Review of Access to New Medicines

Independent review by Dr Brian Montgomery

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1 PREFACE

1.1 I was pleased to be asked by the Cabinet Secretary for Health and Sport to undertake this independent Review of Access to New Medicines and specifically of the impact of the new approach introduced by the Scottish Medicines Consortium (SMC) in 2014 with the aim of increasing access to end-of-life, orphan and ultra-orphan medicines.

1.2 I brought to the Review the perspectives and experiences of a practising clinician and of a Territorial Health Board Medical Director who had latterly spent time as the Board's Interim Chief Executive.

1.3 My aim has been to reflect the views and perspectives of the range of stakeholders who contributed enthusiastically and candidly to this Review. The different stakeholder groups brought a range of perspectives, differing priorities and sometimes conflicting views. I am extremely grateful to everyone who contributed to the Review. My hope is that they feel their views have been considered and presented in a way that is accurate, balanced and constructive.

1.4 By its nature a Review of this sort can appear to focus on negatives or adopt a critical tone. I sought to produce a report that is candid, rooted in reality and which offers constructive criticism. None of the criticism is directed at individuals; it refers to processes and roles. The message is that the impact being sought by the new approach has been achieved however even more can be done to further improve the system and processes, making them more effective and better able to deal with the challenges that lie ahead.

1.5 I must stress that in the course of the Review I encountered high levels of satisfaction with SMC and its processes and more widely with the treatment and care being provided by NHSScotland.

1.6 I would also like to acknowledge the encouragement and support I have received from colleagues throughout the Review. In particular I would like to highlight the open and constructive engagement of SMC colleagues and the advice and support provided by Louise Hester, John Hannah, Kathryn Fergusson and Elisabeth Campbell of the Pharmacy & Medicines Division at the Scottish Government.

Brian Montgomery
October 2016

2 EXECUTIVE SUMMARY

2.1 The Review of Access to New Medicines was undertaken to assess the impact of the new approach introduced in 2014 by SMC. The new approach aimed to increase access to end-of-life, orphan and ultra-orphan medicines.

2.2 This Review concludes that access to end-of-life, orphan and ultra-orphan medicines has increased. Not only that, the stakeholders who engaged with the Review indicated a high level of satisfaction with the current situation and engaged enthusiastically in discussion about how the system for assessment and decision making in relation to access to new medicines could be further improved.

2.3 The new approach has had the hoped for effect in increasing access to end-of-life and orphan medicines with SMC accepting a greater proportion of these medicines for use. However, SMC's rate of acceptance of ultra-orphan medicines has not increased to the same extent. Access to ultra-orphan medicines has increased through the use of Individual Patient Treatment Requests (IPTR) and its successor the Peer Approved Clinical System (PACS).

2.4 When considering ultra-orphan medicines, one size no longer fits all. If NHSScotland now wishes to maintain this increased level of access, then it would be preferable if this was not through continuing reliance on IPTR and PACS. An alternative assessment pathway should be developed for ultra-orphan medicines that preserves the integrity of SMC and its processes yet achieves the intended level of access to these medicines.

2.5 It is important to emphasise that the aim is not to establish a system that enables direct access to all newly licensed medicines. All stakeholders confirmed that Scotland needs to have a system capable of saying no.

2.6 While many stakeholders were pleased with the current increase in access, some highlighted a concern about the sustainability and affordability of the current arrangements going forward. To date the New Medicines Fund (NMF) has effectively met the costs of giving patients access to end-of-life, orphan and ultra-orphan medicines but it is not clear if the NMF will be sustained and if so whether it will be increased to meet the anticipated growth in demand.

2.7 The affordability challenge as it relates to access to new medicines is the challenge of managing the interface between NHSScotland and the pharmaceutical industry. Difficult choices will have to be made as NHSScotland seeks to optimise its use of a finite resource subject to ever-increasing demands while at the same time the pharmaceutical industry operates in a competitive commercial environment.

2.8 Many spoken to in the course of the Review highlighted the need to develop a more sophisticated approach to the measurement of outcomes. All saw a need to move beyond reliance on traditional quantitative metrics. The

aspiration is for a basket of measures that includes real world data, patient reported outcomes and an assessment of wider societal benefit. This will undoubtedly give greater confidence when assessing the impact of new medicines but developing such datasets will be a major task. It will be vital to ensure that the measures are consistent and allow meaningful comparisons which can in turn inform decision making.

2.9 Some of the discussions undertaken to inform the Review sought to link access to new medicines to the approaches being set out in Realistic Medicine[1], the annual report of the Chief Medical Officer (CMO). Those stakeholders involved in the planning and delivery of service were supportive of the general vision articulated in Realistic Medicine but they found difficulty reconciling the principles laid out in the document with the impact of the new approach and IPTR/PACS. They also expressed a concern that medicines were not being treated equitably when compared with other healthcare treatments and technologies

2.10 The Review has benefitted enormously from the knowledge, expertise and enthusiasm of all who contributed to the process. It will be important as the recommendations of the Review are considered and taken forward that there is continuing engagement with the broad stakeholder community already mobilised by the SMC and given specific focus by the Review.

2.11 If the recommendations of the Review are accepted, a number of specific actions will have to be progressed. Some may be able to be taken through existing groups or processes but others will require the setting up of short life working groups, taskforces or other mechanisms and all stakeholders have expressed their willingness to be involved in these processes.

2.12 There would be merit in considering holding a Government-sponsored stakeholder summit meeting to discuss the Review, the issues it has highlighted and the required actions going forward.

3 INTRODUCTION

3.1 Medicines play a significant part in the delivery of healthcare, offering prevention, control, palliation or cure of many diseases. Recent years have seen a growth in the number and complexity of treatments available for a number of conditions and in some instances medicines now offer treatment options where none existed previously. All expectations and indications are that this situation will increase further with the advent of new technologies such as genomics and precision medicine.

3.2 The increase in treatment options has come, in some cases, at a significant financial cost and has challenged conventional methods of assessing cost effectiveness and value for money of new treatments.

3.3 In Scotland, since 2002, all newly licensed medicines have been assessed for suitability for use in NHSScotland by the SMC which has an international reputation as a health technology assessment (HTA) body. Its assessment process concentrates on clinical and cost effectiveness; affordability is not a specific consideration.

3.4 In recent years a higher proportion of medicines for end-of-life and rare conditions when compared with other medicines, have been given “not recommended” status by SMC. Growing concern was expressed by patients, patient groups and the pharmaceutical industry that this appeared to be solely on the basis of cost and consequently patients with certain rare conditions were being denied access to medicines that are clinically effective.

3.5 The conditions treated by these medicines were either end-of-life, where the medicine offered the potential to extend life, or rare conditions where the medicine offered the potential to prevent or slow deterioration of the condition and enhance quality of life. In some instances, the new medicine offered the only treatment option.

3.6 The then Cabinet Secretary for Health and Wellbeing, Alex Neil MSP, asked SMC to review its processes in relation to these circumstances and a Task and Finish Group (T&FG) was established in 2013 under the chairmanship of Professor David Webb. The group reported in December of that year, making nine recommendations all of which were accepted (Appendix 1).

3.7 The key recommendations were the introduction of

- New definitions for “end-of-life” and “ultra-orphan” medicines with retention of the European Medicines Agency (EMA) definition for orphan medicines. (Appendix 2);
- Revised processes for the assessment of medicines falling under these three definitions. (It was recognised that some medicines could be classed as both end-of-life **and** orphan or ultra-orphan);
- Patient And Clinician Engagement (PACE) as an optional addition to the process for the assessment of all three categories and
- A new decision making framework for the assessment of ultra-orphan medicines that was not based on the Quality Adjusted Life Year (QALY).

Overall the intention was to create a more flexible and enabling process for the assessment of these medicines. This is referred to as “the new approach.”

3.8 Two other important related developments took place around the same time. In November 2013, a letter was issued to Health Boards from the Chief Medical Officer SGHD/CMO(2013)20: Access To New Medicines – Transitional Arrangements For Processing Individual Patient Treatment Requests[2]. This required Boards to exclude exceptionality as a consideration for IPTRs and to exercise greater flexibility. This appears to have had the effect of Boards supporting a greater proportion of requests, thus further increasing access.

3.9 The second development was the creation by the Cabinet Secretary of the Rare Conditions Medicines Fund (RCMF) which was replaced in October 2014 by the New Medicines Fund (NMF). This fund was derived from Scotland’s share of the rebate paid to the UK Government by the pharmaceutical industry via the Pharmaceutical Price Regulation Scheme (PPRS). Health Boards can access this fund to cover the acquisition costs and appropriate supporting costs to enable SMC recommended medicines to be made available, recognising that making medicines available may also require investment in diagnostics or other infrastructure and staffing. The fund is available to support the cost of end-of-life, orphan and ultra-orphan medicines whether recommended by SMC or accessed via IPTR/PACS. The stated intent is to ensure that,

“Availability of funding is not a barrier to NHS Board implementation of policy intentions on increased patient access to licensed orphan, ultra-orphan and end of life medicines and that no NHS Board is better or worse off financially on the basis of clinical decisions on prescribing these medicines.”

The NMF is discussed in detail in Section 6.6.

3.10 These factors have combined to create the situation where the majority of patients now access end-of-life, orphan and ultra-orphan medicines either through SMC approval or applications through IPTR or PACS. There is also a perception that media campaigns and political lobbying of councillors, MPs and MSPs positively influences access for individuals or groups of patients.

3.11 There is now a need to clarify or restate the policy intention. All stakeholders consulted as part of the Review acknowledged that universal unchallenged access to new medicines was not desirable.

3.12 The eighth of the T&FG's recommendations was that there should be an independent review of the experience with the new approach.

3.13 This independent Review has been undertaken at the request of the current Cabinet Secretary for Health & Sport and was tasked with answering two core questions:

1. Has the new approach adopted by SMC increased access to end-of-life, orphan and ultra-orphan medicines?
2. How might systems and processes be further improved?

3.14 Underneath these questions sit a series of more detailed issues that fall within the scope of the Review. The full scope and remit of the Review is laid out in Appendix 3. This report follows the order and structure of the defined scope. Much of the discussion that took place with stakeholders was not easily accommodated within the scope as specified and so additional sections on engagement, data and general discussion have been added.

3.15 The medicines covered by the definitions of end-of-life, orphan and ultra-orphan constitute only a part of the total workload of SMC. No other aspects of SMC or its process fell within the scope of this Review. In the course of the Review the overwhelming sense encountered was that there was a high level of satisfaction with SMC and that its processes remain robust.

