

Working with SMC – A Guide for Manufacturers

1. About the Scottish Medicines Consortium (SMC)

The [Scottish Medicines Consortium](http://www.scottishmedicines.org.uk) (SMC) was formed in 2001 to benefit patients by providing NHS Scotland with a single source of advice about the value of each new medicine. Before SMC was set up local Area Drug & Therapeutics Committees (ADTC) advised Health Boards on which new medicines should be approved for use in the local area. The introduction of SMC provided a single point of advice and reduced the duplication of effort across Scotland's Health Boards and the differences in availability of medicines between local areas.

1.1 SMC Remit

The purpose of SMC is to assess the comparative clinical-effectiveness 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) about the status of all newly licensed medicines, all new formulations of existing medicines and all new indications for established medicines. SMC was formed as a consortium of ADTCs, capturing the best of existing practice, experience and skills from across the country, with each Health Board represented in the consortium and participating in its decision-making. SMC has also adopted a cooperative approach beyond clinicians by having senior NHS managers, representatives of the public and the pharmaceutical industry involved in its process.

Since the establishment of SMC the process for assessing new medicines in NHSScotland has become more transparent and understandable. This transparency will further increase in the future, because from May 2014 SMC has [opened its meetings to the public](#). This, and other changes, have been made to the way SMC operates, as a consequence of the [Scottish Government Health's and Sport Committee 2013 review](#) on access to new medicines.

SMC aims to issue its advice as soon as is practical after a new medicine becomes available for use, and therefore requests that companies make submissions as soon as possible after a European Medicines Agency (EMA) positive opinion.

The SMC remit is confined to prescription-only medicines (POMs); it does not assess vaccines, branded generics, blood products (*with the exception of anti-bradykinin and C1 inhibitor therapies*) and diagnostic drugs. [Guidance on the types of medicines that are outwith SMC's remit](#) is available on our website.

In some circumstances an abbreviated submission can be made; this can often be appropriate for new formulations of medicines with a low estimated budget impact. [Guidance on when an abbreviated submission](#) might be appropriate can be found on the SMC website. If you are uncertain whether a product is within SMC remit or whether an abbreviated submission is appropriate, an enquiry can be made via specific forms available on the [website](#).

SMC also has a horizon scanning function that aims to improve financial and service planning within NHS Boards through the provision of early intelligence on new medicines in clinical development. Information on the [horizon scanning initiative](#) can be found on our website. In order to ensure that company products are considered in Health Board financial planning cycles, companies are requested to ensure that they enter all relevant data on medicines in phase III clinical development or those that are three years from being made available to prescribe in the UK onto *UK PharmaScan*. This will allow SMC to extract most of the required horizon scanning data from this source.

1.2 SMC Organisation

The SMC is a committee of around 40 members, who are nominated by ADTCs and others who serve in a personal capacity. All 14 Health Boards are represented and there is a wide mixture of backgrounds to ensure that decisions are made from an appropriately wide perspective, not simply from a clinical viewpoint. Healthcare managers, public partners and the pharmaceutical industry are all members of SMC and take a full part in its decision-making.

As an example, the mix of members in 2014 is summarised below, but there will be some changes over time:

Committee Member	Number
Doctors	15
Primary care	1
Secondary care	14
Pharmacists	5
Healthcare Management	5
Public Partners	3
Pharmaceutical Industry	3
Health Economist	1

Meetings and related timelines

SMC is helped to reach decisions by its New Drugs Committee (NDC), a smaller committee comprised of clinicians, pharmacists and health economists (around 20 members) with a purely technical remit to review the clinical and economic data. This committee makes the first assessment of each submission, which may include an e-mail exchange of questions and answers with the submitting company prior to the NDC meeting. NDC then passes its recommendation to SMC, which, when it meets to consider the medicine, may choose to take a broader view than the strictly evidence-based approach of NDC.

Both SMC and NDC meet monthly, with, for the majority of products, a gap of five or six weeks between a medicine being assessed at NDC and then SMC (Figure 1). Timelines are followed closely to ensure that decisions meet the needs of patients, prescribers and the healthcare system. [Guidance on the sequence of events and the deadlines](#) for the coming year is available on our website.

