NICE National Institute for Health and Care Excellence

Evidence summaries: new medicines – Integrated process statement

Process and methods

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Contents

1 Introduction

This is not the current process. From February 2017, evidence summaries were developed using the evidence summaries: process guide.

1.1 Introduction to integrated process statement

This integrated process statement has been produced to explain how 'Evidence summaries: new medicines' (ESNMs) are developed. It provides an overview of the key process principles and describes all stages of the development of ESNMs. These procedures are designed to ensure that a robust, quality-assured, commentary is developed for the NHS in an open, transparent and timely way, with appropriate input from key groups.

1.2 Background to 'Evidence summaries: new medicines'

The National Institute for Health and Care Excellence (NICE) provides national guidance and advice to improve health and social care. Further information about NICE and its work is available on the NICE website.

The NICE Medicines and Prescribing Centre provides advice and support for delivering safety, efficiency and effectiveness in the use of medicines. The Medicines and Prescribing Centre is responsible for developing ESNMs.

ESNMs provide a summary of the published evidence for selected new medicines that are considered to be of significance to the NHS. This includes new indications for existing medicines and new formulations of existing medicines. The strengths and weaknesses of the relevant evidence are critically reviewed within each ESNM. Importantly, an **ESNM does not constitute formal NICE guidance** and this is clearly stated on each publication.

The context of the rest of the evidence informing the management of the licensed indication(s) or anticipated licensed indication(s) for the new medicine is also summarised to assist local decision-making.

The NHS Constitution gives patients the right to expect that decisions about the funding of medicines and treatments will be made rationally, following proper consideration of the evidence. ESNMs help provide consistent access to the best available information on a medicine to guide local decision-making, for example within a Clinical Commissioning Group (CCG), an NHS Trust, or

across a local health economy. This information from NICE will help to avoid potential duplication of effort when different organisations are producing their own evidence summaries.

The topics for ESNMs are selected in collaboration with the existing NICE topic selection programme. Two types of topics are considered:

- A medicine recently marketed in the UK.
- A medicine that may be marketed in the UK within the next 6–12 months.

In both cases**, topics are considered for an ESNM only if a NICE technology appraisal (TA) is not planned or in progress,** unless the technology appraisal programme will not publish an appraisal consultation document (ACD) within 6 months of the medicine's launch.

2 Evidence summaries: new medicines

2.1 Aims

The aim of 'Evidence summaries: new medicines' (ESNMs) is to inform local planning around the managed use of medicines within a local health system. For the purposes of this process statement, the term 'new medicines' encompasses these areas:

- a medicine recently granted a marketing authorisation in the UK (normally within the past 6 months)
- a medicine with an existing UK marketing authorisation that has been recently licensed for a new indication (normally within the past 6 months)
- a new formulation of an existing licensed medicine (normally within the past 6 months).

2.2 Key audiences

ESNMs are produced for:

- local decision-making groups involved in commissioning and funding services related to medicines (for example, Area Prescribing Committees)
- local medicines management and horizon scanning services
- clinicians[a], involved in local commissioning decisions for planning purposes, for example within a Clinical Commissioning Group (CCG) or NHS Trust.

2.3 Key activities

The key activities involved in the production of each ESNM are:

- identifying, prioritising and selecting the topic
- summarising the key published evidence
- critically reviewing the strengths and weaknesses of the evidence
- placing the new evidence in the context of the wider evidence base for the licensed indication(s) or anticipated licensed indication(s), particularly NICE guidance, if available

- highlighting any potential implications for local decision-making or clinical practice
- identifying any new evidence relevant to published ESNMs through horizon scanning, reviewing and, if necessary, updating or withdrawing an ESNM.

[1] There are restrictions on the promotion of new medicines to clinicians before receipt of a marketing authorisation. Information on yet-to-be-licensed medicines may be provided to clinicians only for use for planning purposes in their role as commissioners.

3 Who is involved in producing 'Evidence summaries: new medicines'?

3.1 The Medicines and Prescribing Centre

The Medicines and Prescribing Centre is part of NICE's Centre for Clinical Practice (CCP). The Medicines and Prescribing Centre consists of a programme director, associate directors and clinical, technical, project and administrative staff. For 'Evidence summaries: new medicines' (ESNMs), senior members of the medicines evidence and medicines education teams within the Medicines and Prescribing Centre are responsible for:

- developing and reviewing processes and methods for producing ESNMs
- identifying potential topics for ESNMs in collaboration with the NICE topic selection team
- preparing ESNMs for publication, including selecting and critically appraising the evidence
- identifying and liaising with external specialist commentators to help ensure the content is relevant and useful
- providing quality assurance of the content of ESNMs
- ensuring timelines and quality assurance standards are followed
- reviewing and updating content of published ESNMs when required.

