



Healthcare
Improvement
Scotland

SMC
Advice on new
medicines

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

Supplement for medicines with European Medicines
Agency conditional marketing authorisation

(Interim accepted advice decision option)

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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 will introduce the interim accepted advice decision option from August 2018. All medicines with European Medicines Agency (EMA) conditional marketing authorisation will be 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 EMA specific obligations (SO), are expected to address the key uncertainties in the evidence presented by the submitting company.

To fully support patient access to medicines that address an unmet clinical need, companies will not be able to opt out of the SMC's interim accepted decision process.

3. Process for submissions for medicines with EMA conditional marketing authorisation

Submitting companies should follow the standard submission process for medicines with EMA conditional marketing authorisation. 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 with EMA conditional marketing authorisation.

3.1 Completion of the NPAF

The NPAF has been updated to request details of the studies that will fulfil the specific obligations set out by the EMA for medicines with conditional marketing authorisation. 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 with an EMA conditional marketing authorisation given the nature of the data available 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 with an EMA conditional marketing authorisation 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 will still be required.

NDC will review the data requirements outlined in the EMA specific obligations 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 address the key uncertainties e.g. an EMA request for mature overall survival data from a final clinical study report may be sufficient if this is the key uncertainty in the 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.

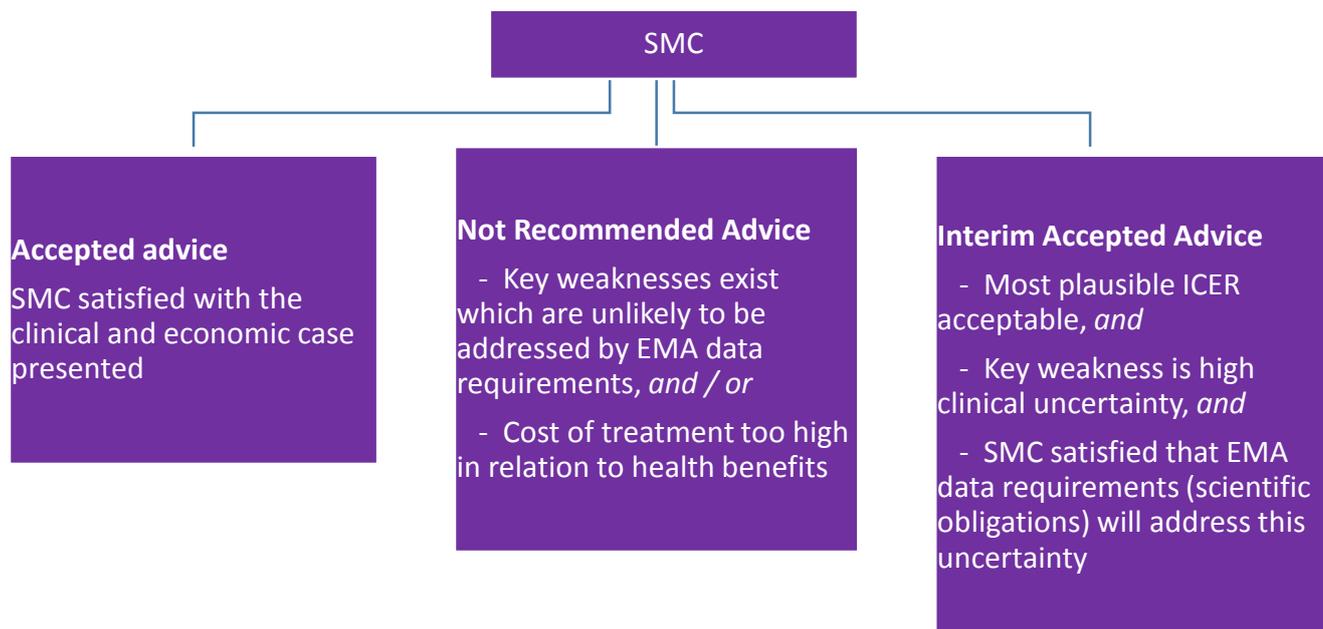
The submitting company will have the opportunity to comment on the NDC DAD and may, if appropriate, provide further clarity to SMC on how the EMA data requirements could support the key areas of uncertainty.