3.16 The Review was not intended to be exhaustive or to provide definitive answers; instead the Review was expected to engage widely with stakeholders and having addressed the core question in relation to the increase in access to new medicines, it was expected to go on to make recommendations that would result in further improvements in processes going forward. By design it concentrated on aspects of the current arrangements for end-of-life, orphan and ultra-orphan medicines that had the potential for improvement and as such the tone and content may appear critical. It should be stressed however that SMC continues to function effectively and enjoys the confidence of stakeholders. Its processes remain appropriate and work well for the majority of medicines it considers. The comments in this report refer to changes and improvements in SMC's processes as they relate to the small number of ultra-orphan medicines under consideration.

3.17 This report is the distillation of the perspectives of stakeholders holding a wide range of views. However, all stakeholders have in common the aspiration that patients get prompt access to medicines likely to be of benefit to them in a way that is uncomplicated, timely and transparent. All stakeholders agreed that the aim was not to achieve universal access to all licensed medicines and that the system has to have the ability to give medicines not approved status if considered appropriate.

3.18 The first of the core questions on increase in access has been relatively easy to address in quantitative terms. What has been more difficult has been to link increased access to improved outcomes. All agreed it will be important to develop systems and processes which report on outcomes. Currently it is possible to look at the impact the new approach has had in terms of the number of medicines accepted by SMC but not in relation to patients treated or their outcomes. This is discussed further in the section on Data, Section 5.

4 ENGAGEMENT PROCESS

4.1 The intention of this Review was not to undertake a detailed scientific analysis. The intention was to seek the views of a wide variety of stakeholders through engagement events, small scale meetings and written submissions and then bring these views together, analyse and present them and use them to inform the conclusions and recommendations of the report. The request was to make the process rapid and "light touch" and not to disrupt the ongoing business of SMC.

4.2 Much of the discussion that took place with stakeholders however was not easily accommodated within the precise criteria of the scope as specified and attempts have been made to place issues, discussion and recommendations in the most appropriate section; where this has proved difficult cross references have been provided. Given the importance of data to the Review a separate section on Data has been incorporated.

4.3 Two engagement events were held. The first, on 21 March, attracted 94 stakeholders and the proposed Review process was explained. There were also presentations from SMC, patient groups and the Association of the British Pharmaceutical Industry (ABPI) on behalf of the pharmaceutical industry. Attendees were given the opportunity to complete forms commenting on their experience of the new approach and their hopes for the Review. The second event took place on 15 July and on this occasion 57 people attended. This event took the form of a progress report and an interactive workshop where stakeholders were asked to comment on some of the more difficult issues emerging from the Review.

4.4 Over the period from March to August the Review had a series of small stakeholder meetings ranging from meetings with individual patients, Patient Interest Groups, Academics, professionals working within the NHS including pharmacists and clinical leads of the cancer networks and with ABPI Scotland. Meetings were also arranged with the health spokespersons of the Holyrood Political Parties. In all over 100 people were involved in this part of the engagement process.

4.5 The Review received 48 written responses from a similar range of stakeholders as had engaged in the small meetings.

4.6 The author also attended meetings of SMC, the New Drugs Committee (NDC) and PACE as an observer.

4.7 As was to be expected a wide range of perspectives was reflected but opinions were perhaps less diverse than might have been anticipated with a general consensus that the changes implemented through the new approach were welcome, appeared to have increased access but would benefit from further development.

4.8 Many of the responses to the Review went into considerable technical detail in relation to the issues under consideration. It is beyond the scope of the Review to replicate that detail in this report but it is important as the recommended actions are progressed that those stakeholders are engaged and every attempt made to ensure that the process benefits from their expertise and enthusiasm.

5 DATA

5.1 NHSScotland has a justifiable reputation for high quality data but there have been three specific areas of challenge for the Review:

- The systems that exist within Boards are appropriate and effective for the service's purposes but they have not been set up to answer the questions posed by the Review;
- The new approach saw the adoption of new data definitions for end-of-life and ultra-orphan medicines which limits before-and-after analyses;
- There are inconsistencies between Boards in relation to the data reported for IPTRs. This is the result of varying interpretation or application of data definitions and has been further complicated by a series of changes in the dataset gathered from Boards annually once again making comparisons across years difficult.

5.2 Within Boards data collection systems related to medicines largely support medicines ordering and prescribing but do not record outcomes. The systems do not allow tracking of the use of medicines in relation to patients. There are a number of local Board-level systems which capture elements of this information and there is a single chemotherapy system for NHSScotland but it is not used in the same way across the three cancer regions. The data challenges experienced by this Review would be addressed by a national electronic prescribing system which includes collection of data on outcomes and side effects.

5.3 Using existing systems some collation of data in relation to the number of times a specific medicine is prescribed is possible but for the purposes of the Review it has not been possible, with sufficient confidence, to equate the number of episodes where a specific medicine is prescribed to the number of patients treated. Similarly, the lack of a national electronic patient record prevents interrogation of data at the patient level. While it is possible to acquire this data from some Boards, a definitive national position cannot be described.

5.4 As stated above, the introduction of the new approach involved adopting new definitions for end-of-life and ultra-orphan medicines. The EMA definition for orphan had been in place since the inception of SMC and was kept. It has not been possible to retrospectively categorise medicines assessed under the previous process according to the new definitions and this has limited the Review's ability to make before-and-after comparisons. A further complication has been that some medicines can be categorised under more than one definition.

5.5 There are similar challenges with IPTR data and although Boards have been required to report on IPTRs to Scottish Government for several years this has been for the number of IPTRs received, the medicines involved and the decision reached. Data has not been requested on the condition being treated. The required dataset for reporting has been modified several times over the years and there has not been a requirement to break IPTRs down

according to the end-of-life, orphan and ultra-orphan definitions. This has prevented year-by year comparisons other than at the highest level and limited the analysis of data to IPTRs for all medicines and not specifically for the categories which are the subject of the Review.

5.6 Going forward there would be benefit in developing datasets and collecting data which take account of outcomes. Outcomes comprise a number of eventualities including benefit accrued but also the stopping of treatment because of side effects or lack of response. There will be a significant role for Public Health Intelligence (PHI), formerly the Information Services Division (ISD), at NHS National Services Scotland (NSS) working with clinical teams and networks to agree and develop appropriate national datasets.

5.7 During the engagement process of the Review there was much discussion about the measurement of outcomes and this is considered in Sections 6.11 & 6.12 and paragraph 8.10.

5.8 A further limitation of the data is that it does not identify the number of patients who might be considered eligible for treatments but who have accepted SMC decisions and chosen not to pursue requests via IPTR or PACS. While the success rate for IPTR and PACS appears high this only reflects the experience of patients who have submitted requests.

5.9 A review of datasets and definitions and processes for collection and analysis would better prepare NHSScotland to meet the challenges that lie ahead. As discussed in Section 6.11, changes in the way that medicines are assessed for regulatory purposes mean that there will be a greater requirement to collect data in relation to individual episodes of treatment which allows assessment of outcomes including side effects. This will require a wider range of data including qualitative measures.

Recommendations

1 Develop, agree and implement national datasets and data definitions for end-of-life, orphan and ultra-orphan medicines and for IPTR/PACS processes. This will ensure that data from Boards is consistent and can be collated. This in turn will allow Boards' data to be used to support functions such as planning and resource allocation.

2 Develop, agree and implement a national chemotherapy dataset and equivalent datasets for medicines used to treat rare conditions

3 Develop, agree and implement sets of outcome measures for classes of medicines or, in the case of very rare conditions, specific medicines

4 Ensure that national systems being developed for electronic prescribing and electronic patient records are prioritised and support the above requirements

5 Establish a multi-agency taskforce or equivalent to report on data requirements to support the assessment and introduction of new medicines going forwards

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

Task and Finish Group Definitions

End-of-Life 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 European Medicines Agency (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)".

Table 1

6.1.1 Discussion with stakeholders revealed a general level of satisfaction with the definitions as laid out in the T&FG Report[3] (replicated in Table 1 above) and applied in the new approach however a number of cautions were sounded. The satisfaction undoubtedly reflects the experience that the definitions as applied have impacted positively on the ability of patients to gain greater access to new medicines. The cautions relate principally to the assessment of ultra-orphan medicines and are explored further in Section 6.3.

6.1.2 Although it was recognised that there are no standard international definitions for end-of-life, orphan and ultra-orphan medicines, concern was expressed that Scotland has taken a different path from the rest of Europe and the United Kingdom and in particular the National Institute for Health and Care Excellence (NICE) in England. It should be noted that the T&FG in responding to the direction of the then Cabinet Secretary consciously sought to foster enablement and flexibility in the process through the application of these definitions.

6.1.3 The extension of the definition of end-of-life medicines to cover a period of three years, as distinct from the period of two years used by NICE, was generally welcomed by patient groups and the pharmaceutical industry however others felt that this introduced different considerations. In particular the tension between length of remaining life and quality of remaining life is not addressed by the definition and remains unresolved.

6.1.4 In discussion with patients and patient groups some patients seeking access to medicines covered by this definition did not regard themselves as at the end-of-life but saw themselves as seeking active treatment with the hope of achieving remission if not cure.

6.1.5 More generally there was a feeling that while the definitions can helpfully be applied to patients' ability to access medicines they do not relate to outcomes.

6.1.6 While there was general satisfaction with the impact achieved by the introduction of the definitions, concern was expressed about their future utility particularly as they apply to ultra-orphan medicines. While the definitions appear to have supported increased access it is anticipated that therapeutic innovations such as genomics and precision medicine, which are likely to impact within the next few years, could see many more medicines classed as orphan or ultra-orphan and the current definitions may lack necessary specificity going forwards. Likewise, the use of combination therapies is anticipated to increase and the current processes and definitions do not readily lend themselves to assessing medicines used in this way.

6.1.7 In several discussions the term "true-ultra orphan" was used to describe a small number of very rare conditions and the associated medicines used to treat them and several stakeholders felt there would be benefit in introducing this further refinement to the definitions. This is discussed further in Section 6.3.

Recommendations

6 Review the definitions for end-of-life, orphan and ultra-orphan medicines to ensure that the definitions used remain suitable to deal with the assessment of anticipated new treatments such as targeted medicines, increasing use of combination therapies and the impact of genomics.

7 Develop, agree and implement a new definition of "true ultra-orphan medicine" to take account of low-volume, high-cost medicines for very rare conditions.

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

6.2.1 The introduction of PACE has been welcomed by all stakeholders, however many feel that it has not been clear how PACE has impacted on SMC decision making and that further development is required. Several patients involved in PACE meetings reported leaving meetings with a sense of strong support from PACE for the medicine under consideration that did not influence SMC to reach a positive recommendation.

