

Guidance to submitting companies for completion of New Product Assessment Form (NPAF) for ultra-orphan medicines

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Introduction

The Scottish Medicines Consortium (SMC) provides advice to NHS boards and their Area Drug and Therapeutics Committees (ADTCs) across Scotland about the status of newly licensed medicines, new indications and formulations of existing medicines. This includes medicines that meet SMC's definition for ultra-orphan medicines.

About this guide

The New Product Assessment Form (NPAF) provides a template for the evidence required by SMC to issue advice to NHS boards and Area Drug and Therapeutics Committees (ADTCs). A specific NPAF for use with ultra-orphan medicines is available from the [Making a submission](#) page of the SMC website. This form is used for both initial assessments and reassessments of ultra-orphan medicines.

This short guide provides information to submitting companies about the specific supplementary methods that are expected to be followed and evidence required to demonstrate the clinical and cost effectiveness through the completion of the ultra-orphan NPAF. It should be read in conjunction with two other documents:

- the Guidance to submitting companies for completion of New Product Assessment Form (NPAF) which contains overall methods guidance for all full submissions
- the SMC Process guide for submitting companies which contains information on the process aspects for ultra-orphan medicines.

Both of these documents are available on the [Making a submission](#) page of the SMC website.

Information on completion of each section of the ultra-orphan NPAF are noted below.

Completion of the ultra-orphan NPAF

Introductory sections

The initial pages of the NPAF require information such as contact details and completion of some basic checklists. Submitting companies should refer to the SMC Guidance to submitting companies for completion of New Product Assessment Form (NPAF), as noted above, for guidance on the information required.

Registration details (ultra-orphan NPAF section 1)

Submitting companies should refer to the information provided under the 'Registration details' section of the Guidance to submitting companies for completion of New Product Assessment Form (NPAF) for the relevant questions in this section of the ultra-orphan NPAF.

Overview and positioning (ultra-orphan NPAF section 2)

Submitting companies should refer to the information provided under the 'Overview and positioning' section of the Guidance to submitting companies for completion of New Product Assessment Form (NPAF) for guidance on the completion of this section of the ultra-orphan NPAF.

Nature of the condition (ultra-orphan NPAF section 3)

This section should provide a description of the ultra-orphan disease or condition and its impact on patients and carers, including:

- severity of the condition, symptoms, pattern of disease progression, level of disability, overall effect on morbidity and mortality
- effect on functioning for example ability to work, participate in education, self-care, undertake activities of daily living
- effect on the patient's quality of life and on family and carers' quality of life
- description of currently available treatment options. These may include disease-specific treatments and/or supportive therapies.
- limitations of currently available treatments including side effects, burden in terms of administration and monitoring, hospitalisation and clinic attendance
- level of unmet need in NHSScotland.

Impact of the new technology (ultra-orphan NPAF section 4)

In addition to information on clinical efficacy, safety and clinical effectiveness as outlined in sections 3, 4 and 5 of the Guidance to submitting companies for completion of New Product Assessment Form (NPAF), companies should consider:

- how outcomes from observational studies including disease registries or early access schemes could supplement conventional clinical study data
- effect of the medicine on patient experience and patient reported outcomes such as health-related quality of life, health status, physical functioning, activities of daily living, adherence to treatment, patient satisfaction with treatment
- how the medicine would be expected to address any areas of unmet need
- for the initial submission, identification of uncertainties or evidence gaps and how these might be addressed.

Value for money (ultra-orphan NPAF section 5)

While SMC recognises the challenges in providing a robust economic evaluation for a medicine used to treat an ultra-orphan condition due to limitations in the data available, an economic evaluation to indicate the value for money is required. General guidance on the methods to be followed for the economic evaluation of medicines can be found in the Guidance to submitting companies for completion of New Product Assessment Form (NPAF) in addition to the specific aspects for ultra-orphan medicines noted below.

Initial assessment

SMC has a preference for a cost utility analysis for such medicines, where appropriate and feasible, 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. The company would be expected to provide supporting rationale for the approach taken. SMC appreciates that in some conditions the economic evaluation will have significant uncertainty, but an estimate of the likely costs and benefits is still required.