If the NDC preliminary advice is 'not recommended', the submitting company can also request a Patient and Clinician Engagement (PACE) meeting and / or to submit a new or revised Patient Access Scheme (PAS).

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:

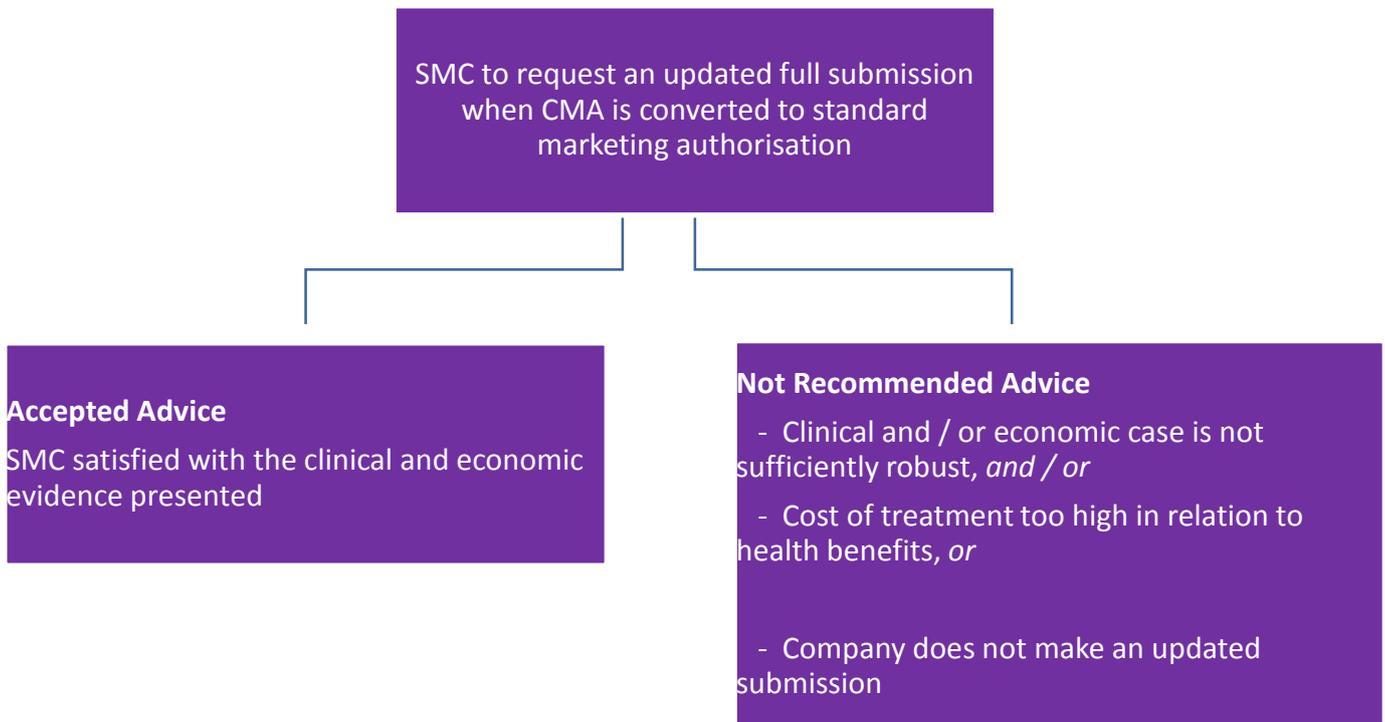


Medicines with interim accepted advice from SMC will be considered for local formulary inclusion, in line with current practice for other medicines accepted by SMC for use in Scotland.

