It would be rare to find that the acquisition cost was not one of the most significant factors in its overall cost-effectiveness, if not the most significant. A considerable part of the problem with access to the medicines that are under discussion is pricing: they are often eye-wateringly expensive. The emotive argument is that the NHS has not used medicines based on the sole criterion of cost. I do not believe this to be the case: health economic analysis using an internationally recognised methodology has shown relative cost-effectiveness of some interventions to be wanting. Societal embarrassment about our ability to provide every health intervention possible should not blind us to pricing by manufacturers that appears to exploit a humane weakness in emotive situations so that they may impose outrageous prices for medicines.

I am happy for this response to be published with my name.

Yours sincerely,

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ABOUT BREAST CANCER NOW

Breast cancer is the most commonly diagnosed cancer in women in Scotland. Over 4,600 women are diagnosed with breast cancer and around 1,000 die from the disease in Scotland each year.

Breast Cancer Now is determined to stop deaths from breast cancer. We believe that if we all act now, by 2050, everyone who develops breast cancer will live.

We are the UK's largest breast cancer charity with an office in London and in Edinburgh. We've already made enormous progress in understanding breast cancer. Now, we're reaching further and doing more than ever before. We're bringing together the brightest minds to discover how to prevent breast cancer, how to detect it earlier and how to treat it effectively at every stage as well as find ways to stop secondary breast cancer.

Our public health campaigns also help thousands every year become breast cancer aware and empower them to take action to reduce their risk of the disease.

We're the catalyst that connects the laboratory bench with the hospital bedside, the GP's office, the politicians' surgery and the policies that govern the health service. We make the voices of patients and their families heard, and support the health service to champion their needs.

BREAST CANCER NOW'S RESPONSE TO THE REVIEW

In responding to the review's call for evidence we have responded to the areas where we are able to add value.

WHAT ACCESS TO MEDICINES MEANS TO PEOPLE

People should be at the centre of the drugs assessment system. As part of our response to this review we therefore surveyed a number of our supporters to find out about their experience accessing new medicines and what unlocking new treatments means to them. One hundred people responded to our survey over eleven days. Half (50%) of the responses came from women with secondary breast cancer or loved ones of those with metastatic breast cancer. Other responses came from people with primary breast cancer and those with a general interest in the issue.

The views expressed through our survey show that when the system isn't working at its best there are very real and worrying consequences for patients and their loved ones. There is frustration and anger among some surveyed at not being able to access new life-extending secondary breast cancer drugs on the NHS in Scotland. A loved one of someone with metastatic breast cancer said that the situation left them feeling "helpless, hopeless, angry and frightened".

The impact of drugs not being available on the NHS leads people to go to great lengths to access the hope that these drugs bring. People have considered moving out of Scotland to access drugs. One family member explained that they are looking at private care abroad. A patient with secondary breast cancer said that she had thought about leaving Scotland and explained that "I shouldn't have to do this to lengthen my life." Others have paid to access drugs not available on the NHS.

An improved system would have a positive personal impact on patients. As one person said, "It means everything and the chance of happiness to know that the very best is being done for my loved one." A secondary breast cancer patient highlighted that better access to medicines would give them hope for the future:

"Being recently diagnosed with secondary breast cancer it would fill me with hope for the future rather than fear if I knew that there was better access to life extending breast cancer drugs in

Scotland. I want to be here to bring up my two daughters and wouldn't want to be in the position of having my life shortened because there were drugs out there that I couldn't access."

The emphasis of any new system therefore needs to be on putting the patient interest first and exhaust every possibility to make new life-extending drugs available on the NHS.

ASSESSMENT OF THE NEW APPROACH

Definitions of end of life, orphan and ultra-orphan

Breast Cancer Now welcomes the definition of "end of life" used by the Scottish Medicines Consortium (SMC).

The PACE process

The Patient and Clinician Engagement (PACE) has improved the transparency of the SMC. Thanks to the PACE process, patients and patient groups now understand better how the SMC process works and can contribute views on the impact of treatments.

However, we can't conclude that PACE has influenced the SMC decisions on breast cancer treatments.

Six breast cancer treatments have been considered using the PACE process. They are:

- Afinitor (everolimus): rejected on 1st submission using PACE, approved on resubmission
- Faslodex (fulvestrant): approved on 1st submission using PACE
- Halaven (eribulin): rejected on 1st submission using PACE, approved on resubmission (with restrictions)
- Kadcyła (trastuzumab emtansine): rejected
- Perjeta (pertuzumab for treatment of HER2-positive metastatic breast cancer): rejected
- Perjeta (pertuzumab for treatment of HER2-positive breast cancer in the neoadjuvant setting): rejected

Afinitor and Halaven were recommended for NHS use in Scotland following resubmissions where we understand the pharmaceutical companies each offered a 'simple discount' to the list price. No significant changes were made to the PACE statements in these resubmissions. In the case of breast cancer drugs, it is therefore not possible to conclude that PACE had a meaningful impact on the SMC decisions.

IPTR / PACS

In 2014, the Scottish Government proposed replacing the Individual Patient Treatment Request (IPTR) with the Peer Approved Clinical System (PACS). PACS is not yet in place across Scotland and IPTR remains the way patients access non-SMC drugs.

IPTR decisions are taken by local Health Boards. Patients across Scotland therefore have to negotiate different local systems to access drugs that could offer improved outcomes. We are concerned that having different decision making processes could mean that some patients could access a drug through IPTR in one part of Scotland where applications elsewhere have been denied. Evidence to the Health and Sport Committee from the Beatson West of Scotland Cancer Centre suggests the current system may have resulted in a postcode lottery for patients:

“There is also some evidence that the IPTR decision making criteria are now quite different between the regions of Scotland and that these differences have resulted in some patients being able to access drugs in one part of Scotland where access would have been denied had they lived in another. This has resulted in some low-level ‘postcode prescribing’ within Scotland, a practice which none of us support.”¹

The PACS system, proposed as part of the reforms in 2014, is expected to be administered locally, but with a national framework and audit from Healthcare Improvement Scotland. When describing how the system would work, the Scottish Government said that variation in local decision making would be “minimised through strict auditing arrangements”². This suggests that decision making will remain at local level with an assessment of the consistency of decision making only after decisions are taken. The system therefore misses the opportunity to get consistency in decision making straight away, thereby leading to the risk that some patients will fall out of local systems before the audit has picked up this practice.

The New Medicines Fund

The Scottish Government has said that the New Medicines Fund / Rare Conditions Medicines Fund has benefitted over 1,000 Scottish patients since 2013/14³. It is clearly benefiting patients, but there is little detail available on how it is performing.

Further data on the fund would be welcome. Particularly:

- Which conditions have been treated using the Fund and how many people with each condition?
- Which drugs have been made accessible through the Fund?

FUTURE REFORM: ACHIEVING A PERSON-CENTRED SYSTEM

As well as a person-centred health service we need a person-centred approval system that assesses drugs for use on the NHS.

To achieve a person-centred process we need a fundamental shift in the way the NHS and the SMC approaches decision making on new medicines. The key principles of such an approach should be:

- Proactive negotiation with manufacturers;
- Flexible decision making;
- Active patient and clinician involvement;
- Consistency and clarity of the process for non-SMC approved medicines;
- A culture of continuous learning and improvement;

Below we outline a number of key suggestions that we believe could help deliver these key principles.

¹ http://www.scottish.parliament.uk/S4_HealthandSportCommittee/Inquiries/UANLM010_CMOC-Beatson_WSCC.pdf

² http://www.scottish.parliament.uk/S4_HealthandSportCommittee/Inquiries/Scottish_Government_Response_-_Access_into_New_Medicines.pdf

³ <http://news.scotland.gov.uk/News/Fund-for-new-medicines-doubles-18eb.aspx>

Proactive negotiation with manufacturers

We believe that every effort must be made to try and make the right decision first time around. Re-submissions mean delays to patients accessing drugs and should be avoided where possible. If a drug is deemed to be effective, every effort must be made to explore all possible options to make it available.

This is why a negotiating mechanism is important. In 2014, the Scottish Parliament's Health and Sport Committee and Scottish Government agreed that a pause should be introduced in the drug appraisal process to allow the SMC and drug companies to explore improvements that can be made to cost-effectiveness. The pause has not been introduced.

Breast Cancer Now is supportive of the concept of a negotiating pause and is disappointed that it has not yet been introduced. We fear that there may be some caution from the SMC on this issue and would like to highlight that an alternative body, perhaps a 'negotiating panel', could be created to take forward such negotiations.

A potential suggestion in this instance could be:

- Giving the SMC the power to refer a submission to a negotiating panel after a submission is rejected by the New Drugs Committee. Three components could form part of the negotiating panel's discussions:
 - PACE submission;
 - The New Drug's Committee's recommendation;
 - SMC modelling of what is required to reach an acceptable cost-per QALY.
- The Patient Access Scheme Assessment Group (PASAG) could assess the viability of offers presented to the panel.

The process should not only be focused on cost, but look at other options to achieve best value. For example, schemes to ensure the managed introduction of medicines over time or ways to further research the benefit of a drug through the NHS could also form part of the discussion.

Flexible decision making

The SMC decision making process needs to be more flexible. As it stands, the SMC can take one of three decisions:

- Accept the medicine for use;
- Accept the medicine, but with some restrictions on which groups or patients should be treated;
- Not recommend the medicine for use⁴.

Drugs are becoming more sophisticated and targeted. It may not always be possible to conclusively prove that a certain drug reaches the SMC's criteria, but the research provided may indicate that it has significant potential to improve patient care.

For example, in certain circumstances, it may be beneficial for the SMC to have the ability to approve a licensed medicine in order for further real world data be collected and allow a more

⁴ https://www.scottishmedicines.org.uk/About_SMC/What_we_do/SMC_Guide_web_final_.pdf

detailed re-submission in the future. In these circumstances, clinicians would have the ability to prescribe these drugs to any of their patients who they deem to be suitable.

With such flexible decision making, patients would get quick access to promising treatments and, over time, it would give the SMC and pharmaceutical company a more detailed case for robust and informed cost-effectiveness negotiations to secure a sustainable deal.

Active patient and clinician involvement

There should be a way of allowing clinicians and patient groups to participate actively at the final SMC Committee meeting.

Currently, drug companies are given the opportunity to answer questions at the Committee, but patient groups and clinicians with first-hand experience of the condition being discussed cannot take part.

The summary of the patient and clinician contribution through PACE is read out at the meeting, but there is no opportunity for them to elaborate on any of the details in the PACE summary or answer any specific questions from the Committee.

Consistency and clarity of the process for non-SMC approved medicines

The proposed PACS system is a step closer to national consistency in how applications will be made to Health Boards to access non-SMC approved medicines. However, Breast Cancer Now fears that PACS will not ensure that decisions are consistent.

We therefore welcome efforts to investigate a single national decision making system, which involves local clinicians and draws on the best expertise across the country.

A culture of continuous improvement

The reforms introduced in 2014 following the various reviews, have made the decision making systems around new medicines in Scotland more transparent. Greater patient involvement is also welcome.

We support this further independent review and hope that its findings will lead to additional improvements that will unlock innovative treatments for women with incurable secondary breast cancer.

Improvement is a process of continual learning. In order to ensure the systems progress at the same pace as developments in treatment it is important that they are regularly reviewed. We would therefore support the idea of a mechanism that facilitates regular review of whether the systems in Scotland are fit for purpose.

This review mechanism could be a feature of the SMC's annual report. Each year, patient groups could be invited to provide feedback on their experience of the SMC process and any improvements for inclusion in the report.

For further information

For further details please contact Breast Cancer Now's Policy and Campaigns Manager in Scotland, Lawrence Cowan, on 0131 240 2850 or Lawrence.cowan@breastcancer.org.

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A personal perspective on the SMC review of Translarna by Michelle Young, mother of a nine-year-old boy Michael Young who suffers from Duchenne Muscular Dystrophy

Dear Sir,

I am advised that you are conducting a review of the efficacy of the targets set on the SMC in 2014 by the Scottish Government. I would like to offer my personal experience and that of my family for your consideration. My son Michael Young has Duchenne Muscular Dystrophy and has been a participant on the Ataluren (Translarna) PTC trial since 2013. We have first hand experience of Duchenne Muscular Dystrophy and live with its effects on a daily basis. Likewise we also have first hand knowledge on how Translarna has benefitted our son.

I would welcome the opportunity to discuss the SMC and PACE process with you face to face, if possible, or as part of a discussion should you arrange one. My family and I have grave concerns relating to the PACE process and SMC final assessment meeting of Translarna.

The following points are our observations of the SMC processes and are in no way influenced by the Translarna decision. We are highlighting our concerns in the hope that the SMC improve and no family feel the concern and distress we have felt. We hope that the SMC processes can be developed to provide robust, vigorous and transparent decision making for ultra orphan medicines.

If you require any clarification then please do not hesitate to contact me.

PACE Patient Submissions

Patients are not permitted to represent themselves in the PACE process and must use an approved Patient Public Partner. In our case that was MDUK. The process allows for two written submissions and attendance of a PACE meeting.

My husband and I were asked to write a statement detailing the effect of Duchenne and the benefits of Translarna. The SMC advised it was important we write about the patient lived experience and the rest of Michael's family and friends asked if they could provide statements as well as Duchenne affects them directly too and they had seen first hand the benefits of Translarna on Michael. Writing the statements was very difficult for all involved. There was a tremendous feeling of responsibility and I spent nearly every night for two weeks as close ones cried down the phone. The process of writing the statements brought to the forefront everyone's feelings about Duchenne and their worries about Michael and his future. As I read their statements I felt tremendous guilt at the pain my family and friends were feeling.

On the first submission MDUK filled in the SMC template and attached the statements from Michaels' family and that of Cormac Fegan's. MDUK were confident their submission showed the extent that Duchenne can affect a family and that it was not just the patient affected. We then submitted a second submission listing other minor points not detailed in the first submission.

Given the importance of the submissions and the PACE meeting I spoke with the SMC Public Involvement Officer, Lindsay Lockhart, on the phone for over 30 minutes when the first submission was sent. I asked if it was acceptable, if all the information we provided was in the correct format, suitably written and asked if it could be improved in any way. I was told it was very good. During this call, (and prior to the second submission being sent), I was strongly advised by Lindsay Lockhart not to repeat anything listed in the first submission. I followed her instruction accordingly. Imagine my horror then that two days before the PACE meeting I discovered by chance that the SMC had only included the MDUK template responses and disregarded in its entirety all of Michael and Cormac's statements. Michael's representation was restricted to a few quotations within the MDUK part.

We were advised that our statements would not be included 'in line with patient fairness'. I cannot see how disregarding multiple statements representing a patient and those affected by the disease is fair. Michael Matheson MSP, John McNally MP and MDUK all wrote to the SMC asking that as a minimum our (Michael's parents') statement be included. This was declined. Had the SMC Public Involvement Officer advised me during our call that our statements were not suitable and had been disregarded I would have summarized our key points in the second submission. We were not given the opportunity to rectify and believe we were misdirected by SMC. MDUK also wrote again to SMC raising their concerns that patient voice was in no way 'maximised' as claimed by them. You can imagine the distress this caused me having to tell my family that the statements that had been so emotional for them to write had been disregarded.

At the time there was much confusion on what parts of the MDUK submission would go forward to the PACE meeting. When we sought clarification the responses were often vague.

We are deeply concerned that the SMC edited the MDUK submission and disregarded information submitted by our family without notifying us or giving the opportunity to correct it. Our family considers Translarna a life enhancing medicine but also the key to allowing Michael access to life saving medicines in the future. Not to be given an opportunity to represent Michael fully and well continues to haunt us.

Questions we have are:

1. Why were people who provided statements not notified they were to be disregarded?
2. Who within SMC decided to edit the MDUK submission and disregard these statements and on what basis?
3. Why did the SMC not make it explicitly clear that only information provided within the template would be included?
4. Why did the SMC fail to give us an opportunity to rectify the submission format given the importance of the information?
5. Why did Lindsay Lockhart fail to inform me during our telephone conversation that the submission was not suitable and why did she say the submission was good?

We recognize the need to have structure and consistency in the submissions received by the SMC but strongly believe that the SMC templates do not allow all the information relating to a complex condition like Duchenne to be listed. If SMC were serious about incorporating the patient 'lived experience' then surely the templates should have sufficient room to include all relevant information. If the SMC will not give feedback on submissions and not offer the opportunity to rectify errors like format then they should

at least have clear instructions detailing not only what is acceptable but what will be disregarded.

PACE Meeting

I attended the PACE meeting with a representative from MDUK. Another two fathers also attended with their representative Patient Public Partners. Our spouses were not permitted to attend and this put further strain on those parents acting on behalf of their sons. I sat beside one father who was literally shaking under the table and thought it cruel that his wife was not permitted to be there to provide support or comfort. Considering the size of the room I see no reason why spouses or partners could not be present.

I think it is commendable to be given the opportunity to speak at the PACE meeting but cannot express strongly enough the burden I and the other fathers felt given that enormity of this meeting and consequences it had for our sons' lives.

We were each given only 5 minutes to present our case. Trying to explain the full natural history of Duchenne, the extent of devastation Duchenne has on a family and the benefits of Translarna in such a short time were impossible. The very short time constraint put additional pressure on those presenting and although those who spoke co-ordinated their presentations we were still pushed for time. I don't think it would have taken significantly more time to present our case fully had we been allowed to do so.

Most of the meeting time was spent with the chairman advising that we would need to summarise (yet further) our submissions to 'no more than 2-3 points and preferably only one point'. Due to the complexity of Duchenne we struggled to do this all to the exasperation of the chairman. In the example of Duchenne what do you choose as your main point? Loss of ambulation, exclusion from future medicines, social exclusion, spinal surgery, requirement for ventilation, severe depression of the patient and parents, impact on siblings, house adaptations, loss of employment, financial strain, heart failure or early death?

The final PACE submission was summarized to no more than a few sentences and in no way showed the full extent of the disease or the benefits of Translarna. We were advised that the submission would be sent to us for comment but we were only permitted to comment on any items that were factually incorrect. We were told we had no say in the overall wording.

We were further advised by the SMC that none of the Patient Public Partners would be permitted to present at the final assessment meeting of Translarna and that a SMC appointed public partner would present the patients' views.

The Public Partner started the PACE meeting by passing a brown envelope to the chairman saying, "can we get the important business of the day out of the way first". I strongly believe it was his expenses form he handed over. I struggle to convey how this made me feel. I was sitting waiting to speak about my dying son, the importance of his life and the most personal of details yet the important business in the Public Partner's mind was expenses. It was callous, upsetting and disconcerting.

The PACE meeting lasted just over 1 hour and only 15 minutes was spent listening to the patients' views. A small amount of time was allowed for SMC staff to ask questions and seek clarifications from the physicians. We were very concerned about what would be

relayed to the SMC at the final assessment given the 'filtered' PACE submission and I asked if the public partner would like to meet so he could ask any further questions and let us know what he intended to present on my son's and the other boys' behalf. This meeting request was declined by the SMC.

Doctors were invited to the PACE meeting. We found out by chance that neither of Michael's physicians had been invited. It was only after continued requests by me and the charities that Dr Guglieri (Lead investigator of Translarna trials at Newcastle Royal Victoria) was invited. Had she not been invited then the experience of the remaining clinicians would have been limited to 2 months experience of Translarna.

Questions we have are:

6. How can the SMC expect a complex condition like Duchenne to be summarized in no more than 2-3 points?
7. Why was the focus of the meeting to reduce patient views to headlines rather than focus on obtaining all the relevant information that could help with the final assessment?
8. Why was most of the meeting time spent explaining the meeting process and then on reducing the patient submissions content?
9. Why were spouses or support not permitted to attend?

Final Assessment

My husband and I attended the SMC final assessment meeting on 1st March 2016 and were deeply concerned with what we saw. We left the meeting feeling it was a foregone conclusion that the SMC would reject Translarna.

The audience was told they would not be permitted to speak or address the SMC committee and if anyone attempted to do so they would be removed from the building with immediate effect. This was particularly difficult when several incorrect statements were made by SMC members and not corrected. To hear incorrect information being presented and not being permitted to correct it was particularly distressing.

We were present for the assessment of four medicines including Translarna. The same amount of time was allotted to each medicine regardless of its importance or impact. Given that Translarna is the first medicine to treat the underlying cause of Duchenne, that it was considered by families to be potentially life saving, that pharmaceutical companies worldwide were watching this decision with a view to investing in Scotland for future trials you would think the SMC would allocate appropriate time yet they spent the same time considering a treatment for warts and green tea extract as they did Translarna.

The PACE submission was read out and the public partner advised the committee that all the patient submissions were included in full. This was incorrect and misleading given we were told our statements were disregarded.

The Public Partner then spoke for a very short period of time, quite eloquently, but only mentioned a couple of points relating to Duchenne. We were stunned when he stopped talking without disclosing the full extent of Duchenne or the benefits of Translarna. We later realized that all he did was read two pages of the MDUK submission verbatim. He failed to tell the committee that all the Scottish boys taking Translarna had benefitted greatly, had not deteriorated since taking the medicine, were all ambulant and that one boy (nearly sixteen years old) remained walking even after a leg fracture (unheard of in

the Duchenne community). Key and vital patient and family information was not presented.

At least half of the allocated time for Translarna was spent by the SMC discussing procedural aspects rather than the impact of Duchenne or the medicine itself. There were queries relating to whether they could base decisions on information in the public domain e.g. unsubstantiated FDA statements in newspapers and the Internet or whether they should include the impact on carers in their decision. If the SMC is fully established should all decision criteria be agreed prior to the assessment of a medicine?

The SMC relied on nominated 'experts' and posed a number of questions to them in written form. These experts were anonymous. Having read the responses to the questions I am concerned about that competency of the experts selected. Multiple responses included "I do not know" or "I cannot comment" or just left blank.

My husband and I saw at least 6 SMC members looking at their phones during the Translarna discussion. One SMC member sat throughout the proceedings chewing gum. Our son is dying and I would have expected a certain level of decorum from the SMC members given the authority and responsibility that has been placed upon them.

One SMC member in plain sight appeared to be reading the Translarna report for what looked like the first time. He spent much of the meeting reading one paragraph at a time and then writing down notes. I would have expected at the final meeting that all the SMC members come well prepared with questions or points of clarification so they were able to make a fully informed decision.

The most worrying aspect of the final assessment meeting was the presentation of incorrect data and the failure of the committee to correct it. There are two examples that come to mind and given they were said right before the final decision I think it would have had an effect of the final decision.

One SMC member stated that the number of eligible boys was not 5-6 as stated but in fact 17 boys. No one in the SMC committee corrected this inaccurate statement and they were left with the impression that final cost to NHS Scotland would be **3.5 times** the correct figure. Had the SMC member read the papers correctly she would have seen that there are 17 boys with the type of Duchenne Translarna treats but that eleven of these boys are non ambulant and therefore not eligible for Translarna. It is foreseeable that one SMC member may misread a statement but why did none of the 20+ other SMC members correct her?

The second example was a statement by a SMC member that "Translarna only provided a little bit of hope for families- there is no concrete benefit". This was the last statement made prior to the vote being taken. When this statement was made many in the public gallery looked towards the public partner to speak and reiterate the benefits shared by the families and clinicians. The public partner sat looking to the ceiling tapping his pen against his cheek. He did not respond. No one in the public gallery was permitted to speak.

We now know the decision on Translarna and that it was rejected on the basis the SMC were 'uncertain of cost effectiveness in relation to benefits'. At no time during the meeting was cost effectiveness discussed or mentioned. Nor was there any debate on benefits of the medicine. How could the SMC say these factors were the basis of their decision and yet not discuss it?

My questions are:

10. How could the SMC say their decision was based on cost effectiveness and benefits yet not mention either of these in the final assessment?
11. Why were PTC not questioned on cost during the final assessment?
12. Why was much of the debate focused on the SMC members understanding decision criteria rather than focused on discussing the condition and the medicine?
13. Why were SMC members permitted to use mobile phones during the Translarna debate?
14. What assurance does the chairman have that the SMC voting members have fully understood and read the literature provided?
15. What experience and competence did the SMC appointed public partner have in relation to Duchenne and Translarna?
16. Why did the public partner fail to present key information relating to impact of Duchenne and the benefits of Translarna?
17. Why did SMC members fail to clarify incorrect and misleading statements?
18. What experience and competence does the nominated experts have relating to Duchenne and Translarna and why were they anonymous?

In summary:

I strongly believe the SMC processes are not suited or developed sufficiently for assessing ultra orphan medicines. There is a great opportunity lost here as with orphan drugs you are able to discuss with each patient what the medicine means to them and what effect the disease has and have an exact view on costs.

My family feels used, misrepresented and manipulated by the SMC. We entered the PACE process being assured that the patient voice would be maximized yet we believe the patient voice is no more than a whisper in SMC considerations.

We believe that the SMC only just tolerate patient representation and do so not because they want to but because they have been told to. They merely 'tick a box'.

We are deeply concerned about the competency and motivation of those selected to represent patients.

We are concerned about the competency of the nominated experts for ultra orphan diseases.

We are concerned about how rigorous the SMC are about understanding ultra orphan diseases and medicines before making their final judgment. We are concerned that in a bid to make a 'quick' response the SMC are not gathering all the information required to make an informed decision.

I am sure you will understand that it has been difficult to put my observations fully and well into writing and I would like to reiterate my willingness to meet and discuss them in more detail for the benefit of the exercise you are carrying out.

Yours sincerely

Michelle Young

ACCESS TO NEW MEDICINES

Dr. Montgomery,

I have written down some observations that I would like you to consider during your review of access to new medicines. In summary I think the process to consider new medicines should be:

Rigorous, Transparent and Robust.

The focus should be on “delivering the best medicine to the patient in the most effective way”.

There is a **Duty of Care** when considering life saving medicines especially for patients who are children and are unable to represent themselves. These children are most vulnerable and deserve our protection.

Points for Consideration (Ultra Rare diseases):

PACE

- **Patients should be full members of the PACE process**
- Patients should have the opportunity to represent themselves if they wish.
- **Patients and patients groups are best placed to nominate experts.**
- The information presented by patients should not be summarized without good reason or without the full approval of the patient.
- Why are patient submissions summarized when information from the pharmaceutical companies, experts, SMC and NDC left untouched? Why is the patient's views considered of less value?
- **The role and responsibilities of the Public Partner needs to be defined** and shared. There is an impression that the Public Partner is there to represent the patient yet in practice the Public Partner is a full SMC member with voting rights.
- If the Public Partner has a vote how do you guarantee unbiased representation? Surely there is a conflict of interest if the Public Partner does not support the medicine?
- How is the competence of the Public Partners assured?
- If the Public Partner presents on behalf of the patients then they should disclose what they plan to say before the final assessment meeting.
- Patients are given only 5 minutes to present complex conditions and the full benefits of a medicine. This is simply not enough time and adds further pressure to the patients presenting at the meeting. The PACE meeting should be focused on obtaining all information not restricting it.
- PACE templates do not provide sufficient space to fully convey all information.
- Personal support should be allowed at the PACE meeting e.g. spouses
- Why are videos not permitted? All communication to SMC through PACE is written in restrictive templates. Video footage may be a more effective means of demonstrating the effects of a disease like Duchenne.

- **There should be greater value and less restriction placed on patient views.**

FINAL ASSESSMENT

- **The SMC should have clear decision-making protocols.**
- Any SMC process queries should be addressed prior to specific medicine assessments.
- The time spent assessing medicines e.g. homeopathic medicines vs. life saving ones should vary depending on impact.
- **Patients should be permitted to speak at the final assessment meeting**
 - They can correct incorrect statements or misunderstandings
 - It is important that they are included in a decision that will have far reaching implications for them e.g. life saving medicines
- **There should be a check that the SMC are ready to make a decision e.g. Gate Compliance.**
 - Do they fully understand the condition, the medicine and its benefits?
 - Have they had sufficient time to consider?
 - Are they certain they have all the information and it is factual?
 - Is there any further clarification required?
 - Is there risk associated with making the decision?
- **Is there a need to have 20+ votes?** Would a smaller group be more effective? In the private sector there is a move to smaller more accountable groups for safety considerations.
- **Voting should be transparent.** Members should disclose their vote and reasons why. This is important for patients and companies to understand what areas need to be developed should they wish to resubmit. It also promotes accountability and due diligence of SMC members.
- Decorum and behaviours need to be considered especially when open to the public.

GENERAL OBSERVATIONS

- There is a growing agreement that diseases like Duchenne will be treated with combination therapy. If SMC is looking for the 'golden tablet' it may never come. The treatment of conditions like Duchenne may never move forward with that approach.
- **Medical trials for Ultra Orphan medicines rarely capture all the beneficial data.** Many companies struggle to define the primary endpoints at the start of the trial let alone capture some of the more subtle but, none the less, important 'quality of life' benefits. E.g. recovery from injury, reduction in severe depression, behavioural improvements, social inclusion, effects on siblings, heart & lung function, and financial impact.
- In the case of Translarna the SMC stated they were unclear of benefits of the medicine but little consideration was given to the absolute certainty of the progression of Duchenne.
- **Pharmaceutical companies expect negotiation on price yet the SMC have a 'closed bid' approach.** This is in stark contrast to NICE and other European countries where cost is negotiated down.

- **Pharmaceutical companies are not best placed to advise on 'costs avoided'**. PTC would not have NHS Scotland costs for supporting Duchenne sufferers e.g. costs for patients who undergo ventilation intervention and require intensive care beds for on average 1 year+ or wages for professional carers for older Duchenne patients.
- There is no greater expert than someone who lives with the disease.
- **The view that patients will take ANY medicine on offer is false.**
- Appointment of experts should be done carefully. Experts should not be anonymous and if they are unable to answer multiple questions posed then they should be discounted and new experts sought.
- Health Board members sit on SMC panel. If they vote no then does that make them biased towards refusing IPFRs and PACS?
- The SMC has an antiquated view that patients are ill informed or incapable of participating in discussions.
- **SMC process is focused on a YES/ NO answer rather than developing novel access routes that are Win/ Win outcomes e.g. managed access schemes.**
- **There is a missed opportunity with Ultra Rare diseases.** In the case of Duchenne and Translarna there were 5 eligible boys; 3 of which had taken the medicine. Feedback could have been collected first hand. There were small enough numbers that benefit could be monitored and assessed at relative low cost.
- The SMC should never make a decision and say they are 'unclear'.
- **In some cases the SMC have presented cost data that is 'theoretical', grossly over-estimated and not realistic to justify a 'no' decision.**
- **The difficulty is not improving SMC processes but how do you improve the culture within the SMC?**
- Who is responsible for regulating the SMC?
- How do we engage pharmaceutical companies early and before they have higher price reference points?
- SMC took just under 6 months to consider Translarna yet European Member states take on average 4 years (NICE ≈ 2yrs)
- Appraise / select / Define / Execute / operate..

Muscular Dystrophy UK submission to the New Medicines Review

Muscular Dystrophy UK welcomes the opportunity to respond to the Scottish Government's New Medicines Review.

Muscular dystrophy and related neuromuscular conditions is an umbrella term used to describe 60, mostly genetic conditions that cause the weakening and wasting of the muscles. All these conditions are serious and progressive, with effects that range from mild to severe disability and premature death, most typically in childhood or early adulthood. Approximately 70,000 people in the UK are affected by one of these conditions.

With some treatments for muscle-wasting conditions in late stage clinical trial and one, Translarna, set to be made available in all parts of the UK with the exception of Scotland, families affected by muscular dystrophy or related neuromuscular conditions (muscle-wasting conditions) cannot afford delays at the regulatory, approvals or delivery stages. It is also essential that clinical trials infrastructure is supported, so that the pipeline for investigation into potential treatments can continue to grow.

With families affected by muscle-wasting conditions, Muscular Dystrophy UK is calling for:

- **The SMC to reverse its decision to reject Translarna for funding on the NHS in Scotland.** The National Institute for Health and Care Excellence (NICE) has recommended Translarna for NHS funding under a Managed Access Agreement. This decision will enable access in England, and is expected to allow access in Wales, Northern Ireland and the Isle of Man. It is unacceptable that boys with Scotland are facing such uncertainty. The SMC, NHS Scotland and the drug's manufacturer have a duty to reach an agreement which will enable access on the NHS in Scotland
- **The SMC to place greater value and less restriction on evidence from patients and family members as part of their appraisal process.** The SMC's current process for incorporating patient and family testimony is truncated, inflexible and does not sufficiently capture the impact a condition has on an individual and their family
- **Greater use of innovative funding arrangements, which can ensure fast access to emerging treatments.** As a matter of urgency, the Scottish Government, SMC and NHS Scotland need to adopt arrangements such as Managed Access Agreements, which can address barriers to access to rare disease drugs including cost and available clinical trial data
- **The New Medicines Fund to be strengthened.** We welcome the Scottish Government's introduction and increase in funding for the New Medicines Fund – a ring fenced fund for rare disease drugs. The fund is currently at £80million and we would encourage any steps the Scottish Government can take to increase this amount.

- **Support for clinical trials and statutory funding for patient registries and databases.** Currently, registries and databases for muscle-wasting conditions are reliant on charitable funding. This form of funding is potentially more fragile, and statutory support is needed to ensure long term security.

How are the views from the Patient and Clinician Engagement process taken into account in decision making?

Has the transparency of the SMC been improved and what further opportunities are there for patient and clinician engagement?

- Muscular Dystrophy UK strongly believes that patients and families members are not treated as full partners in the SMC's decision making process, and that their lived experiences are not sufficiently valued or incorporated within that process.
- The SMC places strict limits on the quantity of written evidence that can be submitted by patients and family members, and also insists that the evidence that is submitted is tailored to a set of pre-determined questions. This leads to important evidence – including evidence from wider family members – being excluded. It is also impossible to capture the wide-ranging effects of a condition in a few paragraphs on a set of generic forms. Muscular Dystrophy UK accepts the need for some kind of standard process, but the current process for collecting written patient testimony is unacceptably restrictive.
- Whilst families are given the opportunity to speak at greater length at the Patient and Clinician Engagement (PACE) meeting the only output from this is a heavily abridged consensus statement. Although families are able to comment on this statement, this is within strict parameters with only précised versions permitted of the testimony they had given at the PACE meeting.
- Families have no speaking rights at the final SMC meeting responsible for determining the SMC's final recommendation. This gives them no opportunity to put their case in person, take questions from committee members or correct any inaccuracies. At the meeting considering approval for Translarna on 1st March, misassumptions from committee members went unchallenged by the Public Partner which caused considerable anger and distress from the families concerned.
- The SMC's patient and clinician engagement process compares very unfavourably to that of NICE, where patient and clinical experts are present at every committee meeting, have full speaking rights and can be questioned closely by committee members to ensure the committee is in full possession of all information when making recommendations.
- **The SMC should urgently reform its patient and clinician engagement process to ensure that patients and families play a full and active role in the appraisal. Muscular Dystrophy UK strongly believes as a matter of principle that patients and families should be able to participate in discussions on decisions that will impact on them more than any other individuals involved in the process.**

How can the SMC process be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier?

Are there opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines?

How are NHS Boards implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund?

- Muscular Dystrophy UK recognises that drugs for rare diseases such as muscular dystrophy are always likely to be more expensive per patient than drugs for more prevalent conditions. We also recognise the significant pressures on the NHS budgets and the need for health commissioners to ensure best value when approving and commissioning new medicines, and for drug companies to offer their product at a reasonable and realistic price.
- Fundamentally, any delays or refusal of approval due to pricing disputes have a detrimental impact on patients and should be avoided at all costs.
- In the interests of ensuring access to treatments for patients, the SMC therefore needs to have access to procedures which can ensure best value for NHSS and reach a companies' best offering at an earlier stage of the process. We are concerned that currently no such process is at the disposal of the SMC.
- Muscular Dystrophy UK endorses the use of Managed Access Agreements as a route to approval for rare disease drugs, and note that this approach has successfully been adopted by NICE to recommend funding for Translarna to treat Duchenne muscular dystrophy and Vimizim to treat Morquio disease.
- Such an approach allows patient access to a treatment, but also mitigates some of the financial risk taken on by the NHS and allows for additional clinical data on the drug's use to be gathered over a longer period of time. It could also permit greater opportunities for a 'once for Scotland' approach, thereby reducing the need for IPTRs to Health Boards and regional disparities and inconsistencies in access to new medicines.
- Muscular Dystrophy UK is calling for the SMC to adopt a Managed Access Agreement process as has been done by NICE in England. We also call on the SMC to enter into discussions with PTC Therapeutics on a Managed Access Agreement for Translarna in order to ensure access to the drug on the NHS in Scotland.
- We welcome the development of the Peer Approved Clinical System and see it a potentially important route to ensure greater consistency between Health Boards when taking decisions on ultra-orphan medicines that have not been recommended by funding by the SMC. However, we believe it is of paramount importance that the SMC develops process such as Managed Access Agreements that can ensure a 'once for Scotland' recommendation at SMC level.

Pfizer Ltd Response
Review of Access to New Medicines – Independent Review by Dr Brian Montgomery
April 29th 2016

Pfizer welcomes the opportunity to respond to the recent Scottish Government Independent Review of Access to Medicines. We would like to offer our thanks to the Scottish Government and the Health & Sport Committee for their leadership in this area, and in particular the intent to improve the systems and processes in order that the SMC say 'Yes' more often resulting in a greater number of patients benefiting from improved health.

We welcome the steps taken to date. However, we recognise that there is a need for further evolution and in particular to fund and evaluate some medicines differently, particularly those for rare conditions and for those medicines which have an adapted or faster regulatory pathway. We urge the Scottish Government to consider the impact of the changing regulatory environment as they continue to provide SMC with guidance, ensuring that it continues to enable the appropriate use of new medicines, supporting NHS Scotland to become a world leader in using these medicines and enabling patients in Scotland to lead longer and healthier lives by improving health outcomes for patients and delivering broader benefits to society.

We share the ambitions that eligible patients should receive medicines at the earliest opportunity. The introduction of a "Pause" needs to be prior to the submission from the company to SMC. We recommend early engagement between companies, SMC, PASAG, clinicians and patient organisations. Further reform is not solely the responsibility of SMC; PASAG and the whole medicines pathway will need to be included in this review.

We would welcome further system-wide change so that SMC and NHS Scotland can progress at a pace aligned with the ambitions of Scottish Government; and in particular with regard to the increased pace of the evolving regulatory frameworks and changes to licensing of medicines. We believe that we need an adaptive HTA system that continues to be flexible, and creates a future proof process that recognises and accepts the increasing number of stratified, immuno-therapy and regenerative medicines coming through company pipelines.

We ask that consideration should be given to further evolution to the current process and have outlined our thoughts on this by answering the questions posed in your scope. In addition, some medicines are now being given "breakthrough" designation by regulators and are made available to patients either pre-licence or with less mature data. To ensure that SMC remains at the forefront of global HTA evolution, further change will be needed, and we recommend that industry, patient groups, SMC, PASAG and clinicians work together to co-create a system that can be implemented throughout the NHS as simply as possible, without more complexity and layers of decision-making.

- **How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice?**

Pfizer support the current definitions and welcome the continued pragmatism of SMC on these and believe that they are working well in practice, our own analysis show that:

- 55 submissions (45 of which were for cancer) have met the new criteria (although 5 medicines did not progress to a PACE meeting),
- 10 submissions met the end of life criteria,

- 9 met orphan criteria, 21 met both end of life and orphan
 - 14 medicines have met ultra-orphan criteria (6 of which also met end of life) and were assessed through the new ultra-orphan framework.
 - just under 2/3rd of the medicines assessed in the new process met end of life criteria
- **How the views from the Patient and Clinician Engagement process are taken into account in the decision making?**

Evidence shows that since 2012 the SMC have increasingly used patient access schemes (PAS), extended the scope and used modifiers and, in 2014, introduced PACE, all with the intention of allowing more flexibility when considering cost-effectiveness evidence. There has been an upward trend in SMC acceptances for medicines that have gone through PACE. However it is difficult to assess the true impact of the PACE statement in these decisions as many were also supported by a PAS and modifiers. However, not all SMC recommendations were aligned with PACE deliberations, which would suggest that an implicit threshold is still a dominant factor in SMC decision making with the cost per QALY still being the greatest decision-making factor.

Pfizer would support further reform of PACE to ensure that it is integral to the whole structured decision-making process, and is not just a stand alone meeting and that the views of the PACE should be more implicit throughout the assessment with a stronger voice in the discussions. Therefore, we would recommend that PACE is instigated earlier in the process and that the clinicians and patient groups involved in PACE are invited to attend and participate in the SMC decision-making meeting. We would also recommend that the Detailed Advice Document (DAD) contained more information that was pertinent to the PACE recommendations and reflective of the SMC decision making discussion.

- **How the new approach to assessment of ultra-orphan medicines is operating in practice?**

We believe that the Ultra-Orphan framework remains over-reliant on the cost-effectiveness element and requires further reform to ensure that it is truly supportive of innovative medicines for rare medical conditions. There has been recent examples where NICE has recommended 3 medicines for very rare diseases, Soliris, Vimizin and Translarna via a Managed Access Agreement. By contrast, however SMC have rejected all 3 of the medicines quoting “The submitting company’s justification of the treatment’s cost in relation to its health benefits was not sufficient and in addition the company did not present a sufficiently robust economic analysis to gain acceptance by SMC.”

In England, NICE has acknowledged that a ‘simple utilitarian approach, in which the greatest gain for the greatest number is valued highly, is unlikely to produce guidance which would recognise the particular circumstances of these very rare conditions.’ NICE Highly Specialised Technologies process guidance acknowledges this, as demonstrated in the recent Translarna decision.

We support a value assessment for this group of medicines and would be supportive of a more flexible managed access agreement process such as that observed within the NICE HST process. We ask that the QALY is removed from the ultra-orphan framework and that a framework which has greater pragmatism is developed where other value elements such as burden of illness, impact on carer’s and wider societal perspectives are considered more fully in the decision-making. In addition we also ask that greater recognition is given to the paucity of data for medicines for very rare conditions and urge that data from across the UK and Europe is considered as part of the decision making process, rather than only Scottish specific information.

- **How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach?**

We recognise that there has been a positive trend in decisions taken by SMC, and Pfizer recently commissioned the Office of Health Economics (OHE) to conduct a quantitative review of the SMC decisions, which we have attached for your reference. Our observations are as follows:

- The overall trend for SMC decisions shows a steady increase in medicines being accepted for use, with an increase in the number of positive decisions on cancer medicines especially for those who received a previous negative recommendation under the old process/methods. However, there is no evidence to suggest that PACE is enabling approval of medicines with a QALY above £60-£70k. This is a particular concern for rarer diseases and may indicate that SMC needs further reform and greater flexibility in rare and ultra-rare medicines.
- The steady increase in Patient Access Scheme (PAS) agreements suggests they have contributed to the upward trend in accepted decisions.
- 50% of SMC recommendations have a cost per QALY below £16,539, and 75% below £31,364
- The average cost per QALY associated with a PACE recommended for use decision is £33,002, a neutral PACE decision £44,620 and where no PACE was invoked £16,480. This would suggest that cost-effectiveness is still a strong predictor in SMC decisions

We believe there is a need to move away from the current focus on cost-effectiveness, measured as incremental cost per QALY and more weight should be given to PACE and the modifiers to allow SMC to make positive recommendations based on the broad concept of value and not necessarily restrained to the implicit thresholds which have not changed in 10 yrs.

To ensure that SMC remains ahead of the curve in HTA and continues to accelerate and manage new medicines into NHS Scotland, we recommend that a degree of flexibility and alternative options can be included as part of early discussions on the managed entry of some new medicine depending on the nature of that treatment being introduced.

- **How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement?**

SMC has led the way on patient and clinical engagement, and we welcome that patient group's and clinicians continue to play a full and active role moving forward. SMC has also always ensured that decisions have a strong clinical focus, so we would recommend that this continues and that PACE participants are invited to attend and participate in the SMC meeting discussion which is held in public.

We would ask that reform of PACE is required to ensure that it becomes an integral part of the SMC process and patient groups feel that they have participated fully in the discussion and decision making. The decision making process needs to be transparent so that it is clearly understood how the patient and clinician submissions are considered in the overall decision making and how this is translated into the final DAD.

- **How NHS Boards are implementing SMC decision under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund?**

We understand that the ABPI will be submitting a response to this affect and respectfully ask that this is considered in this context.

We welcome the use of the PPRS receipts by the Scottish Government to support the New Medicines Fund. We would also outline that Audit Scotland confirmed that the growth in the medicines bill is driven by volume and the growth in the ageing population and increase in long term conditions, the majority of which are treated by medicines in primary care with a high proportion of generic prescribing.

- **How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system)**

Our understanding is that the PACS process is only at a pilot stage and until we see the final outcomes from this we are unable to offer further comment. We would support any new system being transparent and clear in the process and that it does not offer further complexity for clinicians and patients.

- **Whether there are further opportunities to take a ‘once for Scotland’ approach in any aspect of access to newly licensed medicines**

We support a single value assessment by the SMC and therefore would support removal of any subsequent further assessment by the Health Boards. We would want to ensure that there was equity of access to SMC recommended medicines across Scotland.

- **How the SMC process should be adapted to include commercial negotiation with the aim of 1/ ensuring best value for the NHS and 2/ getting a pharmaceutical companies’ best offering price earlier?**

Pfizer would support the ABPI position in that securing the best deal for new medicines is not just about reducing price, it can also be about reaching solutions that make a positive SMC decision possible. We do not believe that commercial negotiation should be the remit of the SMC and we are not aware of any rationale for the SMC to lead on both the HTA assessment and commercial negotiation. The SMC’s role should continue to be that of providing a single value assessment process for NHS Scotland for all new medicines and introducing a new function would be potentially detrimental to that process and devalue the independent position of the SMC.

We also support the introduction of early engagement through a robust horizon scanning process which could provide the opportunity for discussions relating to flexible pricing schemes and managed-entry arrangements. We recognise that capacity is an issue with SMC currently and that some medicines often require more time. We would therefore suggest that further development of the Horizon Scanning process could include a triage system which could include triaging medicines for priority review, particularly those with “breakthrough” designation and also shortening the submission and decision making timelines for other medicines.

- **Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report?**

Pfizer have no comment to make on this point.

- **How the new approach will accommodate advances in new medicines and a developing regulatory framework?**

As the Regulatory Framework evolves so too must the HTA processes at a similar pace to ensure sustainability and close the gap between regulatory approval and access to patients. Some medicines are now designated as “breakthrough innovation” by regulators and can be made available to patients either pre-licence or with data which is less mature than for other medicines. This is to enable patients to benefit more quickly from treatments. This means the existing model of considering the cost and clinical effectiveness of new medicines, by bodies such as SMC will need to change. Such changes have been called Early Access to Medicines Schemes, Adaptive Pathway and the Accelerated Access Review. Solutions being developed in other systems enable a conditional approval by a body such as SMC to enable earlier access to medicines which have demonstrated innovation to regulators but have more limited and less mature data at registration. This means that an alternative approach to approval of these medicines will be needed in Scotland which has greater flexibility than we have currently to enable patients to benefit from early treatment by these medicines.