A slightly different process and timing is available for medicines which treat end-of-life conditions and medicines for orphan or ultra-orphan conditions. If the advice for these products from the NDC is 'not recommended', the pharmaceutical company can request that SMC convenes a [Patient and Clinical Engagement \(PACE\) meeting](#). This is a new process, made available for full submissions and resubmission being made to SMC from May 2014 onwards, as a consequence of the Scottish Government review on access to new medicines. This process will add an additional one to three months to the assessment timelines, but may avoid some of the resubmissions that would previously have been made.

Discussion of Confidential Information

When assessing each medicine, SMC aims to hold most of its discussion in public (Part 1). On occasions however, there may be a need to hold some of the discussion in a closed session (Part 2) without the presence of the public, primarily on account of a need to discuss in depth data highlighted by the manufacturer as confidential for commercial or academic reasons.

Voting

After the discussion on each product has finished, each voting member of SMC is asked to cast their vote on a ballot paper. The votes are confidential. The votes are collected and counted by two members of the SMC staff. The results are made known to the committee once the public has left, after all products have been assessed. Only full members have voting rights and the decisions are determined by a simple majority of those members present.

1.3 Professional Support Staff

The two Committees are supported by a team of clinical reviewers made up of pharmacists experienced in critical appraisal and health economists with experience of health technology assessment and health economic modelling. For each full submission or resubmission being assessed a pharmacist, health economist and an NDC committee member (known as the lead assessor) are allocated to review the company's submission.

The whole organisation is underpinned by a secretariat that provides full administrative and logistical support to the Committees and Assessment Teams and also liaises with the pharmaceutical industry and other external agencies. The work programme and outputs from SMC assessment are all available in the public domain on the SMC website.

1.4 Contact with SMC staff and members

The point of contact for a pharmaceutical company should be with the SMC secretariat. The secretariat will be aware of possible upcoming submissions via the horizon scanning process and, as the expected date of marketing authorisation comes closer, will contact the company asking for confirmation of the submission date. This will generally happen at the time the European Medicines Agency (EMA) issues a positive opinion for the product. At this time the company will be asked to advise the date they intend to make their submission and whether the product could be considered as an end-of-life medicine or a medicine to treat an orphan or ultra-orphan condition. The submission requirements are slightly different for medicines

to treat ultra-orphan conditions, and for this reason companies are asked to provide supporting data on disease prevalence for the full indication in NHS Scotland at this early stage. Ultra-orphan status will then be confirmed by SMC prior to the submission being made. The secretariat can give advice on submission requirements and timings of submissions. The submission should then be made, as per the Guidance on the New Product Assessment Form, via the secretariat.

At present, it is not possible to meet with members of the SMC professional support staff in relation to a submission, before the submission is made – there is no option for a ‘scoping meeting’. However if a manufacturer has a specific question, this can be submitted to SMC in advance of the submission, via the secretariat. If possible the question will be answered. It should be noted that in most cases only generic questions can be answered, as the SMC may not be fully informed regarding the disease area.

The ABPI has two representatives on the SMC, and part of their role is to assist companies with strategic and tactical advice, on the basis of their experience working with the SMC. Companies can contact these individuals via the ABPI Scotland office.

It is the prime responsibility of the manufacturer to submit on time, so that SMC advice can be issued as close as possible to the product becoming available for prescribing in the UK. A company may make a submission for a product once it has received a positive opinion from the European Medicines Agency (EMA), Committee for Medicinal Products for Human Use (CHMP) or approval from the Medicine and Healthcare products Regulatory Agency (MHRA).

However, SMC staff will contact manufacturers regarding their submissions at set stages throughout the process. (*see “appraisal sequence” below*) supplying all manufacturers with information on the progress of their submission, allowing manufacturers to see draft documents about their medicine and sometimes seeking clarification on points of fact.

