

Guidance to manufacturers

Question and answer document on economic submissions to the Scottish Medicines Consortium

N.B. This document is provided to give general guidance to manufacturers making submissions to SMC. Following the advice provides no assurance of getting a positive response. Where a manufacturer is in doubt, they should contact the SMC Secretariat for guidance.

What documents should I know about when completing the economic part of a submission to SMC?

Specific guidance on the economic evaluation is given in the Guidance for Manufacturers document available from the SMC website or from the Secretariat. This deals with each stage of an economic evaluation.

If this does not address an issue, manufacturers can contact the SMC Secretariat for clarification. However, guidance should only be sought on general points about method – SMC cannot become involved in detailed discussions about submissions while they are in preparation.

Does an SMC submission always require an economic evaluation?

The fundamental task of the SMC is to recommend whether a new product should be used in Scotland by comparing its clinical and cost effectiveness with the practice that would be displaced.

Obviously this includes an assessment of the incremental health gain and associated benefits that may result, as well as potential harm; it also includes an assessment of whether the net benefits are sufficient to justify the incremental cost. In general, therefore, manufacturers should include an economic evaluation. This includes where the application is for an orphan drug. SMC recognises that the clinical data may be less extensive for some such drugs. However, evidence to enable the clinical and patient benefits to be compared with costs, over an adequate timeframe, are still essential to inform SMC's decision making.

One of the few exceptions to this rule is if a new product that has shown clinical equivalence to an existing product and has a similar or lower price might not require an economic evaluation. However, great care should be taken over the appropriate comparator when making this claim. The SMC Guidance states that the appropriate comparator is the therapy that would be displaced by the new product: this is not necessarily the same as the comparator in a manufacturer's clinical trials programme.

If a manufacturer is planning to submit a case without an economic evaluation the safest strategy is to contact the SMC Secretariat at an early stage. Failure to do so,

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may result in the submission being returned as incomplete, causing delay to the process.

Does an SMC submission always require a budget impact assessment?

Yes an estimate of the budget impact of the drug over a five-year time horizon must be submitted with all applications. This information is essential to inform on the net costs (higher drug costs from the applicant drug less any subsequent savings in other drugs, adjusted for all anticipated changes to other resources used in NHS Scotland). This information is necessary for the Health Boards to support any implementation decision by the SMC.

What process does the SMC follow after I have made a submission including an economic evaluation?

The first stage is that the submission is forwarded to an economist for review. This has two aspects:

- firstly, if the submission does not include an economic evaluation, is this justified? If it is, the submission should still include a forecast of the budget impact of the new therapy to NHSScotland.
- secondly, is the evidence submitted suitable for critical appraisal? The submission form asks manufacturers to state where in their submission certain key guidance points have been addressed (e.g. “on which page does the submission clearly state the costs used to value resource use?”). This checklist will be reviewed for completeness, with a judgement made at the end about suitability to proceed.

The manufacturer should be informed of a decision from this stage within a week of submission. The Secretariat will also add the submission to the agenda for a meeting of the New Drugs Committee, informing the manufacturer of the timetable.

The submissions are then allocated to an NDC economist for critical appraisal. . The economists work in collaboration with the allocated pharmacist reviewer and a clinical lead involved in the disease area to consider relevant existing practice in NHSScotland and the submitted evidence. To assist this analysis, the reviewers usually require access to original articles describing trials and results to validate its relevance to the Scottish setting. Thus, it is helpful to ensure all references in support of the submission accompany the submission.

Written critiques of the clinical and economic submissions are circulated to the NDC two weeks before the meeting. At the meeting itself, the three reviewers give a brief verbal presentation followed by general discussion. The draft recommendation is then

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revised in the light of these comments and forwarded to the SMC and the manufacturer, to allow for feedback before the SMC meeting.

How much detail is required in the economic submission?

This is difficult to answer and depends upon the nature of the product under consideration, the comparisons that are made, the quality of the clinical evidence available, and so on. The main role of the submission is to provide sufficient evidence for the SMC to judge value in a Scottish setting so it must cover the points set out in the economics checklist. A concise, clearly argued case tends to be more persuasive than a technical case based on a huge amount of detail, except where this is very clearly justified.

What type of economic evaluation should I use?

Again, this depends in part upon what the new product is being compared to, the nature and quality of the clinical evidence and so on. The manufacturer should be aware that the SMC is trying to assess the value of new medicines in the context of a number of pressures upon the NHS in Scotland. To promote consistency across appraisals, SMC has a preference for generic measures of outcome, such as the quality-adjusted life-year (QALY), over disease-specific measures of outcome, suggesting that the manufacturer should give serious consideration to a cost-utility analysis (CUA).

This does not mean that CUA is required every time. Some examples of where it could be argued that it is unnecessary are as follows:

- a medicine that extends life in good quality might be assessed using a cost-effectiveness analysis (CEA) with life-years gained as the benefit measure. The good quality of long-term survival would have to have some proof, however, and not merely be asserted in the submission.
- the QALY does not capture the main benefit of the medicine – contraception is one example.
- utility values appear to lack sensitivity in circumstances where other measures suggest health improvements or disease reductions. Again, this should be demonstrated and not simply asserted. SMC would need to be assured that the changes on the non-QALY measures are valued by patients.

One approach is a cost impact study concluding there are net economic costs savings, in addition to the clinical evidence suggesting the medicine is at least as good as the alternative (e.g. a ‘me-too’ drug). This approach clearly has merits it is not without risk. If the SMC does not agree with some aspect of the calculation of net cost, then this might undermine the claim of net saving – the only evidence the SMC has is then a net cost with no idea of what benefit will be achieved. This might delay

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consideration of the submission or even lead to a judgement of “not recommended”, so this approach (while legitimate) should be used with caution.