We recognise the budgetary pressures that the NHS is facing, and recommend that there is increased flexibility around the development of commercial models between companies and NHS Scotland. There is a need to include wider schemes than just simple patient access schemes, more consideration for performance based outcome schemes, multi-year budgets and medicines that have a number of different indications.

The current cost effectiveness assessment is blunt and is not appropriate for newer combination treatments and many of the precision medicines, immunotherapies and regenerative medicines coming through, which do not fit the “one size” fits all blockbuster drug model currently used. Therefore there is demand for much more flexible models of assessment and pricing. We would not want to see SMC set up to fail as a result of the current SMC methods not being fit for purpose. Pfizer would recommend that all stakeholders, including SMC, Industry, Patient Groups, Clinicians and NHS should collaborate to co-create a framework that can encourage earlier engagement, opportunity for more complex patient access schemes and commercial deals, as well as conditional reimbursement.

- **Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value**

The further development of a Scottish Model of Value needs to introduce further flexibility. It needs to reflect what is important to the Scottish people in being able to access new medicines, ensuring that there is fairness and equity across the system.

It has been highlighted that there is no comparative rigor in assessing cost effectiveness of other interventions that may or may not be cost effective for NHS Scotland. In view of current and future financial constraints facing NHS Scotland, Pfizer would support ABPI and welcome further work being done to address value of not just medicines but of wider healthcare interventions.

Finally, SMC is an intrinsic component of the Scottish life sciences environment. Scotland is and has ambition to further develop its position as a global life sciences leader and destination for investment. Whilst this is outwith of scope of SMC per se, it is important that consideration is given to the wider environment and Scotland’s ability to develop world leading clinicians and researchers of the future. Having a strong base for clinical research and knowledge of the latest innovations and treatments enables universities to compete on the global stage.

Introduction

Thank you for the opportunity to contribute to the Review of access to medicines in Scotland. AbbVie is a global research-based biopharmaceutical company formed in 2013 following separation from Abbott Laboratories. The company's mission is to use its expertise, dedicated people and unique approach to innovation to develop market advanced therapies that address some of the world's most complex and serious diseases. For further information on the company, its people, portfolio and commitments, please visit www.abbvie.com.

Summary and recommendations

This review covers a wide range of issues relating to access to medicines from horizon scanning to local implementation. AbbVie welcomes this inclusive remit as it recognizes that the Scottish Medicines Consortium (SMC) does not work in isolation - there are numerous processes and systems in place both locally and nationally that can affect access to medicines.

AbbVie supports the approach taken by the Scottish Government to date which seeks to improve access to new and innovative medicines, in particular the investment of the Pharmaceutical Price Regulation Scheme (PPRS) rebate to support the New Medicines Fund (NMF) - although greater transparency around the use of the fund would be welcome. The principles underpinning the PPRS agreement (2014) align to some of the aims of this review and we would welcome greater recognition of the role of the industry in supporting the Scheme which aims to establish a fair price framework to provide stability and predictability to the Government and the industry; supports the NHS by ensuring that the branded medicines bill stays within affordable limits; improves access to innovative medicines commensurate with the outcomes they offer patients by ensuring that medicines approved by the SMC are available widely in the NHS; and to reduce bureaucracy and duplication. Under the terms of the PPRS, the amount the NHS spends on branded medicines is capped and any overspend above this cap is paid back to the Government by industry.

As part of the review's consideration of pricing of medicines, it is important to acknowledge the multiple assessments that medicines undergo even after they have been considered cost-effective by the SMC. NHS tendering and local negotiations make further assessments on affordability and, should the review make recommendations for a new process to get to best price at an earlier stage, these subsequent assessments should no longer be required.

It will also be essential for this review to consider developments in the rest of the UK and internationally which aim to provide access to innovative new medicines at an earlier stage in their development. By keeping pace with the changing regulatory and assessment frameworks, the SMC can remain fit for the future.

There is a strong connection between the requirement to create a mechanism that supports early access to new medicines, is more open to innovative pricing schemes and which underpins a Scottish Model of Value. However a priority must be for the Scottish Government to define 'value', as a narrow focus on cost alone may not necessarily offer the greatest value.

- AbbVie recommends greater flexibility for the development of commercial models between companies and NHS Scotland as early as possible to enable a fair price offering. We believe that there should be greater consideration of more complex schemes that incorporate performance-based outcomes, multi-year pricing and multi-indication medicines.
- AbbVie recommends clinicians involved in the PACE process should be in attendance at the SMC meetings and patient groups should be able to offer the input of 'expert patients', being suitably skilled to provide a full patient experience.

- AbbVie recommends that all medicines recommended by SMC are automatically included into local formularies.
- AbbVie recommends a 'Scottish Model of Value' which assesses medicines across a range of determinants; in addition to cost-effectiveness consideration given to wider benefits, such as improved quality of life, greater personal independence and reduced reliance on carers, the ability for a person to return to work and to ease the demand for institutional care.
- AbbVie recommends early engagement between the SMC and product manufacturers, allowing sufficient flexibility in the implementation process that allows for the accelerated assessment and local adoption of new medicines.

This submission focuses on five key areas outlined below:

1. The inclusion of commercial negotiation with the aim of (1) ensuring best value for the NHS and (2) getting to the pharmaceutical company's best offering on price earlier.

It is difficult to respond to the first point without clarity around the definition of 'value' for the NHS. However notwithstanding that, AbbVie is able to make the following comments in relation to this question.

Fundamentally, whilst we recognise the cost pressures that exist within the NHS, we do not support commercial negotiations being included within the remit of the SMC. There are mechanisms within the current system that could support the principle of securing a company's "best offering on price earlier".

AbbVie welcomes the overall objective of Patient Access Schemes (PAS), but believes that there needs to be greater willingness to consider and accept more innovative pricing models including complex PAS. This would require discussions between manufacturers, NHS Scotland, Patient Access Scheme Advisory Group (PASAG) and the Scottish Government at a much earlier stage in the process than the current programme of medicines assessment allows. It would also require the discussions to include value propositions and the social value of medicines under review. Moreover, this would be consistent with approaches emerging in other parts of the UK and internationally to allow for more flexible and innovative reimbursement and support packages to be explored.

In order to support early engagement, we would suggest a clear and concise timeline and forum for such engagement to enable communication and co-operation between stakeholders.

However, the outcomes of such discussion should not then be subject to additional re-negotiations at later stages in the process i.e. conditions of PAS, tendering and local negotiations. Such continued re-negotiations and multiple review steps can erode confidence and trust in the system, reduce predictability and will negate the opportunity to realise the best offering on price as early as possible. The review should seek to make clear that multiple reviews of the same product for the same population are duplicative and not conducive to early patient access and adoption of medical innovation.

We acknowledge there are potential resource implications for the SMC to review, assess and track usage with complex PAS. This function could be undertaken by existing NHS Scotland bodies, such as Health Improvement Scotland (HIS). The outputs of HIS in respect of this would then be available to all those involved in the introduction of new medicines across health boards in Scotland, including Area Drug and Therapeutic Committees (ADTCs), thereby reducing their workload and releasing resources.

There is also a need for this review to clarify the definition of 'earlier' in the context of discussions around price. With the introduction of the UK-wide Early Access to Medicines Scheme (EAMS) to help accelerate patients' access to innovative new medicines, particularly in areas of high unmet need, it would be important

to ensure any proposals taken forward by the SMC reflect early access opportunities as part of a joined up system for innovative treatments for Scottish patients.

It will also be important for this review to consider and be mindful of the outcome of the UK Accelerated Access Review (AAR), which will not report until late June, to ensure there is a joined up approach to respond to the changing regulatory, reimbursement and access framework.

Recommendation: AbbVie recommends greater flexibility for the development of commercial models between companies and NHS Scotland as early as possible to enable a fair price offering. We believe that there should be greater consideration of more complex schemes, that incorporate performance-based outcome, multi-year pricing and multi-indication medicines.

2. How the views from the Patient and Clinician Engagement (PACE) process are taken into account in decision making.

AbbVie welcomes the involvement of clinicians and patient groups in the review of their products; this helps to provide a better understanding of the role of the medicines under review in the treatment of patients and to assess the wider impact on their quality of life. However, we would seek to highlight some current limitations in the PACE process.

AbbVie believes that the role of the patient is crucial in providing an understanding of the impact of the condition and that the role of the patient groups in the PACE process should be further enhanced. However, currently a patient group submission involves the completion of a standard template with limited scope for the provision of 'lived experiences' of the relevant medical and/or the wider benefits of taking the treatment. We would therefore welcome greater flexibility to include aspects outlined above and would welcome greater effort in collaborative ventures to upskill the patient groups, building on the work of the Public Involvement Network Advisory Group.

While SMC considers the cost-effectiveness of the medicine under review, patients may place a very different value on the benefits of their treatment, particularly in respect of end of life products where there may be an added value in their assessment of quality of life, how the product is administered to them and whether it enables the patient to remain at home. This contrasts with the cost-effectiveness assessment undertaken by the SMC, and it is unclear from the current PACE process how much of an impact the input from PACE, and in particular the patient group, has on the final outcome of the SMC technology assessment.

Ongoing engagement with patient groups may become difficult to sustain without transparency around their role and their influence on the final technology appraisal decision. We would recommend that SMC considers adopting the Swedish model of assessment where, in addition to cost-effectiveness, the social value of medicines is taken into account, such as the impact of employment and employability, and the links to the patient's social and economic contribution. This may be particularly relevant in the new model of integrated health and social care and the associated budgetary implications in Scotland.

Recommendation: AbbVie recommends the following minimum standards should be established in the PACE process:

- **The clinicians involved in PACE should be in attendance at the SMC meetings.**
- **Patient groups involved should represent and involve people with a diagnosis and experience of the condition for which the product under SMC review has been granted a licence to provide a greater understanding of the wider social impact of the condition on the individual, such as employment/employability and activities of everyday living.**
- **SMC ensures that the patient group is suitably skilled and informed to undertake the submission.**
- **There is an ongoing review of PACE clinical membership and that it seeks to include clinical sub-specialties to ensure relevant clinical input.**

3. How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund.

From the outset, it is AbbVie's view that although there has been some improvement, the current process by which local NHS boards implement SMC decisions remains inconsistent and, at times, protracted.

We believe there needs to be some consideration given to assist NHS boards to implement and evaluate SMC decisions and that a realistic timeframe for local boards to implement SMC recommendations be put in place, alongside a process of monitoring. In order to overcome the tendency of NHS boards to publish merely holding decisions, when a product is recommended by the SMC, the treatment should be automatically included on to local formularies, even where there is currently 'no clinical demand'.

It appears that discussions and decision-making processes at local health board level can be focused on an assessment of affordability, even when a medicine has been assessed as cost-effective and recommended for use by SMC. The use of a PAS and/or managed entry agreement - allowing for more innovative pricing models to be applied - could assist the affordability discussions and help to minimise the delays in patient access at a local level. Such innovative pricing models may be particularly suited to the budget management needs of the new health and social care integrated joint boards. New medicines, which might realise benefits in social care settings, may be able to be considered in the context of an integrated budget.

An underlying principle of the issues described above is to ensure there are not multiple review processes which add complexity and uncertainty for manufacturers, clinicians and patients alike, and ultimately could cause significant delays with regards to patients accessing treatments they stand to benefit from. AbbVie is aware of examples and disease areas whereby medicines found cost-effective by the SMC have been subject to additional reviews of a less formal nature and based on less transparent processes. In our opinion, a key outcome of this review would ideally be to remove any ambiguity regarding the single assessment that should take place for a new medicine.

In our opinion, the New Medicines Fund is an appropriate use of the PPRS rebate and provides a useful starting model to achieving one of the core aims of the scheme, namely to improve patient access to clinically and cost-effective medicines. The PPRS, which governs 93% of all branded medicine sales, provides an opportunity to ensure budgetary control for patients accessing branded medicines, given that the overall medicines bill of participating members in the UK is underwritten with rebates. However, it is unclear how well understood the part played by manufacturers to underwrite the NMF is by the public or NHS Scotland.

The operation of the NMF could be further enhanced by publicly and regularly reporting on its use. Data made available could include how it is allocated to NHS boards, information on the drugs made available through the fund, the number of patients who have benefitted and the outcomes achieved.

Finally, AbbVie has welcomed the objective of the Peer Approved Clinical Access System (PACS) and believes that if introduced properly, it could help to address weaknesses within the Individual Patient Treatment

Request (IPTR) system. We await the outcome of the pilot of PACS in Glasgow, but would welcome more information on the detail of this pilot and clarity around timescales for implementation. We are concerned that within the current IPTR system, clinicians still have to demonstrate 'exceptionality' despite Chief Medical Officer (CMO) guidance to the contrary. Our own recent experience in the area of advanced Parkinson's Disease found that IPTRs were rejected with the negative SMC guidance cited as justification, although following individual appeals, these patients were given access to treatment, albeit subject to significant delays.

Recommendation: AbbVie recommends that all medicines recommended by SMC are automatically included into local formularies.

4. Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value.

It is unclear if there is any ongoing evaluation of the development of a 'Scottish Model of Value' and how this might align with the work of the SMC in its assessment of new products and indications on cost-effectiveness.

It may be that groups involved in the SMC process could have different definitions of a 'Scottish Model of Value'; for example, cost-effectiveness based value model or an affordability based value model. Indeed, patients and patient groups involved in PACE may place a different value on 'quality of life (left)' to the QALYs applied by SMC. A 'Scottish Model of Value' should therefore reflect what is important to the Scottish population.

However, we believe that some of the pragmatic approaches in relation to the SMC process, such as those in relation to orphan, ultra-orphan and end of life products and the relationship between PPRS and the NMF have helped to begin the process of defining a 'Scottish Model of Value'. It is likely that developments taking place in the rest of the UK, including the Cancer Drugs Fund in England and the aforementioned AAR may require more clarity and greater understanding around the drivers for a 'Scottish Model of Value' and in particular how this will apply to the role and work of the SMC.

In addition, the move to a fully integrated health and social care model, nationally, allows for a 'Scottish Model of Value' which assesses medicines across a range of determinants; not just cost-effectiveness but also considering wider benefits, such as improved quality of life, greater personal independence and reduced reliance on carers, the ability for a person to return to work and to ease the demand for institutional care.

AbbVie has product specific patient support programmes that are an integral part of our medicines and help support patients to improve their outcomes by engaging the patient in decisions about their own health and setting personal health goals, as well as supporting self-administration and the proper use of medicines. Such interventions have been shown to have a number of benefits for the health service that are aligned with NHS Scotland strategic priorities, particularly around patient-centred care, enhancing patient experience, providing patients with the skills, confidence and information to better manage their health and to optimize medicine use, ensuring every effort is taken to provide maximum value to the NHS for treatment. In addition, the provision of such services, for example homecare nurses, can release capacity within the NHS to deliver improvements in other areas of care.

The integration of health and social care presents an opportunity to reconsider how the role of medicines is valued, not merely in the context of cost-effectiveness and affordability to the NHS in Scotland, but to the wider health and social care environment and that any evaluation of a 'Scottish Model of Value' should take 'social value' of medicines into account and the ability of medicines and wider support programmes to release capacity and achieve holistic cross-budgetary care pathway savings.

Recommendation: AbbVie recommends a ‘Scottish Model of Value’ which assesses medicines across a range of determinants; in addition to cost-effectiveness consideration given to wider benefits, such as improved quality of life, greater personal independence and reduced reliance on carers, the ability for a person to return to work and to ease the demand for institutional care.

5. How the new framework will accommodate advances in new medicines and a developing regulatory framework.

The introduction of EAMS by the Medicines and Healthcare Products Regulatory Agency (MHRA) and the AAR may result in medicines being approved with less mature evidence than previously. This will require Scotland and the SMC to take a wiser perspective on future health technology assessment (HTA) in Scotland and links to the issue of a ‘Scottish Model of Value’ and the consideration of innovative pricing schemes to support early introduction.

Solutions being developed in other health technology appraisal systems enable a conditional approval by the HTA body to allow earlier access to medicines that have demonstrated innovation to regulators, but have more limited and less mature data at registration. This means the role of clinical trial data will play an even greater role in the HTA process. A similar approach should be adopted by the SMC and will require much earlier engagement with manufacturers with regards horizon scanning for the HTA of later stage pipeline products.

We believe that the Scottish Government and SMC need to consider systems that enable and encourage early engagement with the product manufacturers and sufficient flexibility in the implementation of a process that allows for the accelerated assessment and local adoption of new medicines possibly in return for enhanced discounting.

Clear funding arrangements and communications plans will need to be established to raise awareness amongst relevant clinicians to ensure as many patients as possible are able to benefit from the innovative medicines available through the scheme.

Recommendation: AbbVie recommends early engagement between the SMC and product manufacturers, allowing sufficient flexibility in the implementation process that allows for the accelerated assessment and local adoption of new medicines.

Dear Sir/Madam

Boehringer Ingelheim is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, Boehringer Ingelheim operates globally through 145 affiliates and a total of some 47,500 employees. The focus of the family-owned company, founded in 1885, is on researching, developing, manufacturing and marketing new medications of high therapeutic value for human and veterinary medicine.

We welcome the review and the opportunity to engage with the process. We hope that the recommendations when published, will promote the use of innovative, clinically-effective medicines that lead to improved patient outcomes.

I am happy to be named both as an individual(Alan Sumner, Head of Corporate Affairs), and company(Boehringer Ingelheim U.K)

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Written Evidence for the Review of Access to New Medicines – independent review by Dr Brian Montgomery

MSD are grateful for the Scottish Government's commitment to continuously improving fair and equitable access for patients to new medicines in Scotland and welcome the opportunity to respond to Dr Montgomery's call for evidence to inform this independent review. We have inputted into the ABPI Scotland response to the review and agree with the comprehensive points they have provided. This submission complements the ABPI response with some examples through our own recent experience and our future planning for the MSD product pipeline.

How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice;

The broader definition of End of life has had a positive impact on medicines within that category achieving an increase in those being recommended. However there are still some categories of medicines e.g. new antibiotics where there is ambiguity as to whether they fit within this definition and where similarly there is an unmet need, potentially fatal outcome for patients if they do not have access and where the acute and urgent nature of the condition means IPTR process is not suitable.

How the views from the Patient and Clinician Engagement process are taken into account in decision making;

PACE has been a well-received addition to the SMC methodology and given both clinicians, patients and companies an opportunity to express the additional value that new medicines can bring outside the clinical and cost effectiveness assessment and this has translated into improved access for those medicines which qualify. However anomalies still occur where there has been an exceptionally positive PACE submission and yet this has, with no clear explanation for the clinicians, patients and company involved in the process, not led to positive recommendation. This happened with MSD's immunotherapy for advanced melanoma where a single PACE meeting led to two different outcomes: a positive for treatment of naïve patients and negative for pre-treated patients, where the medicine was likely to be their only remaining option and was available to patients prior to license via the UK Early Access to Medicines Scheme for this reason. (The committee had also agreed that this medicine met the criterion for absence of other treatments of proven benefit

and secondly as an orphan equivalent SMC could accept greater uncertainty in the health economic analysis.) This would suggest – though the lack of an effective means of SMC explaining its decisions does not allow us to confirm this – that more emphasis/weighting is still given to traditional sensitivity analysis and QALY thresholds by the SMC committee as the determining factors in whether a drug receives a positive recommendation. This also led to an inequality in access for terminally ill patients in Scotland versus the rest of the United Kingdom,

- We would support PACE patients and clinicians attending full SMC meeting to present and answer questions.
- We would support clearer guidance and higher weighting of the PACE evidence in decision making process for EOL/UO/O medicines.
- We would support clear communication as to rationale behind decisions and what impact the PACE submission had on the outcome negative or positive.

How the new approach to assessment of ultra-orphan medicines is operating in practice;

- MSD has had input to and supports ABPI's response on this question

How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach;

- MSD has had input to and supports ABPI's response on this question

How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement;

- MSD has had input to and supports ABPI submission response on this question. Moving forward we would like to see a system where PACE patients and clinicians have equal opportunity to feedback and be involved in SMC committee meetings.

How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund;

- The original New Medicines Review of 2013 made several recommendations covering the process for implementation of SMC advice. There is little evidence to suggest that these have been actively progressed to any degree with PACS pilot only recently being initiated in Glasgow.
- Although work has been carried out to improve consistency of language and information collected at HB level 11 ADTC's still have to assess SMC

positive advice for Formulary and 14 IPTR panels for SMC negative advice. Each has different processes, timelines and approaches to transparency leading to inconsistency of access to medicines and information about them. No new governance has been produced since CMO letter of 2012(1). Accessing information about these processes on HB websites can still be extremely difficult.

- The Scottish Government's commitment to the reinvestment of the PPRS repayments into the New Medicines Fund and resultant increased access to medicines is welcomed. However, MSD cannot comment on the utilisation of the New Medicines Fund as there is no public access to data which could clarify how the fund was allocated across the HBs for SMC approved medicines, IPTR's and what therapy areas benefited from this. We would encourage greater transparency in order to incentivise a long-term sustainable partnership as the basis for future PPRS or next generation agreements.

How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system);

- In the Cabinet Secretary's evidence to the Health and Sports Committee (February) it was reported that there had been a 10 fold increase in IPTRs approved. Again there is no data to date in the public domain which can show the actual number of IPTRs applied for, numbers approved/rejected, therapy areas split or allow evaluation of trends, consistency of decision making and patient access across HB's. We believe public faith in the IPTR process would be further enhanced with the publication of the data behind the information presented to Parliament.
- MSD's experience with the first EAMS product for a life-threatening condition is that clinicians have not been able to access the Advanced Melanoma medicine in pre-treated patients via IPTR in any HB but one; with only a single patient (up to 28.04.16) having had access to the medicine since SMC advice last November (cohort of approximately 40 eligible patients in Scotland) and although CMO(2013) 20 states that exceptionality can no longer be a consideration, feedback we receive from clinicians would suggest that this is still a deciding factor in the ethos of IPTR approval.
- Similarly although overall numbers of IPTR approved have increased the 'hassle factor' and feeling that still remains that applying for IPTR can be an arduous and often unsuccessful process, means that clinicians still either do not apply at all or, if they do and it is turned down, do not apply again in that therapy area.

Whether there are further opportunities to take a ‘once for Scotland’ approach in any aspect of access to newly licensed medicines;

- MSD had input to and support the ABPI response on this question.

How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies’ best offering on price earlier;

- MSD supports the ABPI submission and position on this question. Value and price are two different and independent factors. Assessing value and affordability within the same body will lead to a conflict of interests as many of SMC committee members are responsible for annual budgets and scorecards.
- The integration of health and social care offers SMC the opportunity to take into account the social care savings afforded by some medicines.
- A more flexible approach by PASAG encompassing new innovative PAS and MAA as explained in ABPI submission would allow companies to maximise value for NHS and access for patients to new medicines. A commitment to encouraging improved data collection is also essential to achieve this. MSD have expertise in this area and would be happy to collaborate with SG/NHSS on the development of suitable systems.
- NHS Scotland often benefits from both a PAS and then subsequent tendering processes which have potential to negotiate price further e.g. HCV medicines prices in Scotland are some of the lowest in the UK and Europe.

Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report;

- MSD had input into and supports the ABPI submission on this question

How the new approach will accommodate advances in new medicines and a developing regulatory framework;

EAMS Framework:

- The Early Access to Medicines Scheme (EAMS) has now also been introduced to help accelerate patients’ access to innovative new medicines, particularly in areas of high unmet medical need, where often patients cannot afford to wait. We believe it is critical to review this new scheme alongside the other access to new medicines mechanisms in order to ensure a joined-up system for access to innovation for Scottish patients.

- It is also worth noting, in the context of being forward-looking, that there is an ongoing UK-wide Accelerated Access Review due to report this year. The terms of reference of the review state ‘While noting that some elements of the pathway are devolved, the review’s ambition is to develop a joined-up, globally competitive landscape across the whole of the UK. The DH will work with the devolved administrations where appropriate in order to do this. Issues related to regulation will be addressed on a UK-wide basis, while cost effectiveness and adoption will focus on England.’ The AAR full terms of reference are available at: <https://www.gov.uk/government/organisations/accelerated-access-review/about/terms-of-reference>

MSD’s treatment for advanced melanoma was the first medicine to be made available through the Early Access to Medicines Scheme in Scotland. Therefore, we thought it would be useful to share our early experience and learnings within the context of access to new medicines in Scotland.

Currently there are no guiding principles or operational guidance for Scotland in the public domain and as such pharmaceutical companies do not have a formal framework or process to reference when initiating the scheme in Scotland.

Some of the suggestions below have been implemented at a service level but SMC methodology is no longer fit for purpose when evaluating EAMS medicines and we would hope that this will be recognised and new ways of working identified.

1. Early engagement of all stakeholders involved

We believe in order to ensure consistent access to new treatments for patients in Scotland via EAMS, it is essential that all stakeholders involved including the Scottish Government, the Scottish Medicines Consortium (SMC), the Area Drug and Therapeutics Committees (ADTCs) and NHS Scotland and the company engage early in the process. It would be useful to have the timeline and forum for such engagement clearly defined to ensure early and ongoing communication and cooperation between stakeholders to allow that any potential access barriers can be addressed and overcome as quickly as possible.

We also think the system could be improved by ensuring that, at the point of entry into the EAMS, clear funding arrangements and communications plans are put in place, both to help raise awareness amongst relevant clinicians and ensure that as many patients as possible are able to benefit from the innovative medicines made available through the scheme.

2. A Joined-up system

Medicines that qualify for EAMS must demonstrate that they are a promising, innovative medicine and that they meet the following criteria:

- (a) Life threatening or seriously debilitating condition and
- (b) High unmet need, i.e. there is no methods available or existing methods have serious limitations

With this in mind, in order to ensure equity of access to new medicines for patients, who may be suffering from a life-threatening disease and often cannot afford to wait, we believe it is critical to have a pathway that ensures not only early but also continued access to breakthrough medicines in areas of high unmet medical.

For this reason, we would recommend review of the existing access to new medicines mechanisms and their suitability specifically for EAMS medicines, this would include the following:

- (1) In order to ensure continued equity of patient access from beginning of the EAMS up to routine reimbursement, it is important that appropriate levels of funding are earmarked for new patients in the period following Market Authorisation (when the EAMS must end for new patients according to MHRA's terms) prior to SMC recommendation. Patients suitable for a condition approved by EAMS, by definition, suffer from serious and sometimes life-threatening diseases and therefore can often not afford to wait for access to treatment. If interim funding is not made available for the time between when the EAMS closes and routine reimbursement, which through the additional PACE process can take several months, it will significantly impact on new patients who in some cases only have a few months to live. We are aware that the IPTR process and PACS are currently existing mechanisms that could provide a funding route in this period. We would suggest considering a national IPTR/PACS (with defined criteria on a case-by-case basis for each EAMS product) as part of an entry strategy for EAMS drugs agreed with Scottish Government in operational guidance for new patients presenting in the interim period post marketing authorisation but prior to SMC recommendation. Furthermore, to ensure continuity we would recommend that the ADTC Collaborative should take a collective decision at the start of the EAMS process to fund at the point of a positive SMC recommendation. This would allow access immediately post SMC, without the need for this to go through local formulary process, which could cause delay for patients.

(2) To assess if the SMC/PACE methodology is suitable to assess medicines with significant promise, but where data is still immature and therefore levels of uncertainty may therefore be higher (see below for more detail).

3. New Medicines Evaluation & EAMS Data Collection

The SMC methodology historically has largely focused on mature, randomised trials with comparators in order to conduct a health economic analysis of the medicine. Earlier evaluation of medicines, by its nature, can lead to greater levels of uncertainty within the health economic analysis. Variance in the UK in how health technology bodies are interpreting and handling uncertainty in health economic analysis has led to issues in equitable access to EAMS medicines across the country post-evaluation. Although, we recognise PACE was introduced to provide balance to the SMC methodology for end of life, orphan and ultra-orphan medicines, we question whether it suffices to meet this specific issue around how health economic uncertainty is handled and interpreted.

In addition, although MSD believes that the data collection requirements within EAMS should be decided on a case-by-case basis and be additive, not duplicative, to the clinical development programme, it does represent an opportunity to collect additional data, such as resource utilisation or patient experience, which may be useful to include within SMC evaluation.

Therefore, we believe it will be necessary for new mechanisms to be introduced in the SMC/PACE appraisal process to handle uncertainty that comes with a medicine with significant promise but earlier in its clinical development cycle and also allow for any data collected through the EAMS to be appropriately taken into account.

Antimicrobial Medicines

- The current SMC methodology represents a potential barrier to the Scottish Government's expectation that new antimicrobial medicines should be made available in NHS Scotland.
- Antibiotic resistance is a hugely complex problem with potentially devastating consequences for public health. The Review on Antimicrobial Resistance, chaired by Jim O'Neill, has estimated that the total number of worldwide deaths attributable to AMR could reach as high as 10 million by 2050, with an associated \$100 trillion cost to the global economy, if the issue is not tackled urgently. NHS Scotland has recognised this grave risk and we welcome the implementation of both the UK Five Year Antimicrobial Resistance Strategy 2013-2018, published in 2013, and the Scottish Management of Antimicrobial Resistance Action Plan

(ScotMARAP) 2014-18 (ScotMARAP 2) . These strategies include proposals to stimulate the development of new antibiotics, diagnostics and novel therapies to challenge the growing unmet clinical demand.

- To ensure a sustainable supply of new antibiotics for the future it is essential the right economic models and infrastructure are in place. The current healthcare technology assessment (HTA) methodology poses significant challenges for new antibiotics which rely on non-inferiority clinical trial data and face a highly genericised market. Moreover, the Individual Patient Treatment Request (IPTR) process is unsuitable for acute infections due to the need for rapid treatment, which runs counter to IPTR approvals which are typically committee-based decisions that take time. To encourage innovation and ensure patients' needs are met we would encourage the Scottish Medicines Consortium (SMC) to apply a more flexible approach to the evaluation of antimicrobial medicines.

Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value.

- Changes in the SMC Methodology have gone some way towards and have been much welcomed as the first step in supporting the development of Scottish Model of Value but continuous improvement and additional flexibility of methodology is required to ensure that SMC stays at the forefront of HTA systems globally, Scotland retains its status as a leading innovative healthcare system and provides both NHS and patients with appropriate access to new medicines
- PASAG /NPS methodology and ways of working need to change to embrace and plan for the changing medicines regulatory environment to ensure that pharmaceutical companies, NHSS and patients receive appropriate value and access. This should not focus on merely short term goals but the health of the nation medium to long term.
- As Scotland moves towards an outcomes based healthcare system, the Scottish model of value can be enhanced if medicines usage data is more routinely used, particularly in the case of early access to medicine programmes accompanied by data collection.
- It would be helpful if there was more work to develop a clearer strategy and plan to both define what Scottish Model of Value is and how this is going to be achieved as there is a lack of clarity as to what ,if ,when and how this will be realised and result in continued improvement in NHSS care and patient outcomes.

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with customers to bring innovative healthcare solutions to those who need them the most. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programmes and partnerships.

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For more information visit www.msd-uk.com

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Hi there, response below – we are happy to be ‘Published with name’.

Firstly, thank you to Dr Montgomery for accepting the request from Shona Robison and leading this review.

Dr Montgomery spoke eloquently and with passion at the first meeting and we look forward to assisting you in this process where we can.

On behalf of Mike Matters (SCIO) we comment on what we have seen on the end of the SMC process (public participation) and use comparisons in what experienced at the FDA AdComm process for reviewing applications for orphan/ultra orphan new medicines.

Whilst we cannot comment on the changes implemented by the review from the former system we do feel we can add value in relation to the public involvement element. We feel that this is an area that is welcomed, undervalued by many and needs more work.

- How the views from the Patient and Clinician Engagement process are taken into account in decision making;
 1. Using one person to collate all patient testimony and then relay this devalues and weakens any testimony
 2. Expecting one person who is not a patient or directly affected to speak on behalf of all affected patients without even talking directly to them is simply unacceptable

- How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement;
 1. Public meeting should not be restricted to 30 people for 5 medicines. Should be opened to all interested parties.
 2. Papers issued to public should not be heavily redacted – they should be produced in a format that can be read and removed from the room

- How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system);
 1. There was a serious concern raised by a Pharmaceutical Representative at a conference last year that the UK is too difficult to work with and could put the UK at risk from being approached for future drug trials.

- Whether there are further opportunities to take a ‘once for Scotland’ approach in any aspect of access to newly licensed medicines;
 1. You will never get a mass data set for a rare or ultra-rare disease – this MUST be taken into account. Historical data can be continued to be gathered where there is a safe and effective drug on offer.

- Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report;
 1. We would ask you to consider; has the increase in drugs being approved been mostly for oncology etc? How has the numbers of approvals for orphan and ultra-orphan improved since the last review?

Yvonne Grant

On behalf of Fiona Rankin, Chairperson, Mike Matters

info@mikematters.org

NHS Borders Response to the Review of Access to New Medicines

Dear Dr Montgomery

Thank you for the opportunity to respond to the Review of Access to New Medicines

In providing our response we considered the following areas:

- How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice;
Following the review, the SMC has introduced new processes with the explicit aim of facilitating and speeding up the approval and use of new medicines for treating end of life, orphan and ultra-orphan conditions in Scotland. This change seems justifiable for orphan and ultra-orphan drugs, which treat rare and very rare conditions. The process can deliver effective treatments for such conditions and achieve greater equity of outcome compared to treatments for common conditions, even though they would not be regarded as cost effective in conventional terms. However, the introduction of these processes for end of life treatments seems harder to justify. Why should treatment at this stage of life be prioritised above other life stages and why should different cost effectiveness thresholds apply? The November 2013 direction has led through the IPTR process to substantially greater use of oncology and haematology drug treatments in later life, often to extend life perhaps by a matter of weeks at a cost typically of £15-25,000 per individual. The impact of this in terms of quality of life for the individual is often uncertain compared to a more conservative management course, focussed on symptom control. The impact on NHS Scotland's budget means that services to other patient groups are not funded and often have to be reduced, denying significant numbers (hundreds and even thousands) of other patients treatments of proven effectiveness, that are also more cost effective.
- How the views from the Patient and Clinician Engagement process are taken into account in decision making;
The PACE process has increased the number of new medicines approved by SMC. In turn, this has led to Boards approving more medicines previously not deemed to be cost effective. This is particularly so for end of life medicines which would have previously gone through the IPTR process and the Board's decision may have been not to approve treatment. Changes to SMC processes have increased access to new medicines but may come at the expense of NHS Scotland being unable to fund other treatments due to the finite nature of resources.
- How the new approach to assessment of ultra-orphan medicines is operating in practice;
This change seems justifiable for orphan and ultra-orphan drugs, which treat rare and very rare conditions. The process can deliver effective treatments for such conditions and achieve greater equity of outcome compared to treatments for common conditions
- How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach;
The SMC has approved more drugs in these categories. This has reduced the number of individual patient treatments requests (IPTRs).

- How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement;
 NHS Borders is unaware of any evidence to show that the process has become more transparent or less complex. However, the attendance of members of the public at SMC meetings has allowed decisions to be made in an open forum.
- How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund;
 From a Board's perspective little has changed in this regard. If a clinician submits an application for a new SMC approved drug it will be discussed at our Formulary Committee and a decision made on whether it should be added to the formulary. For an SMC not recommended drug an application will be considered through the IPTR panel for an individual patient or Formulary Committee if applicable to a group of patients. The New Medicines Fund has been used to fund end of life care, IPTR requests and medicines for rare conditions.
- How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system);
 We are not aware of the Peer Approved Clinical System (PACS) having been introduced throughout Scotland. We are awaiting the outcome of the pilot in NHS GG&C.
 Information from the last quarter has shown a reduction in the number of IPTR requests.
- Whether there are further opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines;
 Yes in relation to orphan and ultra-orphan drugs and in some more specialist areas. A good example is the work done nationally on hepatitis C.
- How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier;
 The SMC does not currently have a role in price negotiation. The Patient Access Scheme Assessment Group provides a responsive approach to pharmaceutical industry's submissions.
 We would support adapting an approach to include commercial negotiation at an early stage in the assessment process. However consideration needs to be given to the consequences of doing this.
- Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report;
 The IPTR process has led to substantially greater use of oncology and haematology drug treatments in later life, often to extend life only by a matter of weeks at a cost typically of £15-25,000 per individual. The impact of this in terms of quality of life for the individual is often uncertain compared to a more conservative management course.
 The NHS has a finite budget and areas for investment must be prioritised. NHS Borders is concerned the changes to the SMC process has led to less cost-effective drugs being approved at the expense of more cost-effective treatments. The new processes should be retained for orphan and ultra-orphan drugs but be abandoned for end of life treatments. Towards the end of life, the focus should be on maximising the quality of life for the patient, making them comfortable and supporting them and their family at a difficult time. Funding

at end of life should focus on palliative treatments for symptom control in line with the CMO's annual report, Realistic Medicine.

- How the new approach will accommodate advances in new medicines and a developing regulatory framework;
The change to the SMC processes suggests it would be able to accommodate advances in new medicines.
- Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value.
We have not seen any data to support improved cost-effectiveness of new medicines and the impact of increased access to new medicines on quality of life or life expectancy so it would be hard to determine if the progress made supports a Scottish Model of Value. It is imperative that the Model of Value considers resource implications for NHS Scotland.

The consequences for the change in the SMC process and subsequent decisions made to date for NHS Borders has been an increase in patients being treated as well as more chair time for treatments, more staff time, more medicine preparation time. The lack of resource to fund the other costs associated with the preparation and administration of medicines is putting extreme pressure on services. Resource implications will need to be considered at an earlier stage and perhaps as part of the SMC decision making and should be included in a model of value.

Kind regards

Alison Wilson

Director of Pharmacy, for NHS Borders

Dear Dr. Montgomery,

The changes that SMC has made, in a very short space of time, are extraordinary and commendable. I admire the commitment to change and update the system while recognizing that there are some improvements that can be made.

The following considerations are given with the hope that areas for improvement can be found:

*** How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice;**

The acceptance of the terms orphan and ultra-orphan was much appreciated in the initial review. The definition between the three terms (end of life, orphan and ultra-orphan) seems to have become blurred when drugs are considered by the SMC. Ultra-orphan drugs are, by definition, used by very few patients and are usually very expensive. The initial petitions to the Health & Sport Committee were brought to try to ensure a fair deal for patients with extremely rare conditions. Approvals by the SMC need to be categorized to show that ultra-orphan drugs are being given a fair hearing.

*** How the views from the Patient and Clinician Engagement process are taken into account in decision-making;**

I took part in a PACE meeting in February. The meeting was wonderful and I felt that I had been listened to. I came away believing that the SMC were open to considering a total patient care cost rather than merely the bottom-line drug cost. I completely understand that there is not an unlimited fund of money for drugs and believe that drug companies must give a fair price but the PACE meeting seemed completely at odds with the final SMC decision. The comments given regarding the drug's refusal gave the impression that the PACE outcome had not been conveyed properly or had not been considered. The PACE meeting had acknowledged that the drug in question was 100% effective for patients with PNH, gave patients a normal life expectancy again and also allowed patients to go back to work but the SMC decision information stated that, "the overall health benefits of the medicine meant it would not justify the cost to the NHS". We cannot ever expect all drugs to be available at any cost but we do need to ensure that the PACE meeting discussions are properly conveyed, with adequate medical detail, to the SMC body voting to approve or reject drugs.

*** How the new approach to assessment of ultra-orphan medicines is operating in practice;**

There needs to be more information regarding the split of acceptances between end-of-life, orphan and ultra-orphan drugs.

*** How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach;**

There needs to be more clarity on this.

*** How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement;**

Clinicians and/or patient representatives need to be involved in the SMC decision meeting to ensure the additional cost offsets are completely understood by those who will be voting. When considering drug cost, the SMC must ensure it considers what treatments, care or benefits will no longer be needed by the patient should they be granted a certain drug. The cost of the drug should not be the only factor.

*** How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund;**

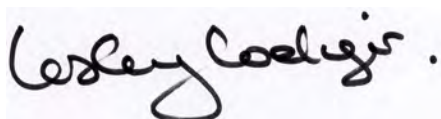
The New Medicines Fund has allowed many patients with rare conditions to get treatment that they would possibly otherwise not have had access to. Health Boards, however, seem confused about which drugs they can use the New Medicines Fund for and whether they will be reimbursed or not. There needs to be more clarity and guidance for Health Boards on this matter.

*** How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system);**

The review guidelines regarding the IPTR system stated that there should no longer be a request for patients with ultra-rare conditions to prove 'exceptionality' as it is impossible to declare one patient significantly different to the ten other patients in the country with the same exceedingly rare condition. On examination of the IPTR forms in several different Health Boards, it appears that this recommendation has not been met. Some boards still have the request for patients to be 'significantly different' on the form while others have removed it from the form but it is still in the accompanying guidance documentation. Health Boards need to be reminded of the initial recommendations.

Many thanks for your consideration of these points. My overall opinion is still that the SMC has to be commended for the work it has done but further improvements are needed to provide us with a truly fair system.

With thanks,



Lesley Loeliger,
Chairman,
PNH Scotland.



Celgene Input to the review of Access to New Medicines in Scotland.

We welcome the opportunity to input to this review and to support the ongoing work to ensure patients in Scotland are able to access the medicines they need. There has been considerable progress in this area over the last number of years and in many regards Scotland has been leading the way, with the SMC continuing to maintain its high standing as a HTA body.

As well as the system reforms which have taken place, the pharmaceutical industry has been working hard to ensure the new medicines we develop continue to be available for patients. In 2014 the current PPRS was negotiated whereby the Pharmaceutical Industry agreed to significant rebates on medicines in order to limit any growth in that spending. Celgene would like to recognise the approach taken by the Scottish Government in using this money in the spirit that was intended during the PPRS negotiations to support the New Drugs Fund. This pricing deal has resulted in significant rebates to the Scottish Government which has been available to support improved access to medicines.

We have also seen a trend over the last few years of the increasing use of Patient Access Schemes by industry to lower the cost of medicines and thus increase cost-effectiveness in line with HTA expectations. The system reforms which have taken place recently in Scotland have further supported the use of these schemes and allowed a continued increase in their adoption, providing the opportunity to reduce medicines prices when it becomes apparent this is needed to demonstrate cost-effectiveness.

To continue this work to provide cost effective medicines for the broadest possible range of patients we would specifically highlight the issue of multiple indication pricing and the need to develop ways for this to operate within Scotland. This will be a key area for future development as research innovation allows mechanisms of disease to be better understood and individual medicines to offer value for patients across multiple conditions.

We look forward to continuing to work with the various NHS bodies in Scotland to evolve the processes by which medicines are made available. It is important to ensure that cost effectiveness and the value of medicines are assessed appropriately so those medicines deemed to offer value are made available to patients as quickly and efficiently as possible.

We have structured our response around selected points highlighted from the review Scope.

Summary

- **There is an opportunity for improved representation of PACE views and Industry expertise at SMC meetings.**
- **There is a need to improve the robustness of the SMC voting process and improve the ability of the SMC chair to facilitate the decision process.**
- **There may be an opportunity to further support the local medicines adoption process to ensure the use of local protocols does not create an additional delay in patients being able to access medicines, or significant variation in patient access across Scotland.**

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Date of preparation: May 2016

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- There is a need to improve visibility of local access to medicines including placing treatment protocols in the public domain.
- A national body such as Healthcare Improvement Scotland should be tasked with monitoring the adoption of SMC guidance at the individual Healthboard level.
- There is potential to improve communication around the new medicines fund and its link to the PPRS in order to increase understanding and confidence in the system that has been put in place.
- The current SMC process allows for pricing adjustments (through the application of a Patient Access Scheme) in line with the principle of providing cost effective medicines where price is linked to value. There is scope to better utilise Patient Access Schemes by taking a more flexible and collaborative approach to their adoption.
- Any steps taken towards commercial negotiation should be done in such a way as to encourage a collaborative process with industry, including taking a more flexible approach to pricing models.
- SMC resourcing should be regularly reviewed to ensure it remains able to fulfill the role asked of it.
- There is a need for improved data capture capability and industry should be a partner in developing this capability.
- A framework to support multiple indication pricing should be developed in collaboration with industry.
- Assessment of medicines value should broaden to include wider societal benefits of treatment such as increased employment, reduced care requirements etc.
- A Scottish model of value when developed should allow for application beyond End of Life, Orphan and Ultra-Orphan medicines.

“How the views from the PACE process are taken into account in decision making.”

Celgene believes the PACE process is a significant step forward by allowing the views of those who are impacted by new technologies to be heard whether that be clinicians or patients. While it appears to be impactful during open committee meetings it is difficult to be sure that the views of the patients and clinicians are truly heard as the committee’s voting is undertaken via anonymous ballot.

Greater transparency in the final decision process would make it more visible how the views from PACE are being taken into account.

“How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new processes.”

It seems from the analyses presented to date that the new processes in combination with an increase in PAS submissions have resulted in increased acceptance rates. However, it is important to consider that the increased acceptance rates have come with an increase in delays. The rate-limiting-factor is usually the number of PACE meetings which can be held each month.

Further consideration should also be given to the impact of SMC’s decisions and whether increased acceptance rates have resulted in increased patient access. Whilst patient access should have increased, there remains considerable variation in uptake of SMC approved medicines across healthboards and we are not aware of any work taking place to evaluate this aspect of access to medicines.

“How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement.”

The move to public meetings has had a positive impact on transparency and allows for a better understanding of the considerations which the committee take into account. It is useful for the company to be able to provide representatives to answer questions of factual inaccuracy or uncertainty. However, there could be increased scope for the contribution allowed to the manufacturer representative as in most cases they are limited to a few sentences only.

Celgene would also support the principle of clinicians and/or patient group representatives who have been involved in PACE meetings being offered the opportunity to attend the SMC meeting in person in order to represent the views expressed at the PACE meeting.

The voting system is still lacking in transparency and may have taken a step backwards from the previous system. Whilst it is not necessary to hold an open vote in front of the public, discussion between committee members (perhaps in a closed session) could be useful and allow the chair to take on a more pro-active role once again and to ensure that members are not voting based on considerations which are out-with SMC’s remit.

“How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund.”

It has been our experience that there can often be significant delays in access to SMC approved medicines. Once clinical need is established the paperwork required for local approval and implementation can be time consuming and often complex. This is particularly so where there is a need for complex clinical protocols or guidelines to be produced or where specific financial planning is felt appropriate.