SMC follows very tight timelines, with an 18 week period between scheduling the company submission for review and release of advice to NHS Scotland for the majority of medicines. Companies should be aware that following submission, they will often be contacted by the SMC secretariat before the medicine is considered by the NDC. There may be requests for further information, clarification on information already submitted or additional analysis in relation to the health economics component of the submission. In some cases the company will be expected to provide significant amounts of information within tight timescales.

While the SMC professional support staff are happy to answer questions about a company’s submission at other points of the process, the staff cannot comment or give opinions on specific aspects of the evaluation of a submission while the assessment process is underway.

After NDC has considered the submission (NDC meets on the last Tuesday of every month) each submitting company will be sent, in confidence, draft advice on the Friday following the meeting. The company is given an opportunity to comment on this draft advice with a two week deadline for response. At this stage there may also be requests for clarification of information submitted or further analysis of information already submitted. Once the company response has been received it is then included in the paperwork for SMC members, alongside the submission. For end-of-life, orphan or ultra-orphan medicines, if the NDC advice is ‘not recommended’ and the company wishes SMC to convene a PACE meeting there is an opportunity to submit a industry PACE statement alongside comments on the NDC draft advice. The company also has the opportunity to submit a new or revised Patient Assess Scheme (PAS) at this time. Further detail on PAS provided below.

After SMC has reviewed the submission, (SMC meets on the first Tuesday of every month), the submitting company will be informed in confidence of the SMC decision, and sent the Detailed Advice Document (DAD), on the following Friday. NHS Boards are also informed of the advice, in confidence, at this stage. Comparator companies are set a copy of the advice on the Monday of the following week. This information will not be made public, however, via the SMC website, until 4 weeks after the SMC meeting. In the intervening period, NHS Boards are expected to prepare for the consequences of the decision and, if relevant, comparator companies are allowed to review statements on their product in the DAD. The submitting company should contact the secretariat at this stage if there are any further issues they wish to raise with regard to the content and wording of the DAD.

If a product is 'not recommended' for use, and the company wishes to consider making a resubmission, a face-to-face meeting with SMC representatives is recommended. These company meetings are arranged via the Secretariat; they normally involve a member of the SMC Executive (usually the vice chairs of NDC and SMC), and a member of the secretariat. It should be noted that individual members of the assessment team are not involved in these meetings. Members of the SMC Executive are empowered by SMC to explain to company representatives how and why decisions have been reached. [Guidance on SMC Policy on meetings with manufacturers](#) can be found on the website.

2. Notes for Manufacturers on Submissions

2.1 Abbreviated Submissions

The SMC will consider an abbreviated submission in some circumstances. An abbreviated submission may be appropriate when the product is not a new active substance, for example for a new formulation of an established product. One of the requirements for an abbreviated submission is that the medicine is expected to have limited impact on the NHS Scotland medicines budget, thus no economic evidence is required.

Separate [guidance on abbreviated submissions](#) is published on the SMC website. Manufacturers should seek confirmation from the SMC secretariat that an abbreviated submission is appropriate in these circumstances.

In addition, SMC will generally accept an abbreviated submission for a medicine that has previously been accepted by SMC on the extension of its marketing authorisation to include use in children or adolescents. [Further information](#) on abbreviated submissions is available on the website.

2.2 Full submissions

SMC makes recommendations on new medicines to NHS Boards based on an assessment of the clinical and cost-effectiveness within the NHS in Scotland. It is therefore important that manufacturers submit clinical and economic evidence according to the principles and standard outlined in the guidance documents.

The only exception to the requirement for an economic evaluation is where a medicine fulfils the SMC criteria for an abbreviated submission (see above).

The SMC assessment of the likely clinical and cost-effectiveness of a medicine is based on the evidence in the manufacturer's submission. In the submission the manufacturer needs to be able to demonstrate the case for the clinical and cost-effectiveness of the medicine through a clear, concise, unbiased and robust case to support the application. Each SMC meeting involves six to eight submissions, therefore it is imperative that manufacturers

provide a concise case. Robustness will be judged on the basis of the methodological quality of the case submitted. The application needs to show that the medicine will:

- (i) provide additional health benefits that are valued by patients compared to current Scottish practice and that this is at a net cost to the NHS that offers acceptable value in relation to other uses of the same resources,
- or
- (ii) offer equivalent levels of health benefit to patients at an equivalent or lower net cost to the NHS.

