Access to newly licensed medicines

Scottish Medicines Consortium

Modifiers

The Committee has previously been provided with information about why the SMC uses “modifiers” in its appraisal process and also examples of these modifiers.

1. Can you clarify under what circumstances the SMC will use modifiers in appraising a medicine, whether or not it is for an orphan disease?

The Scottish Medicines Consortium (SMC) statement on modifiers is attached in full for information. The following description of the new medicines assessment process may assist the Health & Sport Committee in understanding how the process works and where the modifiers fit in to that process.

When a new medicine is licensed for use by the regulatory authority SMC contacts the pharmaceutical company to request a submission on the product, including results of clinical trials and cost effectiveness data.

SMC has a two stage assessment process. The New Drugs Committee (NDC) is the scientific committee of SMC. Its purpose is to appraise all the evidence that is included in the pharmaceutical company submission and reach an initial position on whether the medicine is clinically and cost-effective. It evaluates the submission with the support of medical, pharmaceutical, and health economics experts. There is also written input from clinical experts in NHS Boards at this stage. The assessment on the medicine is discussed in detail at the New Drugs Committee meeting and NDC then makes a provisional recommendation that is shared with the pharmaceutical company.

The SMC Committee takes a broader perspective in reaching a decision on whether the medicine can be accepted for use in NHS Scotland. As well as reviewing the provisional recommendation from NDC and the response from the sponsor company, SMC also considers submissions from Patient Interest Groups. The Patient Interest Group submissions are an important part of the assessment process; they focus on the difficulties the condition presents for patients and the place of the medicine in addressing patient needs. These often supply useful additional perspectives on new medicines and they are very helpful in guiding SMC’s conclusions. SMC also considers special issues related to health care provision in Scotland (such as those related to the highland and island communities), and any relevant societal issues.

SMC uses the cost per Quality Adjusted Life Year (QALY) as a measure to assess the clinical and cost-effectiveness of medicines. The QALY allows comparisons to be made between different medicines for different conditions. Some medicines have a low cost per QALY and these are considered to offer good value for money. Medicines with a
high cost per QALY would not be considered good value for money. A cost per QALY of under £20,000 is generally considered acceptable value for money. For a medicine with a cost per QALY between £20,000 and £30,000 SMC might accept this if the medicine gives significant benefits over existing treatments.

The SMC Committee can consider the application of modifiers for any medicine under assessment where the estimated cost per QALY is relatively high. If a medicine has an estimated cost per QALY > £30,000, and the Committee is confident that the company’s clinical and health economic case is robust, then the Committee will consider whether one or more of the modifiers would allow it to be accepted.

2. What is the decision-making process for determining what modifiers will be used?

3. When a decision has been taken to use modifiers, can you provide more detail as to how they are used and the methodology used to factor them into the appraisal process?

The following description on how modifiers are used within the process covers both questions 2 and 3 above.

The SMC Committee sees the application of modifiers as an important part of the process and there is a proactive approach to considering whether or not any modifying factor will have a bearing on the decision. In addition, companies often state in their submission or their response to the NDC provisional recommendation whether they believe modifiers are relevant. All SMC members are provided with the full company submission and the company response to the NDC provisional recommendation in their meeting papers. This prompts the Committee to consider whether one or more of the modifiers might be relevant to the medicine being assessed. Patient interest groups are asked to highlight in their submissions any patient / carer and family needs that are not being met by existing treatments or medicines. These patient group submissions may also refer specifically to modifiers or describe special factors showing benefits or health gain that might allow SMC to accept a higher cost per QALY. If the company does not make reference to modifiers this does not preclude SMC members from bringing them into the discussion and decision-making. There is a brief presentation on each medicine being considered at SMC and this makes reference to modifiers where relevant.