Celgene suggests where there is need for local implementation work to be carried out, processes allow patients meeting the criteria within SMC approval to access treatment whilst this is completed and that clinicians are made aware of this as part of the ADTC process. Expectations for timelines around development of local implementation of SMC decisions should also be made clear. It is less than ideal for an ADTC to issue a holding position based around the need for development of a protocol or similar. This practice can lead to an inaccurate impression of the time taken to implement an SMC decision and any variation in access across NHS Scotland.

We would also encourage an approach which looks to make available to the general public all information on which medicines are available in an area and in what circumstances they are available. Often medicines are listed on local documents as “available in line with local protocols”. Whilst it is useful to know that these medicines are available it should be clear and transparent what the protocols are in order to be clear on the actual local availability of a medicine.

Celgene would recommend that as a next step a national body such as Health Improvement Scotland (HIS) be given responsibility for monitoring the local adoption of SMC guidance in order to build a clearer picture of this aspect of medicines access.

Regarding the New Medicines Fund: As previously stated we welcome the use of money rebated by the pharmaceutical industry through the PPRS deal to provide this fund. However, the fund is not well understood and it is our experience that very few people are clear on what it is used for and how the money is accessed. It is also

not well understood that it has been possible because of significant pricing negotiations with the Pharmaceutical Industry at the UK level leading to the rebates highlighted earlier.

The lack of understanding of this fund has the potential to mean that there is poor understanding amongst NHS stakeholders as to the ability of NHSScotland to afford new medicines coming through SMC.

Celgene would suggest that there is improved communication of the role of the new medicines fund including which medicines have been funded through the scheme and the role of the PPRS in supporting it.

“How the SMC process should be adapted to include commercial negotiation with the aim of 1. Ensuring the best value for the NHSS and 2. Getting to a pharmaceutical companies best offering on price earlier”

Celgene believes that the best way to ensure the price of medicines is fair for all stakeholders is to encourage the development of a more collaborative HTA process where there is greater opportunity for dialogue around pricing of individual medicines and the value they offer. This allows for greater mutual understanding and for the perspectives of both Industry and NHS stakeholders to be put forward with the aim of reaching a situation where medicines are available for patients. This could include greater discussion with Industry at an early stage as well as ongoing dialogue. We believe the SMC is moving towards a collaborative approach and continuing the expansion of dialogue with the industry and with PASAG to allow for more innovative pricing models, could achieve the aims as stated above without altering the remit of the SMC.

The SMC is a respected HTA body and its evolution has in many regards been leading the way in the UK. We believe it’s purpose should continue to be to provide guidance on the clinical and cost effectiveness of medicines for use in Scotland. A shift in its role towards commercial negotiations would appear to signal a fundamental change in approach to medicines access in Scotland which may have little to do with cost effectiveness or the real world value of medicines. Where price adjustments are needed in order to improve the cost effectiveness of a medicine we believe the current arrangements within the process allow for this to take place in a manner which is consistent with the role of the SMC and with the need for medicines to demonstrate value. Indeed we would suggest these mechanisms are not currently being used to their full potential and that a more flexible and collaborative approach as outlined above could in itself improve access to new medicines further. We would also question how any negotiation approach would sit alongside the development of a Scottish model of Value.

There are a number of areas for consideration in any move towards a model which included commercial negotiation.

- Who would be responsible for negotiating on behalf of NHSScotland?
- Where within the access process would commercial negotiations sit?
- What expectations would there be on which medicines should enter into commercial negotiations?
- How would the increased workload associated with commercial negotiations be managed to prevent further delays to patient access?

As outlined, Celgene would suggest that rather than commercial negotiation, a collaborative approach to explore alternative options to identify the right price in the HTA assessment be adopted. By engaging in such a process both parties can gain a better understanding of the broader impact of our medicines on the pathway & the uncertainties associated with our product’s impact (clinical or economic). That in turn allows us to design a model that provides patients access to drugs, while ensuring NHSScotland gets value for money, by reflecting the agreed

value that an individual medicine brings to a patient group within Scotland. The process should then also allow the consideration of access mechanisms with the flexibility to consider novel approaches to address uncertainty where it exists.

“Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group report.”

As a result of the increased workload associated with the changes in SMC practice we have noticed there are time delays being created within the system leading to some delays in medicines being reviewed. Celgene would recommend that regular reviews take place to ensure the resource in place for SMC is keeping pace with the work it is being asked to carry out. It would also be useful for pharmaceutical companies to be informed of the average delay at the point when they indicate when they will be making a submission. This will allow for more accurate work planning.

Celgene would also highlight that whilst it is important to address the specific issues associated with End of Life, Orphan and Ultra Orphan medicines this should not be to the detriment of other treatment areas.

“How the new approach will accommodate advances in new medicines and a developing regulatory framework.”

Data capture is becoming increasingly important as newer medicines are developed in increasingly specialized areas and with multiple indications across complex diseases.

The principle of conditional approval based on the ability to collect data is an interesting area and one that needs to be looked at further to establish how it might work in the Scottish context. Celgene would suggest that this is an area for collaborative work between NHSScotland and industry to explore how this could best work to ensure the best outcomes for patients.

As new types of therapy are developed there will be a need to regularly review whether current processes are adequate to address the needs of developing science and new approaches to treating disease. Therefore it will be important that SMC remain accessible to individual companies on an ongoing basis in order to discuss and address potential challenges early in the process of making medicines available. Many of the challenges which will be faced are not yet fully clear and so a willingness to engage in discussions around creative and innovative solutions will be increasingly important.

Of particular note is the need to develop a system which allows for multiple indication pricing where a single medicine may offer differing value across a range of indications. This is an issue of critical importance to ensure patients continue to benefit from innovative new medicines as ongoing industry research identifies benefits for new patient groups. Celgene suggests that the SMC develop a clear framework for addressing this area and that they work in collaboration with industry and real-world databases such as ChemoCare to ensure any framework is fit for purpose.

“Whether the progress made to date provides a solid basis for developing further a Scottish model of value.”

Celgene believes the progress to date does provide a solid base for further developing a Scottish model of Value. The PACE process could be identified as a first step towards a Scottish model of Value and it is generally regarded that its introduction has been a positive step particularly welcomed by patient representatives.

The integration of Health and Social care in Scotland illustrates the close inter-relationship between a person's health and the wider implications for society of that health. With a greater understanding of this relationship developing now would be a good opportunity to take a much broader view of the benefits medicines offer to society and to include this within HTA.

Celgene would suggest that any work to develop a Scottish model of Value further should move beyond the areas of End of Life, Orphan and Ultra Orphan diseases and include a much broader range of diseases where there is as much need to acknowledge the significant benefits medicines can offer.

Celgene Ltd

Myeloma UK Roundtable Meeting on Access to Medicines

Summary

Introduction

A multi-stakeholder roundtable meeting was convened by Myeloma UK to build consensus on key issues relating to access to medicines in Scotland and to write a report on the discussion to feed into the ongoing review being undertaken by Dr Brian Montgomery. We considered it more helpful to the Review, the Scottish Government and the Scottish Medicines Consortium (SMC) to ensure that all stakeholder groups jointly discussed the attributes of an access system that would ensure it is fit-for-purpose and works to the benefit of all.

Whilst the Montgomery review is broad in scope, Myeloma UK identified two topics for discussion at the meeting that were considered pivotal to ensuring patients in Scotland have improved access to new and effective treatments. These were as follows:

1. How the drug approval system could be adapted to include a commercial negotiation.
2. How the new approach will accommodate advances in new medicines and a developing regulatory framework.

Attendees discussed and developed key cross-stakeholder recommendations on potential considerations and ways forward on the two issues selected. A summary of the discussions, which were held under Chatham House Rules, alongside agreed recommendations, are outlined below.

The meeting was attended by five representatives from leading patient groups, eight representatives from the pharmaceutical industry (a mixture of both larger and SME companies) and a health economist – all with a remit for Scotland. Additional health economists, clinicians and representatives from the pharmaceutical industry were unable to attend, but their views were sought and included in the write up.

Topic one: How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring the best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier.

Background

Following the Health and Sport Committee Inquiry on Access to Medicines in 2013, a number of reforms were made to national and local access to medicines processes in Scotland, including the development of the Patient and Clinician Engagement (PACE) process designed to increase access to medicines for end-of-life, orphan and ultra-orphan conditions through the SMC.

Whilst these reforms have led to an increase in access, it has been argued that they did not go far enough in amending the system to include a proposed “pause” in the SMC process which would enable discussions around cost-effectiveness during the appraisal process.

Whilst the SMC cannot say “yes” to every drug that they assess, there is the potential for cross-stakeholder collaboration to overcome issues with uncertainty and cost-effectiveness in the lead up to and during appraisals, and to increase the number of first-time drug approvals.

Given that the idea of the cost-effectiveness pause continues to be put forward, it is important to get the scope and details of a revised process right to ensure it is fit-for-purpose and allows a solution-orientated approach to assessing new medicines.

Discussion

SMC pause

- Whilst the Montgomery Review is focused solely on issues with end-of-life, orphan and ultra-orphan diseases, it is important that the topic of “cost-effectiveness negotiations” is considered for all medicines. This will prevent random add-ons the SMC process for certain

disease areas over others and acknowledges that we are moving towards an era where all medicines may be considered “orphan” due to the development of stratified medicine

- Attendees agreed that the cost-effectiveness pause is an inevitability and the narrative and language from Government relating to the pause highlights that it will happen – it is a question of “when” rather than “if”. The important thing for stakeholders to do is to shape the discussion around how it could work in the interests of all stakeholder groups and where it would sit within the medicines approval system
- Key questions related to whether the cost-effectiveness pause would sit within or outwith the SMC appraisal process and at what stage during an appraisal it would sit
- There was agreement amongst stakeholders that this is not something that the SMC has the ability or willingness to facilitate, although it would have a pivotal role in working within a “pause”/cost-effectiveness discussion to ensure there is an understanding of what is needed from stakeholders to find solutions. This is something that could potentially sit within an expert panel within the Scottish Government or Health Improvement Scotland
- It was agreed that rather than an adversarial negotiation on price, it should be a discussion amongst key stakeholder groups about how to ensure patients benefit from a new medicine and the different ways of achieving this end goal
- Arguably, patient access schemes (PAS) are the current way of “negotiating” cost-effectiveness, however, the SMC Patient Access Scheme Assessment Group (PASAG) typically favour straight discounts rather than complex PAS, which involves mechanisms such as outcomes data collection or response schemes. More complex schemes often offer better value than straight discounts, so this is a potential avenue to explore
- Attendees also discussed the importance of crystal clear narrative surrounding the intent of a cost-effectiveness pause within the drug approval process. All stakeholders agreed to meet further to address the specifics around the wording/design of a pause in the process

Early engagement

- There was broad agreement that discussions around cost-effectiveness should not just happen at the stage where a drug has been turned down by the SMC, as this is often too late in the process to address any issues or for pharmaceutical companies to be able to agree cost-effectiveness schemes internally (usually at EU or global level)
- Instead of solely being addressed in a “cost-effectiveness pause” at the end of the process, there should be an “early engagement” function developed as part of drug assessment process in Scotland
- Early engagement should start before a company submission to the SMC and would ensure that key stakeholders are able to discuss the best approach to the appraisal and any potential issues with cost-effectiveness in advance of the SMC assessment process. This would allow solutions to be identified earlier on in the process
- These pre-submission discussions would happen between clinicians, PASAG, patient groups, the pharmaceutical company, the SMC and the Scottish Government (this isn’t exhaustive). It would be a “collaboration” to bring a medicine to patients and would assist in the co-creation of patient pathways (i.e. you could consider issues such as how best to use drugs in clinical practice and clinician opinion on how valuable an intervention is)
- Rather than meeting once, at a point that a medicine has been turned down, there could potentially be a couple of points during the appraisal process where this expert committee would meet to discuss issues around cost-effectiveness. Budget impact of new interventions

is also something that could be discussed at during this phase

- As part of this process, PASAG and the SMC would need to be more flexible in the types of PAS that they are willing to accept as part of pharmaceutical company submissions. A cost-effectiveness discussion would not just focus on discussions around price, it would enable managed access schemes and methods of capturing the outcomes and benefits of a drug clinical practice
- The discussion around cost-effectiveness is linked to the data capabilities of the NHS in Scotland and how we harness the ability that exists across the country to capture information to support drug approval and to assist in the determination of the value of new medicines. This also links to “future proofing” the system, as given the stratified nature of medicines coming down the pipeline the NHS and the SMC will need to be flexible and creative in the way that they approve drugs without the robust Phase III comparative data that has been the norm to-date
- Following the early-engagement process and PACE, if a drug is still likely to be turned down, there might be the potential for a further cost-effectiveness discussion amongst the key stakeholder groups to assess whether there is any further avenues to explore to approve the medicine. However, the early engagement should reduce the need for late discussions on cost-effectiveness
- There is the potential for the Government and NHS Scotland to look towards other countries for successful models of reimbursement and different types of PAS that could be considered in Scotland. Lesson can also be learned on how different health technology assessment bodies are looking at the issue of future proofing their methodology for advancements in medicine

A “triage” process

- The SMC has a horizon-scanning process which looks at new medicines in development. There is the potential to develop upon this function to build a “triage” system into the SMC process where new medicines are “pre-screened” for their eligibility to go through the full appraisal process
- The SMC is there to provide strategic advice to the ADTCs on new innovation and how to invest its resources. There are some interventions that the SMC assess, which could be “pre-screened” and automatically be given a green light given their obvious cost-effectiveness. Using a triage process would allow the SMC to prioritise drugs to go through their appraisal process, increase the capacity of the SMC and allow the identification of drugs for early engagement with the SMC
- Following the implementation of a triage process, an assessment should be made of the additional capacity requirements of the SMC, although the capacity should be improved through improved prioritisation

Topic two: How the new approach will accommodate advances in new medicines and a developing regulatory framework.

Background

Whilst the SMC process currently works well and recent reforms have improved access to medicines for end-of-life and orphan conditions, it is important for the SMC to horizon scan for advancements in medicine which will impact upon the assessment and value of medicines and to evolve their processes to ensure they are prepared for these developments.

The appraisal methods of the SMC are designed to assess data from usually large randomised Phase III clinical trials, however, developments in stratified medicine and adaptive licensing pilots at the

European level highlight that in the near future the SMC will have to appraise early-phase single arm clinical trials and trials with limited data.

Treatments are also increasingly being brought to market across diseases areas in multi-drug combinations and the small molecule nature of medicines is also changing, including the development of gene and immuno-therapy. These developments all have implications for the value of new drugs and the uncertainty relating to the health economic modelling (particularly given the lack of comparative information).

The discussion that took place during this topic is summarised below. This is not an exhaustive list of recommendations and is by no means a finished conversation, it serves as a starting point for gathering cross-stakeholder opinion on this important and wide-ranging topic. It is a topic that should not be seen in isolation to the discussion above on cost-effectiveness.

Discussion

General points

- There was general consensus amongst stakeholders that the issues described above are not just about “future” developments, and that some of this is already a reality. It is therefore crucial that the Montgomery Review starts an important preparatory and discursive process to ensure the SMC appraisal processes are beginning to adapt to these advancements
- There appears to be a current lack of leadership in “future proofing” the NHS and drug approval processes in Scotland for advancements in medicines. This is something that is crucial moving forward and as part of this, it is important for different parts of the health service, researchers and wider stakeholders to communicate and collaborate
- Robust research and analysis needs to take place across Scotland to scope out the advancements in medicines (including stratified medicines and adaptive regulation) and the impact these are likely to have on the health system/drug approval process and how the system needs to be adapted. This should take into account UK-wide and global influences, including on medicines pricing

Increased flexibility in decision-making

- The assessment and approval processes operated by the SMC are going to have to evolve to allow for an iterative and ongoing appraisal of a new medicine rather than a single zero-sum decision on whether or not to make it available to patients
- It is important that SMC develop flexible ways for assessing and approving new drugs, where the health economic uncertainty is higher and the exact value in the real world is undetermined. Developing the SMC’s ability to assess and consider complex PAS and reviewing the ability to approve treatments conditionally in the NHS on the basis of further evidence collection, are critical in this regard
- Conditional approval of new drugs is a viable option, however, there are risks associated with approving drugs and then removing them from national funding if the data collected does not demonstrate good value. Safeguards would need to be put in place to ensure patients do not have to endure a revolving door of approved and not-approved treatments in Scotland
- There is room for “de-risking” the development and approval of new drugs through improved industry collaboration with academic and charity researchers, including through the conduction of UK “bolt-on” studies to develop better understanding of how medicines work in the UK clinical practice. This type of collaboration would allow for data to be collected that supports the health technology assessment process and assists in the reduction of uncertainty

- We need to develop ways to allow clinicians to clearly signal to payers and industry the value of a new medicine. There is a need to involve clinicians in the process earlier to understand what they require from new medicines and how they would use them in clinical practice
- There is also the potential for the NHS and other stakeholders to conduct improved health services research to assist in understanding the types of treatment patients and carer's value, perspectives relating to benefit/risk and also to understand the idea of wider-societal impact. This type of information would help determine other aspects of "value" that medicines bring and is something that could be taken into account in a more flexible appraisal process

Data capability of NHS Scotland

- Future proofing the NHS for medicines advancements, early engagement with stakeholders around cost-effectiveness and improving data collection in the NHS are concepts that are inextricably linked
- As discussed in topic one, good data is important to develop and the Scottish Government needs to harness the capacity of data collection systems in Scotland to ensure that we can continue to measure the impact of a medicine on survival and quality of life following SMC approval, particularly if drugs are approved at an earlier phase and on a conditional basis. Examples of good data resources are the Farr Institute and ISD data in Scotland, but these are often not available to pharmaceutical companies
- It is important to continue to ensure that Scotland is an attractive place for inward investment. Future proofing the HTA system and investing in the data collection systems will assist this
- Existing data collection systems in cancer are not fit-for-purpose as they do not routinely capture the use of oral chemotherapy use in the NHS. This is pivotal information to collect at a time where pharmaceutical companies are proactively developing medicines that allow patients to receive them in the home setting
- There are also issues over how to ensure data entry compliance when using data collection systems within the NHS – there is currently major variation across health boards and cancer networks. It is therefore important that in developing the data capabilities in Scotland that the issue of compliance is addressed to ensure that we gather robust and comprehensive information that is useful
- Research and investment needs to take place to assess what the gaps in data are in the system in Scotland and how we can improve this
- As well as outcomes data, we need data on patient experience and preferences and an increased use of measures such as patient report outcome measures (PROMs), to determine what patient's value from treatments. This can be both collected during clinical trials and also following approval – patients should be seen as partners in the development of innovation

Disinvestment

- There is a need to look at the role of disinvestment in the system and ensuring that the NHS are not paying for treatments that are no longer required. It was discussed that clinicians are best placed to lead on this and their informed, evidence-based decision-making can lead to natural disinvestment (i.e. they chose the most innovative treatments for patients and stop using others)
- It was discussed that at present the NHSS buys costs and not outcomes as a result of a system that does not fit well together and one that doesn't have the ability or agility to bridge the gap between evidence generated from registration trials and the real world clinical needs of patients. As a consequence we have a one size fits all approach to treatment rather than an adaptive flexible system that meets the specific needs of individual or groups of real world

patients. Ideas such as taking whole pathway approaches to the assessment of new drugs and allowing patients and clinicians to co-design these is a fundamental idea to explore

Improved demand-side

- There is a need to strengthen the demand-side in Scotland to ensure that we are signalling to industry and researchers the types of treatments that are needed in each specific therapeutic area. There is the potential to do this through co-creation of the above mentioned flexible treatment pathways and understanding innovation gaps in pathways

Costs/price

- A long-term discussion will need to be had about what we are willing to pay for in the health service, particularly as costs are likely to go up as medicines become stratified. There is a need for a proper concerted look at the system and how it might be developed in a way that is sustainable
- Discussions around the future of medicines need to take place in the context of value and cost-effectiveness rather than around price
- There is the potential for the Scottish Government to have a seat at the table of the PPRS negotiations to ensure that Scottish interests are represented in discussions around the pricing system. Early engagement with the pharmaceutical industry and anticipation of issues around cost-effectiveness will help ensure a better deal in Scotland on value
- Attendees agreed that the New Medicines Fund is not something that is a long-term solution to accessing medicines, particularly as the PPRS may change moving forward, This highlights the importance of co-creating a long-term and sustainable access to medicines system for Scotland

Recommendations

Below is a list of cross-stakeholder recommendations that received broad agreement and consensus during the discussion event and should be factored into the current Review. The new Scottish Government, in collaboration with key stakeholders such as the SMC, industry and patient groups, should:

1. Ensure that co-creation and collaboration are key principles upon which the access to medicines system and the development of treatment pathways in Scotland should be based
2. Explore ways of developing the SMC horizon-scanning process to include “triage” to allow for the prioritisation of innovative, high-cost drugs that need to go through the SMC process (including through a new early engagement process) vs. high-volume low cost drugs which do not require SMC advice given favourable health economics
3. Consider the ways that the medicines approval system in Scotland could be adapted to include robust, early engagement with the pharmaceutical industry and other stakeholders to prepare for and discuss issues around cost-effectiveness as early on in the process as possible. This would sit within the SMC and involve representatives from all key stakeholder groups in a collaboration to ensure drugs are brought to patients efficiently and in a way that represents value to the NHS. This would be part of the “cost-effectiveness negotiations” being considered as part of the review and should ensure that industry are prepared as possible for the appraisal
4. Develop a crystal clear narrative surrounding the intent of a cost-effectiveness pause within the drug approval process, where it would sit within the system, the types of drugs it would assess and who it would involve

5. Conduct research into and develop the data potential of Scotland to ensure that we have the capacity to capture data on patient outcomes and preferences and that it supports the development of managed access arrangements and more complex patient access schemes. This should include a consideration of how we can ensure compliance in data entry across health boards and networks across Scotland
6. Develop the SMC methods to allow for the assessment of more complex PAS, which can sometimes offer better value to the NHS than straight forward discounts. Through earlier engagement with stakeholders and more flexibility, pragmatic solutions can be found to cost-effectiveness
7. Explore ways of future-proofing the SMC process to allow for more flexibility in the assessment of stratified medicines and those approved under early access schemes (such as adaptive licensing) that have more uncertainty but are likely to have a high value to groups of patients in the NHS. As part of a more flexible assessment process, consider ways the SMC could assessed wider societal benefits that newer interventions might bring
8. Commission research into fully understanding advancements in medicine, the impact these are likely to have on the health system/drug approval process in Scotland and how the system needs to be adapted moving forward
9. Strengthen the demand-side for medicines in Scotland by developing ways of signalling to suppliers the types of innovation we need
10. Begin a dialogue on what Scotland is willing to pay for in the health service and affordability. There is a need for a proper concerted look at the system and how it might be developed in a way that is sustainable to the future

Conclusions

The discussion and recommendations in this report represent a “snap-shot” of stakeholder opinion and will be evolved and discussed further in later meetings.

This is the start of an iterative process and provides the basis of future cross-stakeholder discussion and collaboration on the access to medicines system in Scotland. Instead of continually holding reviews on a cyclical basis, as a cross-stakeholder group we were keen to evolve the access to medicines system to ensure that it adapts to the upcoming developments in medicine.

Submission to the Scottish Parliament Health and Sport Committee: Review of Access to New Medicines



Summary

This submission has been developed by Bayer to contribute to the work of the Health and Sport Committee and the Scottish Medicines Consortium (SMC) in the review of access to new medicines in Scotland. The content of our response focuses on those areas within the scope of the review where we can provide the most constructive input.

Significant progress has been made in implementing the recommendations of the rapid review undertaken by the Task and Finish Group. Bayer welcomes the opportunity to evaluate those advances in the access to new medicines framework and explore how the system in Scotland can be improved further.

Overall, the findings of the Health and Sport Committee reflect our positive experiences of the new approach. Specifically, we commend NHS Scotland, and the SMC in particular, for the introduction of the Patient and Clinician Engagement (PACE) process which has given a stronger voice to clinicians and patients in decisions regarding the evaluation of medicines. However, we agree with the views expressed by the Committee, there is clear scope to further expand the role of clinicians and maximise the utility of their experience throughout the process.

The SMC remains one of the first HTA bodies to issue their decision after a European Medicines Agency licence has been granted. Sustaining this approach will present inevitable capacity challenges for the SMC and a full assessment needs to be undertaken of the potential resourcing and planning issues this will pose in order to sustain organisational performance.

While many of the recent changes have been overwhelmingly positive, there remain clear opportunities for further improvement in current arrangements for determining access to new medicines that we would like to focus on:

- Extending the role of clinician and patient involvement
- Clarifying and further describing how the inputs from patients and clinicians will contribute to the overall deliberations of the SMC committees
- Improving the level of transparency and clarity in all committee decisions and their communication so that the rationale for the decision is clear
- Planning that the right capacity and capability exists across the healthcare system to fully support the evaluation process

In addition, Bayer believes that the Committee should give full consideration to three further areas of relevance to the medicines access and reimbursement framework:

- Real world evidence and its application across a healthcare system
- Alignment of regulatory and reimbursement processes
- Innovative pricing and reimbursement models for new medicines

1. Rounding off the Reform Process for PACE right clinician

Bayer supports the principle of an extended role for clinicians with relevant specialist expertise within the PACE process, specifically as part of the final SMC committee meeting. Input from expert stakeholders is key to arriving at an effective and informed decision for patients and the wider healthcare system, and specialist clinical input is fundamental to achieve this ambition.

Bayer would recommend that consideration is also given to involving patient representatives in final SMC committee meetings to allow members to pose questions that may arise during final deliberations.

2. Transparency and Clarity in Articulating SMC Decisions

The Committee discussions clearly highlighted that stakeholders value the role of the SMC and accept that, in some instances, the SMC will have to make negative decisions when the evidence available dictates that such a conclusion is in the best interests of patients and the wider healthcare system. Bayer fully agrees with this position.

Maximising clarity and transparency in decision-making processes and effective communication are cornerstones of good governance which in turn drives public confidence in the system. Further progress in line with the Committee inputs from Lesley Loeliger of PNH Scotland and Professor Rob Jones of the Beatson West of Scotland Cancer Centre would reinforce the rigour and professionalism already demonstrated by SMC in its decision-making.

The SMC has an international reputation as a high-quality HTA body recognised for providing the effective levels of transparency and clarity. Current governance processes could be enhanced further to improve the consistency in decision-making and the communication of decisions. In particular, Bayer believes greater clarity for the SMC committee on how they should handle and consider PACE inputs would be beneficial for all parties to help explain the process followed in reaching a final decision. This could be supplemented by a dedicated training programme and guidelines for committees on reporting and engaging with stakeholders to standardise practices and enable more open and effective dialogue.

3. Capacity and Capability

Capacity and capability in different parts of the system was a strong theme in the Committee debate. With scrutiny of healthcare expenditure increasing and the demands on SMC growing, it is crucial that the necessary workforce expertise and capacity are in place to manage an expanding workload to allow the SMC to fulfil its full range of responsibilities in an effective and efficient way. We believe that confidence in the SMC would be strengthened through the introduction of an organisational development plan which demonstrates that future proofing capacity and capability have been hard-wired into the organisation.

It is apparent from the Committee report that the SMC is providing effective support for patient organisations and their representatives. We strongly believe that this function must continue to be prioritised by the SMC, and could be enhanced further if individuals and groups representing the interests of patients are supported with appropriate training to empower them the necessary skills to help them to express the views and experiences of those they represent as part of the SMC process.

4. Real World Evidence

Bayer noted with interest the Committee's discussion on the potential to generate and utilise real world data for clinical and commercial purposes. Bayer supports efforts aimed at ensuring that medicines deliver value in clinical practice, however careful consideration must be given to the design, implementation and analysis of any real world evidence generation programme.

The practice of collecting clinical data can be extremely complex as demonstrated by the Multiple Sclerosis Risk Share Scheme which took a significant amount of time, effort and resource to set up and required a significant re-design two years after its inception. The development of real world evidence programmes would need to bring all relevant stakeholders together to work in partnership on issues such as:

- Realistic timelines for development and implementation of data collection (e.g. ethical approval processes for new trials or extensions)
- Managing differences between pivotal trial study populations and those patients treated within clinical practice as these differences may actually magnify any uncertainties rather than answer them
- Information governance issues such as consent, data ownership, data storage and access to raw and pseudo-anonymised data
- Data analysis
- Practical data collection and data quality assurance and systems as the history of data collection within clinical practice is patchy at best as evidenced by the on-going struggles in England to get data entered into the SACT database

The SACT database in England is also illustrative of the challenges of generating meaningful data in clinical practice. To the best of our knowledge, the SACT database has only recently started delivering meaningful outputs following six years of concerted effort that has gone into trying to establishing a robust view of systemic cancer treatments across English hospitals. This is not intended as a criticism of SACT, but a recognition of the challenges associated with generating robust clinical data within a very complex and over-stretched healthcare system.

The Committee rightly identified that clinical time can be at a premium especially in rare conditions and the benefits of introducing any additional obligations must be considered against the risks and costs of doing so. If we are to ask more from the clinical community, we must be sure we will deliver excellent outputs to justify the additional demand on their limited time.

Whilst we sound a cautionary tone in relation to real world evidence, Bayer is open to working in partnership with NHS Scotland to explore ways of developing this capability to help deliver benefits for patients and the wider healthcare system.

5. Alignment of Reimbursement and Regulatory Processes

The European and UK regulatory bodies have introduced initiatives such as the Medicines Adaptive Pathway for Patients and the Early Access to Medicines Scheme which can give rise to an early conditional licence being granted on the basis of promising, but still maturing data. However, there is currently a time lag between the point at which licences are granted and when medicines may be reimbursed under an appropriate managed entry agreement that would allow for further collection of safety and efficacy data.

This is a very complex area and any solutions will only be reached with significant dialogue between stakeholders. Bayer would be open to being a partner in such discussions and realising opportunities to accelerate advances in outcomes for patients

5. Pricing and Reimbursement Models

Bayer would be very interested to explore the issues described by the Committee on pricing and reimbursement models further with NHS Scotland and the SMC. We price our medicines fairly according to the value they deliver and believe this is demonstrated by the approval of many of our medicines and indications by the SMC.

Bayer is open to work collaboratively with NHS Scotland to explore how new commercial and managed access arrangements that are flexible and more innovative in their design might be utilised in Scotland. This work could look at:

- Solutions for multi-indication pricing, when different indications of a medicine deliver different value propositions
- Outcome based models of reimbursement
- Conditional reimbursement
- Deferred payments
- Price - volume agreements
- Tendering and negotiations at scale
- Product – service bundling

Moving beyond simple discounts to list price could be a solution to increasing access, especially in cases where medicines have initially not been recommended by the SMC, or when affordability is a challenge, as the real value of a medicine impacts on budgets outside of health although most of the costs sit within the health budget.

The one note of caution in relation to more innovative commercial models is that they involve different workforce capabilities to negotiate, design, implement and administer than simple discounts. However, Bayer is open to work with the NHS Scotland to build this capacity and expertise into the system so that more patients can benefit from new medicines.

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Roche response to the Montgomery Review of Access to New Medicines

Executive summary

- Roche welcomed the Scottish Government's announcements that changes would be made to SMC processes to: deliver consistent, improved access to medicines; improve the approach to individual patient treatment requests through a new Peer Approved Clinical System; and work towards the development of a Scottish Model of Value.
- We believe some of the changes to the SMC, such as the Patient and Clinical Engagement (PACE) are a positive step in the right direction. However, there continue to be challenges due to a lack of transparency and consistency within SMC decision-making processes. For example, it remains unclear what weight is given to the outcome of the PACE process when SMC decisions are made.
- There has been little progress on the development of the Peer Approved Clinical System (PACS). Consequently, patients and clinicians are still reliant on the existing Individual Patient Treatment Request (IPTR) system, which has been shown not to meet patients' needs.
- There has not been any progress on the development of a Scottish Model of Value. This was deemed necessary to identify treatments that were important to the Scottish population and so might require an extra weighting or modifier when reviewed by the SMC. As a consequence, patients in Scotland may be missing out on treatments they could benefit from.
- Roche is keen to work in partnership with the SMC and the NHS in Scotland to identify innovative ways to increase patient access to the medicines they need, aiming to be flexible and innovative in our approach.
- Given our experience of international HTA systems which aim to evaluate whether patients should gain access to specific new medicines, we believe there are a number of principles that a Scottish Model of Value could valuably incorporate:
 - Providing patient access to medicines from licence so that the assessment process does not cause delays in access. The SMC already tries to issue guidance within three months of licence. The PACE process has added some delay and timeliness must not be lost in any new approach.
 - Assessing the benefit of a medicine should not only be based on a simple cost per QALY basis but also by considering wider benefits, such as societal value, unmet clinical need and the potential impact on the standard of care in Scotland compared to the other nations of the UK and the rest of Europe.
 - Ensuring that the data required for a wider assessment of medicines can be collected. This could be through the SMC either instigating a pause or issuing an interim positive decision. An interim decision may be more beneficial for patients. This could provide opportunities for the collection of additional information, including real world evidence, to support the ongoing assessment of a medicine's value in the context of the wider benefits assessed in line with a Scottish Model of Value.
 - Recognition that medicines licensing is moving towards earlier access. The evidence used in earlier licensing will often rely on small datasets of evidence supporting clinical benefit and safety. These data may be insufficient for a health technology assessment. An interim positive decision would enable patients to access the medicine in line with the licence while further real world data were collected.
 - Providing flexibility around reimbursement mechanisms. The SMC already allows positive consideration of complex Patient Access Schemes (PASs), flexible definitions for end of life criteria and orphan and ultra-orphan medicines. The current approach is welcome and should be built upon as a strong foundation in a future system.

1. *How are the agreed definitions for end of life, orphan and ultra-orphan medicines working in practice?*
 - 1.1 It is welcome that the SMC has provided greater clarity and flexibility around the definitions for end of life, orphan and ultra-orphan medicines¹. The role of any one of these new definitions is to ‘trigger’ eligibility for a medicine to be considered through the Patient and Clinical Engagement (PACE) process. These definitions did not previously exist and so the additional flexibility is helpful for patients and manufacturers alike.
 - 1.2 Specifically, the definition of end of life medicines as those “used to treat a condition at a stage that usually leads to death within three years with currently available treatments”² is broader than that currently used by NICE (which is normally less than 24 months), allowing more medicines to be considered under PACE than would be considered by NICE under their “end of life” criteria.
 - 1.3 Similarly, the flexibility to enable rarity to be considered by indication, rather than total licensed indications for a medicine, allows more opportunity for the PACE process to be used.
 - 1.4 Despite positive changes there are still challenges in approving medicines for use at the end of life, particularly those for patients with metastatic cancer and in the combination setting. This is demonstrated by the independent panel review of the assessment of abiraterone. The review led to a delay of more than six months for patients before the treatment was recommended, highlighting problems in the initial review³.
 - 1.5 The progress being made in access to medicines in Scotland is undermined by inconsistency and a lack of transparency in the cost per QALY at which medicines are likely to be approved. For example, pemetrexed for the treatment of locally advanced or metastatic non-small cell lung cancer was approved following the PACE process with a cost per QALY of £58,000⁴, while everolimus for the treatment of metastatic breast cancer was not recommended with a cost per QALY of £36,000⁵. This lack of consistency and transparency in decision-making also leads to unpredictability for manufacturers and patients about the likely outcome of assessments. There needs to be some certainty about the decision-making process so that companies can ensure that they provide the relevant information. Failure often leads to a resubmission to the SMC and further delays for patients.
 - 1.6 Even where the flexibility has enabled positive recommendations, it is not clear how extensive the benefit of these changes has been for patients. To date, Roche has only been able to secure positive recommendations through PACE for two relatively small sub-groups of patients within the licensed indications for our medicines^{6,7}. This means that the number of patients benefitting could be quite limited in comparison to those proven to gain clinical benefit through the full medicine licence.
 - 1.7 Point 1.6 could highlight a potential unintended consequence of how the new definitions are used within the wider SMC decision-making process. Because there is a lack of transparency around the basis of decision-making, and no opportunity for dialogue or negotiation between a manufacturer and the SMC during the process, companies are having to identify sub-groups of patients for whom a positive recommendation might be achieved. This means that companies may make submissions based on a smaller patient population which may be more likely to be accepted by the SMC, but which ultimately means some patients who could clinically benefit are still missing out.

1.8 A key question remains as to whether the new criteria could or should be used as ‘multipliers’ of the QALY threshold as opposed to individual modifiers during the consideration of cost-effectiveness. For example, should a medicine that is used at the end of life for an ultra-orphan condition benefit from twice the flexibility provided for a medicine that is used at the end of life in a more common condition? We would appreciate greater clarity from the SMC on this and it may also be useful for the development of the Scottish Model of Value.

2 *How are the views from the Patient and Clinician Engagement process taken into account in decision-making?*

2.1 It is important that patients’ views are heard as part of the SMC process as they live with the reality of their condition every day and can share their personal experience of the impact of a medicine. Similarly, clinicians can highlight the unmet clinical need for a medicine, consider how it will have an effect on the standard of care offered in Scotland and provide insight into the potential future of treatment if the medicine in question was not available. Roche welcomes the fact that the PACE process now provides a formal opportunity for these patient and clinical voices to be heard during the SMC process, as this was previously lacking.

2.2 Despite the PACE process being used in a number of assessments, there is a lack of transparency about the weight that is attached to the PACE process in the SMC’s decision-making process and the impact this has on final assessment decisions. Given the continued focus on a cost per QALY assessment there is a risk that the outcome of PACE meetings is of limited impact as it provides information on the wider value of a medicine outside what is considered for the cost-effectiveness thresholds. There have been occasions where there has been a clear consensus from the PACE meeting in support of a medicine (as presented at the Committee meeting) but this does not seem to have been reflected in the outcome of the assessment from the SMC⁸.

2.3 In addition, patient and clinician representatives who took part in the PACE process do not take part in the main SMC Committee review, where the final SMC decision is made. This prevents Committee members from seeking clarity on statements contained in the PACE report, and denies PACE representatives an opportunity to question views expressed by the SMC Committee. This lack of dialogue between PACE representatives and the SMC prevents a consensus between all parties being reached on what would be best for patients.

3 *How is the new approach to assessment of ultra-orphan medicines operating in practice?*

3.1 Roche welcomes the new approach to assessing orphan and ultra-orphan medicines, based on both prevalence and incidence. This ensures that medicines measured by one form and not the other are not disadvantaged in the revised process. The benefit offered by this approach of equivalence has enabled patients in Scotland to access medicines that were previously not available, such as patients with advanced ovarian cancer⁹.

3.2 For medicines treating rare conditions it can be difficult to collect sufficient data to carry out a robust cost effectiveness assessment. It is welcome that the SMC is flexible in the data it will accept for medicines which meet these criteria. It remains unclear how much weight these data are given so greater clarity from the SMC on this issue would be helpful for patients and manufacturers alike.

4 *How have the acceptance rates for end of life, orphan and ultra-orphan medicines changed as a result of the new approach?*

4.1 Scottish Government anticipated more medicines would be recommended for use as a result of the changes to the SMC's processes¹⁰. However, neither the Scottish Government nor the SMC have published analysis of the number of medicines recommended and not recommended. We are therefore unable to assess the impact of the changes to date. In addition, it is possible that the impact for patients of an apparent increase in acceptance rates could be limited due to the consideration of medicines for sub-groups of patients rather than acceptance of the full licence as outlined in point 1.6.

4.2 Information is available through the SMC website on the decisions made on individual medicines, but this is not collated to give an overall summary of recommendations. Data need to be compiled and published by the Scottish Government or the SMC so that the true impact of the changes can be understood. These data need to show:

- Both the number and proportion of medicines recommended, broken down by condition.
- How many resubmissions were made before a positive outcome; a figure of total acceptances versus total refusals would not be accurate if several previous negative outcomes were removed from the figures after a medicine was recommended for use.
- Why medicines were not recommended, to highlight where there continue to be challenges in the system.
- Quarterly changes in recommendations to demonstrate the impact of the reforms over time. For example, the number of acceptances may have increased immediately after the new definitions and the PACE process were introduced because of the number of resubmissions of medicines previously not recommended. It is not clear if such an increase would be maintained in the long term.

4.3 It is likely there has been a positive impact from the changes introduced by the SMC, with more medicines recommended. However, it is important to note that the number of medicines assessed by the SMC, and the conditions that they treat will vary year on year. This means that a simple calculation of the number of medicines recommended in different years would not necessarily give the full picture.

Our own experience of the changes is that the SMC has tended to recommend some of our older medicines for small patient populations: Avastin® (bevacizumab) for the treatment of advanced ovarian cancer¹¹ and Herceptin® (trastuzumab) for the treatment of gastric cancer¹². Both of these products were launched with their first indications more than ten years ago, and are not used in combination with another biologic. On the other hand, the number of acceptances for our newly licenced medicines remains unchanged, with both Perjeta® (pertuzumab), used in combination with Herceptin for HER2-positive metastatic or locally recurrent unresectable breast cancer¹³ and Kadcyła® (trastuzumab emtansine) for HER2-positive, unresectable locally advanced or metastatic breast cancer¹⁴ not being recommended. In our view, this would suggest that the changes to the system have provided solutions for older medicines that are standard of care elsewhere in Europe, but that the SMC still does not have the flexibility needed for new, innovative medicines, those used in combination, or the medicines of the future. The system needs to be able to assess these new targeted agents effectively, or patients in Scotland will not be able to access them.

4.4 We are also concerned to note that, of the five breast cancer medicines that have been considered under the new processes, the SMC has only recommended two and recommended

restricted access to another, despite an apparently wide range of cost per QALY estimates¹⁵. There is currently a lack of transparency over what the cause of this variation is, but it may mean that further amendments to the process are required to improve patients' access to new medicines as set out by the Task and Finish Group.

5 *How has the transparency of SMC improved, and what further opportunities are there for patient and clinician engagement?*

5.1 Roche welcomes the efforts the SMC has made towards greater transparency in the assessment process, including its commitment to make meetings open to the public and to include company representatives in these meetings.

5.2 However, there remains a lack of transparency about how decisions are actually made as the Committee votes in private. This significantly reduces the opportunity for public scrutiny of SMC decisions and, in particular, the weight attached to the outcome of the PACE process. Further efforts to improve the transparency of this process would be welcome.

6. *How are NHS Boards implementing SMC decisions under the new approach (both accepted and not recommended), including utilisation of the New Medicines Fund?*

NHS Boards

6.1 We are not aware of significant changes in the operation of NHS Boards' Area Drug and Therapeutic Committees in relation to implementing SMC decisions for accepted medicines.

6.2 For medicines that are not recommended by SMC, there are reports that some NHS boards are refusing to consider applications for a medicine that has not been recommended by SMC under its new PACE processes, unless the request is for an indication outside those considered by the SMC. This type of exclusion is not the intention of the central guidance on IPTR process¹⁶. If the SMC does not recommend a medicine it is critical that a mechanism (currently the IPTR process) is in place to ensure that patients who could gain clinical benefit from the medicine can still access it. The NHS Board position appears to be in contradiction of the guidance issued by the Chief Medical Officer which stated decisions should be made on the basis of clinical need¹⁷.

6.3 Given that the most significant challenges for access to medicines occur during the SMC process and consideration of IPTRs, we believe that efforts need to be concentrated on continuing to reform the SMC, implementing PACS and developing a new Scottish Model of Value.

New Medicines Fund

6.4 It is welcome that the Scottish Government demonstrated its commitment to increasing patients' access to medicines by increasing the budget available through the New Medicines Fund to £80million in 2015/16¹⁸. Previously this funding was predominantly used to provide access to medicines for rare conditions, in particular cystic fibrosis. It would be helpful to have clarity from the review about the current and future funding that will be available for all medicines through the New Medicines Fund.

- 6.5 We understand that the money Scotland received from industry payments to the NHS through the current PPRS agreement has been used for the New Medicines Fund¹⁹. This is appropriate given the intention of the agreement to increase access to innovative drugs commensurate with the outcomes they offer patients and value to the NHS²⁰. Scottish Government committed to publishing data about the use of the New Medicines Fund on an annual basis but this has not been forthcoming.²¹ It is therefore important to understand:
- How the Fund is being spent, broken down by medicine, by process (IPTR, GPTR or SMC) and by NHS Board.
 - How the funding is being distributed to each NHS Board and by what mechanism the resource from the Fund is allocated.
 - If NHS Boards return the funding they receive to local medicines budgets. If not, this effectively reduces the medicines budget available, and spends the resource allocated for medicines elsewhere in the health system. This would not only be undesirable but could potentially undermine the purpose of the PPRS reimbursement mechanism.
- 6.6 It is not clear whether the New Medicines Fund is intended as a ‘seed funding’ mechanism to ensure access to medicines recently recommended by the SMC before funding is in place on an ongoing basis or if the Fund is the long-term funding mechanism for certain medicines. Greater clarity is required to provide patients and clinicians with more certainty about the future of medicines access in Scotland. This is particularly important as the current arrangements are reliant on payments through the PPRS which may be different after 2019 when a new agreement will have been negotiated.
7. *How has the new approach had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system)?*

Peer Approved Clinical System (PACS)

- 7.1 Scottish Government told the Health and Sport Committee that the new PACS system would be piloted and then implemented from May 2014²². It is of great concern that a new system has not been introduced.
- 7.2 Most recently, in March 2016²³, the Cabinet Secretary for Health, Wellbeing and Sport, Shona Robison MSP, explained that a pilot is underway in NHS Greater Glasgow and Clyde for the new PACS system. However, there has been limited information about how the pilot is taking place, how long it will be operating for or what it will be assessing. It is critical that details of the pilot, including how its success is being measured, are made public and a definite date for implementation is given and adhered to.

Individual Patient Treatment Requests (IPTRs)

- 7.3 In the absence of the new Peer Approved Clinical System (PACS) across Scotland, patients and clinicians are still dependent on the existing IPTR system, which has been shown not to work for patients^{24,25}.
- 7.4 Although NHS boards do not include the word ‘exceptionality’ in their published documentation, IPTR applications require clinicians to demonstrate how their patient is different from the rest of the patient population and would have a greater benefit than is normally expected from the medicine²⁶.