3.3 Reassessment of the medicine

If SMC issues interim accepted advice the company will be required to provide a full updated submission when the conditional marketing authorisation is converted to standard marketing authorisation. 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 has the opportunity to provide relevant data in addition to the specified EMA data requirements 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 only medicines with EMA conditional marketing authorisation?

The EMA supports the development of medicines that address unmet medical needs of patients. In the interest of public health, applicants may be granted a conditional marketing authorisation for such medicines where the benefit of immediate availability outweighs the risk of less comprehensive data than normally required, based on the scope and criteria defined in legislation and guidelines.

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).

Introducing the new decision option for medicines with EMA conditional marketing authorisation provides an opportunity to increase access to medicines deemed by EMA to address an unmet need, whilst using an established process to assess ongoing clinical effectiveness. The submitting company is already responsible for the additional data collection and evaluation for submission for EMA so use of this dataset will require limited additional workload for the submitting company and the service in NHS Scotland.

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 data requested as part of the EMA specific obligations would be likely to address those uncertainties. NDC does not have the responsibility for decision making on this matter.

3. What is the SMC voting process for medicines with EMA conditional marketing authorisation?

As SMC decisions are made by majority vote, a two-stage approach to voting for medicines with EMA conditional marketing authorisation 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 resubmit while the medicine has interim accepted advice?

Yes. Where there is substantial new clinical and / or economic evidence for a medicine with interim accepted advice, the submitting company may resubmit before the conversion to standard marketing authorisation.

A full clinical and economic 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 full clinical and health economic review followed by consideration by NDC and SMC committees in line with the usual process and assessment timelines.

While the medicine still has conditional marketing authorisation SMC can issue any of the decision options outlined in Figure 1 which would then supersede the original interim accepted advice.

5. Can I resubmit for a medicine with EMA conditional marketing authorisation where SMC has previously issued not recommended advice?

Yes.

Not recommended advice issued due to previous non-submission

- A full clinical and economic 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) before the interim accepted advice option was available for that medicine

- A full clinical and economic case must be provided, along with relevant supporting documentation, according to the usual SMC process at the point of resubmission.

Depending on the time between the original advice and the resubmission, new clinical and / or economic evidence may be available. Where this is the case the new evidence should be included in the resubmission. Submitting companies are required to provide details of the EMA data requirements in the NPAF which can be considered by NDC and SMC.

Not recommended advice issued (after SMC assessment) where SMC had the option of interim accepted advice for that medicine

- Where there is substantial new clinical and / or economic evidence the submitting company may resubmit to SMC. A full clinical and economic 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.

While the medicine still has conditional marketing authorisation SMC can issue any of the decision options outlined in Figure 1 which would then supersede the original not recommended advice.

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

A full updated submission will be required at the point of reassessment using the NPAF and in line with good practice guidance for standard process as outlined on the SMC website. This should include a full clinical and economic case against the relevant comparators at the point of reassessment.

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

7. At the point of re-assessment of a medicine that holds interim acceptance, is it possible to propose a price increase, for example, if additional evidence indicates that the medicines offers greater value than early evidence suggests?

At the point of re-assessment, where there is an existing PAS in effect for the medicine, a new PAS application pack with updated "PAS Submission" is required. A key concern of Health Boards is the financial/budgetary impact if the price was to rise after re-assessment where Health Boards have risked initiating patients, potentially a significant number of patients, on the medicine while the cost-effectiveness of the medicine was uncertain. Given this, in general, it is unlikely that at the point of re-assessment a pricing proposal that

increases the cost of treatment for patients established on the medicine would be accepted by PASAG. Exceptional circumstances will be considered and an option for companies is to propose a pricing approach that protects the NHS from the financial impact of a price increase on established use while enabling an increase in price for new patients, for example through a rebate arrangement. Any PAS pricing proposal would be considered via the standard PASAG assessment process. In advance of initial submission, companies can discuss their product specific circumstances directly with the PASAG Secretariat.

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

If the company does not provide an updated submission when the marketing authorisation is converted from conditional to standard, 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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