3.2 Other NICE teams

In developing ESNMs, the Medicines and Prescribing Centre works closely with members of other NICE teams. These include

- Topic Selection, to assist in topic identification and prioritisation
- Technology Appraisals, to ensure that there is no conflict or overlap with published, planned or proposed NICE technology appraisals
- Clinical Guidelines, to suggest topics for prioritisation and ensure that there is synergy with published or planned NICE clinical guidelines, including the review and updating of NICE clinical guidelines
- Communications, to carry out an editorial review then to publish and promote the final versions

- Guidance Information Services, to assist at the topic selection stage and to conduct literature searches for the development of ESNMs.

3.3 External specialist commentators

Specialist commentator(s) and/or specialist agencies (for example, the Health Protection Agency for an infectious disease topic) are identified through suggestions from NICE staff, national professional organisations and NICE Medicines and Prescribing Associates (see section 3.5), to review the ESNMs before publication. Specialists are identified early in the production process and provide comments within an agreed timeframe. Specialist commentators are practitioners who have significant expertise in the therapeutic area for which the new medicine is to be used. Their role is to clarify issues about the reviewed evidence and the practical implications of the information contained in the ESNM.

3.4 Manufacturers

When a topic is selected for the ESNM programme, NICE informs the manufacturer of the medicine of its intention to produce an evidence summary and the expected time frame for production. NICE invites them to provide relevant information to support the production of the evidence summary.

The manufacturer is also invited to comment on a draft of the evidence summary, and provides comments within an agreed time frame. The manufacturer has the opportunity to comment on matters of factual accuracy, and respond to any specific questions from NICE about the information they submitted to inform the development of the ESNM.

3.5 The NICE Medicines and Prescribing Associates programme

NICE Medicines and Prescribing Associates are a network of health professionals for whom influencing medicines and prescribing strategy in the NHS is a significant part of their job. They work within their own NHS organisation, health board or service and in their wider local health economy to support high-quality, cost-effective prescribing and medicines optimisation. Details of current Associates are published on the NICE website. NICE Medicines and Prescribing Associates assist with the prioritisation of topics for ESNMs (see section 4.1), and help to identify external specialist commentators.

3.6 Conflicts of interest

NICE staff, NICE Medicines and Prescribing Associates and specialist commentators are required to comply with the NICE code of conduct on conflicts of interest. For more information about how NICE deals with conflicts of interest, please see A code of practice for declaring and dealing with conflicts of interest.

4 Topic identification, prioritisation and scoping

4.1 Topic identification and prioritisation

The topics for 'Evidence summaries: new medicines' (ESNMs) are selected in collaboration with the existing NICE topic selection programme. Two types of topics are considered:

- A medicine recently marketed in the UK.
- A medicine that may be marketed in the UK within the next 6–12 months.

In both cases, **topics are only considered for an ESNM if a NICE technology appraisal (TA) is not planned or in progress,** unless the technology appraisal programme will not publish an appraisal consultation document (ACD) within 6 months of the medicine's launch.

Stage 1: Identifying potential topics

The NICE topic selection process is the primary route to identify significant new medicines. Potential topics for an ESNM can be identified at several points during the topic selection and technology appraisal process and they can include:

- topics that are not prioritised for development into technology appraisal guidance
- topics referred to the technology appraisal programme if the appraisal consultation document (ACD) will not be published within 6 months of the medicine's launch
- terminated technology appraisals
- other topics from the National Institute for Health Research Horizon Scanning Centre (NIHR HSC).

The NICE topic selection prioritisation criteria include the size of population affected, severity of disease, potential resource impact and claimed therapeutic benefit.

Stage 2: Prioritising topics

The NICE Medicines and Prescribing Centre presents a list of medicines identified in stage 1 to NICE Medicines and Prescribing Associates 5 times a year. The Medicines and Prescribing Associates advise NICE on the likely clinical and service impact of these new medicines. The purpose of this stage is to engage with those who have a role in managing the introduction of new

medicines within health communities, with their advice informing stage 3 of this topic selection process.