- 7.5 Patients are still receiving different decisions depending upon where they live, with no predictable outcome for them or their clinicians. The guidance set out by the Chief Medical Officer to NHS boards that decisions should be based on clinical need²⁷ must be restated and mandated, to ensure equitable access to medicines across the country.
- 7.6 It is likely that some doctors are deterred from making IPTR applications on behalf of their patients, as they do not believe they would be successful. This risks masking the full extent of the problems with the system, and the true impact on patients, as applications that are not made will not appear in official statistics.
- 7.7 Scottish Government expects the changes to the SMC processes to reduce the number of patients who have to rely on IPTRs to access medicines²⁸. This would provide welcome certainty to patients and clinicians. However, data on the number of IPTRs approved, the number and impact of positive SMC recommendations, or the budgetary allocations from the New Medicines Fund used to pay for them have not been published and so it is impossible to assess whether this is the case.
8. *Are there further opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines?*
- 8.1 Currently, the SMC reviews new medicines at the time they are launched. Scotland is in the beneficial position of being one of the first countries to have access to new medicines. The cost-effectiveness of medicines at this early stage is still in the process of being evaluated. Many nations evaluate medicines for up to a year before making a decision as to whether the medicine will be reimbursed. Making an early funding decision at this point, before medicines' cost-effectiveness have been fully evaluated, will often mean that companies have a reduced ability to be flexible on price.
- 8.2 In order to overcome these constraints, a preferential approach would be for SMC to exercise flexibility and issue an interim 'conditional' positive decision while additional data are collected on the medicine in real world use. This would provide patients with the benefits of access to the medicines while additional information about the impact of the medicine is gathered to inform a fuller decision.
- 8.3 Another approach, which would delay access for patients in Scotland, could be to postpone the review of the medicine in Scotland while additional data were generated elsewhere to enable SMC to conduct one review with more information. This approach would mean that patients in Scotland would not be able to benefit from the medicine during this period and would effectively mean that medicines became available in Scotland later than elsewhere in the world.
9. *How should the SMC process be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting pharmaceutical companies' best offering on price earlier?*
- 9.1 Roche would welcome opportunities for some flexibility in the SMC decision-making process, which may include a pause, where this enables further discussions between the manufacturer and the SMC which may lead to a positive final appraisal. To our knowledge such a pause has not been used. It is critical that such a pause does not have a detrimental impact on patients.

- 9.2 For example, it will be important to ensure that pauses could not become indefinite. One of the relative strengths of the SMC process over many other HTA processes is the timeliness of its decision-making process. A pause in the process must not undermine this timeliness as this would increase uncertainty for patients, clinicians and manufacturers.
- 9.3 It is important that discussions during a pause are not simply about the price of the medicine. Instead this should be an opportunity to consider the wider potential benefit of the medicine, such as unmet clinical need and societal value. This would also be an opportunity to consider where else the medicine has been reimbursed and therefore the impact of the medicine on improving the standard of care in Scotland. The pause cannot simply be a delay until the narrow cost per QALY thresholds are met.
- 9.4 Rather than simply a pause, the SMC could instead issue an interim 'conditional' positive decision. This could be more beneficial to patients than a pause as it would enable them to access the medicine while further data were collected, such as real world evidence of the impact when the medicine is more widely used. This would then inform a more complete assessment of the medicine based on wider criteria beyond the current narrow cost per QALY assessment.
- 9.5 In addition, in the future, interim decisions may also be required as medicines licensing moves towards earlier access and licensing authorities rely on small datasets of evidence supporting clinical benefit and safety. These would not normally be sufficient for a health technology assessment. An interim decision would enable patients to access the medicine in line with the licence while further real world data were collected to support further assessment.
- 9.6 It should now be possible for the SMC to consider Patient Access Schemes (PASs) put forward by manufacturers appropriate to each indication, given the comprehensive datasets available on the use of cancer medicines within NHS Scotland. It is important that this opportunity is maximised as it would offer value for the NHS and provide access to all patients who could benefit from different licensed indications of a medicine. We would urge NHS Scotland to work towards comparable datasets across all diseases.

10 Have there been unintended consequences of the new approach, the potential of which was noted by the Task and Finish Group Report?

- 10.1 The Task and Finish Group suggested that an unintended consequence of the new appraisal process would be to reduce the incentive for companies to offer patient access schemes to the SMC. Roche is not aware of any circumstances where this has been the case, indeed, companies continue to actively offer patient access schemes.
- 10.2 Other concerns about 'gaming' the system have also proved unfounded. For example, there were concerns that the PACE process could be used to try to drive higher prices. A Roche medicine for the treatment of chronic lymphocytic leukaemia (CLL) would have qualified for the PACE process but we made a submission as normal without changes to the price.
- 10.3 We are concerned that there appears to be a lack of consistency in decisions following the changes to SMC processes, which is making the outcomes of assessments less predictable. This inconsistency is highlighted by the wide range of cost per QALY assessments for medicines which have not been recommended. An unintended consequence of this

unpredictability is that companies are deterred from making re-submissions to the SMC. In the absence of information about the reasons for the initial refusal and without clear parameters within which the medicine would be recommended for use, companies are unable to prepare a robust re-submission.

- 10.4 Whilst Roche recognises the SMC's commitment to transparency, there has been an unintended consequence of the moves to meet in public. As has been noted above in our response to question five, whilst the meetings themselves are held in public, the Committee votes on assessments in private. This reduces the scrutiny of that final decision and what impact changes such as the PACE process have had on the outcome.
- 10.5 As is noted in our response to question one, the changes may have had a further unintended consequence of reducing the number of patients who benefit from a positive decision. Because there is a lack of transparency around the basis of decision-making, and no opportunity for dialogue or negotiation between a manufacturer and the SMC during the process, companies are having to identify sub-groups of patients for whom a positive recommendation might be achieved. This means that companies may make submissions based on a smaller patient population which may be more likely to be accepted by the SMC, but which ultimately means some patients who could clinically benefit are still missing out.
- 11 *How will the new approach accommodate advances in new medicines and a developing regulatory framework?*
- 11.1 Increased knowledge about human genetics is improving our understanding of how we treat and prevent illnesses. Across many diseases, not just cancer, the future of treatment will be more targeted; patient populations will become smaller and more stratified. It is critical that the SMC continues to evolve to reflect these changes to avoid negative impacts for patients.
- 11.2 The data required for a medicine to be licensed is changing, with both the European Medicines Agency and the Food and Drug Administration making efforts to speed up approvals, for example by using rolling information submissions and real world evidence rather than relying only on randomised control trials²⁹. As such, in the future the data required by the SMC for health technology assessment may be different to that required for licensing. This data gap will make it more difficult for the SMC to reach decisions, potentially exacerbating the gap between approval rates for newer and older medicines. This must not be allowed to happen. The SMC process must be under continual review to ensure that patients can get access to newly licensed medicines made available earlier through changes in regulatory processes.
- 11.3 Increasingly, targeted medicines will be used to prevent diseases as well as treatment. This will make collection of data even more difficult. For example, the SMC's usual measures of success such as progression free survival and overall survival will not be relevant for preventative treatments.
- 11.4 As highlighted above, the SMC could issue an interim recommendation for a medicine to be made available through the NHS while additional data on patients' outcomes are collected, so that the assessment is completed and final guidance issued after a defined period of time.
- 12 *Does the progress made to date provide a solid basis for developing further a Scottish Model of Value?*

- 12.1 Roche welcomes the Scottish Government's commitment to develop a Scottish Model of Value³⁰, and we are disappointed that work on this does not seem to be underway. The changes made to SMC processes are a small step in the right direction but more significant changes will be required to ensure that the system secures patients' access to medicines now and in the future.
- 12.2 A Scottish Model of Value needs to reflect what is important to the Scottish population. There needs to be an open debate with the Scottish people about what they value most from healthcare and medicines including the impact on the wider Scottish economy and society. This may mean asking the Scottish population what diseases and interventions are important to them, or highlighting diseases that have a higher prevalence and burden in Scotland compared to elsewhere (for example Multiple Sclerosis). It could also include an evaluation of the wider impact on research and development in Scotland, in building the science base, developing and spreading research capabilities and providing employment opportunities in Scotland.
- 12.3 Roche is keen to work in partnership with the SMC and the NHS to ensure patients can access the medicines they need, aiming to be flexible and innovative in our approach to reimbursement.
- 12.4 Given our experience of international HTA systems which aim to evaluate whether patients should gain access to specific new medicines, we believe there are a number of principles that a Scottish Model of Value could valuably incorporate:
- Providing patient access to medicines from licence so that the assessment process does not cause delays in access. The SMC already tries to issue guidance within three months of licence. The PACE process has added some delay and timeliness must not be lost in any new approach.
 - Assessing the benefit of a medicine should not only be based on a simple cost per QALY basis but also by considering wider benefits, such as societal value, unmet clinical need and the potential impact on the standard of care in Scotland compared to the other nations of the UK and the rest of Europe.
 - Ensuring that the data required for a wider assessment of medicines can be collected. This could be through the SMC either instigating a pause or issuing an interim positive decision. An interim decision may be the more beneficial for patients. This could provide opportunities for the collection of additional information, including real world evidence, to support the ongoing assessment of a medicine's value in the context of the wider benefits assessed in line with a Scottish Model of Value.
 - Recognition that medicines licensing is moving towards earlier access. The evidence used in earlier licensing will often rely on small datasets of evidence supporting clinical benefit and safety. These data may be insufficient for a health technology assessment. An interim positive decision would enable patients to access the medicine in line with the licence while further real world data were collected.
 - Providing flexibility around reimbursement mechanisms. The SMC already allows positive consideration of complex Patient Access Schemes (PASs), flexible definitions for end of life criteria and orphan and ultra-orphan medicines. The current approach is welcome and should be built upon as a strong foundation in a future system.

About Roche



Roche is a leading, innovation-driven pharmaceutical company, with particular expertise in oncology, virology and rheumatology. We are the leading manufacturer of cancer medicines with over 60% of our research in new or existing products relating to the treatment of cancer³¹. We are the single largest supplier of cancer medicines to NHS Scotland and have significant experience in the supply of specialist medicines to the NHS. Roche is the fifth largest investor in R&D globally and the largest in the pharmaceutical sector (\$8.9bn in 2014 (£6.2bn)) and is committed to ensure that this is translated into patient benefits.

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The Janssen division of the Johnson & Johnson family of companies welcomes the opportunity from Scottish Government and Dr Montgomery to respond to the call for evidence on the review of access to medicines 2016. Janssen are happy for this response to be published and attributed to us.

Introduction:

Johnson & Johnson is the largest healthcare company in the world and has a tradition of commitment to Scotland and the UK as a whole, being established here since 1927. Today, in Scotland, Johnson & Johnson has manufacturing sites in Inverness and Livingston, and research and development facilities in Inverness. Janssen are committed to delivering innovative medicines which make an important difference to the lives of patients.

Response to scope questions:

Question: How the agreed definitions of end of life, orphan and ultra orphan medicines are working in practice

Janssen is less certain of how the agreed definition of end of life works in practice. We have had a recent example of where the SMC agreed that our product met the end of life criteria, but were then told that a proportionality factor was taken into account by SMC : even though our product met end of life, the magnitude of benefit considering the life expectancy was not great enough for the end of life criteria to be relevant. This was not something that we were aware of, and we would appreciate further clarity around this.

Question: How the views from the PACE are taken into account in the decision making

Janssen believe that PACE submissions make a positive contribution to the SMC process and we would like to see the PACE outputs have a more formal input to the decision-making framework.

Recommendation: There would be value in a patient/clinician representative from the PACE meeting attending SMC committee meetings to present the PACE statement and/or to answer questions from the committee.

Question: How the acceptance rates for end of life, orphan and ultra orphan medicines have changed as a result of the new approach

Overall, trends for SMC approvals are increasing, although we note there have been occasions where the SMC decisions have not aligned to the PACE recommendations, where the wider value of the medicine was considered.

Question: How the transparency of SMC has improved and what further opportunities there are for patient and clinical engagement

Janssen welcome the opportunity for industry to attend the SMC meeting.

Recommendation: Janssen would like to see the manufacturers participate more fully in the SMC Committee meetings, not just to answer points of clarification, but to participate fully in the discussions. We would also be supportive of patient groups taking a more active role in the discussions and be allowed to present their own submissions. We would also support a patient/clinician representative from the PACE meeting attending SMC committee meetings to present the PACE statement and/or to answer questions from the committee.

Question: How the NHS Boards are implementing SMC decisions under the new approach, including utilisation of the New Medicines Fund.

Janssen has found the NHS boards review of SMC recommendations to be in the main, timely, if not always easy to access on the public websites.

Recommendation: A review by an organisation like NHS HIS on the adherence to the CMO guidance on this topic would be of value.

In relation to the New Medicines Fund, Janssen acknowledges and welcomes the Scottish Government's return of PPRS receipts to the New Medicines Fund, supporting access to new medicines, in stark contrast to England.

Recommendation: The process for accessing the fund seems opaque at NHS board level and some clarification of this may be helpful for both clinicians and patients.

Question: How the new approach has had an impact on IPTRs

It is our understanding that patients and their clinicians that have required access to our medicines through the IPTR process have largely been able to do so. However, not recommended SMC guidance appears to negate any opportunity to access medicines through the IPTR process, even if the company has re-submitted to SMC thus denying access to treatment during the SMC re-submission phase.

Recommendation: An updated CMO letter clarifying access to the new medicines fund for "in SMC process" medicines would be helpful to avoid inequity of access.

Question: Whether there are further opportunities to take a "once for Scotland" approach in ANY aspect of access to newly licensed medicines

There are opportunities and unintended consequences of implementing a "once for Scotland" approach.

The current structure of further assessment of SMC approved medicines by local ADTCs will be negated in a "once for Scotland" approach and Scotland could in effect develop a national formulary. A national formulary would lead to mandatory funding following SMC decisions. This "once for Scotland" approach would end unnecessary duplication of effort and an end to perceived post code prescribing.

Recommendation: Janssen would support a role for ABPI to work in partnership with the NHS to establish processes in the eventuality of a national formulary approach.

With regards to pricing, a 'once for Scotland' approach would mean no further immediate tendering processes for new medicines following a positive recommendation by SMC. Currently as new products enter the market, market forces drive down the price of medicines, a "once for Scotland"

approach would mean NHS Scotland would be unable to capitalise by re-tendering post SMC. Janssen would be unsupportive of this approach.

Question: How the SMC process should be adapted to include commercial negotiation with the aim of (1) Ensuring the best value for NHSS and (2) Getting to a pharma companies' best price earlier

Securing the best deal for new medicines is not just about reducing price, it can also be about reaching creative solutions that make a positive SMC decision possible. Therefore, this review should not be limited to SMC but must also include PASAG and should not only consider "best value" as a discount from list price. This approach fails to acknowledge the social value of medicines which is now key as health and social care come together across Scotland. To ensure a more holistic value assessment of medicines, the discussion must evolve beyond price.

Recommendation: New patient access scheme models must be pursued to support Scotland's "once for Scotland" vision. However, the infrastructure limitations at PASAG need to be addressed to ensure alignment with recent and future progress at SMC.

The majority of patient access schemes (PAS) approved in Scotland are simple discounts from list price, the sustainability of which is dependent on strict adherence to confidentiality. However, this simple PAS preference in Scotland has its limitations and prevents companies from proposing and implementing a range of innovative schemes which provide value for money to NHS Scotland. The number and proportion of specialised products, many in small patient populations is increasing as is the number of products with multiple indications, presenting new challenges for SMC and PASAG.

Recommendation: Other countries use many different processes to secure the best deal on medicines pricing. Janssen would encourage Scottish Government to widen the scope of PASAG to consider alternative financial arrangements for medicines which are used routinely across the globe, and determine whether any of these arrangements could be implemented in NHS Scotland; ensuring systems are in place so that the best value is achieved first time and the need for time-consuming resubmissions to the SMC is avoided. We accept that there is a duty to ensure that money is used wisely and we would therefore suggest that this duty should extend to include a formal review and learning from other countries who also face this situation and who manage to deliver world standard access to innovative medicines within fixed budgets.

To ensure best value Janssen supports an early dialogue process process for pre SMC submission with the key stakeholders: SMC, PASAG, clinical experts, patient groups and the submitting company to establish:

- A more strategic mind-set around pricing of new medicines that focuses on improving patient outcomes as well as seeking to address perceived affordability issues
- Recognition of the need for mechanisms that reflect different levels of value across different indications
- Further infrastructure development and data collection systems that reduce administrative burden across the NHS and capture outcomes and support the true value of medicines.

- Patient group and clinical expert input early in the process, to advise and inform the submissions appropriately
- Decision-making frameworks that accept real-world data

Question: Whether there are any unintended consequences of any aspect of the new approach

We note that there have been medicines that have been approved by the SMC that have been rejected by NICE and Janssen feels that this is a positive endorsement of the changes made in the SMC process. To ensure world leading fit for the future HTA landscape, SMC must continue to evolve in such a positive manner. This continued evolution will support Scotland's ambition towards trade and investment.

The review of SMC in 2013 focused solely on the SMC process. By implementing the recommendations, the SMC process has evolved; however, other parts of the associated HTA system have remained static, namely PASAG. By not reforming both organisations in tandem, a disconnect has been created which has impacted the ability of SMC to say yes (on occasion) to some medicines because of the PAS approach taken by the company.

Recommendation: There is a need for PASAG to be resourced appropriately and given the authority by Scottish Government and the NHS Boards to consider the full range of finance and outcome based schemes in the same pragmatic manner as they currently review simple discount schemes; only then will Scotland's ability to achieve best value for new medicines be significantly improved and supportive of further reform of SMC.

Question: How the new approach will accommodate advances in new medicines and a developing regulatory framework

The SMC reforms from 2013 have been a welcome first step in accommodating advances in medicines, however, in order to stay ahead in the Global HTA stakes and to accommodate the changing pharmaceutical environment, more needs to be done. Specifically, the level of evidence required for license differs greatly from the evidence required for SMC approval. It is clear that the science that underpins new medicines is revealing much more over time about the molecular basis of ill health and the regulators have picked up on this, which has had an impact on the evidence that SMC receives. Highly specialised, targeted medicines for smaller patient populations are now becoming the norm. Regulatory bodies such as the FDA and EMA now recognize that in areas of high unmet need (e.g. metastatic cancer); approval is granted based upon what HTA bodies would traditionally view as an immature or limited evidence base, such as Phase II, single-arm trial data. SMC tends to prefer the highest level of evidence when considering all new treatments, that is, head-to-head, Phase III randomised, double-blinded, controlled trials against the relevant comparator in Scotland. Janssen believes that a fundamental mindset shift on behalf of the SMC is required in order for SMC to evaluate innovative medicines in the context of the evolving regulatory system. -

Question: Whether the progress made to date provides a solid base for developing further a Scottish Model of Value.

The planned scope for a Scottish Model of Value has not been shared with industry but it is clear that for Scotland to remain at the forefront of global HTA there needs to be recognition of the

changing pharmaceutical environment. In some context there has been progress to a wider assessment of value for medicines at the end of life and for rare diseases, with SMC introducing modifiers, PAS and PACE which been shown to be associated with an increasing share of positive SMC decisions over time. However, even with a wider assessment of value, issues around uncertainty still creates problems.

Recommendation: Janssen would ask that the system evolves to cope with uncertainty and is flexible to the needs of future innovation in the medicines environment.

Concluding Comments

Janssen would like to extend our gratitude to Dr Montgomery for the immense time and effort which has been undertaken to review the process for accessing new medicines and hope our comments are found to be helpful and constructive.

For Pharmaceutical & health economic related questions:

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- 07775 551 962

For General questions:

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Re: Review of Access to New Medicines

Prostate Cancer UK welcomes the opportunity to submit evidence to Dr Brian Montgomery, as part of his independent review of Access to New Medicines for the Scottish Government.

Prostate Cancer UK is the leading charity for men with prostate cancer. We fight to help more men survive and enjoy a better quality of life. We support men and provide vital information. We find answers by funding research. And we lead change, raising awareness and improving care. We believe that men deserve better.

Prostate cancer is the most common cancer in men in Scotland, and by 2030 is predicted to be the most common cancer overall. More than 3,000 men are diagnosed with prostate cancer every year in Scotland, and over 21,000 men are currently living with and after the disease. 880 men die of prostate cancer every year in Scotland – that's two men each day¹.

We are committed to delivering positive change for men in Scotland, in line with our new strategy: [‘Ten Years to Tame Prostate Cancer.’](#) To tame prostate cancer we will focus our attention on four priority areas: better diagnosis, better treatment, better prevention and better support. Ensuring that men have access to the latest, clinically-effective medicines in Scotland is fundamental to achieving our goal for better treatment.

Improvements in the approval process since the initial Health & Sport Committee review

Since the Health & Sport Committee inquiry on Access to New Medicines in 2013, there have been a number of positive developments, which have incorporated recommendations previously submitted by Prostate Cancer UK and other patient groups.

The Scottish Medicines Consortium (SMC) now provides more opportunities for patient and public involvement when assessing new medicines and technologies. Key improvements in this area include:

- Additional resources provided to facilitate patient and public involvement - the work of the Patient and Public Involvement Team and the introduction of the Public Involvement Network (PIN) advisory group should be commended.
- The introduction of the Patient and Clinician Engagement (PACE) process for rare and end-of-life medicines have allowed further consideration of the value of a treatment to patients, which may not otherwise be captured in traditional measures of cost and clinical-effectiveness. In most cases, PACE has increased the perception amongst patient groups of being “listened-to” in the SMC process.
- The distribution of SMC decisions prior to publication under embargo has greatly assisted patient groups in preparing communications to patients on the implications of the announcement.

There have also been a number of improvements in terms of the transparency of the SMC process, which have been vital in terms of increasing understanding of the work of the SMC amongst patient groups and most importantly, among patients. In addition to better involvement of the patient and public voice by holding committee meetings in public has been a welcome development.

Furthermore, industry's ability to be at the SMC committee meetings and to answer questions has assisted decision-making.

Further recommendations

Further improvement to SMC processes: Patient and clinician engagement

There has undoubtedly been much improvement in patient and clinician engagement in the SMC drug appraisal process; however there are still some areas for further development.

On two occasions, end-of-life prostate cancer drugs were not recommended by the SMC, following a PACE process. The formal advice was unclear about why the treatments had been rejected and did not seem to reflect what was said by participants at the PACE and committee meetings. In these instances, the manufacturers of the drugs met with the SMC to discuss the decision, but remained unclear about why the treatment had been rejected or what to do next. In both instances, the drug was taken to an Independent Review Panel, with exactly the same evidence used for the initial appraisal, and was subsequently approved.

Observers of the public committee meetings noted that queries raised about aspects of the evidence given at the PACE meeting could not be addressed with those able to respond at the committee meeting. We believe the absence of a first-hand patient or clinician voice at this stage limited the clarity of evidence needed for the positive decision which we then saw from the Independent Panel Review.

In order to address this issue, and to allow better engagement with patients and clinicians, we recommend that expert clinicians from the PACE meeting are represented in the room at SMC committee meeting stage and allowed to offer clarity to queries that may arise.

We also recommend that patient groups, or patients, are offered the opportunity to read out their own PACE submission and respond to queries, should they wish to. Alternatively, patient groups could have greater engagement with the SMC Public Partner who will be reading out the PACE submission on their behalf, to ensure that they have a thorough understanding of the submission and potential questions.

Further improvement to patient access: Make SMC decisions binding

Currently, when a drug is recommended by the SMC, this recommendation goes to each local Health Board's Area Drugs and Therapeutics Committee (ADTC) to determine whether or not it will be routinely available in their area. This process means that there can be variation in patient access to new drugs depending on where they live.

With the latest electoral polls indicating the likelihood of the Scottish National Party (SNP) remaining the party of government in Scotland, it is also worth noting the reference to new medicines and the possible introduction of a new single national formulary in the SNP manifesto:

"New medicines are now more readily available and we will continue to review the appraisal system, to ensure quick, safe and effective access to drugs. We will introduce the option of a pause in the medicines appraisal process to allow for negotiation and potentially avoid the need for reapplication. A new single national formulary – guidance on drug prescribing – will also be introduced to ensure quick and equitable access to new medicines." (SNP election manifesto 2016, 'The Next Steps to a Better Scotland' p3)

This new single national formulary can only work effectively if the recommendations made by the SMC are binding and any failure to achieve this has the potential to prevent the ambition of quick and equitable access to new medicines ever being a reality.

We therefore strongly recommend that SMC-approved decisions should be binding on local Health Board ADTCs, or indeed for a national formulary, to ensure that clinicians can choose to prescribe the treatment for their patient no matter where they live in Scotland.

Further improvement to patient access: National guidance for use of Individual Patient Treatment Requests (IPTRs)

The Peer Approved Clinical System (PACS) - which was intended to replace the IPTRs - is not in place across Scotland. Whilst we are not aware that the absence of PACS is negatively impacting on patient access, in the interests of transparency, the Scottish Government should publicly explain it has not implemented its plans for IPTR reform.

When SMC does not recommend for a new treatment to enter baseline commissioning, the only option available to patients for whom this treatment could be critical is to apply for funding via an Individual Patient Treatment Request (IPTR). An IPTR must be completed by the clinician responsible for the patient for whom the medicine is being sought.ⁱⁱ

While we view IPTRs as a good option for men to access new medicines which have been licensed, but not yet considered or not made available by the SMC, we question the subjectivity with which each request is assessed and the associated bureaucracy that can result in access to new medicines being granted in some areas of Scotland but not in others.

As the IPTR process remains in place across Scotland, it is still operated locally by 14 ADTCs and there is no national guidance in place governing the process and making it fair and equitable. A full review needs to be undertaken on how this is operating, and national or regional network guidance should be put in place to ensure there isn't variation in access.

Evaluation frameworks for continuous improvement, and sharing of information

While the improvements to the SMC processes have allowed patients and the public improved understanding of the system and allowed them to feel more involved, it is unclear whether patients are indeed benefitting from improved access to rare and end-of-life drugs as a result of these improvements, beyond anecdotal evidence and speculation.

We would therefore recommend that quantitative ways of measuring the impact that PACE has had for orphan and end-of-life medicines, as well as outlining the weighting that has been given to patient views in the decision-making process. This could also be applied to other modifiers used by the SMC.

The New Medicines Fund was created specifically to provide on-going funding to make access to orphan and end-of-life conditions easier. There is no information currently publicly available that indicates how this money is being used or what the money is being spent on. There would be value in the Scottish Government sharing how the New Medicines Fund has been used so far and the extent to which it has improved access to new medicines.

Preparation for advances in new medicines

Significant progress is being made in the research and development of stratified medicines with the pharmaceutical industry increasingly investing in this area. Science is increasingly moving towards personalised medicine and we have already witnessed the advances being made in stratified

cancer treatments. These treatments may need to be appraised alongside the personalisation technique, e.g. a genetic test, if it is not already in place. Also it could be difficult to determine the potential population size suitable for a personalised treatment. This is often because the data that determines the basis for personalisation is not routinely collected. There may also be limited treatment comparators. Current SMC processes may not be suited to appraising these types of treatments and should be reviewed to assess their suitability in advance of personalised treatments becoming more prolific.

We welcome the opportunity to input into this review and we look forward to working together in the future to achieve the best outcomes for men with prostate cancer in Scotland.

Yours faithfully,

Lauren Davies
Change Delivery Officer (Campaigns)
Prostate Cancer UK

ⁱ ISD Scotland. Prostate Cancer. Incidence by NHS Board Area of Residence, Scotland 2009-2013 [Internet]. 2015. Available from: https://isdscotland.scot.nhs.uk/Health-Topics/Cancer/Publications/2015-04-28/si_cancer_male_genital_organs.xls

ⁱⁱ http://www.sehd.scot.nhs.uk/mels/CEL2010_17.pdf

Cancer Research UK response to the Review of Access to New Medicines by Dr Brian Montgomery

April 2016

About Cancer Research UK

1. Cancer Research UK is the world's largest independent cancer charity dedicated to saving lives through research. We support research into all aspects of cancer: from exploratory biology to clinical trials, as well as epidemiological studies and prevention research. This is achieved through the work of 4,000 scientists, doctors and nurses.
2. In 2015/16, we spent over £31m on research in Scotland. We receive no Government funding for our research. However, Government investment is critical to partnering and supporting our investment in research in Scottish universities and in the NHS.
3. We work closely with over 20 other cancer charities in Scotland through the Scottish Cancer Coalition¹ (SCC) and we have collaborated on a joint position statement on access to cancer medicines².
4. We welcome the Scottish Government's commitment to improving access to new medicines delivering a new approach to assess end of life, orphan and ultra-orphan medicines, as outlined in the Task and Finish Group Report.
5. Below, we have provided recommendations on the key areas outlined in the scope of the review undertaken by Dr Montgomery:

- The Scottish Government should publish a progress update on the new system and how well it has met each objective of the changes, including expected timelines, patient access and processes for full implementation of the Peer Approved Clinical System (PACS). Within any progress update the Scottish Government should consider comparative analysis of patient access before and after the adoption of the new system.
- Future re-assessment of the definitions of end of life, orphan and ultra-orphan medicines needs to be considered as personalised medicine starts to be adopted across the NHS in Scotland. Furthermore, to accommodate these advances the new system needs continuous assessment and adjustment to match the fast-paced changing environment of drug development.
- The SMC should consider a mechanism for providing feedback to patient and clinical representatives after PACE, with details of how their evidence was used, and where this information could be published.
- Where possible clinicians involved in PACE should be present at the full meeting. This would provide an opportunity where any misinterpretation of their evidence could be clarified.
- The Scottish Government should implement a chemotherapy dataset which would provide outcomes data for all drugs.
- The Scottish Government should make SMC appraisal decisions binding on Health Boards, so these must be followed where a doctor judges that a patient should have an SMC-approved treatment.

¹ <http://www.scottishcancercoalition.org.uk/>

² Scottish Cancer Coalition Position Statement, *Scottish Cancer Coalition Position Statement: Scottish Medical Consortium* (2015) Unpublished.

- In line with the Scottish Government's recommendations, a robust auditing system should be implemented concurrently with the rollout of PACS.
- We welcome the introduction of the PACE process into the new system, however we would like to see more detail on how it affects decision making.
- Greater transparency about how the New Medicines Fund is being spent is needed. The Scottish Government should collect and publish data on actual expenditure from the New Medicines Fund, how it has been distributed across Scotland, its influence on access to medicines and impact on different disease areas.
- This would allow for data comparison across the UK, including the SACT data set in England.
- Area Drug and Therapeutic Committees (ADTCs) should clearly publish their formulary decisions and clear interpretation of SMC guidance on Health Board websites.
- The SMC should implement the proposed 'pause' and the extra time this process adds should clearly be communicated to patients.

How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice.

The Access to New Medicines definitions for end of life, orphan and ultra-orphan medicines are broad definitions which offer greater flexibility in this new system. However, at present we have no evidence to confirm that these new broader definitions are having a direct impact on outcomes. Furthermore, as we increasingly move towards a future where getting the right treatment for the right patient at the right time through personalised medicine becomes achievable, all cancer drugs will technically fall under the ultra-orphan category. As a result, future re-assessment of these definitions needs to be considered as personalised medicine starts to be adopted across the NHS in Scotland.

How the views from the Patient and Clinician Engagement process are taken into account in decision making.

The PACE process, in allowing patients and doctors to better articulate need, appears to have helped shift the balance in appraisals where uncertainty around cost-effectiveness means borderline decisions are now positive.

Some aspects of value can be captured via evidence submissions from patients and clinicians, who are experts in specific diseases and can provide information on quality of life and social impact. The new PACE process has clearly bolstered this for end of life and rare conditions. However the PACE approach does not explicitly demonstrate how submitted evidence from patients and clinicians affects the final decision. The SMC should consider a mechanism for providing feedback to patient and clinical representatives with details of how their evidence was used, and where this information could be published. In addition, where possible clinicians involved in PACE should be present at the full meeting. This would provide an opportunity where any misinterpretation of their evidence could be clarified.

How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach.

A considerably higher proportion of cancer drugs received positive decisions during the period from the end of April 2014 to the end of 2015, compared to the period between November 2012 and April

2014.³ As a result this will likely have helped more patients to have access to newer medicines that might not have received positive decisions under the old system.

How the transparency of SMC has improved and what opportunities there are for patient and clinician engagement.

In 2015 74 patient group representatives were supported to participate in the Patient and Clinician Engagement (PACE) system⁴. This increased focus on PACE in the SMC process as well as initiatives to increase transparency appears to have been very effective.

How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund.

At present, detailed data to indicate which drugs cancer patients are receiving based on incidence rates and existing SMC guidance is lacking. Greater transparency about how the New Medicines Fund is being spent is therefore needed.

The Scottish Government should implement a chemotherapy dataset which would provide outcomes data for all drugs, this would allow for bespoke analysis and broadly support a greater understanding of how well different cancer drugs are working for patients in clinical practice. Furthermore, the implementation of a chemotherapy dataset could allow for more complex submissions to be considered by the SMC.

The Scottish Government should consider the impact of making SMC appraisal decisions binding on Health Boards, so these must be followed where a doctor judges that a patient should have an SMC-approved treatment.

How the new approach has had an impact on access to medicines on an individual patient basis (through individual treatment requests and peer approved clinical system)

We have previously expressed concern that the exceptionality criteria within the Individual Patient Treatment Request (IPTR) system was too restrictive and limited the flexibility doctors had in choosing from a range of treatment options to help their most difficult-to-treat patients. The PACS approach is welcome as in principle it promises to increase this flexibility. However, it is important that the PACS route is used to support genuine need, and not as a mechanism to routinely override evidence-based guidance from SMC. It appears that the balance of spend on IPTRs compared to SMC approved medicines has not changed much under the new system and it's important it does tip more away from the need for IPTRs which lead to uncertainly and inevitable inconsistency in application.

In its response to the 2013 Health and Sport Committee inquiry into access to new medicines, the Scottish Government stated that it "is supportive of introducing robust auditing of NHS Board decision-making about SMC "not recommended" medicines under the new PACS system for individual patients or groups of patients through Healthcare Improvement Scotland and the results to be published in an anonymised way." We support this approach as it is important to better understand the circumstances in which individual requests are being fulfilled and in which diseases these might be important. In turn this should support the decision making of clinicians involved in the PACS process. A robust auditing system should be implemented concurrently with the rollout of PACS.

³ Internal CRUK analysis of SMC decisions for cancer drugs between November 2012 and December 2015

⁴ SMC – Public Involvement Team, End of Year Statistics Report, 2015

In addition, we are aware that an evaluation-based PACS pilot project is underway in Glasgow – the outcomes of this should be published to support decisions on wider rollout. This should provide some detail on the nature of requests in terms of the specific conditions being treated and the treatments being requested.

Whether there are further opportunities to take a ‘once for Scotland’ approach in any aspect of access to newly licensed medicines.

We would welcome opportunities to provide consistency across Scotland in terms of access to newly licensed medicines both for clinical adoption and patients, with the potential for efficiency gains. However wider consideration to a ‘once for Scotland’ approach and its possible impact needs to be undertaken with all relevant stakeholders.

How the SMC process should be adapted to include commercial negotiation with the aim of:

- 1) Ensuring best value for the NHS and 2) getting to a pharmaceutical companies’ best offering on price earlier.**

The SMC should consider earlier negotiations with pharmaceutical companies, working in partnership to agree drug prices that can provide sustainable access to patients while making effective use of limited NHS budgets.

Clearer indications from the SMC earlier in negotiations would allow pharmaceutical companies to consider their submissions on an on-going basis, thus freeing up SMC appraisal channels and allowing for a more productive appraisal process with the overall benefit of improving access. Finally the SMC should be open to more complex schemes and outcome based models.

Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report.

The inclusion of the PACE meeting in the new Access to New Medicines process may have affected attitudes to the resulting decisions, by providing a platform upon which patients and clinicians can make their voice heard. The additional PAS point may have encouraged pricing flexibility from the pharmaceutical industry however due to the confidential nature of those details this is difficult to confirm⁵

How the new approach will accommodate advances in new medicines and a developing regulatory framework

The new approach has the potential to accommodate advances in new medicines however this potential can only be realised with continuous assessment and adjustment to the fast-paced changing environment of drug development. As we move towards more personalised medicines, caring for smaller populations, and utilising new treatment approaches such as immunotherapies the new system needs to be adaptive.

Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value.

⁵ Morrell, L (2016) *Evaluation of the Impact of Scotland’s End-of-Life, Orphan, and Ultra-Orphan Criteria on Funding Decisions*, Unpublished.

Greater patient and clinical input through PACE has certainly added to the value judgement about medicine and provides a better basis, however it remains unclear how this evidence impacts decisions. Therefore, although we welcome the introduction of the PACE process into the new system we would like to see more detail on how it affects decision making.

The effectiveness of any monitoring of the NHS boards Area drug and Therapeutic Committees including the transparency of their operations and their timeliness in publishing local responses to SMC's published advice

ADTC processes are not always clear. They often publish relevant information, for example minutes from meetings and their structures via Health Board websites, though these can be difficult to find.¹ However, where decisions are made on local interpretation of SMC guidance – particularly if there is a gap in the SMC's recommendations (e.g. use of a drug is supported at a certain stage, but there is no recommendation for or against using at a different stage) and local advice is given – it is often not clear where these are published. This makes it difficult to understand whether there is consistency across Health Boards on which drugs patients are being offered. ADTCs should clearly publish their formulary decisions and clear interpretation of SMC guidance on Health Board websites.

The effectiveness of the 'pause' mechanism in the SMC process and whether this mechanism has resulted in greater access to and improved the cost-effectiveness of new medicines

The pause process is not yet in place. We are supportive of the SMC introducing a temporary pause in the process to allow further conversation between the SMC and manufacturer around ways to make the treatment in question affordable to the NHS in Scotland.

Alongside this it should be made clear to patients that the added time would lengthen the appraisal process as a result of the pause, and the resultant implications for access to medicines.

As a member of the ABPI, Bristol-Myers Squibb has noted the draft ABPI response to this inquiry and broadly supports its comments. We would like to supplement the ABPI response with additional points from a company perspective and have been advised that we will have the opportunity to submit further comments following a meeting with Dr Montgomery in May.

Review of Access to New Medicines – Written response from Bristol-Myers Squibb

How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice

Bristol-Myers Squibb supports the current definitions as used by the SMC.

How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement;

We believe that transparency across the health system is critical in ensuring optimal access for patients in Scotland and welcome improvements in the system to make the SMC more transparent.

Greater engagement with the pharmaceutical industry and expanding its role in the process from clarification of points to becoming active participants would further enable it to be more transparent and facilitate a greater understanding across all participants.

Increased transparency around processes, in particular, how input from patients and clinicians is weighted in the overall decision making process and SMC voting would also improve understanding. We also suggest that having the clinical experts at the SMC meeting to answer questions would increase their engagement in the process. Finally, we would also welcome greater transparency over appointments to PACE committees and PACS.

How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund

It is not currently possible for us to make a full assessment of the implementation of SMC decisions and access to medicines at board level, we would hope to see data made consistently and transparently available in a format that patients, clinicians and other members of the health community could fully understand. If this data was regularly made available then equity of access can be better achieved, standards can be established and measured at a national level and we would see greater accountability at board-level.

Scotland has set an example to the rest of the UK by explicitly dedicating money received through the Pharmaceutical Price Regulation Scheme (PPRS) to improving access to medicines through the New Medicines Fund. We would like to highlight the potential difficulty for it to be used transformationally when its current use is primarily restricted to providing access for a single medicine for Cystic Fibrosis. We hope that greater transparency and communication around how to access the fund will facilitate a wider and fairer use of the resource.

How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system)

We do not think that the new approach has had a significant impact upon the reliance upon IPTRs or a positive impact on access following the creation of PACS. Given that the PACS has only recently been implemented we hope that it will play a key role in improving patient

access alongside greater transparency, accessibility and consistency, but are yet to see the desired results.

Whether there are further opportunities to take a ‘once for Scotland’ approach in any aspect of access to newly licensed medicines;

We believe that a single value assessment by SMC is the most robust and equitable method by which patients in Scotland can equally access medicines.

Although mandatory funding for all SMC- approved medicines without additional assessment by health boards would be a positive step to ensure that patients in Scotland receive medicines consistently and without delay we believe there is additional opportunity for Scotland.

Access at the point of licensing for end of life medicines and prompt automatic formulary listing following an SMC recommendation would ensure rapid access for new and innovative treatments.

How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies’ best offering on price earlier

We would echo the concerns of the ABPI around the inclusion of an additional formal step in the SMC process which could act to delay further access to medicines for patients in Scotland.

We believe that for the process to be best equipped for the assessment of new and innovative therapies, particularly the increasing number of immuno-oncology treatments, it must be more pragmatic and flexible in its approach to commercial access arrangements. This will facilitate timely access to a class of medicines which can may deliver long-term survival for some patients across multiple indications.

We have previously stated our support for pilot schemes which have looked at commercial access arrangements including flexible multi-indication pricing. We hope that PASAG will receive the financial and administrative support it needs to ensure that it has the capacity to implement these more pragmatic arrangements enabling it to respond to current and future innovation for the benefit of patients in Scotland.

Bristol-Myers Squibb is committed to ensuring that patients in Scotland are given access to the innovative medicines that are of most value to them and would welcome the opportunity to work with the ABPI, PASAG and NHS boards to develop the processes that combine a robust value assessment with timely and agile commercial arrangements.

How the new approach will accommodate advances in new medicines and a developing regulatory framework

We welcome the SMC’s focus on ensuring that its approach is compatible with the external environment but agree with the ABPI that to ensure that Scotland and the SMC remains at the cutting edge of new medicines introduction some evolution should take place.

Significant “bottle necks” in the process which inevitably result in delayed access for patients in Scotland could be overcome through a combination of enhanced horizon scanning making use of Pharmscan more and increased resourcing for NDC, SMC and PASAG. In addition, to relieving the already high work load this could allow consideration of more pragmatic

commercial arrangements. Greater understanding around the scope and weight attached to the PACE process in combination with greater transparency and engagement with all stakeholders will allow the SMC to anticipate and adapt to the treatment options available to patients in Scotland.

Bristol-Myers Squibb has always regarded the SMC as a body that provides high quality, timely advice. We are concerned, however, that the current process runs the risk of lagging behind other countries such as England where processes have evolved to facilitate patient access to cancer medicines from the point of marketing authorisation and final guidance within 90 days of Market Authorisation.

Bristol-Myers Squibb

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Review of Access to New Medicines 2016

Consultation response

**From Karen Facey, PhD, Evidence Based Health Policy Consultant
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29 April 2016

Respondent's perspective

Although this review focuses on engaging those who have been involved the SMC's "new approach", I hope that these reflections from the founding Chief Executive of the Health Technology Board for Scotland that supported the establishment of the SMC will be of interest. I now provide the perspective of an independent consultant who has been engaged in activities relating to assessment of health interventions from academic and policy perspectives, in Scotland, and internationally, for the past 16 years. In particular I will draw on insights from the world of Health Technology Assessment (HTA), of which medicine's assessment is one part.

Consultation responses

- *How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice*

The definitions of end of life, orphan and ultra-orphan are different to those used in other HTA and regulatory settings, but this doesn't seem to have caused a problem. Most important is to have transparency and consistency. All stakeholders seem to agree that the SMC processes are clear, that published guidance on the web is helpful and that SMC staff are always helpful and willing to clarify issues.

- *How the views from the Patient and Clinician Engagement (PACE) process are taken into account in decision making*

Internationally, there is much interest in the PACE process as a unique way of gathering input from key stakeholders that actually seems to be influencing appraisal decisions. Such a process is particularly important for SMC as it does not have disease specific experts (clinicians or patients) at the SMC table. Some patient groups have recognised the value of working together with clinicians and that the combined perspectives of both stakeholder groups can be more valuable. The joint written statement appears to work well, particularly now that it is presented at the start of the meeting to provide context.

- *How the new approach to assessment of ultra-orphan medicines is operating in practice*

There have only been a relatively small number of ultra-orphan assessments and more work is needed on this assessment process. It is stated that a different assessment approach is used taking into account impacts other than clinical and cost effectiveness based on the framework developed by NICE for their Highly Specialised Technologies (HST) programme including:

1. nature of condition
2. impact of condition
3. value for money
4. patient and clinician engagement
5. impact beyond direct health services and on specialist services
6. costs to NHS and personal social services.

This is a poor framework as it mixes up different things and areas that overlap. Items 3, 5 and 6 relate to economics and could be captured in good economic model.

Items 1 and 2 are fine – but further guidance is needed on what considerations are relevant here. More must be done to identify the unique aspects of ultra-rare diseases - the impacts for children, for families; the lack of specialists, the heterogeneity of disease, the challenges of study, the burden of current treatment (or lack of it) etc.

Item 4 is not a criteria, it is a mechanism by which one could elucidate some of the issues.

Important aspects are missing which are absolutely critical in very rare disease – what are the ethical and organisational issues,

Further must be done to consider how the wider impacts of an ultra-orphan should be assessed taking account of the fact that evidence will be more limited, so wider stakeholder involvement and academic consideration of the ethical and philosophical issues underpinning access to high cost medicines for very rare diseases is needed. NICE is considering its next steps with the HST programme and collaboration with them would be useful.

Furthermore as Member States enact their Rare Disease Plans and expert networks are established, consideration should be given to European collaboration to ensure that pricing strategies for these products are reasonable and to consider whether a European assessment could be appropriate for ultra-orphan products.

- *How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach*

SMC has provided these figures and internationally there is interest to see the acceptance rate move from below 50% to over 70%.

- *How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement*

Transparency

Holding meetings in public has been seen as a very positive step. They are well organised and help stakeholders to understand the deliberative process.

A major issue that continues to limit the transparency of SMC decision making, is the lack of a section in the SMC DAD outlining the consideration of the evidence. NICE has a long section in their reports about this and a table of how evidence was considered. This would be too cumbersome for SMC, but it would be possible for an NDC member to take a note of the key areas of deliberative discussion at the SMC table and note them down in a paragraph at the end of the document.

PACE opportunities

I have been commissioned to co-edit a new book about patient involvement in HTA, which is promoting debate on the underpinning philosophies, purposes and methodologies for patient involvement in HTA. This could provide important insights to future developments. The book highlights that when HTA was developed 40 years ago it was intended to assess the wider impacts of the use of a health technology (medicine) and that this should systematically include considerations of issues relating to patients and their families/carers. However, in the past 15 years HTA has needed to be a rapid assessment and has focused on clinical and cost effectiveness. So the question has always been how do we perform a rapid review that is fair, consistent and transparent?

In relation to patient involvement, it is important to be clear about the purpose of patient involvement and to consider appropriate mechanisms to support effective involvement. Leading on from that, there is interesting new research emerging, which shows that patient input (and clinical input) has most value where there is decision uncertainty, i.e. when there is uncertainty in the evidence of clinical and cost effectiveness. Patient (and clinical) input can help set the context of the burden of illness and current treatments and it can help explain the real added value of a new medicine by interpretation of what the effects of a studied scale really mean.

