Healthcare Improvement Scotland | SMC Advice on new medicines

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

Supplement for medicines eligible for the interim acceptance decision option

Medicines with Great Britain (GB) conditional marketing authorisation, included in the Innovative Licensing and Access Pathway (ILAP) and/or have a positive MHRA Early Access to Medicines Scheme (EAMS) scientific opinion.

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www.scottishmedicines.org.uk

1. Background

The Scottish Government published a review of access to new medicines (2016); http://www.gov.scot/Publications/2016/12/9192/0. One of the recommendations was that SMC should have an additional decision option to accept new medicines for use on an interim basis subject to ongoing evaluation and future reassessment.

2. Implementation of the interim accepted decision option

SMC introduced the interim accepted decision option from August 2018. All medicines with Great Britain (GB) conditional marketing authorisation are eligible for this decision option. SMC may issue interim accepted / accepted restricted advice if the committee considers that the additional efficacy and / or safety data requirements outlined in the Medicines and Healthcare products Regulatory Agency (MHRA) specific obligations, are expected to address the key uncertainties in the evidence presented by the submitting company.

In addition, from September 2021, the interim accepted decision option is also available for medicines included in the Innovative Licensing and Access Pathway (ILAP) and/or have received a positive MHRA Early Access to Medicines Scheme (EAMS) scientific opinion if it is likely that ongoing clinical studies could address key uncertainties in the evidence.

3. Process for submissions for eligible medicines

Submitting companies should follow the standard submission process. The company should use the current New Product Assessment Form (NPAF) available from the *Making a submission* section on the SMC website, which has been updated to take account of additional information requirements for medicines where the interim acceptance decision option may apply.

3.1 Completion of the NPAF

The NPAF has been updated to request details of ongoing studies that will potentially address the key uncertainties, where relevant. For each study, companies are asked to provide a brief description of:

- the study design, including details of blinding and randomisation;
- the main inclusion criteria, that define the patient population included in the study;
- the primary and/or other relevant outcome(s) measured in the study and likely timescale for reporting of these.

SMC recognises the challenges in providing robust clinical and economic evaluations for medicines where there are uncertainties in the evidence base due to immature clinical data, however, a full clinical and economic case should be submitted.

3.2 Evaluation of medicines

New Drugs Committee (NDC) meeting:

As per standard process, a submission for a medicine eligible for interim acceptance will be assessed by NDC on the basis of its clinical and economic case before consideration by the SMC Committee. An appropriate form of economic evaluation to demonstrate the value for money of the medicine remains a requirement.

NDC will review the ongoing studies presented by the submitting company. In its preliminary advice to SMC (the NDC Detailed Advice Document [DAD]), NDC will advise SMC if the additional data could be expected to address the key uncertainties e.g. results of an ongoing comparative study if uncontrolled data has been presented as the key evidence. If a key weakness of the evidence is that the plausible incremental cost-effectiveness ratio is higher than the levels generally accepted by SMC, then the additional efficacy and / or safety data are unlikely to address this issue.