6.2.2 There were repeated suggestions for the development of a framework that would allow the PACE contribution to decision making to be quantified and better understood. When the T&FG made its recommendations it proposed a decision making framework but specifically excluded weighting and scoring. At the crux of this matter is the conflict which has its origins in attempting to include less concrete, qualitative considerations in a new revised decision making process yet at the same time wanting to somehow quantify the impact of these considerations in the ways applied to more traditional quantitative measures. While attempts may be made to better articulate the impact of PACE, by its very nature it is unlikely to be measurable in a way that stands up to consistent replication.

6.2.3 While a weighted decision framework may not be possible attempts should be made to better communicate the considerations that lie behind SMC's decisions and the reasons for these decisions.

6.2.4 While the opportunity for patients, patient groups and clinicians to contribute to the PACE process has been welcomed concern was expressed by some of the patients and patient groups about the role of the SMC Public Partners. It was felt that the role was conflicted between the responsibility to represent the wider public while at the same time acting as an advocate for specific patients or patient groups when reporting on PACE at SMC meetings. There was no criticism of any of the individual public partners but rather a concern about the role the partners were being asked to fulfil.

6.2.5 The comment was made that the patients' message as expressed via PACE was being filtered and diluted by the way that information from PACE was reported to SMC. While the main responsibility for reporting back lies with the chair of the PACE meeting, patients, patient groups and the pharmaceutical industry all have high expectations of the Public Partner to act as the patients' advocate in this part of the process. In some instances, where SMC had reached a not recommended decision despite a supportive PACE statement this was attributed by patients and their representatives, in part at least, to the Public Partner not accurately and adequately conveying the message from the PACE meeting. Patients were also concerned that the Public Partners and other SMC members involved in the PACE process had been unable to deal with some of the questions raised at SMC meetings. As a result, it was felt that there were instances where SMC's decisions may have been influenced by inaccurate or incomplete information.

6.2.6 A different view was expressed by the Public Partners spoken to and by other members of SMC. The conflict referred to above was not seen to pose difficulties and the ability of Public Partners to report objectively and dispassionately on relevant aspects of PACE deliberations to SMC meetings was welcomed and valued. There do appear to be differing expectations of the role and contribution of the Public Partners and this situation needs to be addressed.

6.2.7 There was a strong feeling that the process would be significantly improved by having the patients and clinicians involved in the PACE meeting as active participants in the relevant part of the SMC meeting. This message came not just from patients and patient groups but also from the pharmaceutical industry.

6.2.8 The crux of the issue discussed in the preceding four sections is how to achieve the most acceptable way of working that meets the needs of SMC, allowing it to undertake its business in an effective and efficient way while reassuring patients, their representatives and involved clinicians that their case is being given fair and accurate consideration.

6.2.9 One potential limitation of PACE was felt to be the ability to access clinical expertise from within NHSScotland given the rarity of some of the conditions under consideration and the limited experience with the medicine being assessed. A plea was made for more frequent engagement of experts from elsewhere in the United Kingdom and beyond. There are examples where this has happened but the main problem seems to relate to getting access to scarce clinical time.

6.2.10 The view was expressed by some that PACE should be an automatic part of the assessment of all end-of-life, orphan and ultra-orphan submissions, however it was recognised that PACE carries with it a significant opportunity cost in terms of the time required to prepare submissions and support the meeting. It also introduces a delay in the overall process and taking account of these factors the majority view was that the current arrangements for deciding when PACE should be activated should stand.

Recommendations

8 Review communications of SMC's decisions to patients, patient groups and the pharmaceutical industry with a view to achieving greater transparency.

9 Review and clarify the role of the SMC Public Partner.

10 Consider key participants at PACE meetings being actively involved in the relevant parts of SMC meetings to enhance the quality of discussion and decision making.

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

6.3.1 Discussion with stakeholders on this aspect of the Review produced a variety of responses but running through the responses was a consistent theme that, while the new approach was welcomed and had brought about some improvements, it was not yet suitable for all ultra-orphan medicines.

6.3.2 At the heart of the concerns was the issue alluded to in the section on definitions namely that medicines for very rare conditions, the so-called “true ultra-orphans” are still disadvantaged by the new approach and as such access, if not denied, was being made more difficult as patients and treating clinicians were reliant on IPTR and PACS.

6.3.3 The T&FG discounted QALY weighting for the new approach as applied to ultra-orphans, opting instead to recommend that a decision-making process not based on the cost per QALY should be used for medicines defined as ultra-orphans. The preferred approach was for SMC to use a framework of explicit criteria for evaluating these medicines, without performing weighting and scoring. This was seen to parallel the approach being adopted by NICE and consequently would guard against inequity of access between the home countries of the UK.

6.3.4 There is a widespread feeling that this has not had the expected impact and that an unstated price threshold exists and remains the predominant influencer when true ultra-orphan medicines are assessed. Some take the view that despite the modifications in process and the resultant increased flexibility offered, those making submissions have still not been able to make sufficiently strong clinical or commercial cases to support the use of the medicines under consideration.

6.3.5 Closer examination of the data on the twenty-two SMC decisions since the introduction of the new approach suggests that the success rate for recommendations of ultra-orphan medicines is relatively high at 62%. However, when the medicines are sub-classified as ultra-orphans used at the end of life, ultra-orphans used in the treatment of cancer and other malignancies and ultra-orphans used in the treatment of very rare conditions then the figures for each sub-grouping are starkly different.

6.3.6 Only one out of seven medicines (14%) used in the treatment of very rare conditions was approved despite supportive PACE statements. This compares with 11 out of 12 (92%) approved amongst medicines being used at the end-of-life and 2 out of 3 (67%) approved in the treatment of cancer. The widely held perception is that ultra-orphan medicines used in the treatment of very rare conditions, are all extremely expensive and this is the barrier to their approval. The full break down of approval figures for ultra-orphan medicines is given in Table 2 below (Paragraph 6.4.9).

6.3.7 This finding ties in with the use of the term “true ultra-orphan” in several of the stakeholder discussions. This term acknowledges that there are a small number of high-cost medicines for which the cost-effectiveness data is at a level that, even with supportive PACE statements and the application of modifiers, the medicines still do not attain approval.

6.3.8 Despite the T&FG recommendation that QALYs would not be used in the assessment of ultra-orphan medicines, cost effectiveness remains an important consideration as part of any health technology assessment.

6.3.9 It would appear that the route for patients with these very rare conditions seeking access to medicines has become via IPTR and PACS. This route is associated with a high level of success in contrast to the level of positive recommendations being issued by SMC. Indeed, in some discussions it was suggested that having these medicines considered by SMC was potentially disingenuous and risked undermining SMC’s decisions. In effect almost all patients (85% in 2015/16) using IPTRs are being deemed to have circumstances that exempt them from SMC’s decision. On a practical level the IPTR route is more complicated and serves to delay patients accessing these medicines.

6.3.10 On the basis of this observation there would be merit in considering not just adopting a new definition of “true ultra-orphan” medicine as proposed above, but also exploring the development of an alternative assessment and approval pathway for these medicines.

6.3.11 Despite the new approach the SMC process is not providing patients with increased access to true ultra-orphan medicines. It does seem that even though QALYs are not being applied these medicines are failing to satisfy any test of cost effectiveness. As stated elsewhere this potentially calls to question the role of SMC in the assessment of these medicines. The ability of SMC to undertake a robust assessment of clinical and cost effectiveness is not in question however, it may be that SMC should no longer be the group or process responsible for making the final decision about availability.

6.3.12 A number of possible options exist ranging from making all true-ultra-orphans available but then subjecting them to ongoing evaluation in keeping with Managed Access Schemes (MAS) (see Section 6.9) or creating a different placement of the final decision on availability. This could potentially take the form of a single national PACS for ultra-orphans. This could be based on but different from the arrangement for Board-level PACS as has currently been put in place through the extension of the PACS pilot undertaken in NHS Greater Glasgow and Clyde. Given the small number of cases likely to be involved there would be merit in having a single PACS Panel for true ultra-orphan medicines for NHSScotland. This arrangement would ensure that SMC still contributes to the HTA process but is no longer the final arbiter on availability for true ultra-orphan medicines.

6.3.13 The situation to be avoided is creating a series of individual arrangements for true ultra-orphan medicines as each new one is licensed. While it is now being accepted that one size may no longer fit all it is still important to restrict the number of alternative sizes ideally to one.

Recommendations

11 Develop and implement a new assessment and approval pathway for true ultra-orphan medicines that restricts the role of SMC to health technology assessment and places the responsibility for the final decision on availability elsewhere.

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

6.4.1 The general perception of stakeholders is that acceptance rates, both with restrictions and without, have improved although there was a sense that this might not apply equitably to all three definitions, end-of-life, orphan and ultra-orphan.

6.4.2 It is not possible to draw definitive conclusions because of the short time scale of two years since the new approach was introduced and the relatively small number of end-of-life, orphan and ultra-orphan medicines considered in that period, namely fifty-seven. The drawing of conclusions is further hampered because the definitions in use have only applied since the inception of the new approach and therefore there are no reliable baseline figures against which to measure change. Outwith this Review consideration has been given by SMC to retrospectively applying the new definitions to enable comparison but this has been deemed not feasible. The only definition in use by SMC before the T&FG's work was the orphan medicine definition used by the EMA. The definitions in use for end-of-life and ultra-orphan are new and unique to SMC.

6.4.3 Some retrospective data is available. From 2002 – March 2014, SMC assessed 65 full submissions for EMA defined orphan medicines. Of these 16 (25%) were accepted for use, 25 (38%) were accepted with restrictions and 24 (37%) were not recommended for use. The combined acceptance rate for orphan medicines was 63%. (For the purposes of comparison medicines not recommended through non-submission are not included.)

6.4.4 The T&FG used submissions for designated orphan medicines and medicines within British National Formulary (BNF) chapter 8 (Malignant Disease) as a proxy for previous acceptance rates for medicines used at the end of life or for very rare conditions, the assumption being that cancer medicines would fit the definition for end-of-life medicines. In the period November 2011 to October 2013, the combined acceptance rate for orphan/cancer medicines was 48%.

6.4.5 Published SMC data shows an acceptance rate of 75% for all submissions for end-of-life, orphan and ultra-orphan medicines considered under the new approach. This encompasses the total of 57 submissions however sub-analysis by definition is complicated by several medicines falling under more than one category ie orphan/end-of-life and ultra-orphan/end of life.