Stage 3: Formal approval of topic for review

A final, prioritised list of topics is then compiled by the NICE Medicines and Prescribing Centre using the NICE topic selection prioritisation criteria (based on the size of population affected, severity of disease, potential resource impact and claimed therapeutic benefit), taking into account the advice from the NICE Medicines and Prescribing Associates network. The Director of the NICE Centre for Clinical Practice reviews the list and gives approval to the topics on which NICE should proceed to develop ESNMs. Once approved, the manufacturers of the medicines are informed of the intention to produce these ESNMs and the topics are added to the NICE Forward Planner, as well as being added to the ESNM page of the 'Medicines and prescribing' section of the NICE website.

5 Production

5.1 Equality and diversity considerations

'Evidence summaries: new medicines' (ESNMs) are developed in accordance with the NICE equality scheme.

5.2 Process and timescales

ESNMs are not formal NICE guidance and therefore are not subject to the same intensity of process as other NICE products.

Table 1 shows the key steps in the development of ESNMs.

Table 1 Key steps for developing an ESNM with timelines

Key step	Timescale
Scope topic	Week 1
Contact manufacturer for data	Week 1
Literature search	
Searching for evidence Sifting and selecting the evidence Appraising and categorising the evidence	Week 2 Week 3 Week 3
Authoring the ESNM	
Produce initial draft Internal check of initial draft	Week 4 Week 4
Review of draft ESNM	
Initial draft sent to manufacturers, specialist commentators, NICE Clinical Guidelines team and NICE Technology Appraisals team for review	Week 5
Review comments received and produce revised draft	Week 8
Quality assurance of the ESNM	

Technical check of content by senior adviser	Week 9
Editorial check of content by NICE publishing team	Week 9
Manufacturer invited to check for any remaining factual errors	Week 10
Final check of content by Medicines and Prescribing Centre Programme Director, Associate Director or Consultant Clinical Adviser	Week 11
Sign off and publication of the ESNM	
Guidance Executive sign off	Week 12
Manufacturer informed of date that ESNM will be published	Week 12
Publication on NICE website	Week 13

5.3 Scoping of individual topics

The NICE Medicines and Prescribing Centre holds an internal scoping meeting for each ESNM topic to:

- confirm key contacts at the pharmaceutical manufacturer
- identify specialist commentators (through the NICE Medicines and Prescribing Associates and other existing NICE networks)
- identify terms for a literature search to identify published clinical trial data that reflect the possible indication for the medicines (usually phase III trials)
- confirm arrangements for identifying:
    - proposed or likely indication
    - relevant published trials
    - likely licensing and marketing timeline
    - proposed cost and course of treatment
    - evidence of clinical effectiveness
    - safety issues
    - treatment alternatives
    - likely place in therapy

- incidence and prevalence of (likely) indication (to inform an estimation of use).

5.4 Contacting the manufacturer

NICE asks the manufacturer to support the production of the ESNM by providing the following data (within 10 working days):

- Key published clinical trials relating to the indication being reviewed in the ESNM that have been published in full.
- Key relevant clinical trials that are ongoing or that have been completed but not yet published in full.
- The licence status within the UK, including whether a positive opinion or a marketing authorisation has been granted, and an indication of when the medicine will become available.
- The presentation of the medicine, including form, strength and pack size.
- The expected cost (for medicines not yet available).
- The expected or licensed dose.

5.5 Literature search

5.5.1 Searching for evidence

A literature search is conducted by the NICE Guidelines Information Service. The literature search is intended to locate the best (highest quality) available published evidence relating to the efficacy and safety of the medicine. In addition, explicit reference is made to information in the summary of product characteristics (if one exists) relating to precautions, warnings and undesirable effects and also to published advice from the Medicines and Healthcare products Regulatory Agency (MHRA). Cost information is obtained from the current Drug Tariff, or if the product is not listed there, the current edition of MIMS, or if the product is not listed there, the manufacturer.

5.5.2 Sifting and selecting the evidence

The NICE Medicines and Prescribing Centre sifts the final set of search results using the title and abstract of each article, applying first exclusion and then inclusion criteria. These include the basic criteria as set out below.

First sift

This process removes evidence based on the following exclusion criteria:

- articles of poor relevance against search terms
- publication types that are out of scope:
    - non-English language studies
    - articles if neither the abstract nor full text is freely available online
    - conference abstracts[2]
    - studies that have not been published in full[2].

Second sift

This sift of evidence includes relevant randomised controlled trials (RCTs) that address the use of the medicine within the defined indication under review. The reasons for inclusion and non-inclusion based on the second sift are recorded as well as a 'long list' of those studies that are excluded from the first sift.