As the clinical efficacy data in an orphan drug submission is often limited, SMC will accept a greater level of uncertainty in the economic case. In the event that the clinical and economic case for a medicine is robust but the cost per QALY is beyond the level that would normally be considered acceptable, or for an orphan where there is a high level of uncertainty, the Chair will ask the membership to discuss whether the modifying factors should be considered. The Chair will remind the committee of the stated modifiers (e.g. whether the drug treats a life threatening disease; substantially increases life expectancy and/or quality of life; can reverse, rather than stabilise, the condition; or bridges a gap to a “definitive” therapy e.g. organ transplant) and these will
be considered in assessing both the level of uncertainty and cost per QALY which is acceptable. For example, in considering whether a medicine gives a ‘substantial improvement in quality of life’ the committee will have a detailed discussion on whether this is indeed supported by the clinical evidence in the submission.

Appraising orphan medicines

The Committee notes the information already provided to the Public Petitions Committee concerning the appraisal process for orphan medicines. It also notes the views expressed by the SMC and the Scottish Government concerning the term “ultra orphan medicine”.

4. Has the SMC Committee itself reviewed or considered its own processes for approving orphan medicines?

Yes SMC has reviewed its processes for approving orphan medicines. Between 2002 and 2004 SMC had considered only five orphan medicines but the committee recognised that there was an increasing number of orphan medicines in clinical development. A Short Life Working Group on Orphan Drugs was established to consider whether other approaches to decision making on orphan medicines could be applied. The range of options considered included: a multiplier for the threshold for cost per QALY, whether some QALYs may be worth more than others, the use of modifiers, whether all orphan medicines could be provisionally accepted for a time limited period. The group concluded that the best way forward was to allow SMC to accept greater uncertainty in the economic case for orphan medicines and the output of this group was the orphan medicines policy statement that was introduced in 2007.

In 2008 the National Institute for Health and Clinical Excellence (NICE) in England consulted on whether additional weight should be placed on the survival benefits of drugs and technologies for patients with terminal illness and short life expectancy subject to meeting certain criteria. The Scottish Government Health Department asked SMC to consider the feasibility of such an arrangement in processes for NHS Scotland. The SMC view was that the existing decision making process supported a pragmatic approach that would allow medicines with a relatively high cost per QALY to be accepted in some circumstances. The committee recognized that it would be helpful for transparency of process if these modifying factors could be described. As a consequence the SMC revised statement on modifiers was published in 2010 (copy attached) and this subsumed the previous policy statement that related to orphan medicines only.

5. Has the SMC undertaken any research into the different processes that exist in the UK and beyond for appraising orphan medicines?

SMC does not have a research function therefore we have not carried out formal research into the health technology appraisal processes for orphan medicines in the UK and beyond. There are informal mechanisms, however, to maintain awareness of how
other health technology appraisal bodies in the UK, Europe and internationally consider orphan medicines. The SMC Chair and members of the Executive Team have attended and contributed to international meetings and symposia on orphan medicines. For example, the SMC Chair attended the World Orphan Drug Summit in Frankfurt in June 2011 and presented on the SMC process. This allows SMC to gain a deeper insight into the issue of rare diseases and the European / international policy context.

6. When appraising an orphan medicine what steps does the SMC take to ensure it obtains an expert opinion from a specialist in the disease that the medicine seeks to treat?

The SMC assessment process involves seeking the views and opinions of a range of clinical experts for each new medicine submission. Where possible SMC obtains this input from clinicians in NHS Scotland but when there is difficulty in obtaining responses from clinicians who treat the condition in question it is common practice to seek input from specialists in England. SMC accepts that this can be challenging as often there are few very specialists across the UK with experience of the condition in question. In addition, these specialists may have conflicts of interests (such as their department receiving funding to take part in a clinical trial or payments to contribute to advisory board meetings) that mean their views cannot be taken into account. Although this is challenging for orphan medicines, since clinical expert views were introduced as part of the process SMC has been able to obtain clinical expert input for every orphan medicine considered to date.

7. What is the SMC’s view of the petitioners’ argument that the process is particularly weighted against ultra orphan medicines i.e. a disease affecting fewer than one in 50,000 people in the general population?