6.4.6 Taking account of the earlier comments about "true ultra-orphan medicines" analysis has been undertaken for this Review according to the indication for which the medicines were being assessed. Two broad categories were used, cancer (BNF Chapter 8.1) or rare/very rare condition. The results of these analyses are shown in Tables 2 and 3.

6.4.7 Table 2 shows results for ultra-orphan medicines broken down by whether the medicine is solely an ultra-orphan or whether it meets dual definitions and also by broad therapeutic indication. Table 3 shows similar data for orphan and end-of-life medicines including those satisfying both definitions.

6.4.8 In summary the analyses appear to show a range of acceptance rates which in the main are higher than the figures from before the new approach used by the T&FG. There is however one significant outlier, ultra-orphan medicines indicated for very rare conditions, with an acceptance rate of only 14% representing one out of seven submissions. Arguably these are the "true ultra-orphan medicines." What all of these medicines appear to have in common, with the exception of the one medicine that was accepted (Pasireotide) is significant cost whether expressed as an Incremental Cost Effectiveness Ratio (ICER) or Year 1 budget impact.

6.4.9 While there is no pre-new approach comparator it would appear that access to this sub-group of medicines is extremely limited if access is defined by SMC acceptance for use in NHSScotland. This would appear to be further evidence for the assertion that, for some medicines, high cost is preventing them from being accepted.

	Number of Submissions	Accepted for Use	Accepted with Restrictions	Not Recommended	Acceptance Rate
Total number of ultra-orphan medicines	22	10	4	8	64%
Combined ultra-orphan/ end-of-life medicine	12	7	4	1	92%
Ultra-orphan indicated for cancer/malignant condition	3	2	0	1	67%
Ultra-orphan indicated for very rare condition	7	1	0	6	14%

Table 2

	Number of Submissions	Accepted for Use	Accepted with Restrictions	Not Recommended	Acceptance Rate
Total number of orphan medicines	13	3	8	2	85%
Orphan indicated for cancer/malignant condition	6	1	3	2	67%
Orphan indicated for non-cancer condition	7	2	5	0	100%
Total Number of end-of-life medicines*	9	5	2	2	78%
Total number of combined orphan/EoL medicines*	13	8	2	3	77%

Table 3

*All medicines designated end-of-life or combined orphan/end-of-life are indicated for cancers or other malignant conditions

Recommendations

12 Refine data collection systems to enable meaningful year-by-year comparisons and the monitoring of emergent trends.

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

6.5.1 Feedback from all stakeholders confirmed that SMC and its processes are more transparent. Easily understood information is available from a number of sources and the contribution of Patient Group Partners and the Public Involvement Network were both singled out for particular praise. It was felt that engaging with SMC was still complex and potentially arduous but there were sources of support and the processes felt facilitative.

6.5.2 The move to hold meetings in public was felt to be a significant step in improving transparency but several stakeholders felt there had been one particular adverse consequence, namely the introduction of decision making by secret ballot. Under previous arrangements SMC's decision making had been by discussion and consensus building moderated by the meeting's chair although even then there had been occasions when a show of hands had been necessary. It was felt by some who expressed a view that consensus building was preferable to voting but it was recognised that there may be challenges in achieving this in an open public forum. It was suggested that this might be done in closed session at the conclusion of the public meeting.

6.5.3 This issue has clearly been the subject of much deliberation by SMC and its stakeholders in the course of introducing the new approach. The arrangements currently in place appear to take account of balancing a number of issues including optimising the transparency of discussion at SMC, protecting the confidentiality of individual members of SMC in relation to voting, and respecting the pharmaceutical industry's concerns in relation to the commercial implications of the timing of the announcement of SMC decisions. Nonetheless given the level of concern expressed in the process of gathering information for this review there would be merit in reviewing the position.

6.5.4 It was also commented that although SMC meetings were now held in public they represented only part of a longer process which includes NDC and in some instances PACE which, in common with SMC voting, continue to held in closed session.

6.5.5 Several stakeholders, most notably patients and the pharmaceutical industry, made pleas for greater transparency in relation to decision making. This ranged from voting in public, publishing the outcome of voting and developing a decision making framework document. The inclusion of a section in the Detailed Advice Document (DAD) which outlined how the evidence was considered was suggested but it was recognised that where this had been done elsewhere it had been a complex and labour intensive process. It was felt however that SMC might explore the experience of NICE in this regard.

6.5.6 The handling of information that was deemed “commercial in confidence” was also felt to be a barrier to transparency. It results in documents being submitted which contain sometimes significant amounts of information which has been redacted at the request of the submitting pharmaceutical companies. This is then felt to hamper understanding of the issues. The challenge going forward will be for pharmaceutical companies to make submissions that minimise the use of commercial in confidence data and thus their requests for redaction of the contents of submissions.

6.5.7 Both patients and the pharmaceutical industry asked for greater transparency in relation to decision making when medicines were not recommended, in part to aid with better quality resubmissions where feasible. There was a particular plea to better understand the contribution of the PACE statement to the overall decision.

6.5.8 As highlighted above there was general satisfaction with PACE as having made a good start but there were a number of suggestions on how it might be further developed and improved and these have already been discussed in Section 6.2 above.

Recommendations

13 Review SMC’s processes in relation to decision making by secret ballot.

14 Minimise the inclusion of commercial in confidence information in SMC submissions.

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

6.6.1 It has always been the case that when a medicine is approved for use by SMC it should be made available by Health Boards for use by their clinicians. However, it is not always understood or accepted that this does not automatically equate to a medicine being incorporated into a Board's formulary. This is because formularies generally deal with common treatments for common conditions and many of the end-of-life, orphan and ultra-orphan medicines are by definition indicated only in rare or highly specialist circumstances and may not represent first, second or even third line therapy.

6.6.2 Health Boards have in place mechanisms whereby clinicians can access and use non-formulary medicines but this may require a case to be made that the medicine is more effective than an established alternative. In certain quarters, particularly the pharmaceutical companies, this is perceived as failure to implement SMC decisions however, from a Board perspective, SMC acceptance does not equate to automatic use or incorporation into Board formularies.

6.6.3 For the purposes of the Review it was not possible to obtain comparative data on Board formularies. Neither is comparative data available in relation to processes for non-formulary requests, the number of requests submitted or the outcome of such requests because Boards do not have standardised data systems. Formularies are discussed further in Section 6.8.

6.6.4 The situation for SMC not recommended medicines is different. Where a medicine is not recommended by SMC it can still be accessed via an IPTR or PACS. In these cases, the onus is on the treating clinician to make a case for their patient being treated with the medicine despite SMC advice. This route is discussed in more detail in the next section (6.7) but the experience seems to be that a much greater proportion of IPTR (90%) are being supported compared with the rate prior to the introduction of the new approach (69%). The experience of those Boards involved in the pilot of PACS has been that it is extremely unlikely for a medicine not to be made available.

6.6.5 The NMF is available to meet the costs of the introduction of new medicines as detailed in Paragraph 3.9. There was a concern expressed by patient groups and the pharmaceutical industry that clinicians were unaware of the Fund or the mechanism by which funding could be accessed and consequently they felt reluctant or unable to recommend new medicines for fear that they would not be funded. This was not borne out in discussion with Health Boards and clinicians however there was a lack of clarity on the part of at least one Board as to the full range of exigencies covered by the Fund.

6.6.6 While the NMF and its predecessor the RCMF have served their purpose to date, concerns have been expressed about the lack of clarity regarding arrangements for the future. The agreement on PPRS receipts is set to run in Scotland until 2018/19. So far the monies available have covered the calls made on the Fund but it is anticipated that demands will grow and that maintaining the current level of access to new medicines will only be achievable if the current funding arrangements are maintained and availability of funds keeps pace with demand. Comparisons were regularly made with the Cancer Drugs Fund in England and while the operation of the fund differs from Scotland the trend there has been one of significant growth in demand that has out-stripped the available budget year on year.

6.6.7 While high level data is available on the utilisation of the NMF, limitations are posed on the data and the purposes to which it can be put by the confidential nature of some of the pricing agreements reached with pharmaceutical companies for specific medicines.

6.6.8 The NMF has been welcomed because it has provided a dedicated funding stream which has ensured that patients can access end-of-life, orphan and ultra-orphan medicines while Health Boards are protected from the wider-system impact of funding these medicines.

6.6.9 PPRS has been a welcome source of funds to date but, as highlighted in Sections 3.9 and 6.6.6, the future of this funding stream is unclear however the real point at issue is the willingness to maintain a funding source to cover the costs incurred by Health Boards in providing access to end-of-life, orphan and ultra-orphan medicines. Without such a source Boards will be unable to maintain access for patients without adverse impact on other aspects of service delivery, particularly in the face of the anticipated growth in demand for these medicines.

6.6.10 A number of stakeholders expressed concern that the NMF has resulted in medicines being treated differently from other developments and innovations in healthcare the costs of which have to be met from core funding available to Health Boards.

Recommendations

15 Standardise data collection at Board level in relation to systems and process for requests to access non-formulary medicines.

16 Clarify the future arrangements for the funding of end-of-life, orphan and ultra-orphan medicines.

6.7 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)

6.7.1 The systems in place in Scotland have always been based on SMC deciding on whether a medicine should be available for use in NHSScotland whereas IPTR has placed the responsibility with Health Boards to decide whether individual patients should get access to medicines which have not been recommended for use by SMC. This onus does not change with PACS.

6.7.2 Given the increase in the number of end-of-life, orphan and ultra-orphan medicines accepted for use by SMC, it might have been expected that the number of clinicians and patients accessing medicines via IPTRs would have decreased, and further, a smaller proportion of those IPTRs would have been supported. This has not been the case.

6.7.3 This is in part due to the impact of the letter on Transitional Arrangements For Processing Individual Patient Treatment Requests sent to Health Boards by the CMO in November 2013 (SGHD/CMO(2013)20)[2]. In tandem with the introduction of SMC's new approach this guidance served to increase the number of positive IPTRs decisions from Boards. There has also been a striking increase in the number of IPTRs submitted by clinicians to Boards which is less easy to explain. It may represent greater levels of awareness of new medicines and higher levels of expectation in relation to access even when SMC has reached a not recommended decision. In other words, there appears to be a greater reluctance on the part of patients, patient groups and clinicians to accept decisions by SMC not to recommend certain medicines.

6.7.4 Because of the way that IPTR data has been collected and the change in definitions the ability to analyse the data at any level other than total number of submissions and decisions is limited. As stated above the figures show a significant rise in the number of IPTRs submitted to Boards and an increase in the proportion of submissions approved.