So following on from this, the question is, does PACE allow the right questions to be asked to resolve decision uncertainty. Some of these questions are clear after the draft DAD is available, when the PACE meeting is triggered, but are these questions explicitly addressed in the PACE meeting given the standard PACE submission statement that is used? Furthermore, how are the uncertainties that are raised in the deliberative discussion at the SMC meeting handled? Would it be of value to have a few of those who participated at the PACE meeting, present at the SMC committee table?

- *How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund*

As has been seen in England with the Cancer Drugs Fund, there needs to be a clear process for the use of special funds. It would be interesting to see if the new processes that have just come into place for the Cancer Drugs Fund could be applied to the New Medicines Fund to support evaluation of products that SMC does not recommend.

<https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/cancer-drugs-fund>

- *How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system)*

There is a lack of clarity about the Peer Approved Clinical System (PACS). A few health board websites mention that a new process is being developed to replace Individual Patient Treatment Requests, but indicate that PACS guidance is awaited from Scottish Government. It is disappointing that there has been such slow progress on this major issue.

- *Whether there are further opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines*

For ultra-orphans a once for Scotland (or once for Europe) approach would seem sensible.

- *How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier;*

Internationally over the past two years, there has been much more open interdisciplinary discussion about issues of pharmaceutical pricing both nationally and regarding implications for reference pricing across Europe, as shown by this recent EC report:

<http://www.raps.org/Regulatory-Focus/News/2016/02/25/24409/European-Drug-Prices-New-Commission-Report-on-What-Policies-Work-and-What-Could-Work/>

It is essential that Scotland is involved in these debates.

More open discussion with companies about the veracity of assumptions in economic models could aid pricing (and PAS discount discussions). Agreement on the most realistic assumptions in the economic model would help signal in advance of SMC what the most likely cost/QALY was and if this was seen to be higher than the usual willingness to pay in that circumstance, the company may offer a discounted price earlier. This would need some more time for NDC to do its work and negotiate with the company, but this could save time later and avoid resubmissions.

Internationally there is recognition that the emergence of new technologies such as immunotherapy, gene therapy etc will put a new strain on HTA processes. Currently there is an understanding that HTA bodies assess value for money and that budget impact does not impact the decision directly. The drugs for Hepatitis C have stressed this process and this will become much more challenging with the new therapies that are expected to achieve outstanding benefits (10-12 QALYs) and to be placed at very high price. Discussions are underway to consider very different pricing policies, such as via annuities. Scotland needs to be involved in these discussions.

Given Scotland's outstanding linked medical data, there is a real opportunity for Scotland to lead the way in innovative pricing mechanisms using a wider variety of Patient Access Schemes that are not just confidential discounts, but that are outcome based. Ensuring that only those who will benefit most from treatments are prescribed it, and that the treatment is discontinued if it stops working thus optimizing use of medicines in our health system. Furthermore, linking into collaborative work to collect post HTA data would be valuable, e.g. via the new evidence gathering initiatives in EUnetHTA Joint Action 3.

- *Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report;*

Requiring patient groups to provide submissions for the SMC and then for the PACE meeting and then to be involved in the PACE meeting requires more resources from these voluntary organisations. NICE provides patient organisations with some reimbursement for their submissions and travel expenses. This should be considered in Scotland.

It is welcomed that stakeholders have been involved more in the SMC process, but it is important to evaluate how that input is used in the SMC process to ensure that work continues with stakeholders to focus it on areas that will make a difference to decisions – so that stakeholder's processes can be as efficient as possible and their resources can be invested wisely. Furthermore it is essential that the DAD documents how stakeholder input has been considered alongside other evidence.

- *How the new approach will accommodate advances in new medicines and a developing regulatory framework;*

Important new processes are being developed to support adaptive pathways to medicine's development, including more flexible regulatory pathways in Europe and the USA. Collaborations that seek to pilot such approaches and to determine impacts on HTA are underway (see IMI Adapt SMART programme <http://adaptsmart.eu/>). Scotland should be involved in these important collaborations to discuss the implications of earlier regulatory approval and the more limited clinical data this will yield for HTA.

- *Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value.*

The new approach seems to be glossing over the limitations of evidence in the overview statement in the DAD and the public briefing. This means that we are not being clear about how we determine the added value of a new medicine and that we are doing this assessment to create a fair and transparent process to help us make difficult decisions about limited resources. We need to do more to discuss with the public the wider issues of resource limitations and be clear about our values and principles (e.g. Daniels and Sabin's Accountability for Reasonableness).

We should not be afraid to say the following things where they are relevant - that clinical evidence is poor, that we cannot extrapolate the highly controlled clinical trial evidence to the Scottish setting to show clinical effectiveness, that evidence from short term trials over a few months or years has been extrapolated to 20, 30 or 50 years using assumptions that we cannot validate, that we're not clear who will benefit most from this medicine, who we should treat, for how long, and when they should stop. We should also be clear about opportunity costs related to the specific disease area.

Then we need to be clear how issues such as severity of disease, unmet need, heterogeneity, burden of current treatments, carer burden, patient expectations etc modify our understanding of the evidence and determination of value i.e. we need to gather evidence about these things and explain how we consider them when evaluating traditional clinical and cost effectiveness.

Dr. Brian Montgomery Review of Access to New Medicines: written submission.

Merck has welcomed the changes to the Scottish Medicines Consortium's methodology for the assessment of end of life medicines, orphan medicines and ultra-orphan medicines. The introduction of new, flexible approaches was in direct response to a call from Patient Interest Groups for reform which would increase Scottish patients' access to effective new medicines.

A key element of the changes related to decision making for ultra-orphan medicines. The new process centres on an enhanced Patient and Clinician Engagement (PACE) process, in which specialist clinicians and Patient Interest Groups convene to assess the medicine according to explicit criteria including the nature of the condition and value for money. The PACE process gives patient groups and clinicians a stronger voice in SMC decision making. Whilst a cost-effectiveness ratio is still required in assessments of ultra-orphan drugs, the enhanced PACE process is an alternative to the approach currently taken by NICE when appraising end of life medicines in England, i.e. weighting the QALYs. In the absence of evidence to support the level of weighting that should be applied, SMC did not accept that QALY weighting could be supported. The over-reliance of NICE on this methodology is in sharp contrast. SMC's approach is welcomed and better recognises that the evidence base is by definition limited for ultra-orphan medicines. This is a pragmatic and patient centric approach to decision making that Merck would like to see adopted more broadly across the UK's HTA bodies.

Notwithstanding this, there is remaining opacity and uncertainty with the methodology, particularly for ultra-orphan medicines. A significant number of medicines appraised through the ultra-orphan process have not been recommended by the SMC. In most cases, the reason cited tends to relate to the SMC's assessment of value for money, which in turn is informed by a cost-effectiveness ratio. This implies that there is an ICER threshold beyond which SMC deem medicines not to offer value for money for the NHS in Scotland. Future assessments would benefit from a transparent discussion of the nature of this threshold. Merck do not agree that that rationale for decision making for ultra-orphan medicines should be based on the cost per QALY as these outcomes suggest is continuing to happen. For medicines where uncertainty is still too great to lead to a recommendation, there should be flexibility within the system to allow manufacturers to partner with stakeholders to reduce this uncertainty, through data collection or other means. Such an approach would permit conditional reimbursement of these important medicines but in parallel necessitates considerable effort across all sectors to enhance data collection mechanisms, registries and databases.

Additionally, the future of the Scottish Government's New Medicines Fund beyond 2016 is unclear. The flexibility and pragmatism of SMC's approach which delivers substantially improved access for patients to end of life, orphan and ultra-orphan medicines depends on the security of this fund.



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Independent review of access to new medicines

Response from Parkinson's UK

Introduction

Parkinson's UK warmly welcomes the opportunity to engage with this important independent review. Please publish this response in our name.

Medication is at the very heart of managing Parkinson's. Most of the 10,000 people in Scotland with Parkinson's take multiple medications several times a day to manage their symptoms, which typically affect every aspect of a person's life – including movement, mood, behaviour and cognition.

Parkinson's UK became involved in the SMC process for the first time in 2015. SMC last considered a medication for Parkinson's in 2009. We were involved in the decision around a treatment for advanced Parkinson's called duodopa. It was considered under the PACE (Patient and Clinician Engagement) process because it is defined as an ultra-orphan drug. Duodopa is indicated for use in a very small number of people with Parkinson's – between eight and ten people per year in Scotland, from a population of about 10,000 people. It is not thought of as an end of life treatment, but it is used in cases where all other active treatments have failed to work or are unsuitable.

None of the treatments currently available is disease-modifying. They can help to manage symptoms, but don't alter the underlying progress of the condition. Some of the most challenging symptoms are difficult to treat using current medications and have a profoundly negative impact on quality of life.

Our new research strategy is designed around speeding up the process of developing and licensing new medications to address these issues, and there are several promising new treatments currently in stage three trials. We also strongly support measures that make it easier to re-purpose medications that have been licensed for other indications when there is evidence that they can be used to treat Parkinson's. Accordingly, policy around access to new drugs and treatments will continue to be an important area for Parkinson's UK.

New processes for orphan, ultra-orphan and end of life drugs

In our experience the SMC's definition around ultra-orphan medication has been very helpful. Parkinson's is too prevalent to qualify as a rare condition in its own right, but it is very variable, and some treatments are only clinically appropriate for a very small proportion of people. It is appropriate that such treatments should be considered as orphan/ultra-orphan medicines.

Parkinson's UK is fully aware that we are moving to a future where stratified medicine will have a much greater role. We would expect this to lead to greater numbers of orphan and ultra-orphan applications.

The PACE system

Our experience of the PACE system was broadly positive, although the decision made by SMC did not accord with the recommendations of the PACE meeting.

Parkinson's UK believes that more action is needed to properly reflect both the experiences of patients and carers and the insights of specialist clinicians in SMC's deliberations. The opportunity afforded by PACE is welcome and valued progress on the previous system, but the process inevitably separates both patient and carer experience and condition-specific clinical expertise from the SMC's panel discussion.

Most panel members will not have clinical or personal experience of all the individual conditions and treatments under discussion, and it seems like a missed opportunity not to allow specialist clinicians and patient groups to participate in the SMC meeting itself. In our experience, a few points were raised in the SMC discussion that would usefully have been clarified in some cases by clinicians, and in others by those with specific expertise in working with people affected.

One way of addressing this deficit might be to enable a clinician and patient group from PACE to be invited to attend SMC as "expert witnesses" who can clarify points or answer questions from the panel. We believe that this is particularly important when discussing unusual conditions, or those where symptoms are not widely known or understood.

Strengthening the input of public, patient interest groups and patients and carers

Parkinson's UK believes that SMC public partners have a vital role in SMC's process, but we note that their current remit is very broad. In addition to providing an essential lay, public perspective on SMC's deliberations, they also must represent patient groups and the (separate) perspective of individual patients and carers.

This can be increasingly problematic when the discussion moves away from points that had been covered in the patient group submission or in the PACE meeting. If this happens, the SMC public partner is placed in the difficult position of trying to represent the experience of patients and carers without the insights that come from extensive contact with individuals and families affected by the specific condition under discussion.

Within NHS Scotland, there is increasing recognition of the importance of engaging with third sector organisations directly and also with people who use NHS and care services in order to improve and transform services. It is somewhat surprising, therefore, that there is no space in SMC meetings for either patient groups, or patients and carers themselves, to be directly represented. We note that manufacturers have a role within the meeting. We believe that a similar option may be made open to patient groups, subject to appropriate conflict of interest procedures. Many patient groups will have experience of representing the people with whom they work in front of Scottish and UK Parliamentary committees, with

NHS Boards and other public bodies, and have a good understanding of what is required.

Parkinson's UK would also welcome more flexibility about opportunities to present patient and carer experiences to SMC. For example, the use of photographs and video can be more direct and accurate than explanations in writing or read out by a third party. In particular, video recordings could enable the panel to hear directly from individual patients and carers about their experiences.

Transparency

In common with other patient groups, Parkinson's UK believes that SMC's processes are now more open and transparent than in the past, and we are particularly glad to have had the opportunity to attend SMC meetings and listen to the discussion. We recognise the reasons for taking votes in secret, but wonder whether it would be more transparent to publish the outcome of the votes alongside the decision.

It is somewhat frustrating that so much of the paperwork is redacted for reasons of commercial confidentiality. This presents some issues before and after the SMC meeting. When preparing a patient interest group submission, the brief is not to repeat information that has been presented elsewhere. Patient groups are placed in the position of trying to anticipate what the manufacturer may have said in its submission.

After a decision is made, the economic modelling remains confidential, this can make it very difficult to understand the rationale behind a decision. After the duodopa decision, Parkinson's UK had a very specific query about how social care costs were addressed in modelling in the light of the integration of NHS and social care. We were directed to the model used by SMC as an explanation – but as the modelling was not available to us, we were none the wiser. It certainly does not create the impression of a transparent process.

One of the helpful developments has been releasing embargoed results to patient interest groups five days before publication. We were able to brief our helpline and local advisors, as well as other staff and volunteers who work with people affected by Parkinson's, so that they were able to respond to questions on availability and the implications of the decision.

Getting it right for rare conditions

Parkinson's UK recognises the importance of evidence-based medicine, but we note that it is much more difficult to make the case for treatments relating to under-researched conditions when using peer reviewed research alone. When SMC discussed duodopa, there was a question about quality of life. There is a lack of published research about quality of life in advanced Parkinson's generally, but both the PACE meeting and materials and our patient group submission covered quality of life issues extensively. These materials were not referred to in relation to this question. Parkinson's UK is concerned that this may indicate that SMC's focus on peer reviewed evidence may disadvantage those with a condition where the peer reviewed evidence is limited.

We are concerned that this may mean that treatments for rare and under-researched conditions, as well as those where there is great diversity in the symptoms that people experience, will be less likely to be approved, leaving patients with these conditions less able to access new treatments. We would emphasise the importance of the Panel being able to access clinical expertise directly in these cases.

Implementing SMC decisions locally

In addition to being a core value of NHS Scotland, equity is extremely important to people. Accordingly, most people believe that if a medicine or treatment is accessible in one NHS Board, it ought to be available throughout Scotland, and that if SMC approves a medicine it should be available everywhere. Parkinson's UK is concerned that having individual Area Drug and Therapeutic Committees developing formularies for each NHS Board risks introducing inequity into the system.

Similarly, we are concerned that, where decisions on the outcomes of IPTRs (and latterly PACS) are taken by local NHS Boards there is considerable potential for geographical variations in the decisions that are taken. Indeed, we are aware of anecdotal evidence from other patient groups that some NHS Boards are more likely to reject applications for treatments rejected by SMC than others. We are not aware of any published evidence monitoring these trends, however.

We also note that until late March 2016, only NHS Greater Glasgow and Clyde has been piloting PACS in Scotland, although we note the Chief Pharmacist and Chief Medical Officer's letter of 21 March which indicates that all Boards are now expected to participate in the Stage 2 Pilot of PACS. Parkinson's UK is concerned that there is quite limited information available about how the new systems will work in practice, which is very important given that we may have a role in supporting individuals and families affected during and after the process.

Progress towards the Scottish model of value

Parkinson's UK does not believe that there is sufficient research to support a move to Scottish model of value. We believe that any moves towards value based pricing must be subject to widespread public debate, and very careful scrutiny to ensure that they do not embed additional problems.

For example, there is a high risk that burden of illness (BoI) and wider social impact (WSI) calculations could attribute less value to conditions that primarily affect older people, who are not economically active. They may also be biased in favour of terminal illnesses, and fail to reflect the devastating impact of living with a condition like Parkinson's that is long term, fluctuating, incurable and degenerative.

About Parkinson's

About 10,000 people in Scotland have Parkinson's. About one in ten of these people are classified by ISD as at high risk of hospital admission in the next year.

Parkinson's is a progressive, fluctuating neurological disorder, which affects all aspects of daily living including talking, walking, swallowing and writing. People with Parkinson's often find it hard to move freely. Their muscles can become stiff and sometimes they freeze suddenly when moving. There are also other issues such as tiredness, pain, depression, dementia, compulsive behaviours and continence

problems which can have a huge impact on peoples' day-to-day lives. The severity of symptoms can fluctuate, both from day to day and with rapid changes in functionality during the course of the day, including sudden 'freezing'.

About Parkinson's UK

For more information, please contact our Parliamentary and Campaigns Officer, Tanith Muller, email: tmuller@parkinsons.org.uk, telephone 0344 225 3726.

We're the Parkinson's charity that drives better care, treatments and quality of life. Together we can bring forward the day when no one fears Parkinson's.

Find out more about us at www.parkinsons.org.uk

Review of Access to New Medicines

Submission prepared by Dr Andrew Walker

Declaration of conflicts of interest

I worked closely with SMC between 2002 and 2014 as an economics reviewer and committee member. I now carry out consultancy work with pharmaceutical companies on health technology assessment, ranging from advising on which therapy areas, advising on the design of clinical studies, commenting on submissions to SMC and NICE, and more general commentary on the development of HTA. This work is carried out mainly through my own company, Salus Alba, but I still work for Glasgow University one day per week, and some consultancy work is carried out through the university.

Structure of my submission

The call for evidence issued by the Montgomery Review listed 12 bullet points for feedback. I have numbered them for ease of reference and then re-arranged them so my responses can build on each other and cross-refer.

I will not submit evidence on the following issues:

6. How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund
7. How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system)
8. Whether there are further opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines

Issues 6 and 7 are outside my competence and I am uncertain what issue 8 is referring to.

1. How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach (*issue 4 in the Call for Evidence*)

Since my submission to the Scottish Parliament Health and Sport Committee in January 2016 (can be downloaded from

<http://www.scottish.parliament.uk/parliamentarybusiness/CurrentCommittees/94656.aspx>) the overall pattern of decisions has not changed. However, an analysis of the guidance released by SMC in the first three months of 2016 helps highlight some issues.

- 22 pieces of guidance were issued – the range of medicines SMC deals with is striking, from ‘ultra orphan’ medicines such as eculizumab to new formulations of long-established medicines such as alendronic acid. In the focus on the former the review should not lose sight of the range and quality of work SMC undertake.
- 14 were full submissions, plus one independent review panel decision, and three were abbreviated submissions – despite this being below the peak working rate of SMC, I find amazement in other countries undertaking these assessments that SMC can sustain this workload to a high standard. This amazement only increases when they find the SMC’s resources are a fraction of those for national HTA agencies that SMC is commonly grouped with in forming international opinion on a new medicine.
- When a submission was available for review, 14 of 18 medicines were accepted, a rate of 78% so despite concerns and issues that may be raised in the review, the system is delivering an overall high and sustained rate of positive decisions.

However:

- Eleven of the medicines took the opportunity to use the PACE route, of which 6 were accepted (just over 50%). This may still fall short of expectations of PACE.
- Three of the medicines met the SMC definition of an ‘ultra orphan’ medicine and all were not recommended.
- Six of the PACE medicines were for cancer and four were accepted but all of these were resubmissions or the result of an independent review; the two new medicines were both not recommended. This is encouraging in that medicines initially rejected can be successfully resubmitted but there is a time ‘cost’ from 6-7 months in the best case to several years in more unusual cases.

This suggests PACE is generally working well, but there are still important issues.

2. How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice (*issue 2 in the Call for Evidence*)

The problem in saying whether the definitions are working in practice is that the intentions of those who initiated the review that led to the PACE changes is not completely clear. The initial petitions to Scottish Parliament were regarding access to medicines that would be classed as ‘ultra orphan’; this then joined with issues about the access to specific medicines for cancer, and it seems reasonable to suppose the intent of politicians in supporting the case for change at SMC was to improve access to these two categories.

The actual definitions adopted went beyond that, in several ways:

- The definition of an ‘ultra orphan’ disease was defined as less than 1 person per 50,000 population, which is around 106 patients or less in Scotland. However, PACE also included an additional category covering diseases that had been awarded the European Medicines

Agency designation of an 'orphan', one element of which is prevalence of less than 5 in 10,000, equivalent to roughly 2,600 patients in Scotland.

- On top of that, the PACE definitions also included situations where the EMA orphan definition was met in terms of patient numbers but the medicine had not been awarded orphan status by EMA for some other reason (the so-called 'orphan-equivalent' medicines).
- No account was taken of any other indication for the medicine when determining whether the indication under review should be classed as a rare disease. One of the arguments for special handling of medicines for rare diseases is that low patient numbers mean the price has to be high to cover costs, but this is not true to the same extent if the medicine has many indications.
- In calling for changes that led to PACE Scottish Parliament heard about issues with access to cancer medicines but did not believe cancer should be seen as a special case *in itself*. As a result, the concept of 'end of life' was used in PACE, defined as a situation where the patient was within three years of death with usual care. The danger is that medicines for incurable advanced disease have been given higher status in PACE than medicines that are potentially curative in earlier stages.

My impression is that in a genuine attempt to meet the wishes of Scottish Parliament PACE may have cast its definitions wider than were originally intended by those calling for change.

One consequence has been that submissions reviewed through PACE are very common: on a monthly SMC agenda where up to seven medicines can be reviewed (with full submissions) it is very common to have three PACE medicines and rare to see less than two. I estimate that in the time PACE has been in existence, SMC has issued guidance on 114 full submissions or resubmissions and of these 54 have used PACE (i.e. 47%).

There is an obvious practical problem in that it is not clear this level of additional work was foreseen or that SMC received resources to deliver it on a sustained basis. In terms of the impact on SMC decisions, the consequences are less direct but no less important. My interpretation of PACE was that it created a category for medicines that were different and where the 'normal rules' were not adequate which may suggest cases that were exceptional – the 'ultra orphan' at a cost of £250k per patient per year is an example. The advantage of specifying exceptional cases is that it allows the decision-makers to truly depart from their usual way of thinking with less concern this decision sets a precedent. However, when literally half the agenda is put in this 'special' category, these cases cease to be 'special', by definition, and become 'the norm'.

My suggestion for the review is that consideration is given to either restricting the definitions or possibly creating two tiers of PACE to identify cases that are true exceptions rather than meeting arbitrary definitions such as 5 in 10,000 population or less than 3 years of life expectancy. The quid pro quo would be that once these 'true exceptions' were identified, then SMC decision-making should respond by trying to find a way to accept these cases.

Of course this raises the question of what these special cases should be. I think it is clear Scottish Parliament intended that medicines for very rare diseases should be included, as they were the topic of the original petitions, and that access to medicines for diseases such as cancer should be included.

A case can be made for reviewing which medicines for diseases such as cancer should be included. For example, the current PACE definition is based on 'proximity-to-death' but can a case be made that the medicines we should be making exceptions are those where a cure might be possible or long-term survival is a realistic possibility?

In conclusion, the current definitions work in most cases. However, they are quite blunt and imprecise tools and this has the consequence that some categories such as UO medicines simply do not stand out. I suggest the review revisit the definitions used to weigh the balance between the current system with 47% of full submissions eligible for PACE and around 70% positive, with a trade-off for a smaller proportion qualifying for PACE but a higher proportion being accepted.

3. How the new approach to assessment of ultra-orphan medicines is operating in practice (*issue 3 in the request for comments*)

My comments under this heading build from those above and in my submission to the Health and Sport Committee of Scottish Parliament. To date, SMC has reviewed 15 medicines under the 'ultra orphan' (UO) category of which 9 have been accepted and 6 not recommended (60%). Universally, health care systems regard these as difficult medicines to deal with so that headline rate might be regarded as 'not bad'. However, there is a story underneath these aggregate data: as I have argued before, there are two reasonably distinct groups of medicines in this category, those that also had end-of-life status under PACE and those that did not. The former are typically cancer medicines for quite precise and limited licensed indications, sometimes within a cancer that is quite common overall such as lung cancer – in the SMC's PACE decisions since 2014 there are 8 examples and 7 were accepted. The latter group are more likely to be for chronic diseases and sometimes have very low patient numbers (e.g. in single figures) – there are 7 examples since 2014 and two were accepted.

I do not argue that any of these decisions were right or wrong. However, the medicines in the second group were typical of those that gave rise to the public petitions in 2012 that sparked the whole process of PACE reform – and based on 5 negative decisions out of 7 cases PACE does not seem to have resolved this. These are difficult decisions and this observation is not intended as a criticism of SMC – quite apart from the often limited clinical evidence, other factors include:

- Because the disease being treated is rare does not mean the budget impact is low – for example, the net medicines budget impact of elosulfase alpha would have come to over £3 million per year (before the company's proposed confidential price discount was taken into account) and is probably not untypical (some companies have used commercial confidentiality as a basis to keep budget impact estimates out of the published SMC guidance). If the budget impact was compared across all 114 medicines reviewed by SMC since PACE was set up, I guess this would put this medicine in the 'top ten'. Of course, this means the opportunity cost of accepting this medicine for use in terms of funds diverted from other services would not be trivial in terms of their impact on other patients.

- Cost-effectiveness is accepted as an important and relevant factor in SMC decision-making. The cost per QALY for the end-of-life UP medicines has been on the fringes of what was previously acceptable to SMC making it possible to exercise some flexibility (e.g. around £50k/QALY). However, the cost per QALY for the other UO medicines has often been very high with the figure of £830k for elosulfase alfa being an example that is in the public domain (some companies have used confidentiality to keep cost and QALY figures out of the published guidance but I would guess they are of a similar order of magnitude). For SMC to accept a medicine with a cost per QALY of £830k may make committee members very uncomfortable as it is so far in excess of the interpretation put on cost per QALY for other medicines.

Having noted how difficult these decisions are for the committee the situation is infinitely worse for patients and their families of course; the concern is that for some UO medicines there is no realistic chance the existing process will ever produce positive SMC guidance. As a consequence, without change there will be an on-going need for an ad hoc system of funding for these medicines (if they are to be available at all to patients in Scotland), and pharma companies may disengage from the SMC process (by declining to incur the costs of making a submission for these medicines).

I will briefly consider some options and the reasons I do not think they are appropriate:

- Require UO medicines achieve a cost per QALY comparable to other PACE medicines. This is probably unrealistic: to take the case of the medicine with a cost per QALY of £830k cited above, and assuming a simple pro rata between price and 'cost per QALY', then to achieve a cost per QALY of £50k, £30k or £13k the price discount offered would have to be 94%, 96.4% and 98.4% respectively. (£50k/QALY is a speculative figure for PACE medicines, £30k/QALY is a stated threshold value for non-PACE medicines, and £13k/QALY has been estimated from independent research as the figure for 'routine' NHS spending on other services.) This policy would likely result in an impasse between SMC and the pharma company with patients in Scotland not getting access to UO medicines.
- SMC to set a specific threshold 'cost per QALY' figure for medicines of this type. This has some attraction in that it recognises these medicines are different but it is unclear how a threshold value would be defined, and if £830k is typical of some UO medicines it is difficult to imagine a threshold that does not simply allow everything through.
- SMC to ignore the cost-effectiveness of these medicines and make judgements based only on other factors. As noted above, the budget impact can be substantial especially when summed across a number of UO medicines and funds will be diverted from other health services so other patients lose out. Cost-effectiveness is a way of balancing QALY gains per pound spent across groups of patients and to ignore this is to ignore the opportunity cost. Another problem is that it gives pharma companies the freedom to set whatever price they like, knowing cost-effectiveness is not a factor.
- The status quo to continue. This has the advantage of being known and predictable, but the obvious disadvantage of reliance on individual funding requests for patients to access UO medicines.

- NICE appear to have some success in England by establishing a separate committee to look at what they refer to as ‘highly specialised technologies’ (in practice this means UO medicines other than those for end-of-life). This has delivered some positive decisions, but seemingly by placing very low or zero weight on the cost per QALY, which I have argued against in a preceding section. There are obvious attractions to having a committee who only consider the issues associated with medicines of this type, but it is unclear whether NHS Scotland could justify the resources involved in an additional committee or how such a committee would interpret its remit.

Having rejected these options (although not necessarily every part of every option), I suggest the review should consider the principles it would wish to have underpin the decision-making system for UO medicines. These might include the following:

- An existing policy goal is to reduce dependence on individual funding requests and I assume this will continue to be an aim.
- The SMC system to set a threshold for achieving a positive decision that is challenging but achievable.
- Recognition that in some circumstances the SMC advice has to be negative for the system to have any credibility and cost-effectiveness is a relevant factor to be fair to all patients.
- The system should clearly distinguish end-of-life UO medicines from other UO medicines

The challenge is to define the criteria a medicine has to meet that are ‘challenging but achievable’. One option is to start from a review of recent SMC UO decisions to determine what alternative weight SMC would have had to place on the clinical, cost-effectiveness and supporting evidence for the medicine to have been accepted. This would indicate what would be needed going forward for UO medicines to have a realistic prospect of success at SMC.

4. How the views from the Patient and Clinician Engagement process are taken into account in decision making (*issue 2 in the request for comments*)

As stated above, the PACE process does seem to have made a measurable difference to the rate at which medicines are accepted for use so every other comment has to be seen in this context.

Having attended a number of SMC monthly meetings in the public gallery I observe (1) PACE statements are very common (2-3 every meeting so 24-36 per year) and (2) they are almost universally extremely supportive of the new medicine, seeing few problems, limitations or potential restrictions on its use. Indeed, in some cases committee members have pointed to examples where statements made by PACE seem so positive as to contradict the clinical study evidence before the committee, for example on the frequency and severity of side-effects.

This comment is not intended to devalue PACE statements, especially where they are an expression of unmet need from a patient group. I also recognise the amount of work that goes into these meetings but my point is that faced with three examples per meeting of PACE statements that are

unremittingly positive about the medicines under discussion it is the human nature of any SMC committee member to experience what I might term 'compassion fatigue'.

We are back to the problem of "if everything is special then nothing is special". As I have acknowledged, considerable work and time goes into each PACE meeting and statements yet while each one is robust and helpful if taken in isolation, collectively they do not help the committee to differentiate stronger from weaker medicines. A high priority for the review should be to assess how the same effort could be used to best effect if it sought the same ends by different means.

The issue I see is that the PACE statements do not provide the committee with information that helps them reach a decision. It establishes there is an unmet need and that prescribers and patients want access to the medicine – but the committee feel they already know that. My observation is that they are still struggling with the case made for particular medicines because the clinical evidence may be incomplete or the committee is required to accept the medicine will make a dramatic long-term impact that was only observed in some proxy form in the clinical data available. In short, the main issue the committee faces is uncertainty. I note that when debate about the PACE statement takes place at the SMC meeting, it tends to be about an aspect of the clinical evidence and a member who was present at the PACE meeting might quote a view expressed by clinicians at the meeting. This can be helpful but raises issues about (1) why this very indirect route is being used to seek expert views, (2) how robust it is to have chance reporting of possibly selected views, (3) PACE was originally conceived as having a remit for issues outside of the existing review carried out by SMC staff and considered by NDC.

My suggestion for the review, therefore, is to consider what evidence could be helpful for a decision-maker in making the difference between voting to accept the medicine or not and then determining the most effective way to make this available.

5. How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement (*issue 4 in the request for comments*)

In some respects, transparency has increased since meetings take place in public and representatives from the pharmaceutical company are invited to the meeting table. This helps companies (and patient groups?) understand what factors are discussed – as someone who tries to help companies produce better submissions I know this can be very helpful as they understand the attitudes of the committee.

This requires a lot of extra work for SMC (for which they received increased resources from Scottish Government) but this part of the story has been a success.

However, there are at least two respects in which the system could be said to fall short of transparency:

- Of the SMC committee members at the meeting, typically less than half and sometimes less than a quarter will speak in the discussion about any particular medicine. It is not easy to read the discussion and even when members speak in the debate they do not say which way

they will vote. This has significance when a medicine has been 'not recommended' and the company is seeking to understand the reasons to consider a resubmission.

- Having attended many committee meetings prior to them being held in public my perception is that the nature has changed with the public format possibly being less discursive.
- The other respect in which PACE may have reduced transparency is through pharma companies becoming more aware of rival companies attending the meetings and therefore requiring more data be withheld when SMC issues guidance. In one recent case a company asked SMC to withhold information on the lifetime cost of starting a patient on their medicine and the budget impact for the NHS even though no price discount (which could be sensitive information) was offered. It is hard to understand why the company would make this request or why SMC would agree to it; my assumption is that except where there is a precisely defined need meeting agreed criteria, all information should be shared with patients, the public and prescribers in Scotland through the guidance document.

The first issue could be addressed in two ways: by asking SMC members to nominate the most important factor in their decision on their voting paper, and by expanding the SMC guidance document to include a brief account of this within a report of the topics discussed at the committee meeting.

The review could consider the circumstances under which information about a medicine should be regarded as confidential to ensure consistency and transparency about why it is not always possible to be transparent.

6. Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report (*issue 10 in the request for comments*)

In my comments above I have identified the main unintended consequences I see:

- In a genuine attempt to meet the requirements of Scottish Parliament the definitions of situations where the PACE process could be used were too generous. The unintended consequence is that in outlying cases such as UO medicines the committee feels the PACE card only has limited impact.
- In seeking to give patient groups and clinicians more voice in the process, the number of PACE statements and the lack of differentiation in their degree of support for the medicine has blunted their impact.
- In making the meetings more transparent through holding them in public with pharma companies at the table, the level and nature of debate has changed.
- In making seemingly simple changes to the system, the resources allocated to SMC are stretched to the point where the system suffers backlogs.

Having pointed these out I am pleased to say one consequence we may have feared was that as priority was given to PACE medicines it could be taken away from non-PACE medicines for important

diseases like heart failure, hepatitis C or musculoskeletal diseases. If anything the reverse has happened and the pragmatism members are asked to show for PACE medicines seems to have extended to some extent throughout their decision-making.

Another unintended consequence is an ongoing concern to me about the New Medicines Fund. As I understand this represents the majority (if not all) of the receipts from NHS Scotland for rebates under the UK-wide PPRS scheme, and it is used to help meet local cost pressures both for specific medicines and for more general pressures created through additional approvals under PACE. My concern is that this funding source is not guaranteed and with PPRS re-negotiations happening every few years it could be regarded as non-recurring funding. If the PPRS were switched to another basis and the funding stopped, it seems NHS Scotland could face £90 million of unfunded cost pressures and it is not clear how they would be met.

7. How the new approach will accommodate advances in new medicines and a developing regulatory framework (*issue 11 in the request for comments*)

I understand this point to relate to licensing the medicine at an earlier stage in the development of the clinical evidence, with the possibility that the licensed indication will adapt over time. Having been involved in this type of work for nearly 15 years I think change along these lines is always anticipated in the near future. The latest example is (was?) the EAMS initiative which, as far as I know, has had no noticeable impact on health technology agencies' processes or decision-making.

I hasten to add that the SMC process should be kept under continuous review and should be flexible to cope with change; however, as I have emphasised throughout this comment, SMC can be pragmatic when the need arises. For example, one issue with earlier licensing is a less complete clinical evidence but this is not uncommon and the existing system can cope. For example, the 2015 submission for a lung cancer medicine, ceritinib, was an example where EMA had granted a license based on a single-arm clinical study (no RCT) but SMC system was able to see a way to issue positive guidance first time. Of course, that is not to say there are no issues here at all, but the types of issues are within the experience of SMC.

The main concern I have is if the degree of uncertainty in the clinical evidence increases. This is a familiar issue for many SMC reviews, and the main change that could be reviewed is how SMC thinks about and acts in the face of uncertainty.

Another scenario for changing licensing is where a license adapts as new evidence becomes available, but SMC already has a system where a company is required to resubmit evidence when the license changes in a non-trivial manner, so while the predicted changes may increase the number of submissions I do not see that it raises new issues. For example, SMC was able to issue positive guidance recently for eribulin, a medicine for advanced breast cancer, that superseded earlier advice because the license had changed.

In summary, I do not see a fundamental problem here. I would welcome the opportunity to understand the implications of the changes from someone who fully understands them in case I have missed something.

8. Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value (*issue 12 in the request for comments*)

As I understand it, the concept of Value Based pricing was under discussion at NICE and the initial impression was that this would be a UK wide approach. When it transpired that it was regarded as part of market access which was regarded as a devolved power, it meant VBP became an English initiative and the Scottish Model of Value (SMoV) was coined as a phrase in response. I cannot find any substance beyond this but the concept seems to be attractive to some parties and it maintains a place in the discussion.

In so far as it suggests an overall strategy for accessing new medicines then I am sympathetic. The SmoV could be a set of principles that would be a reference point for judging how the system is performing and any future reform. For example, three principles I would include are:

- From the document inviting this submission you said, “The overarching policy aim of the review is providing safe and timely access to clinically effective medicines at as fair price.” I agree, my only caveat being that price might not be the only variable in a package of reimbursement that is satisfactory to all parties.
- For the vast majority (and possibly all) newly licensed medicines, there is a set of circumstances under which NHS Scotland would make that treatment available for prescription (without the requirement for individual funding requests). The task of all stakeholders involved in decisions about access to new medicines is to identify those circumstances and try all reasonable means to achieve them.
- Stakeholders such as pharma companies will have most incentive to achieve the access desired if the Scottish system is influential and respected internationally.

The SMoV would then be an extended version of these principles, agreed to by all relevant parties. The danger I see is of a somewhat abstract and academic debate about value that is not destined to reach agreement and involve attempts by stakeholders to show every possible factor is important.

9. How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to pharmaceutical companies' best offering on price earlier (*issue 9 in the request for comments*)

In preparing this submission, I saw two main ways forward.

- Option 1 uses the existing SMC process and thinking, and adjusts incrementally for what is judged to be unsatisfactory.
- Option 2 allows for more substantial change in the process and thinking.

In my comments to date I have focused on Option 1 and attempted to make it as robust as possible; however, my preference is for Option 2, for the reasons set out in my submission to the Health and Sport Committee. Briefly these were that the issues with the current system are (1) it has not shown any evidence it can deal with UO medicines, (2) as a reactive system (in the sense it takes a submission from the pharma company to initiate the process) some medicines can be left in limbo if the company disengages with the process to the detriment of patients, and (3) even when SMC is able to say yes, there is no guarantee the NHS has obtained the best price. An example in the final category could be where a medicine has been accepted for one use and is then accepted for a second indication; in many European countries this increased volume would result in negotiations aimed at a lower price, but there is no obvious mechanism to do this.

I therefore propose that a robust review of the evidence should be carried out by SMC. This should build on the strengths SMC already possesses, and increased resources should allow SMC to take the initiative when a medicine is in limbo (my issue (2) above). The aim of the SMC process would no longer to reach a definitive decision on whether to accept the medicine for use or not; rather it is to assemble evidence on the strengths and weaknesses of the medicine, to comment on the perceived balance of strengths and weaknesses, and to identify the circumstances under which patients in Scotland can access the medicine. Following a process similar to the existing SMC system, a document capturing this work would be published online, and this would serve two roles. Of specific interest to Scotland, it would be the document that acted as the starting point for commercial negotiations with the pharma company. However, by being accessible on line many other countries would be interested in reading and understanding SMC's thinking and it would retain its role as one of the most influential HTA organisations, giving Scotland a global profile and ensuring all companies feature Scotland and its circumstances in their launch plans. By retaining respect for its work, SMC can secure Scotland traction in negotiations out of all proportion to its share of the global market for a new medicine.

This also resolves issues around confidential discounts on price and their implications because they would not be introduced at this stage. All the SMC discussion could take place in the public domain because everything submitted could be discussed.

I am aware there has been some interest in getting the best price early on, even before the SMC process. Consider the subsequent process, however. If the company names a price and they cannot then change it, if that price then turns out not to be acceptable to SMC, then months have been lost; commercially that is the company's penalty for 'getting it wrong' but that is no comfort to patients in Scotland who miss out. If on the other hand, the company can change its price then they have no incentive to give a realistic answer at the start.

A second disadvantage of this approach is that if the best price was identified before SMC then all the subsequent analysis would be confidential and could not be discussed in the public meeting, or included in the SMC guidance. This would substantially reduce transparency.

Another disadvantage of the 'get the best price early' approach is that it assumes price is the only variable. Even a cursory examination of HTA assessment of new medicines show there are a variety of options including the pharma company proposing the medicine be used in a limited role within the license, or proposing a rule that can be applied in clinical practice whereby a patient only continues their treatment if a pre-specified level of response is seen. Focusing on price also rules out other types of commercial negotiation such as those linking the unit price to the volume prescribed; this shuts down a lot of potentially useful options for reaching a deal that can achieve access for patients.

The final and most compelling disadvantage to me is that the NHS cannot know the value of the medicine until SMC has done its work; my proposed approach would identify what is good about the medicine so that genuine innovation and breakthroughs are rewarded. In other circumstances it would provide a briefing to the NHS negotiator on what sorts of circumstances they should accept where the whole package on offer (including but not limited to the price) reflects the value of the medicine.

I have some awareness of international systems for HTA and negotiation and I do not know of any system that seeks to get a price deal before the work of the national HTA agency; it just does not make sense.

A concern with my proposal to negotiate after SMC could be the time delay; however, initial discussions could be taking place in parallel with the SMC submission to become familiar with the topic area and treatment options already available. Further discussions could be held as the initial view is formed after the New Drugs Committee's draft guidance is issued; this would then allow all parties to 'hit the ground running' when the final SMC document is available.



Scottish Cancer Coalition

Scottish Cancer Coalition Recommendations on Access to Medicines

Introduction

Below is a Scottish Cancer Coalition (SCC) position paper on recent changes to the access to medicines system in Scotland and recommendations on further ways to enhance and evolve the system to the benefit of patients.

About the Scottish Cancer Coalition

The Scottish Cancer Coalition is a partnership of 23 voluntary organisations dedicated to improving cancer services and outcomes for patients in Scotland, and promoting research and prevention efforts.

This Coalition position paper was put together by a Coalition working group of seven charities – Myeloma UK, Breast Cancer Now, Breast Cancer Care, Prostate Cancer UK, Melanoma Action Scotland (MAScot), Roy Castle Lung Foundation and Cancer Research UK.

For more information, please email Kate Morgan (Myeloma UK) on kate.morgan@myeloma.org.uk.

Key improvements

The Coalition welcomes the following positive developments, as they have resulted in an improved access to medicines system in Scotland:

- Changes that have been made to the transparency of the Scottish Medicines Consortium (SMC) have been transformational in increasing understanding of the work of the SMC amongst patient groups and on how the voice of the patient has been taken into account.
- The introduction of the Patient and Clinician Engagement (PACE) process for rare and end of life medicines within the SMC has increased access to medicines for a number of such conditions, particularly in borderline cases where there is marginal uncertainty around whether or not a treatment represents value to the NHS in Scotland. However, it must be noted that other conditions, such as breast cancer, have not seen such an improvement in access.
- In most cases, PACE has increased the perception amongst patient groups of being “listened-to” in the SMC process.
- Additional resources provided to increase the capacity of the SMC in facilitating patient and public involvement have been very effective. The work of the Patient and Public Involvement Team and introduction of the Public Involvement Network (PIN) advisory group should be commended.
- The distribution of SMC decisions prior to publication under embargo has greatly assisted patient groups in preparing communications to patients on the implications of the announcement.
- The ability of industry to sit in the SMC appraisal meetings and to clarify questions has been a significant improvement to assist decision-making.

- Efforts have been made to streamline the way that the PACE and Patient Interest Group (PIG) forms are read out during the full committee meeting of the SMC, which we welcome as this makes the SMC meeting less repetitive.
- We welcome the removal of “exceptionality criteria” from the IPTR process, as this allows a fairer system of local decision-making for patients.

Recommendations for the future

PACE recommendations

1. Develop quantitative ways of measuring the impact PACE has had on improving access to medicines for orphan and end of life medicines. This could also apply for other modifiers applied by the SMC.
2. A number of cancer drugs have recently been turned down by the SMC, even where the SMC has engaged PACE. Whilst we welcome the autonomy of the SMC in its decision-making and do not think that drugs should be approved where the value has not been demonstrated, there may be ways of “pre-screening” PACE submissions at the New Drugs Committee stage which are likely to be turned down (i.e. where the uncertainty of value is far too high) to ensure that patients and patient groups are not involved in a PACE meeting unnecessarily. These types of drugs are more likely to be approved through negotiations over cost-effectiveness (including PACE) rather than through PACE alone.

General SMC recommendations

1. Introduce a temporary ‘pause’ in the SMC process to allow for further discussion around the cost-effectiveness of the new medicine between the SMC and the manufacturer.
2. Allow expert clinicians to participate in the full SMC Committee meeting on a new medicine to answer questions and clarify areas of clinical uncertainty.
3. Improve the detail included in the final Detailed Advice Document (DAD), including an explanation of how the PACE summary and other modifiers have been taken into account and whether or not a Patient Access Scheme (PAS) was submitted by a company.
4. Make SMC approved decisions binding on Local Health Board ADTCs to ensure that clinicians can choose to prescribe the treatment for their patient.
5. Publish findings on what the impact of the SMC industry early engagement pilots are and how these will be used and improved moving forward.

PACS recommendations

1. The Peer Approved Clinical System (PACS) is not in place across Scotland. Whilst the Coalition is not aware that the absence of PACS is negatively impacting on patient access, in the interests of transparency, the Scottish Government needs to publically explain why this has not been the case and its plans for the IPTR moving forward.
2. As the IPTR process remains in place across Scotland, it is still operated locally by 14 Area Drugs and Therapeutics Committees (ADTC) and there is no national guidance in place governing the process. A review needs to be undertaken on how this is operating and the Coalition would welcome piloting different ways of administering the IPTR process (e.g. through regional networks or nationally) to reduce the risk of regional disparity.

General recommendations

- 1.** Elements of the Accelerated Access Review being undertaken by the Department for Business, Innovation and Skills and the proposed system on the Cancer Drugs Fund are likely to impact on Scotland. Scottish Government should work to understand and influence the affect these policies have in Scotland and the impact they will have on the access to medicines system.
- 2.** Information should be published on how the NMF is being operated and spent across Scotland and the impact it has had on access to medicines.
- 3.** As the PPRS is set to be renegotiated in 2017, discussions are already being held on how this will work and operate. As the New Medicines Fund relies heavily on the rebate from the PPRS, the Scottish Government needs to assess the impact different PPRS pricing models will have on the Fund and also ensure its representation in the renegotiation process.
- 4.** Develop a forward planning document, and have public discussion, on how the SMC and health service in Scotland are preparing for developments such as personalised/stratified medicine and adaptive licensing.



Genetic Alliance UK
Supporting. Campaigning. Uniting.