8. What is the SMC’s view of the proposal that a separate body assess orphan medicines in Scotland as is the case in England?

We believe that the SMC process is not weighted against any specific type or class of medicine, including those used to treat diseases affecting fewer than one in 50,000 people in the general population.

SMC has followed with interest recent developments in England including the establishment of the Advisory Group on National Specialist Services (AGNSS). As the AGNSS remit includes the assessment of the cost effectiveness of orphan drugs for very rare diseases (i.e. orphan products for a clinically distinct group of patients totalling no more than 500 cases in England per year) it will not assess all medicines with orphan designation. Some, but not all, of the orphan medicines that are outwith the AGNSS remit will be appraised by the National Institute of Health and Clinical Excellence (NICE). In England, therefore, there may be three different approaches to orphan medicines; AGNSS, NICE or no assessment. SMC considers this a less equitable position than currently exists in Scotland.
It was expected that only orphan drugs approved by AGNSS for use in England would be available for specialist clinicians to prescribe for patients within designated national specialist services. AGNSS has not issued guidance on any medicines to date, however, and although guidance on two medicines is expected during 2012 we understand that new work has been suspended pending the establishment of the new NHS Commissioning Board for England. It therefore remains the case that the majority of medicines for rare diseases are not subject to any cost-effectiveness assessment in England at present so the approach there is fragmented and not comprehensive for all new medicines.

As outlined in our earlier response to the Public Petitions Committee, SMC believes that there are important strengths in a single, comprehensive assessment process that encompasses all new medicines, regardless of severity or whether the condition they treat is common or rare.

SMC looks at clinical evidence, in the context of modifiers where these might apply, as well as cost-effectiveness. The latter is important and fair to consider in the case of orphan medicines because there is an opportunity cost i.e. paying for these medicines means that funding is not available for something else. The evidence SMC makes its decision on is presented as a result for a typical patient i.e. a gain of 3 months survival at a cost per Quality Adjusted Life Year of £40K. These values are independent of the total number of patients with the condition who are expected to benefit. The same process is used for all medicines but the Committee has flexibility to accept some of them despite greater uncertainty.

The principle of trying to ensure that NHS resources are used most effectively, having regard to the premise that the NHS has limited resources which can only be spent once, underpins all our assessments. The members of SMC apply the same decision making framework across all medicines. We believe this is a key strength of the SMC process. SMC believes that its current methodology is robust, objective, transparent and fair and is therefore appropriate for the assessment of orphan medicines.

10 May 2012
Scottish Medicines Consortium response to the Public Petitions Committee on PE1398, PE1399 and PE1401

The Public Petitions Committee has asked the Scottish Medicines Consortium

- What are your views on the issues raised in the petitions?

1. About the Scottish Medicines Consortium (SMC)

The Scottish Medicines Consortium (SMC) welcomes the opportunity provided by the Public Petitions Committee to describe its role and functions in the assessment of new medicines. The purpose of SMC is to assess the comparative clinical- and cost-effectiveness of new medicines and accept for use those that clearly represent good value for money to NHS Scotland. SMC has a remit to advise Health Boards across NHS Scotland and their Area Drug and Therapeutics Committees (ADTCs) on all new prescription medicines, including new formulations and new indications of existing medicines. Advice is issued as soon as practical after a new medicine becomes available for use. Senior NHS managers, representatives of the public and the pharmaceutical industry are involved in the process. The Patient and Public Involvement Group (PAPIG) subgroup of SMC is responsible for ensuring that the patient/carer perspective is always taken into consideration by the SMC.