The same could be said of a cost-minimisation analysis (CMA). This might be used where a clinical trial shows no difference in the main outcome. However, there may be objective organisational or patient issues that lead SMC to conclude that there are other aspects of benefit beyond the primary outcome selected; again, this might make a simple economic analysis seem inadequate.

In summary, there may be circumstances where a simpler approach than CUA can be used but these should be considered with care by manufacturers. Conversely, submitting a CUA is no guarantee of success!

Do I have to use Scottish data in the economic submission? Does SMC expect me to commission specific pieces of work for the submission?

The generalisability of evidence is a key consideration for the SMC. SMC recognises there are limitations on what can be achieved, especially when the product is so close to its launch date. Taking some of the main components of an economic evaluation in turn:

- (i) Resource use – the SMC would require some reassurance that data used are broadly representative of Scottish patient pathways and clinical practice. Data from elsewhere in the UK are acceptable. Resource use data from other countries or estimated by a panel of experts are regarded with some suspicion and should be avoided if possible, or at least validated for the Scottish setting and included in a rigorous sensitivity analysis.
- (ii) Costs to value resource use – data on Scottish hospital costs are available on a per diem basis from Scottish Health Service Costs, which can be found at:
http://www.isdscotland.org/isd/info3.jsp?p_applic=CCC&p_service=Content.show&pContentID=797
 These costs are updated regularly, the ISD website should always be checked for the latest version.

NHS Reference Costs from the Department of Health are acceptable. Primary care and community costs from the Unit Costs of Health Care publication by Personal Social Services Research Unit, University of Kent, are also acceptable (www.ukc.ac.uk/PSSRU/). Other sources of cost data should be clearly explained.

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- (iii) Ways to value health gain such as utilities – specifically commissioned studies to support the SMC submission are not needed but in the face of concern about the values elicited from any method, the methodology, sample size and nature of respondents should be made transparent and the values be subject to a rigorous sensitivity analysis.

If the economic evidence I have available does not match the guidance then what should I do?

The SMC recognises that not every point of guidance will apply to all economic evaluations; equally, there will be times when data requested by SMC are not available. It is easier for the SMC to understand the evidence presented when the manufacturer makes a clear statement about why a particular approach was selected in preference to another, or why some data items are not available.

What does the New Drugs Committee of SMC particularly value in an economic submission?

The following comments are intended to assist manufacturers and are not a checklist of points that will guarantee success if adhered to.

Firstly, the SMC's concerns may pertain to the clinical evidence but sometimes the economic evaluation highlights these issues. For example, a medicine might have shown a statistically significant difference on a disease-specific outcome measure but the economic evaluation raises the question of what value this has to the patient, and hence whether this justifies the proposed cost. It is an advantage if the submission includes results that directly measure improvements in the patient's quality of life rather than in a proxy measure. SMC places great weight on the patient's perspective on health gain.

Secondly, a rigorous sensitivity analysis may demonstrate the robustness of the base case result. It is well known that economic evaluations are very demanding in terms of data inputs and at this stage of a product's life very little is known with certainty. A well-conducted Monte Carlo simulation is the ideal, but simpler forms of sensitivity analysis can do the same job.

How does consideration by SMC differ from consideration by the New Drugs Committee?

The New Drugs Committee looks at the submission first. This group is composed of doctors, pharmacists, prescribing advisors, a nurse and economists. The main task of this group is to exercise critical appraisal skills to assess the strengths and weaknesses of the scientific case as presented by the manufacturer. It can only assess the drug

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through the information from the submission. Thus NDC makes a recommendation to SMC based on an assessment of the scientific merits of the case.

SMC has a broader representation and includes the groups above plus patient representatives, managers, and representation from the pharmaceutical industry. SMC members receive various documents, including the manufacturer's submission, the economic critique, the summary of product characteristics and the draft NDC Recommendation. A member presents the key points, including those from the economic evaluation, and discussion on these and wider issues that go beyond the scientific arguments is facilitated. SMC then considers its recommendation.

What feedback can I expect and is there a chance for further dialogue with the economic reviewer?

The SMC communicates the NDC draft recommendation and the SMC recommendation to the manufacturer after the relevant meetings. The manufacturer has the opportunity to submit written comments to SMC between the NDC and SMC meetings and these will be taken into account at the SMC meeting.

There is no “face-to-face” contact between manufacturers and reviewers within the process. However, reviewers have the **opportunity** to contact manufacturers for further information or clarification: experience to date has shown the value in this contact. This mainly takes place prior to the NDC meeting and is usually carried out via the secretariat. Manufacturers can contact reviewers but this should be via the Secretariat as well and should preferably be in writing (including e-mail) so that there is a permanent record for future reference. There is no compulsion upon a reviewer to enter into dialogue with a manufacturer and in some circumstances legal advice may be to avoid further discussion.

Economic reviewers may discuss points about the economic guidance with manufacturers but they will not become involved in discussions about a particular submission prior to its submission.

If there is one piece of advice SMC would offer in terms of the submitted economic evaluation right then what would it be?

The economic evaluation needs a sound basic design, including a comparator that reflects SMC guidance, a benefit measure that reflects SMC guidance and data that are plausible in a Scottish context. If manufacturer does not satisfy the SMC on these basic design points then no amount of complex modeling or sophisticated sensitivity analysis will compensate.

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If you have any comments on this document, want to suggest a further question, or want to discuss any point further, then please contact the Secretariat at SMC.