Access to New Medicines in Scotland

Independent Review by Dr Brian Montgomery

Response from Genetic Alliance UK, 28th April 2016

Introduction

1. Genetic Alliance UK is the national charity working to improve the lives of patients and families affected by all types of genetic conditions. We are an alliance of over 180 patient organisations. Our aim is to ensure that high quality services, information and support are provided to all who need them. We actively support research and innovation across the field of genetic medicine.
2. Rare Disease UK (RDUK) is a multi-stakeholder campaign run by Genetic Alliance UK, working towards the delivery and implementation of the *UK Strategy for Rare Diseases*¹, signed by all four health departments in the UK and published by the Department of Health in November 2013. In 2011, RDUK submitted Public Petition PE1398, calling for a thorough review of the processes used to access new medicines in Scotland.
3. Genetic Alliance UK thank the Scottish Government and Dr Brian Montgomery for conducting a review of the reforms carried out by the Scottish Medicines Consortium (SMC) relating to access to new medicines and welcome the opportunity to provide written evidence.
4. Genetic Alliance UK have recently published a Patient Charter on Access to New Medicines for Rare Diseases in Scotland. In October 2015, we held a consultation event with patient organisations to review the processes for accessing new medicines in Scotland. A copy of our Patient Charter was presented to Dr Montgomery at a meeting on Friday 22nd April. The findings from our Patient Charter have informed our response to this consultation and a summary of recommendations can be found at the end of this document.
5. It is the opinion of Genetic Alliance UK that the reforms that have been carried out as a result of the 2013 reviews have resulted in an improved system for accessing new medicines for rare conditions, however there are still improvements that can and should be made.

How are the agreed definitions for end of life, orphan and ultra-orphan medicines working in practice?

6. Before the New Medicines Review in 2013, SMC processes did not recognise the term ultra-orphan or acknowledge the additional challenges of appraising medicines for very rare conditions. The processes that existed prior to the 2013 reforms, even with the modifiers that could be used for orphan medicines, were unsuited to medicines for very rare conditions.

¹ UK Strategy for Rare Diseases. Department of Health, published November 2013, available at: www.gov.uk/government/uploads/system/uploads/attachment_data/file/260562/UK_Strategy_for_Rare_Diseases.pdf

7. The recognition of the term ultra-orphan and the development of a process to address the challenges presented by these medicines has been welcomed. Following the reviews, the QALY information continues to be requested from the manufacturer for an ultra-orphan medicine, but a wider perspective is also taken on its value.
8. When proposing these changes, the SMC claimed that this approach is similar to the interim methods explored by the National Institute of Health and Care Excellence (NICE) for highly specialised technologies (HST) in England, and therefore they expected it to reduce the perceived inequities of access to medicines for rare diseases for residents of Scotland compared to those in England and Walesⁱ. However, inequities are still apparent and example being Translarna, a medicine for the treatment of Duchenne Muscular Dystrophy which received a negative recommendation by SMC in April 2016, followed by a positive recommendation by NICE.
9. It also appears that the process for ultra-orphan medicines has not resulted in an increase in the recommendation rate. When we compared the fifteen months since the reforms to the fifteen months before the reforms, looking only at the orphan and ultra-orphan medicines, the percentage of medicines approved had actually declined slightly. In contrast, the percentage approvals for all medicines assessed (which included both those that went through PACE and those which didn't) increased slightly.

How are the views from the Patient and Clinician Engagement process taken into account in decision making?

10. Genetic Alliance UK welcome the SMC's commitment to strengthen the voice of the patient in SMC decision making. Whilst the introduction of the SMC PACE process has resulted in increased patient involvement and greater patient voice in SMC decision making, it is unclear exactly what effect PACE statements have had on SMC decision making.
11. It is our experience (from attending SMC open meetings) that consideration of cost remains a considerable part of SMC discussions when assessing orphan and ultra-orphan medicines. In certain cases where an orphan or ultra-orphan medicine has been assessed and the PACE statement has been overwhelmingly supportive of its introduction, deliberations over the QALY have taken place and the medicine has been rejected. This would imply that the QALY remains the dominant factor in SMC decision making.
12. Genetic Alliance UK members report that they feel, particularly with regards to a very high cost medicine, nothing that they could have said would have resulted in a positive decision.
13. To date there has been no evaluation of how SMC members reach decisions and as such, it is difficult to assess what impact PACE has on the decision making process. Consultation with SMC members and research into how SMC members make decisions is necessary to evaluate the impact and effectiveness of PACE.

How have the acceptance rates for the end of life, orphan and ultra-orphan medicines changed as a result of the new approach?

14. A study in 2015 found that "The SMC recommendation rate for orphan products, particularly malignant disease and immunosuppressive drugs, has improved from 2013 to 2014 suggesting the revised SMC appraisal process may be more effective in enabling the SMC to provide positive recommendations for orphan products."ⁱⁱ
15. However, when we compared the fifteen months since the reforms to the fifteen months before the reforms, looking only at the orphan and ultra-orphan medicines, we did not see this. Though there were substantial increases in the number of both assessments and approvals after the reforms, the percentage of orphan/ultra-orphan medicines approved had actually declined slightly. In contrast, the percentage approvals for all medicines assessed (which included both those that went through PACE and those which didn't) increased slightly. A recent study has also found that the

upward trend in the proportion of cancer medicines accepted since the adoption of PACE is even greater than that seen across all medicinesⁱⁱⁱ.

How is the new approach to assessment of ultra-orphan medicines operating in practice?

16. Whilst the introduction of the SMC PACE process has resulted in increased patient involvement and greater patient voice in SMC decision making, it is unclear exactly what effect PACE statements have had on SMC decision making. Genetic Alliance UK members report that they feel, particularly with regards to a very high cost medicine, nothing that they could have said would have resulted in a positive decision.
17. In certain cases where an orphan or ultra-orphan medicine has been assessed and the PACE statement has been overwhelmingly supportive of its introduction, deliberations over the QALY have taken place and the medicine has been rejected. This would imply that the QALY remains the dominant factor in SMC decision making. While QALYs can provide a useful indicator of an individual's anticipated health gain following a medical intervention, they do not fully capture the benefit a treatment can offer to patients and families, particularly if they are affected by a rare condition. This remains the case even with the use of modifiers.
18. Evaluation of how SMC members reach a decision is essential to determining how successful the new approach to assessment of ultra-orphan medicines has been. Consultation with SMC members and research into how SMC members make decisions is necessary for the purposes of transparency and to ensure patient and patient group confidence in the process.
19. The SMC have stated that since the PACE process was introduced they have received significantly increased numbers of submissions for medicines of this type^{iv}, which suggests that the increased number of appraisals – and thus approvals – is at least in part due to improved confidence in the processes by manufacturers.

How has the transparency of SMC improved?

20. Genetic Alliance UK welcome the SMC's commitment to improve openness and transparency of its systems and processes. The introduction of open meetings has been a valuable step forward in raising awareness and understanding of how evidence is assessed and interpreted by SMC. From the perspective of patient organisations, open meetings provide an opportunity to witness the way in which their contributions, through the Patient Interest Group Submission and Patient and Clinician Engagement (PACE) meeting, are represented.
21. However, there is still a lack of transparency in how decisions are made at SMC and we remain concerned about the weight of the cost per QALY. We recognise that QALYs can provide a useful indicator of an individual's anticipated health gain following a medical intervention. However, we have concerns about how QALYs are calculated, and the weight they carry in SMC decision making. Patients with rare conditions agree that this method is crude and fails to capture the type and range of symptoms, emotions and disadvantages experienced by patients, families and carers affected by rare conditions. Differences that may be important clinically or to the patient may not be shown by cost per QALY estimates.
22. Whilst the introduction of the SMC PACE process has resulted in increased patient involvement and greater patient voice in SMC decision making, it is unclear exactly what effect PACE statements have had on SMC decision making. Patient groups have reported feeling that too much time is spent at SMC meetings considering cost and that despite overwhelmingly supportive PACE statements, ultra-orphan medicines with a very high cost attached are rejected. It was also noted by one patient group that a particular ultra-orphan medicine was rejected despite a supportive PACE, but accepted upon resubmission following the addition of a Patient Access Scheme. In this instance, the patient group reported that they felt the time that they had taken to participate in the PACE process had been 'meaningless'.

23. Evaluation of how SMC members reach a decision is essential to determining the impact of PACE and the weight given to other factors including the cost per QALY and the Patient Access Scheme. Consultation with SMC members and research into how SMC members make decisions is necessary for the purposes of transparency and to ensure patient and patient group confidence in the process.

What further opportunities are there for patient and clinician engagement?

24. The development of the Public Involvement Team has been a success of the recent reform. The Public Involvement Team provide a valuable source of support to patient organisations participating in the SMC processes. The Patient and Public Involvement Team have developed written resources, reviewed patient submission forms and undertaken a number of patient group engagement activities to raise awareness of the SMC, its role and the value of patient involvement.

25. The Public Involvement Team recognise potential difficulties in engaging with patient organisations for rare diseases, for example, patient organisations may not exist for a particular condition or may not have experience of HTA processes. The Public Involvement Team have worked with Genetic Alliance UK to identify appropriate patient organisations to participate in PACE and to discuss methods for improved patient organisation engagement for very rare condition areas.

26. The Patient and Public Involvement Team has undertaken excellent work to improve the quality of patient group submissions, including developing new submission forms and guidance for providing a Patient Interest Group submission and for participating in PACE. However, further comprehensive training would be welcomed to ensure patient submissions are of the highest quality. Regular training days should be undertaken for both patient representatives and clinicians to not only provide training on how to engage with the appraisal process, but also on the technical aspects of Health Technology Assessment.

27. The SMC are currently expanding a 'PACE mentors' programme to encourage organisations with experience of the SMC process to support other organisations to strengthen their submissions. Genetic Alliance UK support this programme and suggest further steps could be taken. Resources should be developed to share best practice examples with patient groups about to take part in the SMC process. Suggestions from patient groups include developing a repository of patient group submissions or producing informative video to share examples of best practice.

28. Genetic Alliance UK provide a nominated individual to represent rare diseases on the Public Involvement Network (PIN). PIN comprises representatives of patient and carer groups, nominated by umbrella bodies, to ensure that the views of patients, carers and members of the public are used to inform SMC processes and to promote ongoing reform and improvement in patient involvement at SMC. The introduction of PIN has been a welcome development and an important step in improving patient involvement in SMC processes.

29. There is a need for an increase in the number and type of patient voice on all decision making panels at SMC. Patients do not have the opportunity to represent at SMC other than indirectly through the Patient Interest Group Submission or the Patient and Clinician Engagement process. It is the Chair/Principal Pharmacist from the PACE meeting that presents a consensus statement of both the clinical expert and patient/carer representations at the final SMC meeting. It is the role of the Public Partners prepare a presentation of patient group submissions to accurately highlight key issues and messages to present at monthly SMC committee meetings. Public Partners also play a crucial role in the PACE process.

30. Genetic Alliance UK fully respect and support the role of Public Partners. However, we encourage the inclusion of patient perspectives in all decision-making processes in as unfiltered a form as possible. Patients provide an important and unique perspective in decision making, and this input is most valuable when provided in person. While we acknowledge that the current process of public partners reading patient groups submissions in the patient's own words is valuable, it would be

better for patients to deliver these statements directly rather than via an intermediary. Genetic Alliance UK recognise that there is value to having a non-expert public perspective at SMC, however we feel SMC currently conflates public and patient perspectives and that it would be more appropriate for Public Partners to represent a broader social perspective.

31. Patient involvement in SMC decision making could be further enhanced by affording patient representatives membership of the NDC and SMC and voting rights, in a similar role to that currently held by pharmaceutical industry representatives. Patients' experiences and preferences should be represented in all the processes which lead to the availability of new medicines, this would ensure that the benefits which really matter to patients, and the levels of risk they are prepared to tolerate are considered in the decision making process. This is particularly important for serious and rare conditions, where the stakes are so high.
32. Patient representatives (such as patient group members) should be supported as joint decision makers, alongside clinical experts, throughout the process. Similarly, to how industry gets three voting members on the SMC through their industry body (ABPI), it would be appropriate for three patient representatives to also be members provided that they are suitably trained. A trained and disinterested patient can use their insight into the potential beneficiaries' point of view to make decisions as an active member of any body. Additionally, it would be appropriate for two patients who have made submissions to the SMC on a specific medicine to attend the SMC meeting, similarly to how submitting companies do now, in order to answer any specific questions that the panel may have and to address any issues which may require clarification.
33. Expert clinical opinion is a vital component in the SMC decision making process. While the NDC, SMC and local ADTCs may have a range of different specialisms among their membership, this does not always equate to expertise in the condition under consideration. It is essential, particularly in the case of rare conditions, that the appropriate expert clinician be involved in decision making. It must also be recognised, that for many rare conditions, such expertise will lie outwith Scotland. Where necessary, SMC must look to the rest of the UK, or Europe, to ensure that decisions are made on the basis of all necessary information and expertise.
34. Expert clinicians that are invited to participate in PACE must also be experts in the disease area in question and this may require seeking opinion outwith Scotland. For those expert clinicians that are involved in PACE, an invitation to attend the SMC meeting, whether that be in person or by teleconference, to provide answers to any questions the panel may have or to provide clarification on their PACE submission should be extended.

How are NHS Boards implementing SMC decision under the new approach, including utilisation of the New Medicines Fund?

35. Our investigations of formulary uptake reveal that a greater proportion of medicines eligible for PACE were accepted by local health boards than for all medicines, but that this is not true in all cases. Indeed, formulary uptake, both in the rare disease area and more generally, remains patchy and inconsistent.
36. Although there have been several reports of delays and variations in formulary uptake in the more common disease areas, rare disease patient representatives told us that they are not particularly concerned about formulary uptake. This is likely because so few rare disease medicines have up until now been appraised and recommended by the SMC, ie. this is not the crisis point. However, a careful watch should be kept on this issue, as this stage may become more of an issue as a greater number of rare disease medicines make it to this point in the access pipeline.
37. Patient representatives expressed doubt about the value of a full reappraisal of each medicine recommended by the SMC at the ADTC of each health board to determine whether it would be added to local formularies. Citing the consistent problems with availability of appropriately

specialised clinical expertise, patient representatives suggested access to rare disease medicines should be streamlined to avoid this repetition. This could most efficiently be done by making SMC recommendations on orphan, ultra-orphan and end of life medicines binding on health boards.

38. There is a precedent for this in the Scottish context, as previously SMC could designate an innovative medicine for a condition where there are no other treatment options as “unique”^v, which required that boards introduce it within three months. This was removed by SGHD/CMO(2012)1 in 2012 as there had only been one such designation, however this was a result of the unreasonably high requirement for this designation rather than evidence of appropriate levels of formulary uptake of innovative medicines^{vi}.
39. Patient representatives noted that many local health board websites are extremely challenging to navigate. It is important that up to date information about the work of area drug and therapeutics committees and local formularies be published in a transparent and easily accessible manner. Organisational websites are the primary, and sometimes only, source of contact between an organisation and members of the public. It is therefore necessary that it contains the most up-to-date information, explained in a straightforward manner on a site that can be easily navigated.
40. With regards to the New Medicines Fund, patient representatives have noted concerns about the sustainability of the fund, given that funding is gained from a single source. The New Medicines Fund is funded by the PPRS rebate, which the Scottish Government has no role in setting. The lack of guidance on the use of NMF fund also means that we do not yet know how long a new medicine will continue to be NMF funded following a recommendation by the SMC, which also is likely to affect the sustainability of the fund.
41. There is widespread support among patient representatives for the fund to be retained, but with the clarity and transparency on where funds are coming from, and what exactly the fund is being spent on. The Scottish Government should consider publishing annual reports detailing how the New Medicines Fund funds are being spent.
42. Patient representatives have also expressed support for the New Medicines Fund being returned to a single ring-fenced fund rather than allocated to individual health boards. This is primarily for the reasons of accountability – there are concerns that the funding allocations will vanish into health board budgets and any money not spent not enforced as being retained for orphan, ultra-orphan and end of life patients.

Has the new approach had an impact on the reliance on access to medicines on an individual patient basis?

43. Rare disease patients continue to rely on access to medicines on an individual patient basis. Many medicines for rare diseases, particularly those with an ultra-orphan designation, continue to be unsuccessful when appraised by the SMC.
44. Prior to the Health and Sport Committee Inquiry in 2013, rare disease patients faced significant challenges in accessing appropriate medicines through the Individual Patient Treatment Request process. This was due to a number of factors, primarily the restrictive ‘exceptionality’ criteria that had to be met and inequity in decision making across NHS Scotland Health Boards.
45. Genetic Alliance UK welcomed the interim IPTR arrangements which saw the removal of exceptionality criteria and called for a consistent and flexible approach across all Health Boards. The proposed abolition of the IPTR process and the introduction of a Peer Approved Clinical Process (PACS) which put clinical opinion at the centre of decision making was also welcomed. This new system was intended to focus on patient outcomes, and have a reduced reliance on individual requests for medicines.

46. Genetic Alliance UK members have told us that they are finding the interim phase an improvement on previous IPTR arrangements, as it features a combination of added funding (in the form of the New Medicines Fund) and added leniency (the removal, in principle at least, of the exceptionality requirement) which they are finding is slightly increasing patient access via this route.
47. Whilst reliance of exceptionality has decreased and access to medicines through IPTRs seems to have improved, patient representatives have told us that even 18 months after the interim IPTR guidelines were published, a number of health boards were still using either guidance or forms that referred for the need for applicants to be exceptional. It may be due to health boards also expecting the imminent arrival of PACS, and so opting not to make significant changes to their documentation for what was anticipated to be a very short interim period.
48. Genetic Alliance UK welcome the interim arrangements for IPTRs and are pleased that this appears to have resulted in improved access to medicines through this route. However, the interim guidance is no substitute for an improved process which centres around clinical opinion.
49. The transition from IPTR to PACS was due to take place in May 2014 and we understand that a pilot scheme is taking place in NHS Greater Glasgow and Clyde. It should be noted that formal guidance on PACS has yet to be issued publicly and that there are no defined timescales for its introduction. As a result, there is a degree of uncertainty amongst patient organisations about what PACS will look like in practice, how it will operate and how patients will be involved in the process.
50. Genetic Alliance UK acknowledge that it is in the best interest of patients for a pilot scheme to be tested and for a robust system to be introduced to ensure transition between systems is smooth. However, we would welcome greater communication from the Scottish Government regarding the progress of the current pilot scheme and the strategy for phasing out IPTRs and introducing PACS.
51. Details of operational guidance for PACs should be made public as soon as possible and information on timescales be shared to allow patient organisations to prepare for this transition. Training on the new system must also be provided to both clinicians and patient organisations so that they can provide accurate information and support to patients.

Are there opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines?

52. Patient representatives have suggested that discussion and decision making regarding rare disease medicines at ADTC level are unnecessary, citing consistent problems with availability of appropriately specialised clinical expertise. There may therefore be an opportunity to take a 'once for Scotland' approach by making SMC recommendations on orphan, ultra-orphan and end of life medicines binding on health boards.
53. During our Patient Charter workshop, consideration was also given to whether IPTR/PACS decision making at individual Health Board level was appropriate in the case of medicines for rare diseases. Patient representatives are supportive of the idea that IPTR/PACS decision-making be at a level higher than individual health boards, such as regionally. This is because of the concerns about availability of suitable clinical expertise on Health Board IPTR panels. Several expressed the opinion that an ideal system would be one where decisions regarding all patients with a condition are made by a specialist clinical centre for all Scotland. However, it is not entirely clear whether this would address the challenges faced by patients with conditions so rare that there is no specialist clinical centre for that condition in Scotland. It also would likely disincentivise companies from making a submission to the SMC, as it would be perceived as a less difficult route administratively and evidentially.
54. We propose that the best method to address the lack of specialist clinical expertise in rare conditions at health board level, is to encourage IPTR/GPTR/PACS panels (as well as ADTCs more

broadly) to call on the expertise of a list of experts similar to that used by the SMC in gathering evidence for its decisions. Should this be implemented, serious consideration would need to be given to the criteria used to determine whether an individual is an appropriate expert, as well as to how best to both encourage experts to contribute their time to decisions made about patients they are not directly treating, as well as how to enforce local health boards requesting and adequately weighing such expertise.

How should the SMC process be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier?

55. Patient Access Schemes are the current way of negotiating cost-effectiveness, with the SMC Patient Access Scheme Assessment Group (PASAG) appearing to favour straight forward discounts in price from pharmaceutical companies. For medicines where evidence of cost-effectiveness is limited, there may be an opportunity to explore more complex patient access schemes that provide better value for money.
56. At a recent multi stakeholder meeting, hosted by Myeloma UK, there was broad agreement that discussions around cost-effectiveness should happen at an earlier stage of the process.
57. Early engagement should start before a company submission to the SMC and would ensure that key stakeholders are able to discuss the best approach to the appraisal and any potential issues with cost-effectiveness in advance of the SMC process. This would allow solutions to be identified earlier on in the process. A pre-submission discussion between clinicians, PASAG, patient groups, the pharmaceutical company, the SMC and the Scottish Government. It would be a 'collaboration' to bring a medicine to patients and would assist in the co-creation of patient pathways to determine how best to use the medicine in clinical practice and clinical opinion on how valuable an intervention is.
58. PASAG and the SMC should consider ways in which they could be more flexible in the types of PAS that they are willing to accept as part of pharmaceutical company submissions. A cost-effectiveness discussion could focus on managed access schemes and methods of capturing the outcomes and benefits of a medicine in clinical practice rather than concentrating discussions purely on price.
59. Early negotiations should reduce the need for late discussions on cost-effectiveness and involving patients and patient groups in these early negotiations would ensure patients have involvement in the decisions about where the medicine is placed on the patient pathway.

How will the new approach accommodate advances in new medicines and a developing regulatory framework?

60. The new approach appears to be improving access to medicines for end-of-life and orphan conditions although further work is required to ensure that the current approach is suitably robust to deal with ultra-orphan medicines and fit for the future.
61. Developments in stratified medicine and gene therapies will bring a greater level of uncertainty around data and health economic modelling and, as we have seen with the current issues facing ultra-orphan medicines, current processes at SMC are not yet robust when dealing with uncertainty. It is important that SMC develop flexible ways for assessing and approving new drugs where the health economic uncertainty is higher and the real world value is undetermined.

Has progress made to date provided a solid basis for developing further a Scottish Model of Value?

62. At the time of the New Medicines Review in 2013, much mention was made of the PACE process as being the first step in moving toward what was termed a Scottish Model of Value^{vii}. These mirrored discussions were being held in relation to proposed Value-Based Pricing, later termed

Value-Based Assessment, in England. A discussion on developing a Scottish Model of Value is welcomed by Genetic Alliance UK, however we are unaware of any meaningful discussions having taken place.

Genetic Alliance UK Patient Charter on Access to Medicines for Rare Diseases in Scotland

Summary of Recommendations

SMC

- **Recommendation 1:** The role of public partner at SMC should be reviewed and consideration given to increasing the opportunities for patients to provide their perspective in person.
- **Recommendation 2:** SMC Public and Patient Involvement Team should hold regular training days.
- **Recommendation 3:** SMC should consider how to share best practice relating to patient involvement in the SMC process.
- **Recommendation 4:** Membership of the NDC and SMC should include suitably trained patient representatives.
- **Recommendation 5:** Patient representatives that have participated in the PACE process for a specific medicine should be invited to attend the SMC meeting to answer any questions raised by SMC members.
- **Recommendation 6:** SMC must ensure appropriate expert clinicians are involved in decision making
- **Recommendation 7:** Expert clinicians involved in PACE should be invited to attend the SMC meeting to provide clarification or answer questions.
- **Recommendation 8:** SMC should evaluate the significance of the QALY in SMC decisions for rare disease medicines.
- **Recommendation 9:** SMC should consider applying greater flexibility when assessing rare medicines and consider removing the QALY from decision making for rare medicines.
- **Recommendation 10:** Research to monitor the impact of PACE statement on decision making should be undertaken

IPTR/PACS

- **Recommendation 11:** The interim arrangements for IPTRs must be monitored to ensure exceptionality is not a factor in decision making.
- **Recommendation 12:** The interim arrangements for IPTRs should be phased out and replaced by the Peer Approved Clinical System as soon as possible.
- **Recommendation 13:** The Scottish Government should communicate details of the PACS Pilot and the strategy for implementing PACs in Scotland, including timescales for implementation
- **Recommendation 14:** Training and guidance on how PACS works must be provided to clinicians and patient organisations ahead of it's implementation to ensure they are equipped to support patients through the process.
- **Recommendation 15:** Whenever possible, IPTR/PACS panels must feature an appropriate clinical expert in the condition, whether that be by telephone or in person.
- **Recommendation 16:** Health Boards should consider developing a comprehensive list of experts in rare diseases, similar to that used by SMC.

New Medicines Fund

- **Recommendation 17:** The Scottish Government should regularly produce a report on the breakdown of spend under the NMF.
- **Recommendation 18:** The NMF should be retained in its previous form as a single ring-fenced fund, rather than being allocated to local health boards

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- ⁱ Assessment of medicines for end of life care and very rare conditions (orphan and ultra-orphan medicines) in Scotland: Report for the Cabinet Secretary for Health and Wellbeing. Task and Finish Group Chaired by Professor David Webb on behalf of the Scottish Medicines Consortium, December 2013, available at:
http://www.scottish.parliament.uk/S4_HealthandSportCommittee/Inquiries/Assessment_of_medicines_for_end_of_life_care_and_very_rare_conditions.pdf
- ⁱⁱ Marshall, J.D. et al. (2015) Have changes to the Scottish Medicines Consortium (SMC) process following the Routledge review really improved access to Orphan Medications and what factors influence recommendations? *Value in Health*, 18(3), pA93.
- ⁱⁱⁱ Assessing Trends in SMC Advice Decisions (October 2009- September 2015). Office of Health Economics, November 2015. Available at: <https://www.ohe.org/publications/assessing-trends-smc-advice-decisions-october-2009-september-2015#sthash.slwWdbfe.dpuf>
- ^{iv} PACE: Medicines for end of life and very rare conditions. Scottish Medicines Consortium, undated, available at:
https://www.scottishmedicines.org.uk/Submission_Process/Submission_guidance_and_forms/PACE
- ^v CEL 17 (2010) Introduction and Availability of Newly Licensed Medicines in the NHS in Scotland. Scottish Government, May 2010, available at:
https://www.scottishmedicines.org.uk/files/CEL2010_17.pdf
- ^{vi} SGHD/CMO(2012)1: Guidance to Further Strengthen the Safe and Effective use of New Medicines Across the NHS in Scotland. The Scottish Government, February 2012, available at:
[http://www.sehd.scot.nhs.uk/cmo/CMO\(2012\)01.pdf](http://www.sehd.scot.nhs.uk/cmo/CMO(2012)01.pdf)
- ^{vii} Response to the Health and Sport Committee Inquiry into Access to New Medicines. Scottish Government, October 2013, available at:
http://www.scottish.parliament.uk/S4_HealthandSportCommittee/Inquiries/Scottish_Government_Response_-_Access_into_New_Medicines.pdf

Review of Access to New Medicines – independent review by Dr Brian Montgomery
RESPONSE ON BEHALF OF NHS GREATER GLASGOW AND CLYDE

Context

In October 2013 the Cabinet Secretary for Health and Wellbeing directed the Scottish Medicines Consortium (SMC) to undertake a rapid review to establish more flexible approaches in evaluating medicines for treatment at end of life and for very rare conditions. The SMC established a Task and Finish Group with representatives from key stakeholders including clinicians, patient interest groups and the pharmaceutical industry and in consensus [recommended](#) a new approach for the assessment of end of life, orphan and ultra-orphan medicines to deliver substantially improved access to these medicines for patients in Scotland (“the new approach”). In January 2014, following consultation with other parties in the Scottish Parliament, the Scottish Government asked SMC to deliver the new approach set out in the Task and Finish Group Report. The new approach was put in place for submissions received after noon on 7 April 2014 and the first decisions made under the new approach were published in October 2014. In February 2015 the Scottish Government indicated its intention to formally review the new approach in 2015/16. The Scottish Medicines Consortium has adopted a continuous improvement method to the implementation of the new approach and this review builds on that and will take account of the views of the Health and Sport Committee from March 2016.

The review will also consider the wider context of how SMC decisions for these medicines are implemented by NHS Boards, including those orphan, ultra-orphan and end of life medicines not recommended by SMC.

The Cabinet Secretary for Health, Wellbeing and Sport, Shona Robison, has asked Dr Brian Montgomery to lead the review.

Scope of Review

The review should consider the progress made in substantially improving access to orphan, ultra-orphan and end of life medicines for patients in Scotland compared to the former system. The overarching policy aim of the review is providing safe and timely access to clinically effective medicines at a fair price. The review will be forward looking to anticipate, where possible, future developments which will influence this landscape. In particular the

review should consider and make any recommendations it considers appropriate in the following areas:

NHS GG&C would suggest that the scope of the review be wider in that it should not only consider the impact that the changes made to SMC processes have had on the availability of new medicines, but also to examine the impact that this has subsequently had on health boards in Scotland and the opportunity costs of additional spend on medicines.

- How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice;

This is an issue mainly for the Scottish Medicines Consortium, however from an NHS Board perspective it should be noted that the SMC definition for an end of life condition is one that relates to end of life within 3 years of treatment. This differs to that of NICE and the All Wales Medicines Strategy Group which regards end of life as conditions having a life expectancy of less than 24 months. This extension of the definition skews the way in which medicines are considered in Scotland compared to elsewhere in the UK and puts additional burden on the global healthcare budget within NHS Boards by extending the flexibility applied to cost-effectiveness thresholds.

- How the views from the Patient and Clinician Engagement process are taken into account in decision making;

This is an issue mainly for Scottish Medicines Consortium, however, there is certainly a larger number of medicines accepted for use by SMC than prior to the implementation of the PACE process.

NHS GG&C clinicians have strongly supported the PACE process by attendance at PACE meetings and submitting statements. They have voiced their support for continuing to support this process.

- How the new approach to assessment of ultra-orphan medicines is operating in practice;
This is an issue mainly for Scottish Medicines Consortium. It would be helpful to define what 'operating' means in this context. The Scottish Medicines Consortium exists to

provide advice to NHS Boards on the comparative clinical and cost-effectiveness of medicines. Many of the ultra orphan medicines that SMC have not recommended for use have extremely high cost/QALY attached to them. Processes within SMC have been modified to take into consideration many of the issues that relate to ultra orphan medicines. It is acknowledged that this still results in 'not recommended' advice for some medicines where there is clearly an unacceptable argument of cost-effectiveness, but for NHS Boards the continuation of these not recommended opinions suggests that SMC is still able to deliver the equitable advice in relation to best use of NHS resources while using the framework. It is appropriate that the IPTR approach is then used with the revised approach.

Cost per QALYs would rarely be below £100,000/QALY for these ultra orphan indications and can be in excess of £800,000/QALY. It is very difficult to reconcile these figures with our usual acceptable figure of around £30,000/QALY.

We would not support any further attempts to modify the SMC process to increase the frequency of acceptance for use of ultra orphan medicines. This might lead to unintended consequences such as affecting those medicines outwith the end of life and rare diseases framework where the process operates very well and is held in high regard worldwide.

- How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach;
SMC will be able to provide this detail.
- How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement;
Feedback from the NHS Greater Glasgow and Clyde (NHSGG&C) members of SMC suggests that the process is more transparent since the meetings were opened to the public. The Committee took a while to establish a different style of dialogue due to much of the information being discussed being commercial in confidence at the request of the pharmaceutical industry. As there is a two tier process (NDC and main SMC

committee) and all members read the papers prior to the meeting it could perhaps appear that there is little discussion but that often reflects that some submissions raise issues at NDC which may be resolved prior to the SMC meeting. The voting and subsequent private session for the voting results means that the public do not see the whole process from start to finish.

The ability to include the pharmaceutical industry has also been helpful but each additional step/input at the meeting prolongs the meeting further. However, whilst recognising the positives, further involvement of the pharmaceutical industry at each stage in the process does need to be managed to ensure that the perceived risk of inappropriate influence by parties with a direct conflict of interest does not occur. There have been proposals for patients/patient groups to present the PACE, more oncology clinicians to be present and industry to have more input at the meetings. However these proposals all are likely to prolong the meetings without evidence of additional benefit. Members receive all the papers in advance and read them all. The verbal summaries for all aspect of the evidence allow a concise overview and stimulate discussion. There is no evidence to suggest this limits the power of any piece of evidence presented. Additional time could result in requirement for longer meetings or multiple meetings and additional clinician time, all of which pulls valuable clinical resource away from direct patient care.

- How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund; Standard processes apply. Medicines accepted under the new approach are not differentiated in the local process. In terms of implementation, medicines accepted by SMC are still required to go through the local NHS GG&C formulary process to ensure a safe and managed introduction into practice. SMC advice on new medicines is permissive and not mandatory; it does not necessarily show the new medicine fully in context to all other treatment options. Comparators used in SMC decision making are those most likely to be displaced, which is useful for determining cost effectiveness, but is not as useful in meeting the needs of our local clinicians. The local formulary is not about a medicine being available for use, as all medicines accepted for use by SMC are

available. Rather, the formulary has a role in directing the place in therapy to meet the needs of the majority of patients and based on local clinical consensus which enables greater ownership and trust in the decisions. The formulary is also an important educational tool for our less experienced doctors and acts as an engagement tool for our prescribers across primary and secondary care.

The New Medicines Fund has been available to NHS Greater Glasgow and Clyde and has been used to offset costs of the following:

- increased SMC recommendations following the PACE process
- increased rates of IPTR /PACS (pilot) approvals
- historical IPTR approvals for long term medicines such as eculizumab
- to make ivacaftor available under a patient group treatment request agreed nationally.

IPTR decisions in NHSGG&C have never considered funding consequences and have only ever considered specific patient clinical characteristics. Pre-review, if specific clinical characteristics of the patients differed from clinical trial populations and the patient was likely to gain additional benefit as a result of these differences then patients would have been able to access medicines in NHSGG&C which were not recommended by SMC.

The New Medicines Fund has been welcome as this has avoided the need to divert funding from other Board priorities to meet the demand for access to new medicines for patients with rarer conditions and at end of life. The New Medicines Fund is derived from receipts recovered via the Pharmaceutical Price Regulation System (PPRS) which in turn is recovered from profits for medicines already funded by Health Boards. It should be recognised that there remains a finite resource for healthcare and reallocation of the overall NHS budget at source to the New Medicines Fund does redirect funding that may have been available for other priorities. This has meant that, whilst central financial support has been provided to improve access to less cost effective medicines, Health Boards continue to face the challenge of prioritising cost effective medicines alongside other competing healthcare priorities. To avoid future pressure on affordability of more cost effective medicines, additional funding for end of life, orphan medicines and

medicines for rare conditions approved through these routes should continue. It is noted that the new medicines fund has been reduced by a third for 2016/17 and there is no indication of a long term commitment which could provide a serious financial challenge. While initial returns may suggest that this is a reasonable approach, most of the ultra orphan medicines will require long term commitments by NHS Boards to supply those medicines, often for a patient's lifetime. If this approach continues the cumulative effects of further new medicines for rare conditions being provided will inevitably cause huge stress, not only on any new medicines fund, but on the wider budget when such monies could have been spent on cost effective interventions.

Traditionally the Pharmaceutical Pricing Regulation Scheme (PPRS) contributes to the global budget. This has helped the overall management of medicines expenditure but under the current arrangements resource is directed towards medicines that are known to be not cost-effective. This results in pressure on the medicines budget which is planned on the basis of making cost effective medicines available.

- How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system);

An increased rate of IPTR proposals and IPTR approval rate has been observed in NHS GG&C, possibly as a result of the modification of the process to introduce greater "clinical flexibility" as proposed by the review through transition to PACS guidance. While it may be expected to see a reduction in IPTRs over time as the new processes come into effect, there will always be medicines that remain not recommended and therefore requests for IPTRs will continue.

Peer Approved Clinical System (PACS) is currently being evaluated by NHS GG&C and several other health boards on Scotland. We understand that there is a possibility that PACS could operate alongside the IPTR process. Were this to happen it would result in an additional complexity through operation of a two tiered system which may be difficult for the public and clinicians to understand and which may produce inconsistent decisions between both processes.

- Whether there are further opportunities to take a ‘once for Scotland’ approach in any aspect of access to newly licensed medicines;

There could be opportunities for ‘once for all’ approach for some aspects of the process. The most obvious relates to any negotiation on price for the PACS scheme – in the pilot the individual Board negotiated price. This would be better done nationally by procurement experts such as our national procurement colleagues. However there is clearly opportunity for price negotiation for all new medicines as part of the access arrangements.

Any work involving ultra orphan medicines has the potential not just for a ‘once for Scotland’ approach but for a UK approach as the numbers of patients involved for each medicine are so small.

NHSGG&C does not believe that a once for Scotland formulary is the best use of resource. A local Board utilises formulary as a tool to encourage mindful prescribing, to support doctors in training and to engage clinicians in both primary and secondary care to discuss the right medicine for the right patient at the right time. It is for the majority of prescribing in the majority of patients and not about a list of available medicines. Even if there was a national list of medicines available for use in NHS Scotland, there will still be a requirement to ensure safe local implementation of a new medicine and this may require development of guidance or protocols for use.

- How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies’ best offering on price earlier;

The SMC is not a negotiating group. It is a consortium of ADTCs. Negotiation on price requires specialist knowledge. In NHS Scotland this is provided by National Procurement which sits within NHS National Services Scotland. They are best placed to carry out price negotiations. Pricing is not a devolved responsibility and so there is a UK component to branded medicines pricing via the Pharmaceutical Price Regulation Scheme (PPRS) in addition to a European and global market context. There must be realistic expectations to price negotiation. However the new processes may well have weakened the

negotiating position by accepting medicines that are less cost effective and an inference that the threshold has increased. In reality the pharmaceutical industry can offer a higher price and still be accepted due to the increased flexibility.

- Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report;

While the new approach has achieved wider access to new medicines this has resulted in millions of pounds being spent on medicines that were previously not deemed as cost effective. PACS widens this approach further. NHS Boards have a duty of care to their whole population and money spent on non cost effective medicines, regardless of the source, results in opportunity costs for other members of the population who may be denied another more cost effective intervention as a result.

It could be argued that if access to these ultra orphan medicines is going to be granted irrespective of the SMC assessment via a separate process, as appears to be the case, then that assessment process is not worthwhile. Publication of “not recommended for use in NHS Scotland” decisions in these rare conditions creates huge and unnecessary distress to families and may impact on public confidence when reported in the media. In addition resource that could be spent on direct patient care is being utilised to support the SMC process for ultra-orphans.

We understand that the consideration of ultra orphan medicines provides significant challenges for the SMC assessment process. However, it is still essential that evaluation of medicines continues to ensure there is equity across all patient groups, be they for common or ultra-orphan conditions.

As stated previously there may be an assumption from the pharmaceutical industry that the threshold for acceptance has increased and therefore NHS Scotland is in a weaker negotiating position than existed prior to the new arrangements. This is reflected in the observation that since the introduction of the new approach, end of life medicines now considered by SMC typically come with base case ICERS in the range of £50,000/QALY rather than the previous £30,000 threshold.

- How the new approach will accommodate advances in new medicines and a developing regulatory framework;

The developing regulatory framework and in particular the policy drive for earlier access to new medicines even before safety and efficacy has been fully demonstrated, such as through the EAMS approach certainly provides challenges for Health Technology Assessment (HTA). The evidence being considered is derived earlier in the medicines development, has more uncertainty about benefit and less certainty about safety. There could be more impact from adverse drug reactions than previously experienced when a medicine is made available earlier and this may contribute to a different cost effectiveness profile.

- Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value.

NHSGG&C has no knowledge of developments in this area. There are now an increasing number of medicines being accessed that would not previously have been considered as cost effective options for NHS Scotland.

Examining the clinical and cost effectiveness of interventions is an essential method of helping healthcare organisations who require to operate within finite resources to prioritise their healthcare delivery. Within health technology assessment the cost per quality adjusted life year (QALY) is a well accepted indicator that allows a consistent approach when evaluating medicines. Medicines are now being made available with cost per QALY much higher than previously accepted. This may have made more end of life medicines available to certain patients, but research is ongoing at the University of York¹ which has suggested that even the conventional threshold of cost effectiveness of cost/QALY of £30,000 is too high and by approving more costly medicines, more harm is being done to other patients. In a finite healthcare budget, decisions that increase access to medicines with more marginal benefits impacts on ability to deliver other healthcare services. Currently there is limited opportunity to assess whether or not the additional investment in medicines is delivering improved outcomes. More research is

required to determine the effectiveness of medicines when used in “real world” i.e. outwith the restrictions on patients recruited to clinical trials.

It is also clear that medicines are treated in a different way to other healthcare interventions. There is no comparative rigor in assessing cost effectiveness of other interventions that may or may not be cost effective for NHS Scotland. In view of current and future financial constraints facing NHS Boards in Scotland, NHSGG&C would welcome further work being done to address value of not just medicines but of wider healthcare interventions to inform debate and aid the difficult decisions regarding prioritisation of interventions facing the NHS

Approach

The review will be undertaken independently of the Scottish Medicines Consortium and the Scottish Government and consult widely with those who have been engaged in the new approach, building on feedback already received by the Scottish Medicines Consortium, Scottish Government and Health and Sport Committee of the Scottish Parliament.

The review will have access to commercial in confidence information held by the Scottish Government on the basis that the confidentiality of this information is strictly upheld. The review will not significantly impact on the ability of the SMC to continue its work, and subject to this, is expected to report to the Scottish Government in around four months.

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ABPI Scotland Submission

Review of Access to New Medicines – Independent review by Dr Brian Montgomery 17 May 2016

Summary of key points

- The key to overcoming barriers and implementing successful reform is to work together with all stakeholders in partnership. Everyone in Scotland has an interest in getting this right. The opportunity exists for Scotland to use these reforms to help drive the Scottish health economy and improve health outcomes for Scottish patients.
- Medicines are set to deliver some of the biggest advances in treatment and there is a very strong pipeline of new medicines coming to the market over the next 5 years.
- SMC assesses the clinical and cost-effectiveness of new medicines. This means that medicines spending is already scrutinised more than any other area of NHSScotland spending.
- The success of the review will be determined by its implementation. A system of monitoring and evaluation of the review outcomes must be set-up.
- The current definitions for end of life, orphan and ultra-orphan medicines are working well.
- The current model of assessment of ultra-orphan medicines is not suitable and should be reformed.
- PACE is a relatively new system and it should be reviewed and adjusted to ensure it is having the desired effect. Better integration of PACE outputs is needed into the main SMC decision making process.
- We believe that SMC acceptance rates have improved, but the contribution of how individual changes have impacted on individual decisions is not clear, due to the introduction of multiple changes in parallel.
- The current SMC voting system should be reviewed by the SMC User Group Forum.
- PACS should be developed and implemented following the publication of the results of the pilot. The recommendations of the Accelerated Access Review should be considered in a timely manner – early stage routing of high impact medicines with a joined up approach across SMC and health boards would allow NHSScotland to be a rapid adopter of AAR opportunities.
- The SMC should not have a role in pricing negotiations, but earlier and more frequent dialogue and engagement between pharmaceutical companies and Scottish stakeholders would be welcomed in relation to fully aligning value propositions with commercial propositions.
- Making Scotland's health data practically useful will be central to advances in medicines assessment.



- Scotland has the opportunity to develop a world-leading medicines assessment process. Developing a range of different routes for assessing medicines with different characteristics which would serve Scottish patients well.
- PASAG needs to be reformed to help facilitate new approaches, along with the consideration of new commercial models which will facilitate earlier and greater access for Scottish patients (building on the 'once for Scotland' concept).
- There needs to be greater transparency on how the New Medicines Fund is being used. The medicines which have benefited from the fund should be disclosed into the public domain, with the development of criteria for determining the use of the fund going forwards.

Introductory comments

ABPI Scotland is grateful for the opportunity to submit to the Review of Access to New Medicines. This is an important review, and we have added in supplementary points below, as well as addressing the review questions in turn.

World-leading medicines assessment and health data as a driver of the Scottish economy

A large part of the importance of this review lies in its importance in unlocking the potential of Scotland in this area. World-leading medicines assessment is within Scotland's grasp as we enter the era of increasingly sophisticated and targeted medicines. Getting our HTA right would have huge benefits for Scottish patients and for NHSScotland; quicker access to the most cutting-edge treatments.

The potential prize in this area also extends to Scotland's economic potential. ABPI Scotland have been working hard with a number of stakeholders, not least the Scottish Government, to make Scotland a more attractive destination for global pharmaceutical investment. Scotland's history of medical research is a great source of national pride. There is no reason that Scotland cannot continue to be at the cusp of continuing medical innovation, and having a world-leading assessment process for new medicines would be an important step towards this.

The pharmaceutical industry in Scotland currently supports 8,000 jobs and generates £824m in GVA for Scotland. The pharmaceutical industry is also Scotland's second biggest industrial spender on R&D, accounting for 17% of the total.¹ ABPI Scotland will continue to work with all stakeholders to try to improve these figures by making Scotland as attractive a destination for global pharmaceutical investment as possible. As a monopoly purchaser, NHSScotland has huge potential to help promote and grow both the pharmaceutical sector and the wider life sciences sector in Scotland.

Our submission will point to health data as a key component in helping us achieve this. This is because a modern NHSScotland will need to improve its collection and use of data, not because it is a panacea, but because it is a necessary and central component to unlock potential new approaches, some of which we outline below. Health data cannot solve any of the issues around medicines access alone, but it is clear that without improved health data, these issues will not be solved.

¹ Economic impact of the pharmaceuticals industry on the Scottish economy (October 2015) – Fraser of Allander Institute, University of Strathclyde (commissioned by ABPI Scotland)



The affordability of new medicines to the Scottish Government

Our submission is also written in the context of a particularly tough financial environment for NHSScotland, for reasons that are well-known. The pharmaceutical sector has recognised this, and the current agreement on pharmaceutical prices (the Pharmaceutical Price Regulation Scheme or PPRS) has ensured that the medicines bill remains affordable for NHSScotland. Pharmaceutical companies have paid, through the PPRS rebate, an estimated £115 million (2014/15 and 2015/16) back to the Scottish Government, with a further £60 million estimated for 2016/17. We are not aware of any other industrial sector that offers such a deal to the Scottish Government. This money is paying for the Scottish Government's New Medicines Fund and increasing access to new medicines in Scotland.

This additional money notwithstanding, we appreciate that it is difficult for the Scottish Government to continue funding NHSScotland to the levels expected, and so it is inevitable that there will be a degree of attention on the cost of medicines. However, it must be borne in mind that NHSScotland's spending on medicines is already scrutinised more than any other area of NHSScotland's budget, despite it making up only around 10% of the total. It is worth reiterating that the role of the SMC – a role that ABPI Scotland fully supports – is to determine which medicines are clinically and cost effective.