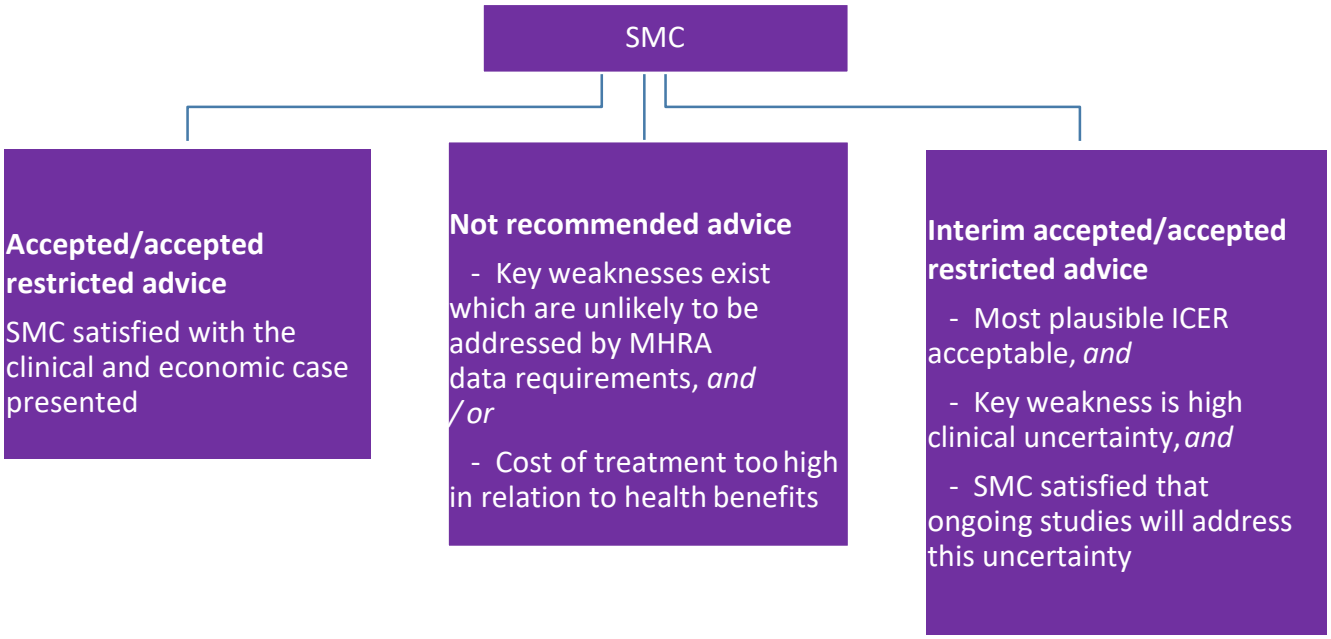
The submitting company will have the opportunity to comment on the NDC DAD and may, if appropriate, provide further clarity to SMC on how the ongoing studies could support the key areas of uncertainty.

If the NDC preliminary advice is 'not recommended', the submitting company can also submit a new or revised Patient Access Scheme (PAS) and, if the medicines has been validated as meeting orphan (equivalent) and/or end of life criteria, request a Patient and Clinician Engagement (PACE) meeting.

SMC meeting:

As part of its review and decision making process, SMC will assess the information provided by the company in addition to other sources of evidence including patient group submissions, clinical expert comments and, where relevant, the output from the PACE meeting. The SMC decision options at initial assessment are outlined in Figure 1.

Figure 1:



Medicines with interim accepted advice from SMC will be considered for local formulary inclusion, in line with current practice for other medicines accepted by SMC for use in Scotland.