2.3 Positioning within licence

SMC has a remit to consider the full indication covered by the marketing authorisation for a new medicine. In making a submission to SMC, however, in some circumstances the company may wish to make a case for the clinical and cost effectiveness of the medicine for a narrower population than that covered by the full licensed indication(s). For example, where the company wishes to make the case for the medicine when positioned for use in a specific patient sub-group in order to maximise its cost effectiveness..

- (i) Where a submission covers only part of the marketing authorisation for a product the submitting company must detail all other aspects of the marketing authorisation that are within SMC remit but have not been covered in the submission.
- (ii) Where a submission positions a medicine for use in a sub-group of patients narrower than that covered by the marketing authorisation the submitting company should ensure that the proposed population for treatment is appropriate and valid within the licensed indication under consideration in the submission.

The manufacturer must state explicitly on the registration page under 1b) that SMC is asked to consider the use of the medicine when positioned for use in a sub-group of the population covered by the marketing authorisation.

2.4 Resubmissions

If 'not recommended' advice has been issued for a product, and the company wishes to consider a resubmission, they can request, via the Secretariat, a face-to-face meeting with SMC, with the aim of better understanding why their product was not recommended thus allowing an appropriate focus for the resubmission.

The resubmission will follow the same process and timelines as all other submissions. Where possible SMC will ensure that the assessment team involves a pharmacist and an economist who were not involved in the previous submission, but the assessors can be briefed by the original assessor if required.

2.5 Submissions for medicines for end of life conditions or very rare conditions (orphan and ultra-orphan)

SMC has introduced a variation to normal process for the above medicines, primarily related to the ability to request a PACE meeting should the NDC recommendation be 'not recommended'. Companies must therefore read the appropriate guidance on the [SMC web-site](#). The definitions of orphan and ultra-orphan medicines are based on the full population of the licensed indication irrespective of whether or not the company wishes SMC to consider the product when positioned for use in a sub-population of the licensed indication. The

definition of end of life medicine may be based on a sub-population of the licensed indication where the manufacturer provides adequate justification.

3. The New Product Assessment Form (NPAF)

The NPAF provides a template for the evidence to be provided within the company submission. Detailed [guidance notes](#) for the completion of the new product assessment form are available on the SMC website. These include a description of the type of information expected to be submitted within each section of the form, an indication, where appropriate, of the expected source of the information, and how the information should be presented.

The [deadline dates](#) for submitting NPAFs to SMC can be found in a timetable on the website. Incomplete submissions cannot be scheduled for assessment. Once an NPAF has been submitted to SMC no amendments can be made.

Submissions should be concise, but also seek to include all relevant data. The required information is stated for each section of the document and applicants should focus on these requirements and not include any information that is not directly relevant to the indication under review. As far as possible, manufacturers should limit the electronic size of the document since it may have to be distributed across servers with varying limits to file size. For guidance, most submissions have a file size of around 1 to 2 megabytes.

The submission should be a stand-alone document. It should focus on information related to the indication for which approval is sought, rather than all available data for the medicine. Appendices may be used for information that exceeds the level of detail requested in the guidance but only when considered essential and not to present core information. For example it is not acceptable to attach a key study as an appendix and to complete the efficacy section with 'see Appendix X.' In some cases it will be more appropriate to include data as a supporting document, referenced in the text, than as an appendix. SMC also requires completion of an Excel budget impact template for all full submissions. A blank template can be found on the [SMC website](#).

3.1 SMC Review Checklists

The SMC/NDC use [checklists](#) as part of their review process, as these improve consistency and aid in supporting an efficient review process. Blank copies of the economics checklist and clinical checklist are made available to industry, via the SMC website. It should be noted, however, that this is provided to aid understanding of the SMC review process. It is not a 'tick-list' for submitting companies i.e. providing all the information on the checklist does not mean that no other information is required. The full NPAF Guidance must be followed.