Every single medicine approved for use by the SMC has been evaluated and proven its cost-effectiveness. The same cannot be said of other areas of NHSScotland spending, for example medical devices and technologies, procedures, IT infrastructure or contracted out services. The NHS Greater Glasgow and Clyde Director of Finance Mark White queried this to the Scottish Parliament earlier this year:

*"It is a fair challenge. Looking at the whole healthcare system and the patient journey, I do not think that many other areas are scrutinised as much as medicines are, and we have already debated the wider costs with regard to added value, knock-on effects and wider implications. It is true that the same rigour is not applied to many other parts of the system. Perhaps a debate for another time is whether that should be a further development of the process."*²

Price and value are not the same thing, and it is beyond doubt that medicines offer enormous value to NHSScotland and to wider Scottish society. In the last 30 years alone, death rates from HIV have fallen by 80%, deaths from cancer have fallen by 20% and recent pharmaceutical advances mean 90% of people living with Hepatitis C can now be cured through a 12-week course of medicines. The effective use of preventative care, vaccines and medications can slow disease progression, avoid illness and reduce costs.

We do recognise that the Scottish Government has many competing priorities when it comes to allocating spending. That is why ABPI Scotland is happy to work with Government and its agencies to find solutions that make medicines accessible and healthcare more sustainable, while securing future innovation. The pharmaceutical industry wants to be part of the solution in continuing to make medicines more accessible to Scottish patients.

² Health and Sport Committee Official Report (23 February 2016) - <http://www.scottish.parliament.uk/parliamentarybusiness/report.aspx?r=10388>



Implementation and evaluation

It is ABPI Scotland's view that there must be some measurement applied to the outcomes of this (and previous) reviews. This should apply both to the application of any recommendations, new guidance etc but also to the effects these new recommendations are having.

For example, it is impossible to know what effects the previous reforms to the SMC have actually had. Of course all stakeholders are able to give their views on whether the processes work more smoothly or not, and obviously we can all see how the SMC have applied the previous recommendations quickly and effectively. But there is currently no way to assess whether more patients are getting access to more new medicines than they otherwise would have. Patient access and use of new medicines has to be the ultimate determinant of success. ABPI Scotland and our member companies would be happy to work with any and all stakeholders to help deliver this.

Questions posed in the Review scope document

Question 1. How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice

1.1 ABPI Scotland are happy with the agreed definitions, and believe them to be working well. The new criteria are more flexible than those used elsewhere in the UK, something for which the SMC should be commended.

Question 2. How the views from the Patient and Clinician Engagement process are taken into account in decision making

2.1 We do not know how the views from PACE are taken into consideration during decision-making, and whether this is being done on a consistent basis. It is impossible to be sure without greater transparency. Anecdotal feedback from the ABPI member companies is that the process is giving patients and clinicians a greater voice in the process, an outcome that ABPI Scotland supports.

2.2 The PACE process would benefit from greater transparency around the output, how that output is used in decision making and, precisely, what impact this actually has on decisions. At the moment it seems quite an arbitrary and inconsistent effect.

2.3 Strengthening patient and clinical views would be welcomed by ABPI Scotland, something we believe could be done by making the emphasis and consideration given to PACE submissions more clearly defined.

2.4 There are concerns amongst the ABPI member companies about the delays that occur as a result of including a PACE submission. It has generally added an additional month to the submission process, but delays as long as three months have been reported to us. We believe this to be a resource issue, rather than a problem of process. It would be helpful if more PACE meetings could be held each month.



ABPI Scotland Recommendation –

There should be greater clarity as to how PACE outputs have been used and taken into account in decision making. NICE for example include a description of which different elements were included in their decision-making process and the precise impact and contribution of each factor to the decision made (short-term).

ABPI Scotland Recommendation –

The SMC and the SMC User Group Forum should examine if, and how the PACE process might be made available to different categories of medicines (for example where there is high un-met need) (mid-term).

Question 3. How the new approach to assessment of ultra-orphan medicines is operating in practice

- 3.1 The broader decision-making framework for orphan medicines is working well in practice.
- 3.2 However there is strong feeling among the ABPI member companies that further changes are required in the way that ultra-orphan medicines are assessed. There is an overreliance on the QALY, and a requirement for too much detail around sensitivity analysis. There are many examples of appraisal processes that are used to evaluate ultra-orphan medicines, and the SMC should look to these optimise its process (eg the NICE HST Programme).
- 3.3 The current process and level of analysis is much the same as for ‘standard’ medicines. ABPI Scotland does not believe that this is appropriate for ultra-orphan medicines, and that this could result in such medicines not being approved for use in Scotland. The SMC Task and Finish Group (T&FG) made this point quite clearly in its 2013 report:

“After consideration of a range of sources of evidence, including international literature...the T&FG concluded that the rationale for using a decision-making process not based on the cost per QALY was clear for medicines that would be defined as ultra-orphans.”³
- 3.4 The SMC T&FG report went on to suggest a number of other approaches that are more appropriate to the assessment of ultra-orphan medicines.
- 3.5 ABPI Scotland research demonstrates that 3 medicines have been assessed solely under the new ultra-orphan process (during our review period of 1 May 2014 to 6 July 2015). One of these medicines was accepted and 2 were not recommended.
- 3.6 Our research shows that 6 medicines have been assessed under the new ultra-orphan + end of life processes during the review period. 3 of these medicines were accepted, 2 were accepted with restrictions and one was not recommended.

³ Assessment of medicines for end of life care and very rare conditions (orphan and ultra-orphan medicines) in Scotland – p11 (December 2013) – SMC Rapid Review Task and Finish Group - http://www.scottish.parliament.uk/S4_HealthandSportCommittee/Inquiries/Assessment_of_medicines_for_end_of_life_care_and_very_rare_conditions.pdf



3.7 The same ABPI Scotland research shows that of the 93 medicines reviewed by the SMC during the review period of May 2014 to July 2015 using both new and existing processes (full submissions and resubmissions only), 78 (84%) were accepted or accepted with restrictions, and 15 (16%) were not recommended.

3.8 ABPI Scotland would like to see greater emphasis put on the ultra-orphan framework, and a recognition that 'standard' QALY based assessment process are not appropriate for ultra-orphan medicines.

ABPI Scotland Recommendation –

The current model of assessment of ultra-orphan medicines is not optimal for these medicines. The SMC User Group Forum should review the process and methodology for appraisal of ultra-orphan medicines, so that there is greater focus on the ultra-orphan framework and less on the cost/QALY.

Question 4. How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach

4.1 ABPI Scotland believes that there has been an improvement in the number of medicines being recommended for use by the SMC.

4.2 ABPI Scotland does not know which factors (or which combination of factors) have had the biggest impact upon decision-making (ie PAS, PACE, end of life, orphan or combinations of these).

4.3 As outlined in our answer to the previous question, there is an ongoing problem with the assessment of ultra-orphan medicines (see question 3).

4.4 Our own research shows that of the decisions made by the SMC between the 1 May 2014 and 6 July 2015, 108 of the 139 medicines assessed (78%) were accepted for use or accepted for restricted use, whereas 30 (22%) were not recommended for use in NHS Scotland.

4.5 When considering only full submissions and re-submissions (n=93), 78 (84%) were accepted for use or accepted for restricted use, whereas 15 (16%) were not recommended for use in NHS Scotland.

4.6 Compared to decisions made pre-reform, the acceptance rate for new medicines has increased by 50% from a prior-five-year average of 33%. The corollary is that the number of new medicines not recommended has decreased from a prior five year average of 35% to 16%.

4.7 ABPI Scotland is not aware of any publically available information that demonstrates whether or not the reformed SMC processes have resulted in greater access to, and use of, these medicines for patients through their NHS boards. This is a major weakness when trying to assess the effectiveness of the reforms undertaken, and their impact upon patient access to new medicines, a point we made in our introductory comments (above).

Question 5. How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement

5.1 ABPI Scotland believes that holding meetings in public has increased the transparency of the SMC process, particularly from the point of view of the public/patients.



- 5.2 ABPI Scotland does have concerns around the current voting mechanism. We have concerns that voting in public has made decisions less predictable than before (based on the discussion), and that anonymous voting is less transparent with regards the reason for a decision being reached (particularly from a manufacturer perspective). There may be advantages in moving back to consensus decision making which is not anonymous but having this part of the discussion in private (as per the NICE process). This should be explored.
- 5.3 It is ABPI Scotland's view that at times the decision made does not reflect the nature of the committee discussion. A consensus approach was more productive, with voting being used only where consensus was not achieved. This can be regarded as best practice in this area and therefore should be revisited.
- 5.4 The lack of transparent reasons for a negative SMC decision has a tangible effect. If companies are unclear why a particular submission was rejected, any amendments and resubmission will take longer to prepare, with consequent slowing patient access. Routine constructive written or verbal feedback would be helpful to companies in this regard.
- 5.5 Anecdotal feedback from the ABPI member companies acknowledges the greater input from patients and clinicians brought about by PACE, and suggesting ways in which the PACE input could be considered differently (please paragraphs 2.2 and 2.3 above).
- 5.6 A greater role for the medicine manufacturer would also be helpful. We believe they could contribute even more by being permitted to play a more active and constructive part in the discussion.
- 5.7 We recognise that PACE is still a relatively new process. Establishing formal feedback to companies, and also to patient groups and clinicians, on the usefulness of their submission will help strengthen future submissions. To this end, some official guidance from SMC on writing a PACE submission would be useful for health charities and patient groups.

ABPI Scotland Recommendations –

A review of the voting method by the SMC and/or the User Group Forum, and how voting in public is working, should be put in place.

A feedback mechanism for both patient groups and manufacturers on what could be improved in their submissions be established.

Question 6. How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund

- 6.1 As far as ABPI Scotland is aware, implementation of recommendations is not measured (at least not publically) so this is unknown.
- 6.2 There should be transparency around how the NMF is being used, what it is funding and what the process is for NHS boards and/or clinicians to access it. There is currently no way of knowing whether the NMF is working successfully or not, or even whether it is being utilised properly.
- 6.3 There should be a process in place to track the SMC's decisions through NHS boards to measure how they are translating into patient use.



ABPI Scotland Recommendation –

Health Improvement Scotland should routinely and regularly monitor and publically report on NHS board translation of SMC decisions, and subsequent patient uptake of SMC approved new medicines.

The use to which the new medicines fund has been put should be made publically available and criteria developed and consulted upon to ensure optimum use of the fund going forwards.

Question 7. How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system)

- 7.1 As PACS has not yet been implemented we await to be able to assess its effectiveness.
- 7.2 ABPI Scotland believe that the flaws in the IPTR system as identified by the Scottish Parliament's Health and Sport Committee in 2014 most notably its inequity, persist.⁴
- 7.3 With regards IPTRs, there is a lack of information on what they are being used for and under what circumstances. There absolutely should be a system to deal with unusual cases, but it should not be normal for it to be used.
- 7.4 Beating Bowel Cancer's 'triple-lock' system idea is worthy of consideration. Indeed ABPI Scotland were under the impression that this would form the basis of PACS. This system requires 1) clinician to apply based on individual clinical need 2) expert peer to support 3) panel simply ratifies.
- 7.5 ABPI Scotland is concerned by reports that some NHS boards will not consider IPTRs once a medicine has been 'not recommended' for use in NHSScotland by the SMC.

ABPI Scotland Recommendation –

The outputs from the PACS pilot should be shared with stakeholders and consulted upon.

Question 8. Whether there are further opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines

- 8.1 ABPI Scotland strongly supports that idea that once a medicine has been assessed by the SMC, it should not undergo any additional assessment or restrictions at a local NHS board level.
- 8.2 ABPI Scotland would point the Review in the direction of the UK Government's Accelerated Access Review (AAR), which is due to report in July 2016. The opportunity exists to recognise particularly promising or important medicines earlier in the process. Increased dialogue between the manufacturer and key stakeholders allows potential difficulties to be discussed early (for

⁴ Letter from Convener of the Scottish Parliament's Health and Sport Committee to four NHS boards (5 March 2014) - http://www.parliament.scot/S4_HealthandSportCommittee/Inquiries/Access_to_new_medicines_-_letter_to_NHS_boards.pdf



example budget impact, service design, supporting data and diagnostics, alternative assessment pathway etc). The end goal is to speed-up patient access, streamline the assessment process and remove the need for duplication.

8.3 We would like to see a mandate sit either with SMC or with another body to implement early-stage 'routing' of medicines that would utilise a suite of potential options depending on the medicine being assessed. These routes could include:

- Patient Access Schemes – encompassing both simple and complex PAS (see comments below on reform of PASAG).
- Managed Access Agreements (MAA's) – which could include payment by results.
- Abbreviated submissions – this could include resubmissions, expedited assessments.

The assessment route taken would be agreed based on a number of factors, which could include unmet need, significant service or cost impact, likely PACE submission, what data will be required to implement etc.

ABPI Scotland Recommendation –

SMC, Health Improvement Scotland (through the ADTC collaborative), health boards, patient, clinician and pharmaceutical industry stakeholders are convened for a short-life working group to develop an enhanced process and methodology for early engagement. This would investigate alternative options for the managed access of certain high impact new medicines and the process to determine the most appropriate route for any subsequent assessment by SMC and mechanism for achieving rapid uptake across NHSScotland.

ABPI Scotland Recommendation –

A short life working group to be created to look at what early engagement means, what it should entail and what needs to happen to make sure it works for all stakeholders. This would allow Scotland to be proactive in rapidly implementing some of the new concepts which will be set out in the Accelerated Access Review intended to allow NHS patients to get earlier access to important medicines.

Question 9. How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier

9.1 The SMC should not have a role in pricing negotiations. To do so would hamper the SMC's role and reputation as an evidence-based assessment body that judges clinical and cost efficacy.

9.2 More frequent, and earlier, opportunities to engage and enter dialogue with stakeholder agencies (be that SMC, or other bodies) is welcomed by ABPI Scotland. The earlier any potential problems are addressed, the fewer delays there should be to patient access.



9.3 Discussions around aligning commercial and value propositions are to be welcomed and in general should happen once the value proposition of a medicine is established via the SMC process (including any PAS agreements, MAAs). These should usually happen after the value of a new medicine has been established. Free pricing helps maintain the UK as an early launch market; the SMC is often one of the first HTA reviews and leads the way in establishing the cost-effectiveness of new medicine.

Question 10. Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report

10.1 We refer to our answer to question 5 (above) about the voting system.

Question 11. How the new approach will accommodate advances in new medicines and a developing regulatory framework

- 11.1 Currently, the new approach is very limited in its ability to accommodate either advances in new medicines or the developing regulatory framework.
- 11.2 Again we refer to the work around the Accelerated Access Review. Early engagement and discussion on a new set of options for the kinds of new medicines coming in the future will be vital. Please see the earlier responses to question 8 and question 9, where we discuss early engagement.
- 11.3 Other factors would include a reformed PASAG, and Scotland starting to use its world-leading data in a more uniform practical way that benefits patients.

ABPI Scotland Recommendation –

A Short Life Working Group should be created to develop a gap analysis to review the suitability and accessibility of key datasets, conditional approvals, interim funding and the other options available to Scotland. This would be with the aim of supporting the assessment of value and supporting the use of MAAs for medicines where this approach is suitable. The SLWG could also make recommendations on the appropriate processes to support accessibility and availability of data fit for this purpose.

Question 12. Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value

- 12.1 ABPI Scotland is unclear about what is intended through the development of a specific 'Scottish model of value'. We understand that much of the work around reforming SMC processes is part of moving us towards a Scottish model of value.
- 12.2 We understand that Scottish model of value has been included in the SMC User Group Forum (SMC UGF) work plan for 2016.



- 12.3 In terms of progress that we would like to see, we refer to our answers to questions 9 and question 11, where we discuss the improvements that we would like to see.
- 12.4 ABPI Scotland sees an opportunity for Scotland to be ground-breaking in its approach to HTA, and we are very keen to work with all stakeholders to ensure that we take this opportunity.

Additional comments

The need for PASAG reform

New Patient Access Scheme (PAS) models can be explored to support the 'once for Scotland' vision. Whilst appreciating and recognising the willingness to engage with submitting companies, the current evaluation infrastructure limitations at the Patient Access Scheme Assessment Group (PASAG) need to be addressed to ensure alignment with recent and future progress at SMC.

Many PASs approved in Scotland are 'simple' discounts from list price, the sustainability of which is dependent on strict adherence to confidentiality. However, this 'simple PAS' preference in Scotland has its limitations and prevents companies from proposing and implementing a range of more innovative and potentially more beneficial schemes. This is particularly so as the number and proportion of specialised products, many in small patient populations, increases, along with the number of products with multiple indications. These new products will continue to present difficulties for the SMC and PASAG unless we make headway on addressing ongoing issues.

PASAG cites the administrative burden on the NHS boards as the main reason for not approving financial or outcomes based schemes (often referred to as 'complex PAS') and has a preference for 'simple' discounts. We accept that such schemes can be administratively burdensome, but in order to deliver greater value for money for NHSScotland more creative solutions are required, and the additional administration will be a resource cost that must be factored into the 'Scottish model of value'. The pharmaceutical industry will be happy to discuss how we can collaborate to help with any additional burden.

Failure to include 'complex PAS' will in our view, severely hamper NHSScotland's ability to secure the best deal for new medicines – something that the Scottish Government has recently obliged NHSScotland to when procuring pharmaceuticals.

What is required?

ABPI would like the Scottish Government to widen the scope of PASAG to allow it to consider alternative commercial models put forward by companies and determine whether these arrangements could be implemented in NHSScotland. This would also involve ensuring systems are in place so that the best value is achieved first time and the need for time-consuming resubmissions to the SMC be avoided.

There is a need for a clear flexible framework for PASAG that provides a suite of different models/mechanisms to cater for different products and circumstances, and creates appropriate channels for discussion and negotiation. NHSScotland would also have to be willing and able to implement these. ABPI Scotland would be happy to discuss what could be included in this suite of options.

These arrangements are not currently factored into value assessment and/or pricing arrangements.



The PASAG process was not included in the SMC reforms of 2013. PASAG need to be resourced appropriately and given the authority by Scottish Government and the NHS boards to consider the full range of finance and outcome based schemes in the same pragmatic manner as they currently review simple discount schemes; then Scotland’s ability to achieve best value for new medicines will be significantly improved.

Failure to reform PASAG will mean that current inflexibilities in the PASAG decision-making process will not support the Scottish Government ambition to reach the best deal for Scotland, first time.

ABPI Scotland Recommendation –

ABPI Scotland proposed the creation of a framework with PASAG that facilitates a suite of options that cater for the complex mix of medicines and indications in the pharmaceutical portfolio. ABPI Scotland is keen to have further discussions about what this would include, and it should be tied-in to wider reform in the context of a once for Scotland approach (see question 8).

Some examples of the types of schemes that could work within a new framework

A range of schemes are given below as an example (this is not an exhaustive list), divided into finance-based and outcomes-based schemes. All require some kind of value assessment before they can be applied. Some are currently available in the UK.

Finance-based schemes

<p>Simple discount</p>	<p>The scheme most favoured by PASAG and NHSScotland. Majority of PAS approved by PASAG since its inception have been simple discounts. For SMC appraised medicines a confidential discount is agreed. The company applies the discount when invoicing NHS organisations.</p> <p>Advantages of this approach are a low administration burden for all (NHSScotland, company, clinicians); certainty in terms of NHSScotland receiving the benefit and a direct line between the discount and the relevant payer and that confidentiality allows the net price to be maintained.</p> <p>For multi-indication products, companies are unable to price according to the value of each indication, as the discount is priced to the first and/or lowest priced indication.</p> <p>Whilst this is ideal for the Scottish Government/NHSScotland, it compromises commercial viability for companies, limits use of this mechanism, and in some cases stops companies from launching in early indications.</p>
<p>Dose capping (including use of free stock)</p>	<p>A company offers a number of free doses up-front or provides free supply following a set number of doses.</p> <p>Products can also be provided free of charge (or at a discount) for a finite period at the start of treatment.</p> <p>In both instances, the extent of overall benefit will be dependent on actual duration of treatment (although this may be based on limited experience).</p> <p>This approach addresses affordability concerns for the NHS by limiting cost whilst not impacting duration of therapy and still allowing clinicians to make prescribing decisions</p>



	<p>according to the needs of their patients.</p> <p>For the company, the offer of free (or discounted) drug following a set number of doses enables uncertainty around duration and/or cost to be addressed.</p> <p>However the overall value to the company is realised only if patients continue treatment to or beyond the forecast duration and NHSScotland systems mean that these schemes are generally associated with an administrative burden.</p>
Budget capping	<p>Budget capping helps address affordability concerns by offering certainty in expenditure and budget management for the Scottish Government, NHSScotland and the company. Multiple indications can be accommodated and potential for off-label use of the medicine is reduced.</p> <p>For the company, revenue is limited to a finite amount and potentially damages the realisation of commercial success for medicines that offer real patient benefit. It relies heavily on accurate forecasting of potential NHSScotland uptake.</p>
Patient number capping	<p>This has been implemented under the CDF in England and involves a cap on the number of patients allowed access to the medicine. A further arrangement is introduced for patients additional to the cap, such as a discount or performance-based arrangement.</p> <p>For the company, there is a guarantee of access up to a specified number of patients and for the NHS any further risk is shared with the company. The success of the scheme is highly reliant on accurate forecasting.</p>
Multi-indication pricing	<p>Whilst the number of medicines with multiple indications is increasing, there is no mechanism for a company to make different arrangements across the full range of product indications.</p> <p>In reality, pricing is established at the level of cost-effectiveness of the first indication, which is generally in patients where establishing cost effectiveness is most difficult (e.g. in smaller patient populations, those with a high burden of or advanced disease).</p> <p>Implementation of a price adjustment under the current system means that the resultant price can make existing (or future) indications either more or less cost effective, with the risk for patients, clinicians and NHSScotland that companies may choose not to launch in indications which will tie them to a single price. This could disadvantage some patients.</p> <p>Options include around this include the generation of a blended ICER in value assessment; a blended price across the total patient population which accounts for the price at which each indication offers value to NHSScotland; payment at different prices for each indication followed by a reconciliation exercise at agreed time-points.</p> <p>For companies, this approach also relies on accuracy of forecasting and/or a retrospective mechanism agreeable to all parties. There is a need to revisit the discount on the introduction of each indication.</p>

Outcomes-based Schemes

These fall into two broad categories: ‘pay for performance’ and ‘coverage with evidence development’ (including ‘future value rebate’ schemes). Both aim to address clinical and/or economic uncertainty.

Pay for performance	<p>Outcomes are tracked during ‘real-world’ use and payment, rebates or free stock and are dependent on achievement of agreed patient outcomes.</p> <p>It is currently possible to get approval for these schemes although they are not favoured</p>
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	<p>and in fact only one 'pay for performance' scheme has been implemented (the Velcade Risk-sharing Scheme in 2009).</p> <p>These schemes represent genuine risk sharing between the company and the NHSScotland. The company bases the arrangement on the outcomes derived from clinical trials and the NHSScotland only pays for use in patients where the medicine proves effective. The schemes have a life-span that can be limited to the time it takes for outcomes to be established with confidence.</p> <p>The existence of emerging patient registries, provide an ideal potential vehicle to address uncertainties, build use and reimbursement on the basis of real-world outcomes, and maximise the value of the investment made in developing the registry.</p> <p>Certain circumstances need to be in place for these schemes to work effectively, for example biochemical markers that assess and enable tracking of performance of the medicine and a common patient pathway to enable consistent application across NHS boards. The company will need to design a system and support NHS boards in set-up and implementation which requires a degree of consistency across NHS boards to enable this to happen.</p> <p>Investment in resources (time, manpower, money) can be considerable not only for the company but also for the NHS board. Patient pathways may need to be adapted and investment made in administering the scheme. There have been examples where NHS organisations have opted out and foregone the rebate as administration has proved too onerous.</p> <p>Where implementation is complex, ABPI Scotland believes Pay for Performance schemes should generally be limited to exceptional circumstances where uncertainty cannot be addressed in other ways.</p>
<p>Coverage with Evidence Development (CED)</p>	<p>Evidence is collected in a real-world setting to address a particular aspect of uncertainty. Price and/or funding is subsequently contingent on an analysis of the data generated (eg through a subsequent NICE appraisal).</p> <p>There is very little experience in the context of medicines in the UK, with the possible exception of the Multiple Sclerosis Risk Share Scheme.</p> <p>A 'future value rebate' scheme (Votrient in renal cell carcinoma), where the company committed to a rebate if results of a Phase 3b study did not confirm the original value assessment, has also been approved. There are currently more questions than answers, including:</p> <ul style="list-style-type: none"> • What kinds of study come under the banner of CED? Arguably, CED could include not only collection of real-world data in observational studies, but also extension of Phase IV studies where drug is paid for by the NHS, or even extension of Phase III studies. • Study design: who decides the protocol, by and with whom, how is it approved? • Who pays and for what? • Who collects the data, who oversees collection? • Who is responsible for ensuring good practice in study design, data collection and reporting, patient safeguards, etc? • How is the reimbursable price during data collection agreed and by whom?



	<ul style="list-style-type: none">• Over what time period is data collection undertaken?• How will the data collected be used?• If the decision on final reimbursement is dependent on SMC, will SMC accept observational rather than RCT data? <p>These questions will need to be answered, in collaboration with the pharmaceutical industry, if CED is to achieve its potential as valuable addition to available schemes.</p> <p>Again, ABPI Scotland believes it should be limited to exceptional circumstances where uncertainty cannot be addressed in other ways.</p>
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'Infrastructure' schemes

In these schemes, the company agrees to provide infrastructure and support (eg nurses, clinics, patient pathway design) to NHSScotland so that the service is able to adopt the new medicine. The company is able to secure rapid adoption and patients, clinicians and the company benefit from use of the medicine to best-practice standards.

NHSScotland is relieved of the requirement for immediate investment in new services, including recruitment, up-skilling and training. There are issues around agreement of exit strategies and willingness of NHSScotland to take on the cost of care of patients once services have been established.

These arrangements are not currently factored into value assessment and/or pricing arrangements.

ABPI Scotland

May 2016

Cystic

Fibrosis a fight we must win

Submission to Dr Brian Montgomery's *Independent Review of Access to New Medicines*

Cystic Fibrosis Trust

May 2016

Introduction

This paper outlines the Cystic Fibrosis Trust experience of and comments on the recommended changes made to increase transparency, improve patient involvement within the SMC appraisal process for the appraisal of orphan, ultra-orphan and end of life medicines.

Summary

Since the implementation of the Scottish Government New Medicines Review recommendations in 2014 that among other positive steps saw the formation of the Patient and Clinician Engagement (PACE) process, the Cystic Fibrosis Trust agrees that there is greater transparency and communication from SMC via the Public Involvement Team and that support through the process is significantly improved.

The role of the Public Partners has been clarified in recent meetings with SMC. However, for associated patient groups we would seek verbal clarification at patient group submission to SMC that the Public Partners role is not to represent but to convey burden of disease, unmet need and the patient story at SMC meetings.

The Trust supports the move to pre-notify patient groups, which facilitates better communication with the cystic fibrosis communities which has been a more recent development.

The Cystic Fibrosis Trust has proposed a solution provide a model for access to new medicines for smaller patient groups using real time registry data* to assess impact of new treatments and arrange with pharmaceuticals reimbursement costs depending on outcomes.

The proposed model could be applied in appraising both ultra-orphan and orphan indications and provide an opportunity to move beyond traditional appraisal routes where data uncertainty contributes to inadequate cost-effectiveness confidence and negative recommendations. Please see the Cystic Fibrosis Trust's new medicines proposals attached.

*The Cystic Fibrosis Trust hosts and sponsors the UK CF Registry, a patient data registry providing health data for 99% of the UK cystic fibrosis patient population.

PACE and decision making influence

The Cystic Fibrosis Trust has attended two PACE meetings for three drugs:

- Ivacaftor (kalydeco) 2-5 year olds went to PACE, 2016: not recommended
- Orkambi went to PACE, 2016: not recommended
- Nebulised Aztreonam lycine (cayston) went to PACE, 2015: recommended

On the whole we welcome the addition of the PACE meeting to the appraisal process and our experience of it has been beneficial. By allowing a voice to both patient groups and clinicians we were able to highlight elements of the drug, condition or disease group rather than what was presented in the written PIG submission.

During one meeting audible gasps were heard from the SMC attendees when discussing some aspects of the disease such as the isolation the disease causes for family and friends. Although noted in the submissions, this was better conveyed in a face to face discussion.

This however has highlighted duplication of or inconsistencies in important information in the final PACE statement from ones noted on Patient Interest Group submissions and therefore would consider that a variation of the PACE platform or questions requiring to be asked be more valuable earlier in the appraisal process.

Although the PACE meeting is a positive inclusion in the process patient groups would not be aware of the impact of their statement on a decision at the final SMC date. An audit of impact of PACE at the SMC decision making meeting amongst committee members would provide further transparency and context for the usefulness of the process.

Clinicians' opinions

Overall feedback on the changes and PACE process suggested that clinicians felt their opinion was valued and were pleased they had been given a voice in the process. However, it was felt the patient voice should be more represented through all stages of the process.

The Peer Approved Clinical System (PACS), to replace the Individual Patient Treatment Request (IPTR) due to partly being administered unequally across health boards is being piloted in Greater Glasgow and Clyde NHS Health Board (GGCHB) but not more widely implemented despite this being a recommendation since 2014.

There is concern that drug funding may come from GGCHB budget rather than from the New Medicines Fund (NMF) if PACS is not used as intended, for example for ivacaftor should be guaranteed to clinics by the NMF.

Who benefits from access to new drugs?

The Cystic Fibrosis Trust attached with this submission the review data concerning the effects of ivacaftor one year on for paediatric patients who are 6 years old and older in Scotland.

The positive effects of ivacaftor, under the NMF, cannot be overstated for this patient group who otherwise would have continued with cystic fibrosis decline and death (for older patients) without the drug. Scottish Cystic Fibrosis registry data shows a median age of death from the disease at 26, which is two years less than the UK median at 28. As ivacaftor, and now Orkambi herald a new drug pipeline in the treatment of cystic fibrosis we believe that clinical data obtained since 2014 could be used to help shape a Scottish model of value for ultra-orphan and orphan medicines going forward as noted in our proposed solution.

Further opportunities for Patient Engagement

For the patient voice to be represented further in new medicines appraisal process we would encourage consideration of Patient Groups being represented at SMC meetings when new drugs are considered. This would add more value to the process if done in a correct and safe manner.

We are very positive about the review recommendations which are moving in the right direction to a Scottish model of value.

About the Cystic Fibrosis Trust

The Cystic Fibrosis Trust is the only UK wide charity supporting those with the condition and their families and researching cystic fibrosis to enable our community to live a life unlimited by their condition.

More than 2.5 million people in the UK carry the faulty gene, around one in 25 of us – most without knowing.

There is currently no cure for cystic fibrosis and most treatments target only the symptomatic expression of the disease rather than the underlying cause, including physiotherapy, exercise, medication and nutrition.

However, new medicines that target the basic genetic defect are being developed for more and more people with cystic fibrosis and the Cystic Fibrosis Trust is committed to ensuring people get time access to effective medicines.

We predict that more than half of the cystic fibrosis population in the UK will live past 41, and improved care and treatments may mean that a baby born today can be expected to live even longer.

However, in 2014, the median age at death was just 27. Many people with cystic fibrosis still die as children.

For further information on any of the above issues facing people living with cystic fibrosis please contact policy@cysticfibrosis.org.uk

Scottish Directors of Public Health

Final Response from the Scottish Directors of Public Health on the Scottish Medicines Consortium Review (the Montgomery Review)

31 May 2016

Dear Brian,

The Scottish Directors of Public Health (SDPH) welcomes the opportunity to respond to the Scottish Medicines Consortium (SMC) Review. As you will be aware, in collaboration with the NHS Board Directors of Pharmacy, the SDPH advised on the content of the response from the Board Chief Executives. In this response we wish to highlight the issues we wish the review to take into account from a population health perspective.

Firstly, we recognise the considerable workload undertaken as part of the review whilst maintaining “business as usual”.

Secondly, we acknowledge that the revised SMC process has increased access to new medicines for a small number of patients with specified conditions. From a population health perspective, however, the consequences include:

- a change in the balance between the risks and benefits of those drug treatments that have been considered for funding through this mechanism
- an increase in investment in what would previously have been identified as non-cost-effective medicines;
- reduced access to medicines for patients with other chronic diseases,
- a potential to widening of health inequalities between patients eligible for consideration by SMC and patients with similar or greater needs but non-eligible conditions.
- a risk of avoidable harm to the wider population arising from unintended consequences of the new processes that focus on access to medicines rather than health need and ability to benefit from health care intervention. These unintended consequences include the disinvestment in more effective and cost-effective prevention, treatment and care that is required in order to finance access to new medicines.

In this paper we highlight three broad areas on which you requested our views:

1. An overview of the areas that must be addressed in the review
2. A brief outline of the more detailed submission of evidence that can be developed;
3. How we can ensure SMC processes and associated measures can be made more robust, timely, and equitable and tailored in response to need.

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1 Areas that must be addressed in the review

We consider that the following issues need to be addressed in the SMC review.

Population characteristics

- Consideration of how changes in the Scottish population in the next two decades may influence the processes developed for the SMC to date, and what new issues may arise.

Assessing health gain / value

- Until recently, the SMC has used health maximisation (cost per QALY) as the basis for its assessments of health gain and value. Whilst this has created a useful comparator between medicines, the absence of evidence to support the quantification of the benefits from technologies, service implementation, and population or preventative interventions, means that it is difficult to draw direct comparisons. This tends to distort the overall value of a drug based gain.
- Ensuring that there is an appropriate balance between absolute and relative cost-effectiveness of medicines designed to treat a specific condition and the evidence of the benefits and risks of treatment is critical. The increasing acceptance rates for SMC applications suggest that the threshold for treatment has reduced though there has been no study of additional benefits and harms.

SMC Independence and Conflicts of Interest

- The SMC must remain as an independent advisory committee and be able to demonstrate that it is not subject to undue influence from external bodies whether these are patient lobby groups, pharmaceutical companies, health boards, or political parties.
- It has always had very strict rules regarding conflict of interest regarding its core members, but less attention is paid to potential influences on patient groups or individual clinicians, especially via indirect funding from industry. How can we ensure that all involved in SMC processes are trained in critical appraisal and the understanding of risk, benefit, opportunity cost and measurement of quality of life?
- Consideration also needs to be given to how best to include public and patients groups not directly affected by the treatment under consideration. Currently, there is little or no opportunity for those other patient groups who will be disadvantaged by the diversion of resources that results from the new process have any balancing input.

Application of decisions

- A national “compassionate use” programme is an important aspect of any system for appraising the appropriate use of new medicines. The application of such schemes requires care. . Where there has been no previous effective treatment for a condition, the use may be clear. But what about its application to a specific sub-group of patients, or where treatment resistance associated with lowered

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thresholds has undermined the real or perceived effectiveness of standard treatments?

- To supplement the work of SMC, there is a requirement for a national second stage to address how medicines will be introduced and withdrawn systematically. This 'put to use' process would build on the Area Drugs and Therapeutics Committee Collaborative to create a 'best for Scotland view on the place of the therapy' with a single formulary and a requirement to commission and receive reports on pharmacovigilance, equity and opportunity costs.
- An example of such an approach can be seen in New Zealand, where the role of PHARMAC's within the health system is to make decisions on which medicines are funded in order to get the best health outcomes, from within the available budget. PHARMAC's decisions need to represent good value for money for the benefit of all New Zealanders. It seeks to balance the needs of patients' access to healthcare against its responsibilities to the taxpayer. The PHARMAC Board is required by law to manage pharmaceutical expenditure within budget and reports directly to the Minister for Health.
- However, there are differences in the healthcare systems between New Zealand and Scotland that mean that the approach in New Zealand would require to be considered within the NHS Scotland health landscape. The New Zealand system is a transparent approach to value and affordability within a fixed budget.

Value for money

- Cost effectiveness must remain a feature of the work of SMC. However these considerations need to be widened to consider overall affordability, particularly since the increasing spend on a limited group of medicines for a restricted group of patients is outpacing the uplift in NHS funding, even with the allocation of the new medicines funds. That said, the actual cost of the new drugs that have been prescribed should be identified as they may be a relatively small amount in comparison to the overall drugs budget.
- Financial comparison should be extended to consider the opportunity cost of SMC decisions. The current spend on new and high cost medicines is distorting patient pathways by focusing investment on certain interventions rather than on others, regardless of evidence of benefit.
- Investment in certain acute specialties rather than primary care: the new medicines fund does not cover the infrastructure required to deliver new and complex medicines safely, so additional infrastructure costs in acute care further reduce investment in pharmacy and pharmaceutical care in other areas. The most obvious example is the current cuts to smoking cessation, in part to fund lung cancer treatment with new and end of life drugs.

Research considerations

- Patient safety is crucial but there is limited investment in pharmacovigilance studies and short-term follow up predominates in those studies that are carried out. We need to maximise the potential of using ISD data for such studies.
- Patients with rare conditions must have the opportunity to participate in global trials and all should be enrolled routinely in follow up research. However, the excess NHS costs of such research should be fully funded by industry.
- Compliance with open data standards is a requirement for use for use of medicines and technologies in Scotland. In the short term, we should be seeking

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commitment by companies to work towards this, reflecting the requirements of the International Committee of Journal Editors for transparency, scrutiny, reproducibility, and access to trial data by other researchers.

Equity

- The pattern of investment in research and development by commercial companies does not reflect the burden of preventable disease in Scotland or globally. This means that some patient groups will inevitably receive greater attention than others. With increasing costs per QALY for some treatments, this means that some patient groups will be better served than others. This will have the effect of increasing health inequalities is not recognised and addressed.
- There has been no equity audit of the current scheme to ensure that the socioeconomic gradient in disease is reflected in the distribution of treatment. The rapid acceptance of strict rationing of access to new medicines for Hepatitis C versus cancer medicines with far more limited benefit suggests that the requirement to demonstrate vertical equity has not been considered.
- Clearly, there is a piece of work there for public health to think about the equity issues regarding new drug and health interventions in a systematic way and help build such considerations into SMC and other processes.

2 Ensure SMC processes and associated measures enable patients to equitably access effective treatments that meet need and avoid unintended inequalities

First, the SDPH recognises that SMC – in all its incarnations - fulfils an important role within the universal health care system in Scotland, is well-respected internationally and deserves the confidence of political and strategic decision makers. However, the requirements, expectations and context which creates such confidence has changed over time; not least because of the evolving nature of stakeholder engagement and involvement. An SMC remains essential to any universal healthcare system. Difficult decisions are difficult. One Committee should take them. There should be no parallel process for the approval of new medicines.

Revising the processes and focus of SMC without cognisance of the wider impact on health and the health system risks undermining SMC's expert role, is hazardous and can lead to unintended consequences.

SMC previously provided an objective view that supported clinicians and patients in making difficult decisions. We understand that, without support, doctors, patients and relatives tend to overrate treatment benefits and underestimate treatment risks and adverse consequences. That is why research evidence and longer term pharmacovigilance, pharmacoepidemiology and studies of patient outcomes, and effective ways of engaging patients, public and politicians in knowledge translation are essential.

We recognise the need for robust mechanisms that enable exceptional use of otherwise unapproved medicines. These fall into two groups for which complementary criteria apply: experimental and compassionate use. Experimental use should be an n = 1 trial in exceptional circumstances, with all the safeguards that

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entails. Compassionate use programmes are for those situations in which ‘medicine is expected to help patients with **life-threatening, long-lasting or seriously debilitating illnesses**, which cannot be treated satisfactorily with any currently authorised medicine¹.

¹See:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000293.jsp

The medicine must be undergoing clinical trials or have entered the marketing-authorisation application process and while early studies will generally have been completed, its safety profile and dosage guidelines may not be fully established.’

Other, costly exceptions to the use of SMC processes cannot occur without justification and SMC should reserve the right to make decisions about medicines without manufacturer involvement if they choose not to engage with SMC. The emergence and maturity of *Realistic Medicine* as a concept and set of principles is a new, welcome and practical framework within which SMC can adjust and flourish.

Whilst the review of SMC processes has resulted in wider access to new medicines for a small number of patients and conditions there have been adverse consequences including:

- increased investment in what would have traditionally been recognised as non-cost effective medicines;
- lack of opportunity to explain the partial role of medicines in treating patients with cancer, rare and common chronic conditions;
- limited understanding of the infrastructure required to support safe and effective use of complex and multiple medicines in everyday life;
- differential funding of care for conditions in which manufacturers have invested.
- preferential care for patients who are eligible for new treatments;
- fragmentation of care for patients with rare conditions rather than developing and agreeing common standards of care, treatment goals and the role of medicines;
- potential widening in inequalities in outcomes for specific conditions if medicines and additional interventions are effective in selected patients; and
- potential for overall reduction in health gain associated with cuts to funding for more effective interventions.
- NHS Scotland needs to take balanced and consistent decisions, implement them fairly and then maintain them until new, peer reviewed, evidence emerges. SMC
- provides a recognised focus for one aspect of treatment, the cost-effectiveness of medicines in isolation, taken in optimal circumstances. The increasing percentage of the health budget spent on medicines that are SMC approved means that single focus decisions need to take the wider opportunity cost of such decisions to patients, the population and the NHS. These opportunity costs are not simply financial; the resultant transfer of funding from one part of the patient pathway to another has the potential to undermine the overall gains in quality of

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life and reduction in mortality from the condition by over-treating with medicines of limited benefit while reducing resources available to address co-morbidity or provide practical support and specialist palliative care. More broadly, transfer of resources from one condition to another, from one section of society to another, if sustained, will pose risks to the universal nature of the health service.

SDPH are aware of these unintended consequences and wider issues associated with the most recent review of SMC. These have been explained fully in the contribution from pharmacy colleagues.

We consider that the current review provides an opportunity to explore, understand, and where necessary, recommend changes in process that address:

- 1) the unintended consequences of the separation of processes relating to the access to new medicines from a societal discussion on value and maximising health gain;
- 2) a proper consideration of the opportunity costs of investing in pharmaceutical interventions which would have previously been deemed not to be cost-effective and would not have been accepted for use in Scotland;
- 3) how best to gain best value in a way that maximise affordability and sustainability of implementation of SMC decisions; and
- 4) how SMC processes can be enhanced to reflect the context of realistic medicine and the comparative benefit and value associated with pharmaceutical and non-pharmaceutical interventions, especially in the context of the shift to prevention.

In these ways we consider that the system can provide more equitable access effective treatments that meet need and avoid unintended inequalities.

Yours sincerely



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West of Scotland Cancer Network Response to the Review of Access to New Medicines – independent review by Dr Brian Montgomery

Context

In October 2013 the Cabinet Secretary for Health and Wellbeing directed the Scottish Medicines Consortium (SMC) to undertake a rapid review to establish more flexible approaches in evaluating medicines for treatment at end of life and for very rare conditions. The SMC established a Task and Finish Group with representatives from key stakeholders including clinicians, patient interest groups and the pharmaceutical industry and in consensus [recommended](#) a new approach for the assessment of end of life, orphan and ultra-orphan medicines to deliver substantially improved access to these medicines for patients in Scotland (“the new approach”). In January 2014, following consultation with other parties in the Scottish Parliament, the Scottish Government asked SMC to deliver the new approach set out in the Task and Finish Group Report. The new approach was put in place for submissions received after noon on 7 April 2014 and the first decisions made under the new approach were published in October 2014. In February 2015 the Scottish Government indicated its intention to formally review the new approach in 2015/16. The Scottish Medicines Consortium has adopted a continuous improvement method to the implementation of the new approach and this review builds on that and will take account of the views of the Health and Sport Committee from March 2016.

The review will also consider the wider context of how SMC decisions for these medicines are implemented by NHS Boards, including those orphan, ultra-orphan and end of life medicines not recommended by SMC.

The Cabinet Secretary for Health, Wellbeing and Sport, Shona Robison, has asked Dr Brian Montgomery to lead the review.

Scope of Review

The review should consider the progress made in substantially improving access to orphan, ultra-orphan and end of life medicines for patients in Scotland compared to the former system. The overarching policy aim of the review is providing safe and timely access to clinically effective medicines at as fair price. The review will be forward looking to anticipate, where possible, future developments which will influence this landscape. In particular the review should consider and make any recommendations it considers appropriate in the following areas:

- How the agreed definitions for end of life, orphan and ultra-orphan medicines are working in practice;

The SMC definition for end of life is a condition at a stage that usually leads to death within three years with currently available treatments. This differs to that of NICE and the All Wales Medicines Strategy Group which regards end of life as conditions having a life expectancy of less than 24 months. This extension of the definition skews the way in which medicines are considered in Scotland compared to elsewhere in the UK and puts additional burden on the global healthcare budget within NHS Boards by extending the flexibility applied to cost-effectiveness thresholds.

- How the views from the Patient and Clinician Engagement process are taken into account in decision making;

Scottish Medicines Consortium is best placed to answer this, however, the introduction of PACE appears to have a positive influence the decision making process. A larger number of cancer medicines are now accepted for use by SMC than prior to the implementation of the PACE process. This includes medicines which were previously not recommended after one or more previous submissions.

Clinicians from Boards within the West of Scotland Cancer Network (WoSCAN) have strongly supported the PACE process by attendance at PACE meetings and submitting statements. They have voiced their support for continuing to support this process.

- How the new approach to assessment of ultra-orphan medicines is operating in practice;
- How the acceptance rates for end of life, orphan and ultra-orphan medicines have changed as a result of the new approach;

SMC are best placed to answer this however cancer patients have benefited from this new approach with a number of treatments now accepted through this assessment process including treatments which were previously not recommended.

With the continuing evolution of precision medicine more future cancer medicines are likely to meet the criteria for orphan and ultra-orphan status and will benefit from this new approach.

- How the transparency of SMC has improved and what further opportunities there are for patient and clinician engagement;

We are aware of proposals for cancer clinicians to have more input at SMC meetings by attending committee meeting to speak to the PACE recommendations. The value of this increased input should be carefully weighed against the impact this will have on diverting valuable clinical resource away from direct patient care. For example, clinician attendance at PACE meetings can result in clinic lists being reduced or cancelled; attendance at a further meeting would place additional strain on services.

- How NHS Boards are implementing SMC decisions under the new approach (both accepted and not recommended) including utilisation of the New Medicines Fund;

Standard processes apply for implementation: in WoSCAN any cancer medicine accepted by SMC is still required to go through the regional process to advise our constituent Board ADTCs and support local services to safely implement advice. This is achieved by providing a regionally agreed protocol specific to the new treatment to support safe prescribing, dispensing and administration and incorporating the advice in the relevant disease specific clinical management guideline which guide clinicians on place in therapy in the context of the overall treatment pathway.