2. Orphan medicines

Orphan drug legislation was introduced in the EU in 2000 in an attempt to improve the availability of medicines for rare diseases, described as ‘orphan medicines’. This created incentives for pharmaceutical companies to develop medicines for rare diseases. The EU criteria for orphan medicines are those defined by the Committee on Orphan Medicinal Products (COMP) and set out on the European Medicines Agency (EMA) website. In terms of the rarity of the disease, in the EU an orphan drug is defined as one for which the frequency of the disease is less than 5 per 10,000 of the EU population. ‘Ultra orphan’ is a term used by NICE but not, as far as we are aware, formally recognised by relevant regulatory agencies. The number of new treatments for rare disorders has increased over the past 10 years. Over 800 medicines in development have been designated as orphans and there are now 74 orphan medicines with a marketing authorisation from the EMA (i.e. licensed for prescribing in the UK). This reflects the success of the Orphan Drugs Regulation in Europe.

3. SMC methodology

When a new medicine is licensed for use the pharmaceutical company is asked to make a submission on the product, including results of clinical trials and cost effectiveness data, to SMC. SMC has a two stage process. Firstly, the New Drugs Committee (NDC) critically evaluates the submission with the support of medical, pharmaceutical, and health economics experts. The NDC then makes a provisional recommendation that is shared with the pharmaceutical company concerned. The advice from NDC, together with feedback from the company is then considered by the SMC committee. Patient
Interest Group (PIG) submissions, focusing on the difficulties the disease presents for patients and the place of the medicine in addressing patient needs, are also an important part of the SMC’s assessment process. They often supply useful additional perspectives on new medicines and they are very helpful in guiding SMC’s conclusions.

4. SMC assessment of orphan medicines

For an orphan medicine the submitting company is required to make the case for clinical and cost-effectiveness in the same way as for all new medicine submissions. In reaching a decision on whether the medicine can be accepted for use in NHS Scotland, SMC recognises that efficacy data are very often limited due to the rarity of the condition and may therefore accept a greater level of uncertainty in the economic case. SMC explicitly state that we will accept greater uncertainty in the health economic case when assessing a medicine with an orphan indication. There are also situations when a higher cost per Quality Adjusted Life Year (QALY) may be acceptable and this is factored into our process. These additional factors, termed ‘SMC modifiers’, such as whether the medicine: treats a life threatening disease; substantially increases life expectancy and/or quality of life; can reverse, rather than stabilise, the condition; bridges a gap to a “definitive” therapy, or provides a licensed alternative to a previously unlicensed medicine will also be considered in assessing both the level of uncertainty and cost per Quality Adjusted Life Year (QALY). These modifiers are always actively considered when reaching a decision on a medicine with orphan status (according to the EMA Committee on Orphan Medicinal Products (COMP)).

These modifiers form part of a global judgement taken by SMC, which is also influenced by input from clinical experts and Patient Interest Groups as well as the clinical and cost-effectiveness data on the new medicine submitted by the manufacturer.

When a modifier, or any other special issue which may have been highlighted by the sponsor company, by clinical experts and/or by Patient Interest Groups, is a factor in SMC acceptance of an orphan medicine this is stated in the health economics section of the SMC detailed advice document.

5. SMC advice to date on orphan medicines

Up to and including October 2011, SMC has assessed 51 full submissions for orphan medicines of which 10 (20%) have been accepted for use and 21 (41%) accepted for restricted use. The remaining 20 (39%) were not recommended. For a further 12 medicines the manufacturer did not make a submission to SMC so these were not recommended. Three orphan medicines have been accepted for use after assessment through the SMC abbreviated submission process. The corresponding figures for medicines without orphan status assessed by SMC are: up to and including October 2011, 422 full submissions have been assessed of which 127 (30%) have been accepted for use, 189 (45%) accepted for restricted use, and 106 (25%) not recommended. These figures illustrate that the acceptance rate for orphan medicines
submitted to SMC (61%) is lower than the acceptance rate for medicines without orphan status (75%) but that this difference is justifiable.

Summary details of the advice relating to all orphan medicines is attached for information. Full details are available on the SMC website.