3.2 Key points on methods

- It is the company's responsibility to clearly demonstrate the case for the cost-effectiveness of a medicine submitted to SMC. If the company does not submit economic evidence according to the principles and standard outlined in the guidance the SMC will be unable to accept the medicine for use in NHS Scotland.
- The perspective adopted on costs should be that of the NHS in Scotland and social work.
- The evidence submitted must be assembled systematically and synthesised in a transparent and reproducible way.

- All data used to estimate clinical and cost-effectiveness must be presented clearly in tabular form and include details of data sources.
- Clinical and cost-effectiveness needs to be considered over an appropriate time horizon relevant to Scottish practice and patients and all relevant treatment options for the specific patient groups should be compared.
- In general, cost-utility analysis is the preferred form of economic evaluation, with health effects expressed in terms of quality-adjusted life-years (QALYs).
- The SMC considers modelling a relevant framework within which available evidence can be synthesised and estimates of clinical and cost-effectiveness generated. The annual discount rate recommended for both costs and benefits is 3.5%.
- Uncertainty surrounding the estimates of cost-effectiveness needs to be included.

Further guidance on methods is provided in part C of the [Guidance to Manufacturers](#) on Completion of the NPAF.

For the assessment of ultra-orphan medicines, a different [decision-making framework](#) will be used, similar to that used by the National Institute of Health and Care Excellence (NICE) for highly specialised technologies (HST). The QALY will be requested but a wider perspective will be taken on the value of the medicine.

3.3 Key points on references

- All evidence included in the submission should be referenced throughout the NPAF and references should be numbered in the order in which they first appear in the text. Each reference should have only one number that is repeated if it is cited more than once.
- At the end of the submission a list of all references should be provided in the Vancouver style, numbered and ordered strictly in accordance with their numbering in the text. Author/date styles of referencing should not be used. Submissions have been received where listed references did not correspond to the citation in the text, including some with mixed referencing styles. These are unacceptable. Referencing through the use of word processing devices such as footnotes/endnotes is also not acceptable.
- Electronic copies of all references cited in the submission should be sent to the secretariat in a zipped file to be received no later than the monthly deadline for receipt of company submissions. Should the file size exceed 20 MB, please condense into separate files and send each file separately. Each reference should be provided as an individual electronic file and should be in an electronic format that can be searched i.e. Word or Portable Document Format (PDF). Scanned documents are not acceptable other than in exceptional cases where it is impossible to provide a document in a searchable format.
- Full versions of in-house clinical study reports and/or drafts for publication should be provided where these have been used as data sources. These are required for assessors to make factual checks and to gain a comprehensive understanding of relevant study methodology, conduct and results. Synopses and selective extracts are not sufficient.
- On request from the submitting company, SMC will treat data from these sources (that are not otherwise in the public domain) as commercial in confidence (CIC)

and the information will not be disclosed in any form to persons or organisations outwith the SMC committee and NDC, SMC clinical and economic assessors and secretarial staff.

- These data will be annotated (by underlining) to indicate that they are CIC in paperwork provided to the SMC committee and NDC, and will be removed from the SMC Detailed Advice Documents that are issued to the NHS and posted on the SMC website.
- While SMC encourages full referencing of the evidence presented, please avoid the inclusion of unnecessary references such as those that duplicate evidence provided by more robust sources.

Further guidance on referencing, including the use of abstracts and posters as sources of information, is provided in part A of the [Guidance to Manufacturers](#) on Completion of the NPAF.

3.4 Confidentiality of Information

Information provided in company submissions will be treated as confidential and will only be available to members of SMC and NDC, SMC clinical and economic assessors and secretarial staff. Commercial in confidence (CIC) information will also not be available to members of the PACE group. During public meetings, those members of the public who are present will have access to a redacted copy of the NDC draft DAD. Should confidential information need to be discussed, a closed 'part 2' meeting will be held.