Up to 3 RCTs can be reviewed for an ESNM. If more than 3 RCTs have been identified for possible inclusion, they are prioritised taking into account the following considerations:

- whether patient-oriented outcomes[3] were reported and if so, whether these were primary or secondary outcomes
- whether an active comparator was used, and whether this reflects usual UK practice
- whether the population in the study reflects the typical UK population for which this medicine is likely to be used (bearing in mind the licensed or proposed indication and NICE guidance)
- the size of the available studies.

5.5.3 Appraising and categorising the prioritised evidence

The NICE Medicines and Prescribing Centre prioritises the evidence for critical appraisal and records the reasons for non-inclusion of evidence. The full text of the prioritised evidence is appraised using an assessment form suitable for the type of evidence. If a European public

assessment report (EPAR) has been published, it is used to supplement the information included in the published study report, if this is necessary.

5.6 Authoring of the ESNM

The NICE Medicines and Prescribing Centre drafts the ESNM using a standard template, which includes sections relating to the following:

- synopsis of key points from the evidence
- relevance to NICE guidance programmes
- general information about the disease or condition
- product overview, including drug action, licensed or proposed indications, course and cost
- review of the available evidence, with relative strengths and weaknesses of evidence for clinical effectiveness and safety
- context, including treatment alternatives and their cost
- estimated impact for the NHS, including likely place in therapy and estimated usage

5.7 Review of the draft ESNM

The NICE Medicines and Prescribing Centre sends the draft ESNM to the identified external specialist reviewers, the manufacturer, the NICE Clinical Guidelines team, and the NICE Technology Appraisals team for review. Any comments received are considered within the production of the revised draft. Actions are also recorded. Feedback to commentators is available on request to NICE.

5.8 Quality assurance of the ESNM

Quality assurance of the ESNM is carried out by the NICE Medicines and Prescribing Centre. This involves a detailed check of all content, to ensure all sections of the document contain statements and conclusions that are fair and balanced. They must accurately reflect the evidence reviewed and be substantiated by an explicit and appropriate source of evidence. This is carried out to a standard checklist. A further check for clarity, grammar, spelling and style is also undertaken by the NICE Medicines and Prescribing Centre. All drafts and any changes to drafts are recorded for audit purposes.

In conjunction with the NICE publishing team, the NICE Medicines and Prescribing Centre produces a near-final draft. The manufacturer is given the opportunity to review the near-final draft to check for any factual errors and any necessary corrections are made by the Medicines and Prescribing Centre. Once sign-off is received from the Medicines and Prescribing Centre Programme Director, Associate Director or Consultant Clinical Adviser, NICE Guidance Executive reviews the ESNM, and if appropriate, approves the ESNM for publication, ensuring that due process has been followed in its development. The manufacturer is informed of the scheduled publication date, and may request an embargoed copy of the ESNM to be sent to them 24 hours before publication.

5.9 Publication of the ESNM

The final ESNM is uploaded and made available online through the Medicines and Prescribing Centre page of the NICE website.

The NICE Communications team develops a communications plan for the ESNM, together with the Associate Director within the Medicines and Prescribing Centre, and is responsible for disseminating the ESNM once it has been published.

[2] Studies that have been reported only as conference abstracts or otherwise not reported in full are excluded because they cannot be critically appraised. However, the ESNM may indicate if key clinical trials are ongoing or have been completed but not yet published in full.

[3] Patient-oriented outcomes are those that are of direct clinical importance, such as mortality, rates of cardiovascular events, or quality of life. This is in contrast to disease-oriented, surrogate outcomes, such as changes in blood pressure or biochemistry.

6 Review

Every 'Evidence summaries: new medicine' (ESNM) states the date of its publication. The literature search (section 5.5) is repeated every year to check if relevant new evidence has been published. In addition, whether or not to update published ESNMs is considered on a continuing basis by the Medicines and Prescribing Centre at NICE, in the light of its current awareness activities (see Medicines and Prescribing Alerts on the NICE website). Examples of circumstances when an update or withdrawal of an ESNM might be required include:

- new information or data becoming available that materially affects the efficacy or safety information within the ESNM
- NICE publishing a technology appraisal that provides guidance on the use of the medicine in the stated indication.

7 About this integrated process statement

The integrated process statement for 'Evidence summaries: new medicines' (ESNMs) provides a high-level overview of the process for developing ESNMs and will be supported by the forthcoming NICE methods manual.

For published ESNMs, see the NICE website.