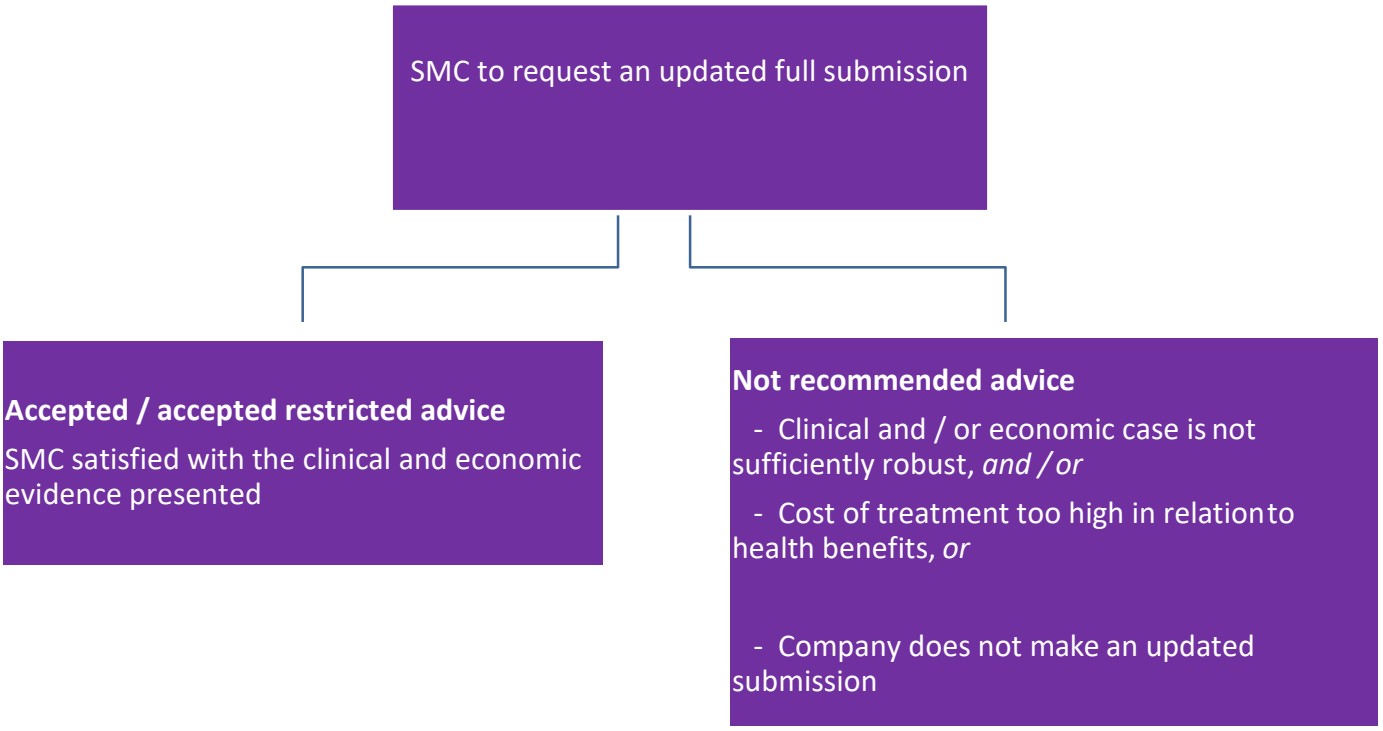
3.3 Reassessment of the medicine

If SMC issues interim accepted advice the company will be required to provide a full updated submission in agreement with SMC

- when the conditional marketing authorisation is converted to standard marketing authorisation (if relevant)
- for medicines that do not have a conditional marketing authorisation, SMC will liaise with the company to agree on further regular points of contact about the clinical evidence, to ensure a practical and mutually acceptable date can be set.

The updated submission must be provided in line with SMC Guidance to submitting companies including the relevant comparator(s) and within the context of the current treatment pathway in Scotland at the point of reassessment. The submitting company may also provide relevant data in addition to those from ongoing clinical studies to support their clinical and economic case e.g. observational or real world data. The SMC decision options at reassessment are outlined in Figure 2.

Figure 2:



3.4 Patient access schemes (PAS)

See PAS application packs and guidance on SMC website.

The submitting company must provide a new PAS application with their updated submission in line with PAS guidance at the point of reassessment.

If the medicine is accepted for use at the point of reassessment the updated PAS will come into effect.

In the event that the medicine is not recommended for use, at reassessment or due to non-submission, the previously established PAS would continue to be in effect for the minimum period specified in said PAS agreement.

Frequently Asked Questions

1. Why are only certain medicines eligible for the interim accepted decision option?

The MHRA supports the development of medicines that address unmet medical needs of patients. In the interest of public health, certain medicines are eligible for different regulatory pathways depending on the seriousness of the condition and/or lack of currently available treatment options.

GB Conditional Marketing Authorisation

A medicine may be granted a conditional marketing authorisation where the benefit of immediate availability outweighs the risk of having less comprehensive data than normally required. The marketing authorisation holder will be required to complete specific obligations (ongoing or new studies, or collection of pharmacovigilance data) with a view to providing comprehensive data confirming that the benefit-risk balance is positive. Once comprehensive data on the product have been obtained, the marketing authorisation may be converted into a standard marketing authorisation (not subject to specific obligations).