6.7.5 It appears that clinicians and patients are increasing their use of the IPTR systems to successfully access medicines given not recommended status by SMC. Between 2012 and 2016 the number of IPTRs submitted rose from 389 in 2012-13, peaking at 918 in 2014-15 and dropping to 696 in 2015-16. In the same periods the approval rates were 69%, 82%, 90% and 87% respectively. (Table 4)

	Total IPTRs	Approved	Rate	Not Approved	Rate
2012 - 2013	389	268	69%	121	31%
2013 – 2014	426	351	82%	75	18%
2014 – 2015	918	829	90%	89	10%
2015 – 2016	696	608	87%	88	12%

Table 4

6.7.6 It is not possible with the same degree of confidence as applies to SMC data (Paragraph 6.4.9) to differentiate end-of-life, orphan and ultra-orphan medicines within IPTR data but it is possible to make broad assumptions in relation to the available data. On the basis of this it does appear that the proportion of IPTRs that are for end-of-life, orphan and ultra-orphan medicines has changed being around 30% in 2012-13 and rising to around 60% in 2014-15 and 2015-16.

6.7.7 Using the same data subject to the same assumptions, it appears that in 2012-13 medicines that would now be classed as end-of-life, orphan and ultra-orphan had a lower approval rate at around 45% compared with other medicines at 80%. This difference appears to have narrowed with the figures for 2014-15 being in the region of 88% and 94% respectively and the same figures for 2015-16 being in the region of 85% and 91%. These figures are shown graphically in Chart 1.

6.7.8 Even given the limitations of the data it is clear that there has been an increase in the number of IPTRs submitted and an increase in the number of IPTRs being approved both in absolute and percentage terms. This is further evidence of increased access.

6.7.9 There was a strong concern expressed by several stakeholders that the system has evolved to the point where, in relation to access to end-of-life, orphan and ultra-orphan medicines the most likely outcome, regardless of SMC's decision, is that the patient will get access to new medicines. The question is not if access will be granted but when.

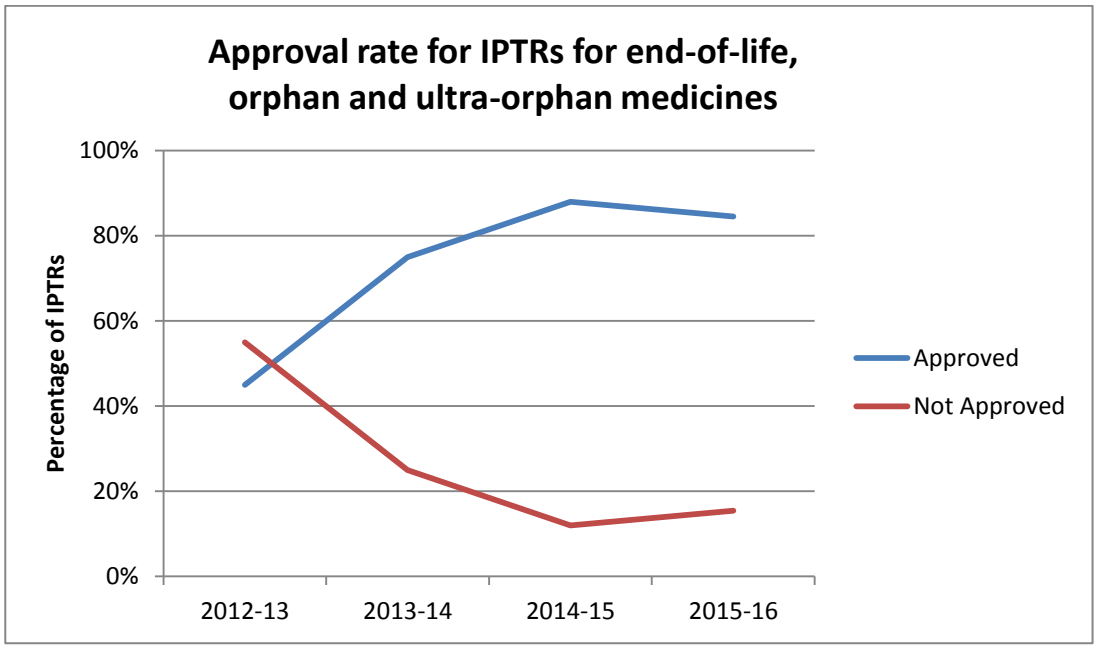

Chart 1

Recommendations

17 Review the data set and definitions for data relating to IPTRs collected by Boards with the aim of achieving consistency and comparability and also extending the dataset to include data on outcomes.

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

6.8.1 Since the inception of SMC there has been a "Once for Scotland" approach to the managed introduction of new medicines in NHSScotland. This has worked well and there are several areas where this approach could be further developed.

6.8.2 Arguably in circumstances such as those encountered when dealing with end-of-life, orphan and, in particular, ultra-orphan medicines, consideration should be given to a "Once for the United Kingdom" or even a "Once for Europe" approach. Despite the undoubted strength of its health technology assessment capability, Scotland lacks the critical mass to effectively negotiate and procure high-cost, low volume medicines such as ultra-orphans.

6.8.3 A single National Formulary for NHSScotland has been suggested and key to the success of such an initiative will be how the formulary is developed and implemented. There would be undoubted gains in NHSScotland adopting a national approach to formulary development and use. A possible process and benefits are discussed in Paragraph 6.8.6.

6.8.4 Formularies perform two primary functions. They can be a comprehensive compendium of all medicines available for use or they can be decision-support tools which promote and support the safe and effective use of medicines in the management of medical conditions. The former is the British National Formulary (BNF) which needs no replication. The latter can take a number of forms but there is demonstrable value in having locally-developed and clinically-owned formularies.

6.8.5 Most Boards have their own formularies which have been developed to meet local need largely in relation to higher volume, lower cost activity. These formularies provide clinicians with advice on the management of specific conditions and detail therapeutic options based on clinical and cost effectiveness. Usually this is presented as a number of ranked choices. Not every medicine for ever condition will be or needs to be included in a formulary but as every medicine approved by SMC is by definition available to clinicians in every Scottish Health Board, there are local mechanisms for clinicians and patients to access non-formulary SMC approved medicines. See Section 6.6.

6.8.6 Where the "Once for Scotland" approach would be of benefit is to have a more coordinated approach to the development and use of formularies. A successful approach would retain the local sensitivity and ownership associated with Board-level formularies while achieving a greater harmonisation and consistency between Boards. This could be achieved by building on the work already led through Healthcare Improvement Scotland (HIS) as it brings together Board Area Drug & Therapeutics Committees

(ADTCs) to look at and address issues of shared concern. The impact is likely to be similar to that hoped for by those who advocate the introduction of a single national formulary for NHSScotland but the process is likely to engender greater engagement and ownership.

6.8.7 One area where the apparent lack of a "Once for Scotland" approach was commented on repeatedly is the approach to IPTRs and PACS. It is important to remember though that these are processes dealing with the specific circumstances of individual patients in contrast to SMC processes which take a population view. They are also processes dealing with requests for medicines which SMC has already concluded are not recommended for use in NHSScotland. As a result, the deliberations of IPTR panels on individual circumstances will legitimately reach differing conclusions despite apparently similar circumstances. As the accountability for the decision lies with Health Boards these differences are generally interpreted as inconsistencies between Health Board processes rather than differences between the circumstances of individual patients.

6.8.8 While Boards have complied with the guidance in relation to IPTRs they have undoubtedly put in place different processes which reflect local circumstances. The variations largely reflect the capacity and expertise available to individual Boards to address IPTRs.

6.8.9 A "Once for Scotland" approach or process would improve transparency and consistency and build greater confidence in the IPTR system and its successor PACS. This could be achieved by elevating the processing of IPTR/PACS requests to a single national panel or perhaps regional IPTR/PACS panels following consistent methodology.

6.8.10 This already happens in some instances. Where the medicine being requested is being used to treat cancer or a rare condition the clinical consideration usually takes place within the cancer centre or equivalent expert centre. The expert centre's IPTR panel or equivalent makes a recommendation which is subject to confirmation of funding and as funding is dealt with at the level of the patient's Board of residence the recommendation is passed to the Board of residence for final decision. The introduction of the NMF has removed affordability as a consideration. It is unlikely that the Board of residence would not accept the clinical recommendation of the expert centre therefore access would be granted in the majority of cases.

6.8.11 As long as the focus of requests is on the individual patient, this would not result in the same decision for every request for access to a medicine given not recommended status by SMC. If the aim though is to achieve the same decision for every request then the process actually becomes one which is about reversing SMC decisions rather than considering whether there are specific circumstances in which an SMC decision should not apply to an individual patient.

6.8.12 PACS has now been introduced as the alternative to IPTR with the expectation that it will help address the perceived inconsistencies and weaknesses of IPTR. Initially PACS was piloted in NHS Greater Glasgow and Clyde and more recently the pilot has been extended to all Boards but a comprehensive evaluation has not yet been undertaken or published. Consequently, the information available to the Review is based on informal feedback from people involved in the pilot.

6.8.13 PACS is seen as a more consistent process driven by clinical opinion which helps address some of the apparent variability seen with Board-level IPTR processes. Concern has been expressed though that the PACS process does not allow a not supported decision. In other words, a vigorously pursued PACS application will inevitably result in access being granted. This concern is the origin of the "not if; but when" concern highlighted in Paragraph 6.7.9.

6.8.14 The discussions with stakeholders in relation to IPTR and PACS highlighted yet again the pleas for consistency and transparency in relation to processes and decision making. As noted elsewhere all stakeholders accepted that the system had to have the ability to reach not recommended decisions but the discussions stopped short of providing a consensus on the circumstances under which these would apply.

6.8.15 Patient Access Schemes (PAS) and the associated Patient Access Scheme Assessment Group (PASAG) already represent a "Once for Scotland" approach to NHSScotland's relationship with the pharmaceutical industry. There is the potential for a different and more effective mechanism regarding the pricing and procurement of medicines and this is discussed in Sections 6.9 and 8.

Recommendations

18 Explore opportunities to learn from and collaborate with other health economies in relation to the assessment and managed introduction of new medicines and other health technologies.

19 Standardise NHSScotland's approach to formulary development and use.

20 Review and evaluate the experience of PACS to date with a view to deciding on any required modifications and thereafter agree the final model and timescales for implementation in NHSScotland.

6.9 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

6.9.1 There is a need to differentiate between the full process for the assessment and managed introduction of new medicines for use in NHSScotland and the part that SMC and its processes play in that wider process.