Information that is commercial or academic in confidence will be annotated by underlining in the DAD that is made available to committee members and will be removed before making the DAD available to the public. However, it is important to state why the data are confidential and the timescale within which they will remain confidential should be detailed. SMC will respect confidentiality, but reserves the right to include data that are already in the public domain e.g. as a published abstract or conference poster. In such cases, SMC will not exceed the level of detail in the published source and the submitting company will have an opportunity to review the Detailed Advice Document (DAD) as part of the routine consultation process, as outlined below. SMC is committed to adhering to the guidelines agreed with ABPI that appear on the SMC website.

4. SMC decision making

4.1 Where a higher cost per QALY may be accepted

The SMC does not have a formal threshold cost per QALY below which cost-effectiveness would be considered demonstrated. Nor does SMC have a fixed upper limit on willingness-to-pay for a QALY. The cost per QALY is only part of a wider judgement of the value of a new medicine. Where the cost per QALY is relatively high, other factors also play a role in SMC's assessment and may modify the final decision (see below).

4.2 Modifiers

In assessing the relative clinical and cost effectiveness of new medicines, the SMC requires a robust clinical and economic case to be made and for the medicine to demonstrate value for money. In some specific situations SMC may exercise greater flexibility in its decision making to allow consideration of additional factors. These additional factors, known as modifiers, may allow SMC to accept either more uncertainty in the health economic case or a higher cost per [Quality Adjusted Life Year](#) (QALY). There are specific modifiers that apply to medicines for EMA designated orphan conditions.

Further information on SMC [modifier's policy](#) can be found in the website.

4.3 PACE Meetings

When a PACE meeting has been convened, the output from this meeting, which includes a wider perspective from clinician and patient groups who are experts in this disease area, will be considered by the SMC when making its recommendation. The output from the PACE meeting will be a major factor in the SMC decision.

4.4 Patient Access Schemes

[Patient access schemes](#) (PAS) are schemes proposed by pharmaceutical companies to improve the cost-effectiveness of medicines, thereby facilitating patient access. Patient access schemes will be considered by NHS Scotland to facilitate access by patients to medicines:

- (i) that are not, or might not be, in the first instance found to be cost-effective by SMC

or

- (ii) where a patient access scheme has been accepted in the context of a NICE Multiple Technology Appraisal. All PAS submitted with a NICE MTA must be evaluated for acceptability in Scotland by the Patient Access Schemes Assessment Group (PASAG) and the MTA endorsed by Healthcare Improvement Scotland

PAS schemes are examined by a body separate from SMC. The Patient Access Scheme Assessment Group (PASAG) has been established to undertake an objective and independent assessment of PAS submitted by companies on a national basis.

Manufacturers should submit any PAS at the same time as they are making their submission to SMC. Both submissions must be made via the SMC secretariat. PASAG then reviews and makes a recommendation on the proposed PAS to SMC for consideration alongside the manufacturer's SMC submission. For medicines to treat end-of-life conditions or for orphan or ultra-orphan conditions, if the NDC advice is 'not recommended', the company has the option to submit a PAS at that point, or to modify the current PAS.

[Full guidance covering submission of a patient access scheme and the SMC approach where a comparator medicine has been accepted for use on the basis of a confidential PAS](#) is available on the SMC website.

5. Freedom of Information

SMC is not a "Scottish Public Authority" for the purposes of [Freedom of Information \(Scotland\) Act 2002](#) and thus is not subject to the terms of that Act.

However the 14 Scottish NHS Boards who form the SMC are the public authorities listed in the Act.

SMC acknowledges the benefits of fostering greater transparency in carrying out its functions and, to that end, has adopted a culture of openness wherever possible in its dealing with information and wishes to act within the spirit of the legislation by providing a response to information requests. As such all information received may be subject to disclosure under the Freedom of Information (Scotland) Act 2002.

On receipt of a request for information, the SMC secretariat will contact your designated company representative to confirm that you are agreeable to the release of the information being requested and to give you the opportunity to identify information that is deemed as commercial in confidence.

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