Healthcare Improvement Scotland | SMC Advice on new medicines

# Guidance to Submitting Companies for Completion of New Product Assessment Form (NPAF)

Supplement for medicines for extremely rare conditions (ultra-orphan medicines)

NHS SCOTLAND

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Please note – Scottish Government announced the introduction of a new ultra-orphan definition and approach to the assessment of medicines for extremely rare conditions in June 2018. The new definition came into effect from October 2018. This supplement provides guidance on the assessment of medicines meeting the previous ultra-orphan definition introduced following the 2013 review into access to new medicines.

Submissions will be assessed using the new ultra-orphan approach from April 2019. Further information is available on the SMC website under *How we decide and Revised process – ultra-orphan medicines for extremely rare conditions*.

# 1. Background

The Scottish Government's inquiry into access to new medicines (2013) concluded that existing cost-effectiveness thresholds are not always appropriate when considering medicines for end of life or very rare conditions. The Scottish Medicines Consortium (SMC) was asked to apply more flexible approaches in the evaluation of these medicines, as a first step in a wider process to determine Scotland's requirement for a value-based approach for the health technology assessment of new medicines.

SMC processes include the option of input from a Patient and Clinician Engagement (PACE) group for these medicines. There is also the opportunity to submit a new or revised Patient Access Scheme (PAS). In addition, the assessment process for ultra-orphan medicines involves the option to apply a broad decision-making framework.

This supplement provides guidance to submitting companies in relation to ultra-orphan medicines. For guidance on end of life and orphan medicines, refer to the Guidance to submitting companies on completion of new product assessment form available from the *Making a submission* section of the SMC website.

# 2. Definition

SMC defines medicines used to treat ultra-orphan (extremely rare) conditions as follows:

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).*

The definition of ultra-orphan status is based on the full population of the licensed indication relevant to the submission, 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.

# 3. Process for submissions for medicines with ultra-orphan status

In SMC's routine contact with companies about submission requirements after receipt of a positive opinion from the Committee for Medicinal Products for Human Use (CHMP), the company will be asked to indicate whether the product will be used to treat an ultra-orphan condition (see definition in section 2) and to complete a proforma providing supporting evidence, i.e. data on disease prevalence for the full indication in NHSScotland. SMC will confirm to the company that the medicine meets the criteria for the ultra-orphan assessment process before the submission is made.

A submission for an ultra-orphan medicine should use the New Product Assessment Form (NPAF) available in the *Making a submission* section on the SMC website, which takes account of the additional information requirements.

## 3.1 Completion of the New Product Assessment Form (NPAF)

SMC recognises the challenges in providing robust economic evaluations for medicines used to treat ultra-orphan conditions given the nature of the data available. A cost-utility analysis is requested for such medicines as this allows comparability with other medicines across the value for money spectrum. However, where an evaluation using quality adjusted life years (QALYs) is not feasible, SMC will accept cost-effectiveness analysis using appropriate natural outcome measures. Cost-consequence analysis may also be provided where the submitting company judges that there are multiple relevant outcomes not readily captured within a QALY based assessment or cost-effectiveness analysis using a single outcome measure. SMC appreciates that in some conditions the economic evaluation will have significant uncertainty, but an estimate is still required.

Given the nature of extremely rare ultra-orphan conditions, submitting companies may also wish to provide a sensitivity analysis supporting the base case economic evaluation that adopts a wider perspective than the conventional NHS perspective. This will permit the evaluation to reflect wider costs and benefits relevant to the patient and their carer, such as out of pocket expenses, lost earnings and carer quality of life gains from the new treatment.

A submission for a medicine used to treat an ultra-orphan condition requires completion of Appendix A 'Ultra-orphan decision-making framework' in addition to the pharmaco-economic case and budget impact template provided in sections 6 and 7 of the NPAF. Companies should consult the Guidance to submitting companies for completion of the NPAF for good practice guidance on all economic evaluations.

For appendix A, the table below sets out the factors companies should consider when completing the NPAF. In some cases the information required will be a summary of other information within the NPAF.

| Decision making criteria | Evidence |
|---|---|
| Nature of the condition | • Description of symptoms and functioning with current treatment<br>• Limitations of current treatment options<br>• Effect on carers' quality of life |
| Impact of the new technology | • Summary of key efficacy findings from section 3 of NPAF<br>• Summary of any important adverse events associated with treatment from section 4 of NPAF<br>• Summary of key clinical effectiveness points from section 5 of NPAF including clinical significance of health gain associated with treatment<br>• Discussion of spectrum of benefits within the patient group and potential for treatment continuation rules |
| Costs to the NHS and Personal Social Services | • Summary of year 1 and year 5 gross and net budget impact from section 7 of the NPAF, with and without PAS where relevant.<br>• Assessment of any significant budget impacts falling on any non-NHS organisations<br>• Summary of key uncertainties in relation to budget impact |
| Value for money | • Summary of the base case cost-effectiveness ratio or cost-consequence analyses, from the economic analysis in section 6.<br>• Summary of key sources of uncertainty in the economic analysis and impact on base case cost-effectiveness ratio |
| Impact beyond direct health benefits and on specialist services | • Impact of the technology in allowing patients to contribute to society / improve family functioning/continue in education<br>• Impact on carers quality of life of the new treatment (note development of formal tools such as Carer Experience Scale)<br>• Cost-effectiveness ratios showing the adoption of a wider perspective on costs and benefits<br>• Assessment of impact on NHS staffing, infrastructure and training requirements |

## 3.2 Evaluation of medicines used to treat ultra-orphan conditions

### New Drugs Committee (NDC) meeting:

A submission for a medicine that will be used to treat an ultra-orphan condition will continue to be assessed as normal by NDC on the basis of its clinical and economic case before consideration by the SMC Committee. An economic evaluation to indicate the value for money of the medicine will therefore still be required, but with the flexibility in approach as described in section 3.1 above. NDC will also review the information presented by the company in Appendix A but this will not be part of the decision-making process for NDC. If the draft NDC advice is 'not recommended', the submitting company will be offered the opportunity to request a PACE meeting and / or to submit a new or revised PAS. For guidance on PACE, refer to the Guidance to submitting companies on completion of new product assessment form (NPAF) available in the *Making a submission* section of the SMC website.

### SMC meeting:

SMC will adopt a broader decision-making framework, examining the nature of the condition, impact of the medicine, impacts beyond direct health benefits and costs to the NHS using the criteria set out above. As such, the economic analysis will be a factor within the decision-making framework but will not be the predominant factor in the SMC decision.

As part of its review process, SMC will assess the information the company has provided within Appendix A as well as other sources of evidence to populate the framework, e.g. from SMC clinical experts, Patient Group submissions and, where relevant, the output from PACE meetings. This will ensure SMC is provided with as complete a picture as possible of the relevant aspects upon which the decision will be based.

The SMC DAD for medicines used to treat ultra-orphan conditions will be structured according to the ultra-orphan decision-making framework, incorporating information from the PACE statement and Appendix A where relevant.

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