6.9.2 None of the stakeholders consulted felt that SMC had a role to play in commercial negotiation. SMC's role and acknowledged strengths lie in health technology assessment and that should remain SMC's primary function.

6.9.3 When discussing this aspect of the Review stakeholders were realistic about the competing priorities involved and recognised that the challenge is how to best manage the interface between NHSScotland and the pharmaceutical industry. A situation where NHSScotland seeks to optimise its use of a finite resource subject to ever-increasing demands while the pharmaceutical industry operates in a competitive commercial environment and seeks to maximise return on its investment and meet the expectations of its shareholders.

6.9.4 The clear, shared interest of all parties evident to the Review is to give patients access to new medicines likely to be of benefit to them in a way that is clinically appropriate, timely and affordable.

6.9.5 Currently there is little in the way of formal price negotiation on behalf of NHSScotland. While consideration of price is part of the development and submission of PAS this process is led by the pharmaceutical companies and the proposed PAS is agreed, or not, by PASAG. This process has been successful in agreeing a number of simple discounts for high-cost medicines but it is a process that is used by the pharmaceutical companies usually in response to anticipated or actual failure of submissions to achieve SMC support.

6.9.6 With PAS to date there has been a preference to pursue simple discounts because of the lesser administrative burden on Health Boards. Some complex PAS have been accepted which rely on ongoing data collection which then influences the actual amount paid. There is a definite enthusiasm on the part of the pharmaceutical industry to explore the potential of this approach and to develop more formal MAS for use in NHSScotland. Several stakeholders also commented that this approach will be necessary to cope with some of the anticipated changes in the way that new medicines will enter the market in future. This is discussed in section 6.11. MAS should be developed as an additional option rather than a replacement for PAS as simple PAS are likely to remain appropriate for a number of new medicines.

6.9.7 To date there has been a reluctance on the part of NHSScotland to enter into payment-by-results schemes despite enthusiasm on the part of the pharmaceutical industry because of the perception that the establishment of systems to support the on-going requirement for data collection is complex and labour intensive and the costs could potentially exceed any gains from the complex PAS. It is going to be difficult to maintain this position and for the reasons outlined in Section 6.11 and elsewhere, NHSScotland now needs to explore complex PAS and other MAS with a view to their early adoption.

6.9.8 The general approach of NHSScotland to the negotiation of prices for end-of-life, orphan and ultra-orphan medicines has tended to be reactive. There is now a need to be more proactive to better deal with the growing competing priorities facing health and social care and the increasing challenge of making best use of the public purse.

6.9.9 It was suggested by one stakeholder that the new approach has actually weakened the negotiating position of NHSScotland. The concern is that the explicit move away from the use of the QALY to assess ultra-orphan medicines indicates that higher costs will be tolerated. Consequently, it was felt that incentives for pharmaceutical companies to offer reduced prices had been removed. In similar vein the increased success rate for IPTR applications may also encourage pharmaceutical companies to maintain higher pricing strategies.

6.9.10 There was a general feeling that the negotiation on pricing has to be part of a different set of relationships and the discussion needs to begin earlier in the pathway of a medicine's introduction. It also needs to involve a wider group of stakeholders than just NHSScotland and the pharmaceutical industry. All of those who contributed to this Review expressed an interest in being involved in discussions about how pricing strategies might be agreed. The need for robust data and data handling expertise to support a new process was highlighted and the Farr Institute was seen as having a significant contribution to make in this regard. As well as addressing issues of cost and affordability a suitable new process will be better able to address issues such as horizon scanning, optimal use of the medicine, outcomes, value and whole system impact. Any future mechanism to set pricing has to possess a level of sophistication capable of dealing with issues such as multi-indication pricing and managed access schemes.

6.9.11 This different relationship between NHSScotland and the pharmaceutical industry will inevitably harbour a tension between the collaboration required to jointly optimise use of and access to medicines, and the competitive stance required to have a commercially robust negotiation on price. These two aspects of the relationship are not mutually exclusive and each has to inform the other particularly in relation to assessment of value as discussed in Section 6.12. It is also important to accept that the relationship has to involve input from the full range of stakeholders already engaged with SMC and this Review and not just NHSScotland and the pharmaceutical industry.

6.9.12 There is active discussion outwith this Review about the introduction of a pause in the process. There is a lack of clarity amongst stakeholders on exactly what this means and how it might operate. Having a mechanism which creates the opportunity for pharmaceutical companies to review their pricing rather than having to resort to full resubmissions is welcomed by some, however other stakeholders spoken to during the Review are concerned that a pause will delay decisions on access and potentially create an environment which could present opportunities for gaming.

6.9.13 It was suggested that one of the limitations of the current system is the number of decision options open to SMC. The choice is effectively binary albeit that an approval decision can be associated with restrictions. It was felt by some that giving SMC an option to give a conditional yes would helpfully enhance the nature of price negotiations and pricing strategies and would be compatible with a move to the adoption of MAS.

6.9.14 A conditional yes would fit with MAS as used elsewhere including in NHS England. SMC would have the option to approve a medicine subject to ongoing data collection and evaluation with the option that if the medicine failed to deliver the anticipated outcomes the pharmaceutical company would refund the costs and the medicine would have its use restricted or would be withdrawn.

6.9.15 Some reservations were expressed about the ability to withdraw a medicine that had not lived up to expectations once it had been established in practice. Despite these reservations it was conceded that such a system would have to be explored particularly in relation to the anticipated introduction of medicines in the future where a medicine would be licensed on the basis of demonstrating potential but before having a conventional evidence base established.

6.9.16 NHSScotland has already demonstrated the benefits of negotiating for medicines using National Procurement within NSS. The most recent success has been the procurement of the new medicines for Hepatitis C. There is the opportunity to learn from and build on this experience and although the circumstances in relation to volumes and critical mass are different when considering end-of-life, orphan and ultra-orphan medicines, there are still parallels in relation to the timing of the negotiation and the mobilisation of expertise.

6.9.17 Discussion with stakeholders and some of the scoping undertaken in support of this Review suggests that NHSScotland could learn from the experience of other countries. New Zealand, Canada and several European Countries were mentioned but none offers a simple, readily-adoptable solution. There would be merit in undertaking a more detailed evaluation of experience elsewhere.

Recommendations

21 Explore MAS with a view to early adoption in NHSScotland. These should build on the experience of complex PAS within NHSScotland and payment-by-results schemes in operation in other health systems.

22 Review the proposal to introduce a “pause” in light of some of the wider changes and actions recommended in this report.

23 Give SMC the additional decision option of “recommend for use subject to ongoing evaluation and future reassessment.”

24 Make greater use of National Procurement in NSS to lead negotiations on behalf of NHSScotland on the cost of new medicines

25 Undertake a comparative review of the arrangements in place in the healthcare systems of other countries for the introduction of new medicines and specifically end-of-life, orphan and ultra-orphans, seeking to learn from their experiences.

6.10 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

6.10.1 A number of sources felt that there had been unintended consequences associated with the introduction of the new approach. Most of the comments came from sources within the NHS.

6.10.2 It was felt that the new approach poses significant challenges for the capability and capacity of the system particularly if the demand for assessments continues to grow as anticipated. This is impacting not just on SMC and its associated processes but also patient groups, clinicians and the pharmaceutical industry. The time involved in preparing and assessing submissions is significant and makes substantial calls on a sometimes small cohort of professionals and lay experts. This can impact on clinical activity and carries a significant opportunity cost. Continuing to properly resource the system will be challenging as the required resource is not just financial.

6.10.3 The introduction of the new approach has had the unintended consequence of creating a system where access to ultra-orphan medicines used in the treatment of rare conditions has not increased. This has resulted in an increase in the use of IPTR and, in the pilot Boards PACS, with the experience being that the majority of requests are supported despite SMC's original assessment. This is discussed in Sections 2, 6.3, 6.7, 6.8 and 7.

6.10.4 The approach to the use of medicines may have changed. The improved access brought about by the new approach, whether by SMC decision or IPTR/PACS, has given clinicians more options and often treatments are being applied more aggressively and for longer periods of time than current evidence would justify. Several clinical stakeholders commented that current clinical practice associated with end-of-life medicines was at odds with the principles underpinning Realistic Medicine[1]. It was felt that in some cases the use of medicines aimed at extending life was at the cost of pursuing alternative non-drug treatments aimed at enhancing quality of life and providing high-quality supportive care.

6.10.5 There was a view that the new approach has actually weakened the negotiating position of NHSScotland. Because there is an expectation that higher costs will be tolerated it was felt that this removed incentives for the pharmaceutical companies to offer reduced prices. This is discussed in more detail in Paragraph 6.9.9.

6.10.6 More generally, concern was expressed that medicines were increasingly being treated differently from other types of care in relation to cost and cost effectiveness or prioritisation. Comparisons were drawn with a number of new and emerging non-medicines technologies. In May 2016 HIS and the Scottish Health Technology Group (SHTG) followed a consultation paper published in January 2016 with an action plan entitled,

"Driving improvement in non-medicine technologies."[4] Both publications resonated with this Review.

6.10.7 The point was made that medicines have always been subject to greater scrutiny than other technologies because data is more readily available and that one aspiration should be to replicate the rigour applied to the introduction of new medicines to other new technologies.

6.10.8 Some stakeholders saw that the introduction of secret voting at SMC meetings had clouded transparency in a way that had not been intended. This is discussed in Section 6.5 above.

6.10.9 Several clinical stakeholders voiced concern about the impact of the introduction of the new approach on the morale of SMC members. In some quarters there were concerns that by inference a highly-regarded process had been criticised and even undermined. This feeling has been further compounded by the apparently large proportion of SMC decisions which have been "overturned" by the high success rates for requests made via IPTR and PACS. It was seen as a significant success that the high level of clinical engagement both through direct involvement with SMC and in support of its decisions had been maintained through the implementation of the new approach.

6.10.10 Several of the highlighted unintended consequences cannot be readily addressed as discrete issues. Mitigation will be dependent on further change to the system for access to new medicines. The unintended consequences identified will have to be borne in mind as this Review's recommendations are considered and taken forward to ensure that, as much as is possible, they are not replaced by a new and different set of unintended consequences.

Recommendations

26 Monitor the demands made on SMC and its associated processes and ensure that the available capacity and capability and support mechanisms are adequate for SMC's needs.

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

6.11.1 The Review was involved in much interesting discussion about what lay ahead and how we might collectively address the anticipated challenges to best effect.