6. Societal considerations of valuing rarity

Societal considerations are important in relation to medicines for rare diseases. Societal attitudes toward cost effectiveness have been explored in a number of reports produced by NICE's Citizens' Council including one on Ultra-orphan drugs (November 2004). This concluded that the criteria the NHS should take into account when deciding to pay premium prices for ultra orphan drugs are, in descending order of importance:

• The degree of severity of the disease
• If the treatment will provide health gain, rather than just stabilisation of the condition
• If the disease or condition is life-threatening

Key findings were that rarity on its own is an insufficient reason to justify paying a premium for treatment and that the degree of severity and the amount of health gain are the more critical factors. NICE states that: “Decisions about whether to recommend interventions should not be based on evidence of their relative costs and benefits alone. NICE must consider other factors when developing its guidance, including the need to distribute health resources in the fairest way within society as a whole.”

More recent data on the views of the general public on this issue are available from outwith the UK. In a survey of the Norwegian general population, people were asked whether society should pay more to treat rare diseases than it does for common diseases. The results showed that although respondents supported equity of access to healthcare for people with rare diseases, they did not support providing care for people with rare diseases when the cost of that care was at the expense of people with common conditions. Two citizen's juries held in Canada had similar findings; opting for health policy that would ensure that effective interventions are made available to the largest number of patients. A preference for treating small numbers of patients was expressed only if the patients were severely ill and the treatment could produce substantial health gain to all of them, bringing them back to normal functioning.

There may also be an issue in relation to how rarity is defined. Globally there are over 6000 identified rare diseases, so collectively the number of patients affected by rare diseases is considerable. To illustrate this, the Rarer Cancers Forum states that between 30% and 50% of all cancers are classified as rarer and an estimate recently quoted in the Scottish media is that in total more than 350,000 people in Scotland will be affected by a rare disease.
7. SMC views on the issues raised by Petitions PE1398, PE1399, PE1401

SMC fully supports the principle that people with rare conditions should be able to access clinically and cost-effective interventions including medicines through the NHS. We believe that SMC helps to ensure that new medicines with the most significant benefits are available across Scotland and improves consistency in their availability from one NHS Board to another. Difficult decisions have to be made in order to spend available resources wisely and this is increasingly important in the current fiscal climate. If money is spent on medicines that do not offer good value, it means that this money is not available to be spent for other treatments that could provide benefits to patients (termed the ‘opportunity cost’).

Although the SMC acceptance rate for orphan medicines submitted to SMC (61%) is lower than the acceptance rate for medicines without orphan status (75%), SMC believes that these figures are reassuring because de facto the evidence base for orphan medicines is often weaker than for other medicines, the SMC modifiers described above do not always apply to the medicine under review and the prices charged for these drugs can make it impossible for them to meet conventional measures of good value.

SMC believes it is important to highlight the extremely high acquisition costs associated with many orphan medicines. This has attracted recent attention in the medical literature, where it is noted that the pharmaceutical industry already receives incentives to develop medicines for rare diseases, and arguing that an unintended consequence of the orphan drugs legislation may be exploitation of the rules for profit. Within NHS Scotland we have the Patient Access Scheme (PAS) which allows the pharmaceutical industry to reduce the cost of a drug where the drug has been shown not to be cost effective. This was set up in 2009 to try to help enable access and to date overall, 25 medicines with a PAS have been reviewed by SMC with 13 accepted for use or restricted use contingent on the PAS being available in NHS Scotland.

If more value or weight is to be put on the health improvement associated with treatments for rare conditions than for common conditions this raises important equity issues. There is evidence from England and elsewhere that the public’s willingness to pay for medicines that treat rare diseases is not unlimited.

SMC considers the clinical and cost-effectiveness of all new prescription medicines, regardless of severity or whether the condition they treat is common or rare. The principle of trying to ensure that NHS resources are used most effectively, having regard to the premise that the NHS has limited resources which can only be spent once, underpins all our assessments. The members of SMC apply the same decision making framework across all medicines. We believe this is a key strength of the SMC process. SMC believes that its current methodology is robust, objective, transparent and fair and is therefore entirely appropriate for the assessment of medicines with orphan status.

Scottish Medicines Consortium, 7 November 2011