While we welcome the increased access to new cancer medicines the capacity to meet the consequent increased demand for services is posing a significant challenge for our constituent Boards in terms of clinical capacity to deliver these new medicines. Boards will need to balance the drive to introduce these treatments as quickly as possible after SMC acceptance against maintaining safe delivery of systemic anticancer therapy (SACT). For example, the new immunotherapies require careful management and monitoring to ensure early diagnosis of adverse effects to minimise the risk of life threatening complications. Planning and implementation of the patient pathway will include education of clinicians who may care for the patient takes time. Current horizon scanning for new treatments focuses on medicines budget impact, intelligence on service impact has become a critical requirement to facilitate safe and timely implementation.

- How the new approach has had an impact on reliance on access to medicines on an individual patient basis (through individual patient treatment requests and peer approved clinical system);

The network does not have a role in the access to medicines through IPTR or PACS.

- Whether there are further opportunities to take a 'once for Scotland' approach in any aspect of access to newly licensed medicines;

Even if there was a national list of medicines available for use in NHS Scotland, there will still be a requirement to ensure safe local implementation of a new cancer medicine. There may be benefit in a shared approach to the development and approval of national cancer clinical management guidelines to support consistent and equitable implementation. There is already consensus for a number of disease groups which are supported by national MCNs and some of the regional MCNs collaborate. This would require further exploration to determine benefit/added value vs resource required to support a national approach.

- How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier;

We support additional negotiation to achieve best price for NHS Scotland as early in the process as possible. The new processes may, however, have had the unintended consequence of weakening the negotiating position by accepting medicines that are less cost effective and thus an inference that the threshold has increased. The pharmaceutical industry can offer a higher price and still be accepted due to the increased flexibility.

We also have concerns regarding the emergence of complex Patient Access Schemes. The network has supported PASAG to review the feasibility of some schemes. Different schemes are being proposed by different manufacturers with vary complexity, approach and information. These are time consuming both to initially assess feasibility and then for Boards to administer these in practice diverting clinical staff from patient facing services. It is unclear to us how these schemes improve access and benefit NHS Scotland versus simple discounts.

- Whether there have been unintended consequences of any aspect of the new approach, the potential of which was noted by the Task and Finish Group Report;

We understand that the consideration of ultra orphan medicines provides significant challenges for the SMC assessment process. While we welcome increased access for cancer patients as a result of this process it is still essential that evaluation of medicines continues to ensure there is equity across all patient groups, be they for common or ultra-orphan conditions.

There may be an assumption from the pharmaceutical industry that the threshold for acceptance has increased and therefore NHS Scotland is in a weaker negotiating position than existed prior to the new arrangements. We understand through colleagues in NHS GGC, that since the introduction of the new approach, end of life medicines now considered by SMC typically come with base case ICERS in the range of £50,000/QALY rather than the previous £30,000 threshold.

- How the new approach will accommodate advances in new medicines and a developing regulatory framework;

The developing regulatory framework and in particular the policy drive for earlier access to new medicines before safety and efficacy has been fully demonstrated through the licensing process (eg EAMS) provides challenges for Health Technology Assessment. The evidence being considered is derived earlier in the medicines development, has more uncertainty about benefit and less certainty about safety.

- Whether the progress made to date provides a solid basis for developing further a Scottish Model of Value.

WoSCAN has no knowledge of developments in this area. There are now an increasing number of medicines being accessed that would not previously have been considered as cost effective options for NHS Scotland. Despite this there is much criticism from pharma on HTA methodology not meeting requirements for precision medicine and the need to consider wider societal benefits. However, as far as we are aware, a better alternative has not been proposed.

Examining the clinical and cost effectiveness of interventions is an essential method of helping healthcare organisations who operate within finite resources to prioritise their healthcare delivery. Within health technology assessment the cost per quality adjusted life year (QALY) is a well accepted indicator that allows a consistent approach when evaluating medicines. Medicines are now being made available with cost per QALY much higher than previously accepted. In a finite healthcare budget, decisions that increase access to medicines with more marginal benefits impacts on ability to deliver other healthcare services. Currently there is limited opportunity to assess whether or not the additional investment in medicines is delivering improved outcomes. More research is required to determine the effectiveness of medicines when used in “real world” setting. WoSCAN will support the pilot work underway in NHS GGC to develop the methodology to provide outcome data.

Medicines are treated in a different way to other healthcare interventions. There is no comparative rigor in assessing cost effectiveness of other interventions that may or may not be cost effective for NHS Scotland. In view of current and future financial constraints facing NHS Boards in Scotland, WoSCAN would welcome further work being done to address value of not just medicines but of other healthcare interventions such as early detection of cancer, surgery and radiotherapy to inform debate and aid the difficult decisions regarding prioritisation of new interventions.

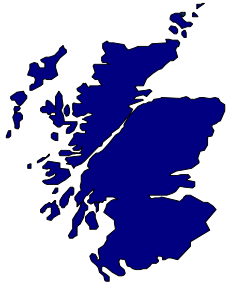
Approach

The review will be undertaken independently of the Scottish Medicines Consortium and the Scottish Government and consult widely with those who have been engaged in the new approach, building on feedback already received by the Scottish Medicines Consortium, Scottish Government and Health and Sport Committee of the Scottish Parliament.

The review will have access to commercial in confidence information held by the Scottish Government on the basis that the confidentiality of this information is strictly upheld. The review will not significantly impact on the ability of the SMC to continue its work, and subject to this, is expected to report to the Scottish Government in around four months.

Prepared by Mary Maclean Regional Cancer Care Pharmacist on behalf of the West of Scotland Cancer Network

May 2016



NHS Scotland

Directors of Pharmacy



NHS Forth Valley Pharmacy Services
Falkirk Community Hospital
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Date: 2nd June 2016

Dear Dr Montgomery

Review of Access to New Medicines

Thank you for taking the time to attend the Directors of Pharmacy (DoP) group meeting on 19th May to discuss the review of access to new medicines.

As advised at the meeting, the DoP group and the Directors of Public Health (DsPH) group have provided evidence to inform the Board Chief Executives (BCEs) response to the review. The evidence focused on the BCE priority areas for consideration i.e. resultant impact on additional investment, affordability, opportunity cost, sustainability, value and equity.

In addition we noted that it was disappointing that the launch of the review did not have an NHS perspective to complement the ABPI presentation and patient voice. This we believe set an uncomfortable tone for the review within the NHS. This in combination with the overall fatigue which the politicisation of access to medicines has created over the last 3-5 years is challenging for pharmacists in their capacity as professionals with responsibility for the safe and effective delivery of pharmacy services and in their responsibility for the governance of the safe and effective use of medicines.

The DoP group welcome this additional opportunity to highlight a number of key issues:

1. Whilst it is recognised that there may be a need to value medicines used at end of life or for rare conditions differently to reflect public preference, the flexibility now applied at SMC and NHS Board level has created a number of concerns around:

- equity, such that more cost effective interventions (medicines and non medicines) may be bypassed in favour of this group of medicines or that patients with common, chronic diseases are treated differently in terms of the value placed on treating their conditions.
- an absence of the necessary robust mechanisms to capture evidence of benefit
- a considerable service capacity challenge with respect to both clinical service provision and the redirection of clinical and financial team resources to track those medicines approved via IPTR/PACS processes. It is noted that this has increased further since your review commenced.

2. The cumulative impact of Scottish Government requirements for both increased flexibility by SMC in its decision making process, and the additional flexibility in the IPTR process applied at Board level is significant. This has put considerable strain on systems to enable the cost effective use of these medicines.

3. There is a disconnect between the policy on access to new medicines and parallel policy and strategy such as the Quality Strategy, National Clinical Strategy and Realistic

Medicine. Specifically, that access is one dimension of quality but it has gained a disproportionate portion of the assurance system for the safe and effective use of medicines for patients and public. The policy is focussed solely on access and does not recognise the broader aspect of clinical decision making that includes clinical judgement about appropriateness, benefit and safety for individual patients.

4. The policy shift has to date, been partially funded by the New Medicines Fund. If there is a political desire to significantly shift access to new medicines on an ongoing basis there needs to be a sustainable model of funding put in place that addresses the full service implications of such a move. Without a sustainable funding model Boards will ultimately be forced to decide whether they support the use of the less cost effective medicines approved via PACE when compared to more cost effective interventions as they seek to discharge their responsibilities to meet local clinical needs within the finances they have available.

5. In the longer term the influence of the PACE process and the approval of less cost effective medicines for use in NHS Scotland may bring significant cost pressures to the NHS. In addition the shift in willingness to pay as a result of the higher value accepted for end of life treatments and rare conditions, may yet lead to unanticipated consequences in terms of pricing of medicines coming to the market in the future. It is also likely that the wider population will come to expect a level of acceptance of medicines related value, both in terms of acquisition cost per patient and cost effectiveness, which is out of step with the costs of other aspects of healthcare delivered in Scotland. The new arrangements are not sustainable to support medicines for use at end of life and for rarer conditions and therefore could not be extended to include further groups of medicines.

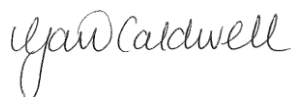
There is a need to move to a position where non cost effective medicines remain somehow separate to the mainstream to allow their value to be defined, through outcome data and assessment of evidence and a fair price to be negotiated to achieve value for the public of Scotland.

The review needs to be reframed within the context of realistic medicine and the comparative benefit and value associated with medicine and non medicine interventions.

As discussed the DoP group members are supportive of your offer of a structured questionnaire to explore the NHS Board issues in more detail.

We look forward to meeting with you again to discuss related issues and enclose our response to the Health and Sport Committee (Appendix 1) which you may find of interest.

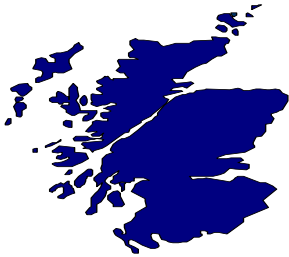
Yours sincerely



Gail Caldwell

Chair of the NHS Scotland Directors of Pharmacy group

Appendix 1



NHS Scotland
Directors of Pharmacy



Health and Sport Committee

Access to new medicines – Call for Written Views

January 2016

The NHS Scotland Directors of Pharmacy (DoP) and the Scottish Association of Medical Directors (SAMD) welcome the opportunity to respond to the request from the Health and Sport Committee to follow up on its 2013 inquiry into access to new medicines and to seek an update on the effectiveness of the changes made to the Scottish Medicines Consortium's system for approving new medicines.

The NHS Scotland Directors of Pharmacy (DoP) and the Scottish Association of Medical Directors (SAMD) are of the view that the Scottish Medicines Consortium (SMC), as a consortium of NHS Board Area Drug and Therapeutics Committees remains a valuable source of advice to NHS Boards on the clinical and cost-effective use of new medicines.

Question 1

1. To what extent have the new SMC process (implemented in April 2014) for approving medicines, current Individual Patient Treatment Requests and the new Peer Approved Clinical System (PACs) for rare conditions and end of life medicines become more transparent, less complex and delivered improved access to new medicines?

SMC processes changes are clearly described via its website and include patient, clinician and industry specific fact sheets to aid understanding of approval processes. The changes SMC has made in response to the policy recommendations and the impact of the changes made by SMC are outlined in the attached update report. The opening of SMC meetings to the public and industry provides enhanced transparency of decision making. The developments in SMC to support public involvement have also helped improve transparency and engagement.

The new SMC processes, including the Patient and Clinician Engagement (PACE) system, has improved access to 28 end of life and rare diseases medicines that previously may not

have been accepted on the basis of cost effectiveness. It should be noted that the additional SMC process steps have increased the complexity of the assessment process and extended timelines for assessment.

Under the previous SMC processes it is likely that these medicines would not have been accepted for routine use and the route of access to NHS funded treatment would have been through the individual patient treatment request process (IPTR).

In the longer term the influence of the PACE process and the approval of less cost effective medicines for use in NHS Scotland may bring significant cost pressures to the NHS with the potential for greater diversion of resources away from other more effective and cost effective treatments including non drug treatments. In addition the impact of the policy directive to value medicines used at the end of life and for very rare conditions differently in NHS Scotland may add to the cost pressures on the NHS. The willingness to pay more for medicines used at the end of life and for very rare conditions, may lead to unanticipated consequences in terms of the cost of medicines for NHS Scotland.

As we enter the era of personalised medicines, potential treatment populations will become smaller and therefore more medicines may be classified as orphan or ultra-orphan with the option for health technology assessment through these new, more flexible processes. This may have a huge impact on budget with greater expenditure on very expensive medicines with potentially marginal benefit.

The Scottish Government New Medicines Review recommended the replacement of the existing system of IPTRs and a move to a new system called Peer Approved Clinical System (PACS). Ministerial announcements indicated that the national guidance would be available in spring 2014. Whilst the CMO/CPO Letter "Access to Medicines – Transitional arrangements for processing individual patient treatment requests", SGHD/CMO(2013)20, 5 November 2013 and the subsequent letter: "Proposed approach to deal with the transitional period from IPTR to PACS", 11 December 2013 offer some guidance there remains significant scope for interpretation and application of interim arrangements at individual Health Board level.

If PACS is to be implemented, the DoP Group and SAMD are supportive of the Scottish Government's commitment to the development and provision of a national system including a centralised patient support team to assist patients going through the request process, training materials for clinicians, a register of specialists to assist boards, improvements to the patient information currently provided through Health Rights Information Scotland and the implementation of robust auditing arrangements via Healthcare Improvement Scotland.

A pilot to develop the PACS process which is limited to consideration of ultra-orphan medicines not recommended by SMC has recently been launched in NHS Greater Glasgow and Clyde. In the meantime, Boards continue to operate under the guidance of CEL (2010) 17 "Introduction and Availability of Newly Licensed Medicines in the NHS in Scotland" and SGHD/CMO (2011)3: Implementing CEL 17 (2010): Introduction and availability of newly licensed medicines in the NHS in Scotland – Good practice guidance for NHS Board management of individual patient treatment requests (IPTRs).

The general view across the DoP group and SAMD is that following the introduction of more flexibility within the IPTR system, there was a rise in the number of IPTR requests and the acceptance rates for IPTRs. Scottish Government continues to request and receive data in relation to IPTR activity. Comparison of these data is particularly difficult given the relatively small numbers involved and the need for confidentiality when considering individual drugs or conditions where patient numbers can be very small (less than 5).

In relation to improving access to medicines that represent the best in therapeutic value and outcomes, the NHS Scotland Directors of Pharmacy (DoP) and the Scottish Association of Medical Directors (SAMD) would support further consideration of mechanisms to monitor patient outcomes as recommended in the SMC Task and Finish Group Report: Assessment of medicines for end of life care and very rare conditions (orphan and ultra-orphan medicines). It is recognised that there is a need for the NHS to work with partner agencies to ensure that medicines approved for use under the new process deliver the predicted benefits.

Question 2

The effectiveness of any monitoring of the NHS boards Area Drug and Therapeutic Committees including the transparency of their operations and their timeliness in publishing local responses to SMC's published advice?

NHS Board ADTCs are required to work to the CMO timelines for local adoption / decision making with regards to new medicines approved by SMC. In February 2012 the Scottish Government issued SGHD/CMO(2012)1 "Guidance to further strengthen the safe and effective use of new medicines across the NHS in Scotland."

One of the aims of this guidance was to standardise a timeframe for NHS Boards to consider Scottish Medicines Consortium (SMC) accepted medicines and to publish advice accordingly.

The timeframes stipulated were:

- NHS Boards are expected to reach a decision on a SMC Accepted medicine within 90 days of the issue of SMC advice to NHS Boards (this advice is confidential for the first 30 days).
- NHS Boards are expected to publish on the Board website, the formulary decision within 14 days of the decision being reached.

Additionally NHS Boards were expected to issue standard advice to reflect formulary decisions. This information is freely available to the public on Health Board internet websites. The use of these timelines, standard categorisations of decision making and internet publication have helped improve transparency of decision making. Board ADTCs have been working throughout 2015 via the ADTC collaborative, hosted by HIS, to further refine and standardise the reporting categories used by NHS Boards to provide greater transparency and improve public information and understanding in terms of decision making.

Throughout 2014/15, NHS Boards have also worked informally with the ABPI to help improve its interpretation and subsequent data capture of NHS Board decisions to ensure that the pharmaceutical manufacturers of new medicines have an accurate picture of how new medicines are to be used in NHS Scotland.

Question 3

How the New Medicines Fund has been used and the extent to which it has improved access to new medicines for those with rare conditions?

The New Medicines Fund (NMF) represents a significant investment from Scottish Government to allow NHS Boards to implement Government policy with regard to improving access to medicines associated with end of life and medicines for the treatment of rare conditions. These medicines may not have received approval for use from the SMC in the past due to their lack of cost effectiveness. It is noted that the increase in access to new medicines is due to changes in SMC and associated Individual Patient Treatment Request (IPTR) processes and not the New Medicines Fund.

Question 4

The progress towards developing value-based assessments of new medicines and the Scottish model of value?

Progress toward developing value based assessment is challenging and it is recognised that there are other areas of care with treatments that may provide greater health gain but which are not currently afforded the level of flexibility that has been applied to end of life and rare conditions. If this policy was to be pursued it would have to be determined which patient groups and which disease states are more important and therefore more deserving than others.

The PACE process affords an opportunity for SMC to take a wider view of the value of medicines used at the end of life and for very rare conditions

The new framework for assessment of ultra orphan medicines (medicines used to treat a condition with a prevalence of 1 in 50,000 or less (or around 100 people in Scotland)) allows SMC to use a broader decision-making framework, examining the nature of the condition, impact of the medicine, impacts beyond direct health benefits and costs to the NHS using the criteria set out above. PACE meetings are held for these medicines. Cost-consequence analysis may be provided where the submitting company judges that there are multiple relevant outcomes not readily captured within a standard health economics (Quality Adjusted Life Year (QALY) based) assessment or cost-effectiveness analysis using a single outcome measure. For these medicines, the economic analysis is a factor within the decision-making framework but will not be the predominant factor in the SMC decision.

The SMC is in a position to help determine and enable the research required to underpin an evidence-based approach to the development of a Scottish Model of Value by the Scottish Government.

Question 5

The effectiveness of the 'pause' mechanism in the SMC process and whether this mechanism has resulted in greater access to and improved the cost-effectiveness of new medicines

The PACE process involves a 1 to 3 month pause in the SMC assessment process and this offers pharmaceutical companies an opportunity to submit a new or revised Patient Access Scheme (PAS) aimed at improving the cost-effectiveness of the medicine. As demonstrated in our response to question 1, there has been an increase in the numbers of medicines accepted for use in NHS Scotland following a PACE process.

NHS Boards should continue to receive timely advice about all new medicines. It is recognised that the assessment process is best served by pharmaceutical companies offering a competitive price from the outset.

Gail Caldwell

Chair

NHS Scotland Directors of Pharmacy

Dr A Russell

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Dear Dr Montgomery

ACCESS TO NEW MEDICINES REVIEW

NHS Fife welcomes the opportunity to respond to the request regarding the impact of the recent changes to the NHS Scotland processes for the introduction of new medicines.

NHS Fife has contributed, through a number of routes, to the response that is being submitted on behalf of the Chief Executives Group but we would like to take this opportunity to reiterate a number of points from an NHS Fife point of view.

The review of SMC processes has resulted in new definitions for end of life, orphan and ultra orphan medicines; a new process of Health Technology Assessment (HTA) for such medicines with increased patient, clinician and industry involvement and an increased transparency of SMC decision making for all medicines. The SMC review has delivered what was asked by the Scottish Government (SG) - wider access to new medicines. We believe about 30 medicines have been accepted for use in NHS Scotland as a result of the Patient and Clinician Engagement (PACE) process; medicines which would likely not have been accepted previously due to relatively poor cost effectiveness. The increase in access applies to a very small number of patients across a discrete number of conditions. Importantly, as yet there is no evidence that the additional investment in these medicines is delivering improved outcomes and health gain.

NHS Fife is concerned that this wider access to medicines has come at a high cost in terms of additional investment, affordability, opportunity cost, sustainability, value and equity. We believe this review gives an opportunity to engage in dialogue with the wider public on decisions about resource allocation on medicines. We see this review offering an opportunity to highlight these fundamental issues in the wider context of health and social care and ensure they are explored and the implications fully understood.



Affordability and Opportunity Cost

From an NHS Fife perspective, since the review into access to new medicines, budgets are under increasing pressure. The increasing spend on a limited group of medicines and growth in prescribing outpaces the uplift in NHS funding and is not fully addressed by our allocation of approximately £3 million from the New Medicines Fund (NMF) between 2014 and 2017.

As well as more medicines being accepted for use by SMC, NHS Fife has approved in the region of 30-40 Individual Patient Treatment Requests (IPTRs for medicines that have not been recommended for use, generally on the basis of poor cost-effectiveness), and this increased flexibility utilised in the IPTR process is further contributing to the financial pressure. This is impacting on the limited clinical and service capacity to safely and effectively deliver these medicines, most of which are for specialist use only.

Furthermore, a Peer Approved Clinical System (PACS) is being piloted for ultra orphan medicines that have been not recommended by SMC. This PACS process leaves the decision to treat with the prescriber supported by a clinical specialist. There is no opportunity for the NHS Board to consider clinical effectiveness or cost effectiveness and where the place of medicines sits in a treatment pathway alongside other potential interventions.

There is an administrative burden on staff in terms of the required monitoring and financial tracking associated with these processes. The focus to date on patient outcome has been limited to IPTRs. We are concerned that the introduction of PACS brings with it a responsibility to collect meaningful data in such small patient numbers may not be possible for any one system to demonstrate clinical or cost effectiveness of these decisions.

The cumulative impact of these new processes with the resulting increased access to medicines is extremely challenging from both a clinical service and financial perspective.

Increased access to medicines with marginal clinical benefits impacts on our ability to deliver other medicines and healthcare services with greater proven patient benefit. Additionally even though the NMF funds the end of life medicines there still remains the opportunity cost of the use of this sum of money. Further funding of end of life medicines is inconsistent with the principles of "Realistic Medicine" and with service changes required to support delivery of the SG 2020 Vision and National Clinical Strategy.

The introduction of the new SMC processes, flexibility around "value" and continued pressure for even wider access to medicines is resulting in a shift of public perception of the value of medicines but not necessarily for other healthcare interventions which are equally clinically and cost effective. We are concerned that society may come to expect the prescribing of medicines whose value is out of step with other aspects of healthcare delivered in Scotland. This could lead to patient and public expectations are out of line with the current financial position within NHSScotland, further impacting on opportunity costs of these policies.

Sustainability

The clinical capacity to deliver these new medicines is not always taken into account when increasing access to new medicines. The desire to bring these medicines into use more quickly has resulted in increasing pressure on services in terms of clinical capacity, infrastructure and service funding.

The changes to medicines regulation in Europe and the UK are focussed on accelerated access policies e.g. including Early Access to Medicines Schemes and is creating additional pressures on clinical capacity and funding.

The impact of the introduction of a new medicine on service capacity, sustainability and affordability should be considered alongside clinical and cost effectiveness data.

Evidence of Benefit

We know that Health Technology Assessment (HTA) is about examining the clinical and cost effectiveness of interventions, not affordability; however, with the many competing demands and continuing financial pressures across public sector services we must ensure that we are getting value for money and providing interventions which are safe, effective and offer clear benefit for patients.

We therefore call for further study of the benefits of these medicines, investment in pharmacoepidemiological studies, particularly the examination of outcomes in “real world” patients, routine participation in and follow up of clinical trials for our patients, and clear information on the balance of risk and absolute benefit.

Evidence of benefit should be considered alongside equity of access to medicines and non medicines interventions in future.

Equity

Medicines used at the end of life and for very rare diseases are now treated differently to medicines for more common chronic conditions (which present a greater burden to the system and are predicted to increase) and indeed to other healthcare interventions in NHSScotland. The consequence is that more cost-effective interventions are bypassed in favour of less cost effective interventions. The focus on these medicines introduces inequity in the system that HTA seeks to prevent.

There is not an equitable approach to HTA or access across all health technologies and interventions. It is critical going forward that consideration is given to a more proportionate approach across medicines and other interventions as recently agreed by the European Commission.

Pricing of Medicines

Pricing and the Pharmaceutical Price Regulation Scheme (PPRS) are not devolved responsibilities so NHSScotland is bound by UK negotiations on medicines pricing. This has to be seen in the context of a European and global market. We are a relatively small player in these bigger markets.

SMC's role is to conduct HTAs; it does not have a role to negotiate the price of medicines. The current Patient Access Scheme system, administered by the Patient

Access Scheme Assessment Group (PASAG), applies to a minority of SMC submissions and is responsive to a submission from a pharmaceutical company – it is not proactive. PASAG can influence manufacturers to reduce the administrative burden of schemes but does not negotiate or seek to influence pricing.

Whilst there must be realistic expectations to price negotiation with consideration of any unintended consequences of change, we support additional negotiation to achieve the best price for NHS Scotland as early in the process as possible to maximise efficiency for NHS.

The SMC definitions for end of life, orphan and ultraorphan medicines are now broader than those currently used by the National Institute for Health and Care Excellence (NICE) and the European Medicines Agency (EMA). NHS policy that extends willingness to pay will affect pricing strategies as the pharmaceutical industry may increase prices even further.

Summary

Whilst the review of SMC processes has resulted in wider access to new medicines for a small number of patients and clinical conditions, NHS Fife is concerned that this has resulted in increased investment in medicines that have poor cost effectiveness. This could be seen to be to the detriment of patients with chronic diseases, by creating inequalities between these patients and those who have end of life and rarer conditions and has not moved us towards the ultimate goal of maximising health gain for the wider population.

The effects of the policy are long term and cumulative and this causes issues for NHS Boards in terms of equity, value, affordability and service delivery. Increasing expenditure on medicines with poorer cost effectiveness for a small number of patients, yet substantial cost has not yet produced evidence of additional benefit and outcomes.

There is now an apparent disconnect between the policy on access to new medicines and parallel policy and strategy such as the Quality Strategy, National Clinical Strategy and Realistic Medicine. Specifically, access is only one dimension of quality and may be in danger of producing a distorted understanding of the safe and effective use of medicines for patients and public which we are aiming to drive locally.

This distorted understanding and the issue of inequity may ultimately drive demand for increased flexibility in other groups of medicines. The current arrangements are not sustainable to support the current medicines in early access schemes and therefore should not be extended to include further groups of medicines without further work to understand clinical benefit.

The issue of obtaining best value and, value in the context of non medicine related interventions, must be considered. Future actions and recommendations should be reframed within the context of wider societal value, realistic medicine and the comparative benefit and value associated with medicine and non medicine interventions.

The past four years of scrutiny and review on access to new medicines and SMC specifically have significantly challenged NHS Fife in delivering the overall NHS agenda.

We ask this review to address the equity, sustainability and financial governance issues presented to all boards by increasing access to less cost effective medicines.

NHS Fife thanks you for the opportunity to participate in this review and would be happy to provide any further input should that be required.

Yours sincerely

DR FRANCES M ELLIOT
Medical Director NHS Fife

Brian thanks for this timely reminder.

As you will know SAMD is very focussed on how the National Clinical strategy and realistic medicine play into everyday clinical practice. From an NSD perspective we have a number of key challenges in supporting appropriate use of a number of high cost low volume meds. We are currently working with one of the NHS GG&C teams to invite development of a new drugs protocol which is explicit about 1st, 2nd and 3rd line therapies with clear markers for escalation and most importantly review of clinical benefit and cessation of therapies that are not making a difference. Mike Bisset is currently chairing a group looking at Inherited Metabolic Disorder and here the advice to start therapy in Adults is by a team in NHS England who have no financial responsibility for the prescription and currently we have no specialist service (for adults) in Scotland to challenge the use or monitor / recommend change once commenced. This latter is an example where a Scottish service might bring about savings in that being able to modify the usage of a high cost drug in one patient would probably pay for most if not all of the salary of the specialist in Scotland.

I would wish to reinforce the detailed response offered by Lindsay McClure during the consultation period. Her points about opportunity to get into a more mature relationship with the pharma industry should be include in any recommendations. If you have not already had a conversation with my new colleague Craig Wheelans - I would commend this to you – Craig does have a seat on one of SMC advisory panels and his career path has included time working inside one of the major PIs
Mike

Dr Mike Winter

Medical Director, PCF SBU

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Hi Brian


Further to Gillian at SAMD's request to provide comments you may get a version of this from CMO as I have been in correspondence with her about access to ultra-orphan drugs but below is my contribution to the discussion.

I have concerns about the current Peer Approved Clinical System in Scotland as I do not believe that it provides us with a robust national process for managing access to ultra-orphan drugs. Leaving 14 Boards to make their own interpretation and modification to the current GG&C process is not going to deliver a standard and consistent process. One PACS process and perhaps even one PACS group for Scotland would provide the consistency in decision-making that is required. I also feel that to be credible the PACS process must take clinical effectiveness into account and have as a possible outcome 'not supported' as opposed to just 'yes' or 'yes with the following caveats..'

Hope that is helpful.

Best wishes

Iain

 #hello my name is...

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Dr Brian Montgomery
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Date: 16 June 2016
Your Ref:
Our Ref: TD/AT/EW
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Dear Dr Montgomery

NHS Lothian/SCAN Response To The Montgomery Review

NHS Lothian and SCAN welcome the opportunity to respond to the independent review on Access to New Medicines. NHS Lothian considers that if the purpose of the review is to consider whether the changes directed by Scottish Government has resulted in increased access to medicines for end of life, orphan and ultra orphan medicines then the answer is clearly yes. SMC has accepted more of these medicines and where SMC has "not recommended" a medicine Health Boards have been advised to apply maximum flexibility through their IPTR processes. Most recently a new approach through the use of the pilot Peer Approved Clinical System (PACs) for ultra orphan medicines has resulted in a process which further increases access.

The questions to be considered therefore are perhaps more to do with the value to patients, the public and the Scottish purse of these changes. NHS Lothian and SCAN are aware of and have had sight of responses from other Health Boards and from Health Board Chief Executive Officers (CEOs). It is our view that we are very supportive of the views expressed by these groups and in order to avoid simply repeating arguments that have already been made, we wish to emphasise particular issues which we consider merit in depth consideration.

It is our view that the full cost of implementing this policy shift requires to be assessed. This is difficult at present as information seems to be limited to the number of additional patients treated and the size of the New Medicines Fund. Clearly this is not sufficient to assess if the money spent has improved care for those patients in a meaningful way and what the opportunity cost of this approach has been.

We were disappointed that those present at the launch of the Review of Access to New Medicines did not hear the view of the NHS. Presentations were given by the Pharmaceutical Industry, patients and the Health Technology Assessment Agency (SMC) but the Service was not invited to speak. It is hoped that this was an oversight but it meant that the predominant message from the launch was a view from stakeholders of a wish to further widen access. This may be a good thing but there is undoubtedly a cost to other patients in choosing this direction of travel and we hope as a Service to ensure that this perspective is fully considered.

About 30 (thirty) new medicines have been accepted for use in NHS Scotland as a result of the changes to SMC processes these medicines would probably not have been accepted previously due to relatively poor cost effectiveness. The increase in access has affected a relatively small number of patients across a discrete number of conditions. Importantly, it is yet unclear whether the additional investment in these medicines is delivering improved outcomes and health gain. In addition to this we would wish to consider the losses incurred by other patients in our system in directing resources in this way. The University of York has published work identifying that the standard £30,000k per QALY is above the threshold that the NHS can afford based on current funding.

The reasons for allocating funds to medicines that have a cost/QALY above this requires to be clearly articulated. It could be argued that patients in these categories should be treated differently from others due to the rarity of their condition, or because of the "Rule of Rescue" applies whereby society will often choose to allocate large amounts of resources at the end of life. It would be important to quantify how much society is willing to spend, and if the public can accept that this may deprive others of health care.

There is one budget for the NHS and although a New Medicines Fund was created this may take resources from one area and direct their use towards these particular new medicines, perhaps at the expense of more cost – effective treatments. Where a new medicine is cost-effective but not end of life, orphan or ultra orphan, Health Boards are obliged to fund from their standard allocation yet a medicine that is less cost-effective by conventional measures is funded. In addition to this, although the New Medicines Fund covers the cost of the products it does not fund the services required to provide the product. The Edinburgh Cancer Centre (ECC) along with other cancer services across Scotland notes an 8% increase in activity as a result of changes to demographics, diagnostics and treatment options. Provision of these new medicines places increased pressure on these services. It is our view therefore in terms of an assessment of value to patients and the public, that both of these things have yet to happen.

In terms of the public purse, the review asks "How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies' best offering on price earlier". It is our view that SMC is not a negotiating group and to be seen to negotiate access to medicines based on price would undermine the assessment of the clinical value of the medicines. It is possible that National Procurement or another body could be asked to negotiate with the industry but we are conscious that there is already a five year negotiated agreement on the cost and value of branded medicines (PPRS) and Scotland plays its part and signs up to this. There must be realistic expectations about price negotiation and if Government is not content with prices currently offered then support for SMC and the Service when they consider the price too high and/or value too low would be enormously beneficial.

At present the pharmaceutical industry are getting a message that Scotland will pay almost any price for this group of medicines. The fact that in most cases the medicines that have been accepted by SMC since the changes have been implemented has resulted in only a small increase in the cost/QALY make good commercial sense as the industry will not wish to push too far. However, if this is coupled with the change in processes post SMC whereby there is increased access to "Not Recommended" medicines at HB level this means that it is often difficult to not use medicines deemed not to be cost-effective despite the highly credible work done by a Scottish HTA agency.

We remain concerned for the patients who are disadvantaged by this approach. Scottish Government is asking the NHS to treat these patients and continue to treat everyone else as well. If this is required then the full cost of implementing these new medicines, the service costs as well as the medicine costs, requires to be funded. If this happens it would be more of a level playing field for all patients.

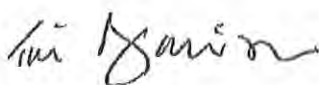
We would wish to emphasise however the need for Scottish cancer patients to get European standard of care which does require greater access to new medicines. This recognises the need to drive prices down and thus increase value.

We are aware that the Cancer Drugs Fund in England has changed following investigation into the evidence around costs, benefits and lack of outcome data. It may be worthwhile to ensure that Scotland does not have similar challenges describing the benefits for Scottish patients.

In order to be clear of the benefits of the policy approach, we had hoped that the Scottish Model of Value (SMoV) would be developed, but to our knowledge no work on SMoV has been initiated by Scottish Government.

In summary, the value to patients, the public and the Scottish purse should be considered. This requires a thorough evaluation of the costs of implementing these changes, not just in terms of the additional number of patients treated but by measuring what the benefits and disbenefits were for this patient group, measuring the impact on services and other patients and calculating the opportunity cost of this approach. The effects of the policy are long term and cumulative and this causes issues in terms of affordability, equity and service delivery. We would request that further changes to increase access are not imposed on SMC and the service without this evaluation.

Yours sincerely



TIM DAVISON
Chief Executive



alpha-1 uk
support group

Supporting alphas, their families,
carers and friends since 1997

23rd June, 2016

Dear Dr Montgomery,

Re: Independent Access to New Medicines Review

Our patient group has recently participated in the PACE process of Human alpha-1 proteinase inhibitor (A1PI) (Respreeza), SMC No. 1157/16, and two representatives of our charity attended the PACE Meeting on 14 June 2016. As such, we would like to provide feedback of our experience of PACE for the purpose of the review you are conducting on behalf of the Scottish Government.

We very much welcome the establishment of the PACE pathway as an opportunity to elicit information from rare disease patient communities and expert clinicians. In our view, patient and clinician input on the disease, the unmet clinical need, and the expected benefits from a new medicine is invaluable to help inform health technology assessment of rare/ultra-rare/end-of-life disease treatments.

However, our experience of the PACE Meeting and the upstream process prior to the meeting, has raised our concerns regarding certain aspects of this process which, from our perspective, was far from ideal and not conducive to achieving the aims that the SMC set out to achieve with PACE.

1) Identification of patient group stakeholders and initial engagement by SMC

Our patient group was invited to participate in PACE only days prior to the deadline for patient group submissions. We were initially contacted by the Genetic Alliance on behalf of the SMC Public Involvement Team. The SMC team had apparently been unable to identify our patient group, despite the fact that we previously had personal contact with a member of the SMC Public Involvement Team. In addition, our group has a prominent web presence (a simple Google search would have been sufficient to find the two relevant patient groups in the UK/Scotland).

Despite having negotiated an extension of the formal patient group submission deadline with the SMC team, we were granted only a relatively short timeframe (less than two weeks) for completion of our submission. It was made clear to us that a deferral of the PACE timelines would not be considered as a consequence of the SMC's failure to contact us within a reasonable timeframe prior to the patient group submission deadline. It was fortuitous that we were able to draw on results from a national patient survey for our submission that we had previously conducted for a different purpose. Otherwise, we would not have been in a position to provide high-quality information that was elicited in a systematic fashion and which is clearly more robust than anecdotal evidence.

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Patrons: Professor R.A. Stockley MD, D.Sc, F.R.C.P. / Professor William MacNee MBChB MD FRCP(G) FRCP(E)

Not giving patient groups sufficient time to collect the best possible information to address the questions posed in the PACE submission form defeats the very purpose of the PACE exercise. It needs to be recognised that many rare disease patient groups are limited in their ability and resource to obtain representative information from patients within very short timeframes.

2) Lack of adequate clinical expertise and poor quality of clinical input

Our group has a long history of engagement and collaboration with the AATD clinical community within the UK and globally. As such, we are aware of all centres and clinicians in the UK that have a special interest and experience in managing AATD patients. We also receive regular feedback from patients across the UK about their experiences of struggling to find a clinician with knowledge of the condition and its complexities. Consequently, we are aware that there is a lack of clinical expertise in AATD in Scotland, with only one centre regularly managing AATD patients and therefore being able to develop the relevant expertise that only comes from direct clinical experience of the condition.

We repeatedly raised our concerns with the SMC, both in telephone conversations and by email, that we were not confident that sufficient clinical expertise in AATD exists in Scotland to allow the SMC to capture information that provides insights beyond that likely to be included in the manufacturer's submission. We offered to provide the SMC with names of recognised experts in the field from England (or elsewhere) who have a proven track record of managing AATD patients. We suggested a particular clinician who works in England and who is the only clinician in the UK who has experience of using the medicine under consideration in routine clinical practice (namely, for over ten years when they practised in Spain where the medicine has been available and where they managed the National AATD Patient Registry for many years).

However, the SMC repeatedly assured us that they had sourced sufficient clinical input for PACE via Managed Clinical Network and, in this particular case and according to the process, a nomination of clinicians outside Scotland was not appropriate.

However, we were shocked at the quality of the clinical stakeholder input detailed in the PACE documentation we received prior to the PACE meeting. The five (unnamed) clinicians who had responded to specific questions about the disease and the therapy under consideration clearly had very little knowledge and clinical experience of the condition. Few of them were familiar with the concepts underlying the efficacy evidence of the new medicine, and none of the clinicians had ever used the therapy. Two physicians stated the number of AATD patients in their practice (4 and 7 respectively): the estimated prevalence figures of AATD in Scotland and the number of respiratory specialists in Scotland indicate that this number of patients is no greater than would be expected for any average specialist in Scotland and, in any case, is an insufficient number to gain a good understanding of the disease and the issues faced by patients.

This was in stark contrast to the SMC's assurance that adequate expertise had been sought and found in Scotland. We also understand that the search for a suitable clinician participant at the PACE Meeting was ongoing until just a few days before the meeting, which does not attest to a robust and confident approach to identify the best possible and experience-based clinical views to evaluate the potential added benefit of the therapy under consideration.

Furthermore, only one of the three clinicians who were selected to attend the PACE Meeting provided a PACE clinician submission in advance of the meeting. One clinician provided their submission only hours before the meeting, and the third clinician provided their submission several days after the PACE Meeting. The only clinical submission available in advance of the meeting did not address any of the questions posed in the template, despite specific prompts included in the questions; the very limited information provided by the clinician suggested either a complete lack of personal experience of managing patients with AATD, or a failure to engage in the process (further suggested by his late arrival at the PACE Meeting).

During the PACE Meeting, the same clinician demonstrated a lack of familiarity with the methodology used in the relevant clinical efficacy studies of the therapy under consideration and key published literature, an only superficial understanding of the natural history of AATD and only generic, rather than specific, understanding of the clinical and societal issues relating to AATD.

Whilst the second clinician provided an insightful submission (despite it being only provided hours before the meeting), the third clinician, who was not listed on the agenda, did not contribute any commentary during the meeting at which they too arrived twenty minutes late. This clinician only provided a PACE statement after the meeting, thereby eliminating the true independence of their statement (particularly as it was almost identical to that of the first clinician). The question arises as to what the purpose was for this clinician to be included in PACE at all, and to be formally listed in the summary PACE document, thereby falsely implying that they contributed to the output.

It should not have been left to the patient group representatives to provide the necessary clinical supporting evidence during the PACE Meeting, but unfortunately this was the default position created by the shortcomings of the physicians' knowledge and contributions throughout PACE.

The approach adopted by the SMC in identifying clinicians with (supposedly) adequate clinical experience and expert opinion on the issues under assessment raises the question as to whether their process is fit-for-purpose: the most informed clinical perspective requires hands-on experience of managing the condition, but the choice of clinicians by the SMC would suggest that its motivation is one of needing to "tick the boxes" and comply with a political agenda rather than one of identifying the most suitably qualified clinician.

We understand that it is challenging to find clinical expertise for all rare conditions in Scotland, but patient groups and clinical expert centres outside Scotland are great sources for information and can assist in recommending suitable clinicians with the necessary expertise and willingness to engage in PACE. However, we did not

experience willingness by the SMC to truly attempt to find the best possible clinical expertise (outside Scotland) and, sadly, the PACE output is testimony to the lack of clinical perspective which would have been crucial to frame and support patient experiences and to provide an additional dimension for the appraisal of the medicine in question.

We are concerned that the process of identifying adequately experienced clinicians for PACE is driven primarily by politics; i.e. the focus on obtaining this expertise from within Scotland and the reliance on recommendations from the Managed Clinical Network. The latter appears to lack the application of any objective criteria or filters to confirm that the selected clinicians are not only self-proclaimed experts, but in fact qualified to comment on questions that require both a certain degree of expertise with the condition in question and an interest to engage in the process with a view to add value.

3) *The PACE Meeting*

Our PACE Meeting started late, and there was a rushed atmosphere from the very beginning of the meeting. It was clear that the Chair aimed to finish the meeting at the scheduled time, despite the late start. The sustained feeling of rush was not conducive to providing an atmosphere where the patient participant felt comfortable to discuss very personal issues related to living with the disease.

Two of the three clinician participants arrived twenty minutes late, thereby missing the delivery of the patient's powerful and poignant personal statement. How could they have provided clinical support or perspective of the patient's statement when they did not hear it? Both these clinicians had not prepared a summary statement and were clearly unprepared for the meeting. They did not appear to have read the detailed documentation provided to all participants prior to the meeting, and they arrived without any documentation to refer to during the meeting – they did not even have a piece of paper and pen. It did not become clear prior to, during or after the meeting what their involvement with AATD has been during their career. As mentioned above, one clinician did not make a single verbal contribution throughout the meeting, and only provided a rudimentary PACE statement several days afterwards.

This approach gave the impression of disrespect towards the attending patient who went far outside her comfort zone to deliver a heartfelt and very personal statement, and disrespectful towards the patient community that made a significant effort in providing high-quality input into PACE, and towards the PACE process in general considering its importance in the ultimate SMC decision.

The SMC Public Involvement Team advised us in advance of the meeting that we would not be expected to comment on any topics that would be considered to lie within the clinicians' remit. However, it became clear during the meeting that, with the exception of one clinician who was not a physician, the attending clinicians were unable to comment on any questions relating to the clinical trial methodology and results, potential patient subgroups that may benefit most from the therapy etc. Consequently, it was left to patient representatives to fill these gaps. Although it is

not uncommon for rare disease patient groups to be extremely well informed about the condition, clinical research and the therapeutic landscape, it should not have been the patient representatives' role to provide technical information that should fall within the clinicians' scope of expertise.

Regarding the short one-hour duration of the PACE Meeting, that we were not even fully granted due to a late start, the Chair clearly had to rush through the agenda. One hour was entirely insufficient to delve deeper into a number of issues that we feel would have been important and beneficial to discuss in order to provide a broader picture in support of the therapy under consideration.

We strongly recommend that the duration of PACE Meetings is significantly extended going forward. NICE scoping meetings are a very good example of a meeting environment that is conducive to an open and respectful discussion that teases out information which has not already been provided in the formal process leading up to the meeting.

4) Adherence to process and access to assistance by SMC team

The SMC Public Involvement Team was always accessible to us and provided advice, guidance and support whenever required. They were always courteous and provided responses to our queries in a timely manner throughout the process.

Our experience was that, although the SMC claimed to strictly adhere to the formal process, their interpretation of the process was at times arbitrary and seemed to be primarily aimed at "getting the job done", rather than focusing on managing the process in the interest of achieving the best and fairest possible outcome.

Despite the late stage at which we were contacted by the SMC, we were given a short and strict deadline, whilst one clinician PACE statement had not been submitted until the day of the PACE meeting and another one only several days later.

The SMC did not permit us to nominate three patient representatives to attend the PACE Meeting (the maximum number allowed), despite the fact that the only other patient group that had submitted a PACE submission, was unable to nominate an attendant for the meeting. If PACE is aimed truly at eliciting information based on patient experience, it surely should not matter with which patient group, if any, patient participants are affiliated. The questions posed in the PACE patient group submission form and during the PACE meeting do not discriminate based on patient group membership, and patient views are equally valuable and relevant irrespective of affiliation. For this particular issue, process is taken too far and is counter-productive in achieving what PACE sets out to do.

We also felt that the final PACE statement lacked some of the important points discussed at the PACE Meeting, such as the emotion and distress that was expressed by the patient attending the meeting, as well as details of benefit observed with the therapy under consideration in other countries. We highlighted these points during the review round of the PACE output, but feel they were still not adequately addressed in the final PACE statement.

Not reaching outside Scotland to obtain relevant clinical expertise was likely to have been the single most detrimental determinant resulting in the lack of a relevant clinical perspective and a rather “toothless” final PACE statement, which is not conducive to achieving a meaningful impact on the final SMC recommendation.

We hope this feedback is helpful and, although rather critical in some areas, assists in improving the process and the experience of PACE stakeholders in the future. As part of the rare disease community we feel very strongly about the need to improve platforms that allow for patients, clinicians, health care providers and payers to work together in the interest of addressing the high unmet medical need, enhancing access to effective medicines and health outcomes whilst providing “value for money”.

Please do not hesitate to contact us if you have any questions or would like to discuss any of the above further.

Yours sincerely,



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