6.11.2 There was a shared view of an exciting emerging situation described as precision medicine and associated with highly-targeted therapies informed by genomics. This will potentially bring many benefits but also challenges around using the technologies to achieve optimum benefit. Treatments are likely to be used with a greater degree of confidence but many more could be classed as orphans and ultra-orphans under the current definitions. Highly-specialised, targeted medicines for smaller patient populations are anticipated to become the norm.

6.11.3 Given the relatively small number of patients suitable for treatment the medicines have the potential to be extremely expensive and the costs would not be confined to the medicines. Many will bring with them a requirement for diagnostics or other supporting services to enable their use.

6.11.4 Internationally there is a move to give patients earlier access to medicines which have shown potential benefit and this is being seen in a number of ways in other health systems. Novel approaches to so-called "breakthrough" medicines and Early Access Schemes (EAS) are already in place elsewhere.

6.11.5 There is a move on the part of regulatory agencies to grant licenses at an earlier stage when compared with the processes for medicines that do not meet the definitions for end-of-life, orphan and ultra-orphan. Because these medicines are used to treat such small populations it means that the evidence bases normally expected of new medicines will never be established. Consequently, licenses are being granted with the requirement for ongoing evaluation of the medicine and even linkage to completion of clinical trials.

6.11.6 This means that in the future the level of evidence required for licensing will be less than that required by SMC for its health technology assessment. The risk then becomes that none of these medicines will be accepted for use by SMC and the IPTR/PACS route becomes the norm. It will be important as discussed in paragraph 6.3.12 to ensure that SMC's contribution to the assessment process is revised and remains relevant.

6.11.7 There are a number of opportunities. If Scotland is to avoid creating a system that makes it difficult for patients to access new medicines or, worse still, denies them access, then the existing system needs to evolve. The introduction of a conditional yes (as discussed in Section 6.9 above) accompanied by the on-going collection and evaluation of data in collaboration with the treating clinicians, pharmaceutical companies and other agencies such as the Farr Institute would better align SMC's

processes with the direction of those of the regulator and work to the advantage of patients.

6.11.8 A different approach will be required that takes account of different and novel types of data including so-called “real world” data, patient reported outcomes and other quantitative measures. There is also likely to be an increasing need to develop and use metrics linked to prevention and preservation of function rather than more traditional outcomes. This will best be achieved by working with a broad set of stakeholders to agree datasets and data definitions to support the ongoing evaluation. Much can be learned from the databases and patient registers held by some patient support groups and in some instances these could provide solid starting points.

6.11.9 These revised processes should be encompassed within a MAS that ensures that access to new medicines is informed and driven by meaningful data.

Recommendations

27 Consider through wide stakeholder engagement the best way for NHSScotland to take advantage of the opportunities afforded by anticipated developments in the way that new medicines will be introduced in the future. This is likely to be through the establishment of a multi-agency taskforce or equivalent group.

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

6.12.1 In the course of the engagement undertaken by the Review there was limited awareness of the concept of a Scottish Model of Value and no sense that any particular progress had been made with the issue since the introduction of SMC's new approach.

6.12.2 There was doubt that the experience of the new approach in relation to end-of-life, orphan and ultra-orphan medicines would provide a solid basis for the further development of a Scottish Model of Value because of the highly specific considerations of this particular agenda. There was strong agreement though that the experience could and should inform any developmental of a model.

6.12.3 The situation with end-of-life, orphan and ultra-orphan medicines is highly unusual and may even be unique. Many of the medicines transcend the conventional measures of cost effectiveness but these considerations are displaced by others such as the extreme rarity of the conditions and the lack of alternative treatment options. The view obtained through this Review is that, in the current situation, there is justification for considering these medicines according to different parameters and using different weightings from other treatments. A future Scottish Model of Value ideally would provide a framework that makes this unnecessary.

6.12.4 Any framework has to develop an accepted model of value that is sophisticated enough to deal in multiple currencies of which money is only one. Discussions in this Review moved between cost, cost-effectiveness, affordability and value accepting that they are all different but inter-related. The most challenging to define is value and in a Scottish Model of Value it will be important to ensure that it is measured and expressed in broad but consistent terms. These terms cannot be confined to clinical effectiveness and medical outcomes but need to take account of personal considerations and wider societal factors. The metrics need to be applicable not just to this small group of medicines but to an array of treatments and interventions in a way that informs and supports meaningful comparisons and difficult choices.

6.12.5 Each of the stakeholder groups spoken to had helpful and interesting perspectives on what constituted meaningful measures of success in relation to treatment with medicines. The measures extended beyond traditional, often binary outcome measures and looked at qualitative information such as patient reported outcomes, real world data, societal impact such as ability to work and maintain physical and financial independence, preservation of function, prevention of deterioration whether of the primary condition or through prevention of the development of co-morbidities and wider impact on families. The list is long and complex but there is a need to work with stakeholders to agree meaningful frameworks and metrics that stand up to repeated use and comparison. A system that developed a new framework and metrics for every new medicine that required ongoing evaluation would be neither efficient nor effective.

6.12.6 In keeping with the comment made in Paragraph 6.10.7 about the high level of scrutiny applied to medicines, the principles outlined should be applicable not just to the evaluation of new medicines but to other non-medicines health technologies.

6.12.7 Ideally a Scottish Model of Value would not be confined to health or healthcare interventions but could be used across all aspects of public life in circumstances where informed choices have to be made about the use of finite and increasingly scarce resources.

Recommendations

28 Consider how the experience of NHSScotland's systems for the assessment and managed introduction of new medicines can inform the development of a Scottish Model of Value. This is likely to be through the establishment of a multi-agency taskforce or equivalent group.

7 CONCLUSIONS

7.1 Discussion, comment and recommendations run through the various sections of this report. This section deals in the main with the core questions highlighted in Paragraph 3.13.

7.2 Access to end-of-life, orphan and ultra-orphan medicines has increased. If this situation is to be maintained there are two significant issues that need to be considered. Firstly, the assessment and decision making process for ultra-orphan and true ultra-orphan medicines and secondly, the funding mechanism and affordability of maintaining the increased level of access.

7.3 It appears that access to end-of-life and orphan medicines has increased as a result of the new approach. SMC is accepting more of these medicines for use in NHSScotland however, SMC acceptance of ultra-orphan medicines remains low. This is even more striking when one looks specifically at ultra-orphan medicines used to treat very rare conditions. In this report these are referred to as true ultra-orphans. Access to ultra-orphan medicines has increased as a result of more IPTR for these medicines being supported by Health Boards.

7.4 One of the main issues that will have to be considered in light of this Review is whether Scotland has achieved the level of access it set out to and whether the intention is now to maintain this level of access across all three definitions of end-of-life, orphan and ultra-orphan medicine. The T&FG was not set a target for access but it appears that the rates of acceptance for end-of-life and orphan medicines are on a par with the other medicines considered by SMC. Similarly, IPTR data would suggest that access to ultra-orphan medicines is at a rate similar to SMC acceptance for other medicines.

7.5 If the increased level of access being delivered by the current arrangements is felt to be satisfactory then maintaining it will require aspects of the assessment and decision-making system to be revised. The system should deliver its assessments and decisions in a manner that achieves this desired level of access and is consistent, timely and transparent.

7.6 One size no longer fits all and since the introduction of the new approach SMC decisions have delivered increased access to end-of-life and orphan medicines while IPTR has become the default route for ultra-orphan medicines. However, a system that relies on individual applications to access medicines and in effect overturns SMC decisions is not efficient or effective and an alternative pathway as discussed in Section 6.3 is recommended. This would create better alignment of processes and SMC would continue to assess and comment on the clinical effectiveness and cost effectiveness of the medicine but the final decision on availability would sit elsewhere. This approach preserves the integrity of SMC and its processes across the full range of medicines it considers yet achieves the intended level of access to ultra-orphan medicines.

7.7 Getting to this point will require further focussed discussion involving stakeholders through a taskforce or similar.

8 DISCUSSION

8.1 As might be expected this Review has raised a number of issues that have their origins in the Review but have ramifications not just for the wider healthcare system but for health and social care and other publicly funded services.

8.2 At the core of these issues is the challenge of how to manage the tension between optimising the use of finite resources in a way that ensures that difficult choices are made with confidence and an acceptable balance is reached between providing individual patients with the best experience of care and investing in the health and wellbeing of the wider population. This is in essence the tension articulated in the Institute for Healthcare Improvement's Triple Aim[5] which lies at the heart of Scotland's 20:20 Vision for Health & Social Care[6] and the associated Route Map[7].

8.3 All expectations are that the challenges highlighted in this Review with respect to ongoing access to new medicines will be replicated across a wide range of healthcare and other technologies to which clinicians and patients will seek access in coming years. The rate of development of often costly innovative technologies is seemingly exponential and is accompanied by expectations in some quarters that these innovations will be introduced at earlier stages of their development. This will often be without a traditional evidence base but instead with the expectation that the evidence base will continue to be accumulated as part of managed introduction and managed access schemes.

8.4 Suggestions of a new paradigm may not be overstated and the consensus view of the stakeholders contributing to this Review is that the existing structures, processes and relationships are unlikely to meet the challenge going forward. There are however significant strengths within the existing paradigm. SMC and its associated systems and processes function effectively, are highly regarded and enjoy the confidence of patients, the public, clinicians and the pharmaceutical industry. The new approach has had the sought after impact for end-of-life and orphan medicines. There is a need though for reflection and further evolution of a system already based on a philosophy of continuous improvement.

8.5 The suggested new paradigm needs to have at its heart a different set of relationships between all of the stakeholders. These include patients and the wider public, organisations representing patients' interests, NHSScotland including SMC, Territorial Health Boards, Special Health Boards such as HIS and NSS and their constituent parts, the pharmaceutical industry, academia including organisations like the Farr Institute and Scottish Government.

8.6 The new relationship has to be positioned further upstream in relation to the introduction of medicines than previously. To date the interaction between the various players, and certainly that between NHSScotland and the pharmaceutical industry has tended to begin only once a medicine has been

granted a license and a submission to SMC is being considered. All spoken to consider this to be too late, missing as it does the opportunity to collaborate on issues such as horizon scanning, the optimal use of specific medicines, wider assessments of impact and value and more pragmatic pricing strategies.

8.7 Even within groups of stakeholders there will be a need to behave differently. NHS Boards and clinicians involved in developing treatment strategies will have to share intelligence to better inform horizon scanning. Pharmaceutical companies will have to move to greater collaboration with their competitive rivals particularly in the area of the introduction of new medicines which will be used as part of combination therapies or multi agent regimens.