Innovative Licensing and Access Pathway (ILAP)

The aim of ILAP is to allow safe, timely and efficient development of innovative new medicines for patients. These medicines will be used to treat serious conditions and/or for conditions where there is a lack of treatment options. SMC is a partner in ILAP, alongside the MHRA, the National Institute for Health and Care Excellence (NICE) and the All Wales Therapeutics and Toxicology Centre.

MHRA Early Access to Medicines Scheme (EAMS)

EAMS aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need. Evidence collected during the EAMS period can be used to inform the submission to SMC.

The interim acceptance decision option can allow earlier access to innovative medicines that address an unmet need, while further data to support clinical effectiveness are gathered.

2. Can NDC propose interim accepted advice in the NDC DAD with its preliminary advice to SMC?

No. The role of NDC committee is to consider the key uncertainties in the clinical and economic evidence presented by the company and to advise SMC if the ongoing clinical studies would be likely to address those uncertainties. NDC does not have responsibility for decision making on this matter.

3. What is the SMC voting process for medicines eligible for the interim accepted decision option?

As SMC decisions are made by majority vote, a two-stage approach to voting for medicines eligible for an interim accepted decision will be adopted.

At the discretion of the Chair, to avoid inadvertent disclosure of the final decision, a closed session may be called. The Chair will ask members to vote in the usual way.

Vote 1: If the majority vote is to accept the medicine then a second vote will not be required. The medicine is then accepted for use in line with the indication or restricted population as proposed by the company.

If the majority vote is to not recommend the medicine then a second vote will be required.

Vote 2: Members will vote to accept the medicine on an interim basis or to not recommend the medicine for the indication or restricted population as proposed by the company.

4. Can I submit while the medicine has SMC interim accepted advice?

Companies should liaise with SMC to agree an appropriate date for reassessment. For medicines with conditional marketing authorisation this will be when the conditional marketing authorisation is converted to full. For medicines with a standard marketing authorisation this will be in agreement with SMC.

An appropriate case must be provided, along with relevant supporting documentation, according to the usual SMC process at the point of reassessment. The submission will be assessed in line with the usual process and assessment timelines.

At this stage SMC will decide to accept the medicine (or accept with restrictions) or to not recommend the medicine, which would supersede the interim accepted advice.

5. Can I resubmit for a medicine where the initial SMC advice was to not recommend the medicine?

Yes.

Not recommended advice issued due to previous non-submission

- An appropriate case must be provided, along with relevant supporting documentation, according to the usual SMC process at the point of submission.

Not recommended advice issued after SMC assessment

- Where there is substantial new clinical and / or economic evidence the submitting company may resubmit to SMC. An appropriate case must be provided, along with relevant supporting documentation, according to the usual SMC process at the point of resubmission.

The resubmission will be assessed with a clinical and health economic review followed by consideration by NDC and SMC committees in line with the usual assessment timelines and the decision options in Figure 1 will be available.

6. We are planning a submission to SMC and the currently available treatments include a medicine that has interim accepted advice. Is it a relevant comparator?

Yes. If the medicine with interim accepted advice is in use at the time of the submission to SMC and has been identified as a relevant comparator then a case should be made against this medicine.

7. What type of submission should be provided at the time of reassessment?

An updated submission will be required at the point of reassessment in line with good practice guidance for standard process as outlined on the SMC website.

If there are few changes to the original submission then it would be helpful to highlight new information in the NPAF.

8. What happens if the company does not provide an updated submission for reassessment?

If the company does not provide an updated submission for a medicine accepted on an interim basis when requested, SMC will issue not recommended advice. This will replace the previous interim accepted advice.

9. What happens if SMC issues not recommended advice following reassessment or failure to resubmit?

Patients already taking a medicine that was previously accepted on an interim basis

Where a patient continues to derive clinical benefit it is expected that the patient would remain on the medicine until the patient and clinician consider it appropriate to stop treatment.

Other patients

Where SMC advises that a medicine is not recommended for use in NHS Scotland but a clinician thinks it may be of benefit for a particular patient then the clinician should follow the relevant local health board procedures to seek access.

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