Given the nature of 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.

Reassessment

The guidance relating to value for money for the initial assessment above remains valid for the initial assessment and reassessment of ultra-orphan medicines. However, at reassessment, value for money will be taken into account as part of the decision-making process. This section provides additional guidance to inform a submission for reassessment in terms of its consideration of cost effectiveness.

SMC does not have a fixed upper limit on willingness-to-pay for a QALY and this applies equally to ultra-orphan medicines.

The challenge for decision making for ultra-orphan medicines reflects that of all other medicines; it is to strike a balance between decision making based upon explicit, stated principles and the need to retain some flexibility to respond to the circumstances of any particular case. This section sets out some general principles but in any individual decision it is the responsibility of the SMC to weigh the factors and issue guidance that it feels to be consistent with the full range of evidence (economic and other, quantified and qualitative).

SMC may also consider other factors in relation to end-of-life and orphan medicines such as added benefit from the patient, carer and clinician perspective that may not be fully captured in conventional clinical and economic analysis (these are included in the Patient and Clinician Engagement [PACE] statement). SMC conventional modifiers may be applied to all new medicines assessed, if appropriate. Guidance on the application of modifiers can be found in the SMC Process guide for submitting companies.

As mentioned, the SMC does not have a fixed upper limit on willingness-to-pay for a QALY for ultra-orphan medicines. As such, incremental cost-effectiveness ratios (ICERs) are not considered in isolation by SMC and are used as part of their decision-making process. However, it is recognised that other Health Technology Assessment (HTA) agencies do set out levels of acceptable levels of willingness-to-pay. SMC notes sections 6.2.22 to 6.2.24 from the National Institute for Health and Care Excellence (NICE) guidance for their highly specialised technologies process, as follows:

NICE guidance [NICE Health Technology Evaluations: The Manual](#):

“6.2.22 For highly specialised technologies, the committee will consider the size of the incremental QALY gain in relation to the additional weight that would need to be assigned to the QALY benefits for the cost effectiveness of the technology to fall within the highly specialised technologies £100,000 cost per QALY level.

6.2.23 For this weight to be applied, there will need to be compelling evidence that the treatment offers significant QALY gains. Depending on the number of QALYs gained over the lifetime of patients, when comparing the new technology with its relevant comparator(s), the committee will apply a weight between 1 and 3, using equal increments, for a range between 10 and 30 QALYs gained.

6.2.24 The weighting is applied as described in table 6.2 below.

Table 6.2:

Incremental QALYs gained (per patient using lifetime horizon)	Weight
• less than or equal to 10	1
• 11 to 29	1–3 (using equal increments)
• greater than or equal to 30	3"

Costs to the NHS and Personal Social Services (ultra-orphan NPAF section 6)

In addition to completion of the standardised SMC budget impact Excel template to show an estimate of the NHS budget impact, companies should include an assessment of any significant budget impacts for any non-NHS organisations.

The budget impact template is available on the [Making a submission](#) page of the SMC website and the information set out in section 7 in the SMC Guidance to submitting companies on completion of the New Product Assessment Form (NPAF) should be referred to for completion of this section of the submission.

Impact beyond direct health benefits and on specialist services (ultra-orphan NPAF section 7)

This section should describe potential impact of the medicine other than clinical benefits, adverse effects and on health-related quality of life, this may include:

- opportunity for patients to contribute to society, improve family functioning, continue in employment or education
- impact on carers' quality of life (for example using tools such as the Carer Experience Scale) and ability to work
- impact of adopting a wider perspective on the cost effectiveness of the medicine (for example incorporating loss of earnings, carer disutility)
- implications of the introduction of the new medicine on the NHS including staffing, infrastructure and training requirements.

Summary information for submitting patient groups (ultra-orphan NPAF section 8)

Submitting companies should refer to the information provided in the Guidance to submitting companies for completion of New Product Assessment Form (NPAF).

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