8.8 The new relationships have to acknowledge and deal with the tensions created by being both collaborators and customers and this will be challenging. There is evidence of a willingness to change and move away from what has been seen as an adversarial role where SMC's expectation of the pharmaceutical industry has been to make submissions capable of meeting SMC's criteria, while the pharmaceutical industry has had an expectation that SMC has to justify not recommending medicines for use in NHSScotland. In this latter regard there has been a repeatedly expressed frustration on the part of the industry that SMC does not provide adequate explanation for its decisions. Arguably the introduction of the new approach laid the way for a shift from a competitive to a more enabling process but further progress will require a more fundamental rethink on the quality and positioning of the relationships.

8.9 Discussions that took place in the course of the Review demonstrated a willingness on the part of all stakeholders to collaborate on developing new ways of working. A repeated theme was for the need to begin that collaboration much earlier in the process of bringing new medicines to market but also to continue it after medicines had been accepted for use to ensure there was ongoing evaluation of the impact of medicines. The approach was characterised as a collaboration informed and driven by data. This collaboration and the involvement of academic partners such as the Farr institute was seen as a way of addressing some of the challenges of optimising the use of medicines, agreeing affordable pricing strategies and coping with the revisions to the regulatory framework for new medicines.

8.10 During evidence gathering from stakeholders much was made of the need to take a more sophisticated approach to benefits that includes patient-reported outcomes, wider societal benefits such as the ability to continue working or a reduction in care or support requirements. The term "overall budget impact" was used on several occasions and requires the application of sophisticated health economic modelling which takes account not just of medicine costs but of whole system value and impact and introduces the concept of multiple "currencies" not just financial cost. The integration of health and social care presents Scotland with a particular opportunity in this regard.

8.11 One of the key findings of this Report is that despite the new approach, access to true ultra-orphan medicines used in the treatment of very rare conditions has not increased as measured by SMC recommending such medicines for use. It is unlikely that any further revision to SMC processes is likely to change this. In other words, in terms of process, one size no longer fits all but every attempt must be made to restrict the number of alternatives to one rather than have a series of exemptions on a case-by-case or medicine-by-medicine basis. This will require the development of an alternative pathway with a revised contribution from SMC in relation to true ultra-orphan medicines.

8.12 Mention has to be made of the difficulty highlighted by several contributors in reconciling the direction outlined in Realistic Medicine[1], particularly when it comes to the challenge to reduce the harm associated with over-investigation and over-treatment, with the drive from both clinicians and patients and their advocates to access new medicines at the earliest opportunity. It was suggested that in relation to end-of-life, orphan and ultra-orphan medicines this was influenced by the lack of alternative management strategies. It does confirm the need to pursue as a matter of priority the discussion initiated by the publication of Realistic Medicine[1] in Scotland and comparable initiatives such as Prudent Healthcare[8] in NHS Wales.

8.13 As the recommendations are progressed there will be additional sources of expertise from which NHSScotland can benefit. Boards should work with PHI on developing and refining datasets. The Farr Institute could add further expertise and rigour to the development of revised datasets and systems to undertake evaluation of new medicines both prior to launch and as part of the ongoing evaluation following introduction to clinical practice. The expertise of National Procurement at NSS will be essential in developing a different approach to affordable pricing.

8.14 There is a danger that in trying to address the issues raised in this Review and its recommendations that actions are taken at the wrong level or on too small a scale. At the heart of the Review are a number of fundamental questions about NHSScotland and its continuing ability to deliver the healthcare that the people of Scotland want and expect. This is in large part down to agreeing the priorities for funding from a finite resource. This will involve difficult choices but these choices have to be made by the correct stakeholders armed with the correct information. In this regard initiatives such as “Creating a Healthier Scotland – What Matters to You?”[9] will be key.

9 SUMMARY OF RECOMMENDATIONS

9.1 Develop, agree and implement national datasets and data definitions for end-of-life, orphan and ultra-orphan medicines and for IPTR/PACS processes. This will ensure that data from Boards is consistent and can be collated. This in turn will allow Boards' data to be used to support functions such as planning and resource allocation.

9.2 Develop, agree and implement a national chemotherapy dataset and equivalent datasets for medicines used to treat rare conditions.

9.3 Develop, agree and implement sets of outcome measures for classes of medicines or, in the case of very rare conditions, specific medicines.

9.4 Ensure that national systems being developed for electronic prescribing and electronic patient records are prioritised and support the above requirements.

9.5 Establish a multi-agency taskforce or equivalent to report on data requirements to support the assessment and introduction of new medicines going forwards.

9.6 Review the definitions for end-of-life, orphan and ultra-orphan medicines to ensure that the definitions used remain suitable to deal with the assessment of anticipated new treatments such as targeted medicines, increasing use of combination therapies and the impact of genomics.

9.7 Develop, agree and implement a new definition of "true ultra-orphan medicine" to take account of low-volume, high-cost medicines for very rare conditions.

9.8 Review communications of SMC's decisions to patients, patient groups and the pharmaceutical industry with a view to achieving greater transparency.

9.9 Review and clarify the role of the SMC Public Partner.

9.10 Consider key participants at PACE meetings being actively involved in the relevant parts of SMC meetings to enhance the quality of discussion and decision making.

9.11 Develop and implement a new assessment and approval pathway for true ultra-orphan medicines that restricts the role of SMC to health technology assessment and places the responsibility for the final decision on availability elsewhere.

9.12 Refine data collection systems to enable meaningful year-by-year comparisons and the monitoring of emergent trends.

9.13 Review SMC's processes in relation to decision making by secret ballot.

9.14 Minimise the inclusion of commercial in confidence information in SMC submissions.

9.15 Standardise data collection at Board level in relation to systems and process for requests to access non-formulary medicines.

9.16 Clarify the future arrangements for the funding of end-of-life, orphan and ultra-orphan medicines.

9.17 Review the data set and definitions for data relating to IPTRs collected by Boards with the aim of achieving consistency and comparability and also extending the dataset to include data on outcomes.

9.18 Explore opportunities to learn from and collaborate with other health economies in relation to the assessment and managed introduction of new medicines and other health technologies.

9.19 Standardise NHSScotland's approach to formulary development and use.

9.20 Review and evaluate the experience of PACS to date with a view to deciding on any required modifications and thereafter agree a process and timescales for full roll out and implementation.

9.21 Explore MAS with a view to early adoption in NHSScotland. These should build on the experience of complex PAS within NHSScotland and payment-by-results schemes in operation in other health systems.

9.22 Review the proposal to introduce a "pause" in light of some of the wider changes and actions recommended in this report.

9.23 Give SMC the additional decision option of "recommend for use subject to ongoing evaluation and future reassessment."

9.24 Make greater use of National Procurement in NSS to lead negotiations on behalf of NHSScotland on the cost of new medicines.

9.25 Undertake a comparative review of the arrangements in place in the healthcare systems of other countries for the introduction of new medicines and specifically end-of-life orphan and ultra-orphans, seeking to learn from their experiences.

9.26 Monitor the demands made on SMC and its associated processes and ensure that the available capacity and capability and support mechanisms are adequate for SMC's needs.

9.27 Consider through wide stakeholder engagement the best way for NHSScotland to take advantage of the opportunities afforded by anticipated developments in the way that new medicines will be introduced in the future. This is likely to be through the establishment of a multi-agency taskforce or equivalent group.

9.28 Consider how the experience of NHSScotland's systems for the assessment and managed introduction of new medicines can inform the development of a Scottish Model of Value. This is likely to be through the establishment of a multi-agency taskforce or equivalent group.

10 Glossary

ABPI	Association of the British Pharmaceutical Industry
ADTC	Area Drug & Therapeutic Committee
BNF	British National Formulary
CMO	Chief Medical Officer
DAD	Detailed Advice Document
EAS	Early Access Schemes
EMA	European Medicines Agency
HIS	Healthcare Improvement Scotland
HTA	Health Technology Assessment
ICER	Incremental Cost Effectiveness Ratio
IPTR	Individual Patient Treatment Request
ISD	Information Services Division
MAS	Managed Access Scheme
NDC	New Drugs Committee
NICE	National Institute for Health and Care Excellence
NMF	New Medicines Fund
NSS	NHS National Services Scotland
PACE	Patient and Clinician Engagement
PACS	Peer Approved Clinical System
PAS	Patient Access Scheme
PASAG	Patient Access Schemes Assessment Group
PHI	Public Health Intelligence
PPRS	Pharmaceutical Price Regulation Scheme
QALY	Quality-Adjusted Life-Year
RCMF	Rare Conditions Medicines Fund
SHTG	Scottish Health Technology Group
SMC	Scottish Medicines Consortium
T&FG	Task and Finish Group

Task & Finish Group Recommendations

1 SMC should introduce new, more flexible approaches for the assessment of EoL medicines, orphan medicines and ultra-orphan medicines;

2 SMC should adopt the following methodologies, which will substantially improve access to these new medicines:

- Medicines for EoL and orphan medicines - If the SMC New Drugs Committee (NDC) advises that a medicine does not meet the conventional thresholds for cost-effectiveness, a PACE Meeting may be convened to allow SMC to clearly establish the views of clinicians and Patient Interest Groups on the need for the medicine, its clinical benefits, optimal place in therapy and the patient perspective. The output of the PACE Meeting will play a significant part in informing the SMC decision for the medicine, with a more powerful influence than the current modifiers;
- Ultra-orphan medicines - 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. A new framework of explicit criteria for evaluating these medicines, without performing weighting and scoring, will be introduced. A PACE Meeting may also be convened for these medicines;

3 SMC should work with stakeholders to introduce these new approaches as quickly as possible;

4 SMC should encourage early resubmissions for medicines that have been 'not recommended' for use under the current system;

5 SMC should ensure that any changes to how SMC works must be clear and understandable to the public. It was also agreed that the definitions should be applied in an enabling way, to allow flexibility;

6 SMC should work with patients and clinicians to ensure there is understanding of the new processes and to enable and maximise their contributions;

7 Scottish Government should engage with the NHS to give further consideration to mechanisms of monitoring patient outcomes after treatment with EoL, orphan and ultra-orphan medicines;

We note the Scottish Government's intention that the SMC's system of medicines appraisal is given time to establish itself. On this basis, the following two recommendations are made:

8 There should be an independent review of the experience with the new SMC approaches, and a decision on when this should be initiated would be taken no later than 12 months after the new approaches are introduced;

9 SMC should work with the Scottish Government to determine and enable the research required to underpin an evidence-based approach to a Scottish Model of Value.

Task and Finish Group Definitions

End-of-Life 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 European Medicines Agency (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)".

Remit and Scope of the Review

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;

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

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

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

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

- 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;

- 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;

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

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

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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