NICE National Institute for Health and Care Excellence

Evidence summaries: process guide

Process and methods

Published: 23 January 2017
nice.org.uk/process/pmg31

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1 Introduction

1.1 Introduction to process guide

This process guide provides an overview of the key principles used for developing evidence summaries. Each stage ensures 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

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.

NICE's medicines and technologies programme (MTP) provides advice and support for delivering safety, efficiency and effectiveness in the use of medicines. The MTP is responsible for developing evidence summaries. 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. Evidence summaries provide consistent access to the best available information on a medicine to guide decision-making, nationally within NHS England and locally, for example within a clinical commissioning group, an NHS trust, or across a local health economy.

What are evidence summaries?

Evidence summaries provide a summary of the best available evidence for selected medicines[1] that are considered to be of significance to the NHS including:

- **new medicines**
    - a medicine that has recently been granted a marketing authorisation or recently launched 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 recently granted a marketing authorisation or launched in the UK (normally within the past 6 months)
- **off-label use of licensed medicines**

  - a medicine that is used outside of its marketing authorisation (off-label use of medicines)

- **unlicensed medicines**

  - a medicine that is used when there is no licensed medicine for a condition

  - a medicine that is used when there is no licensed medicine appropriate for a significant proportion of people needing treatment for a condition.

Full systematic reviews, meta-analysis and cost-effectiveness reviews are not carried out when producing evidence summaries. Topics are considered for an evidence summary if a NICE technology appraisal is not planned or in progress, or the technology appraisal programme will not publish an appraisal consultation document within 6 months of a medicine's launch. Previous inclusion of an unlicensed or off-label medicine in a NICE guideline is not necessarily a reason for it not to be selected for an evidence summary.

The strengths and weaknesses of the relevant evidence are critically reviewed within each evidence summary. Importantly, an evidence summary **does not include recommendations and does not constitute formal NICE guidance**.

Evidence summaries should not be considered to promote the use of unlicensed medicines solely for economic reasons.

[1] NHS England may commission an evidence summary for any medicine to inform a commissioning policy for that topic area.

2 Evidence summaries

2.1 Aims

Evidence summaries aim to:

- provide a summary of the best available evidence relating to the use of a medicine for a specific condition within the context of other NICE guidance in that therapeutic area
- inform national commissioning decisions about medicines, for example by NHS England
- provide consistent access to the best available information on a medicine to guide local decision-making and planning, for example, by the regional medicines optimisation committees (RMOCs), within an area prescribing committee (APC) across a clinical commissioning group (CCG) or NHS trust within a local health economy (this helps avoid potential duplication of effort at a national, regional or local level)
- provide information for healthcare professionals to inform their decision-making and support the development and updating of local formularies
- help inform the public about a medicine and condition to help them make decisions about the medicine
- provide information about an unlicensed medicine or off-label use of a licensed medicine that is being considered when there are no suitable alternatives licensed for that situation
- inform the development or updating of NICE guidance.

2.2 Key audiences

Evidence summaries are produced to inform the decision-making of:

- groups involved in:
  - commissioning or funding services using medicines (such as NHS England, RMOCs and local APCs)
  - developing medicines optimisation policies
  - individual funding requests, for example, within a CCG or NHS trust
- healthcare professionals caring for individuals

- healthcare professionals[2] involved in local commissioning decisions for planning purposes, for example, within a CCG or NHS trust
- patients and the public
- local medicines optimisation and horizon scanning services.

2.3 Key activities

Producing an evidence summary involves:

- identifying, prioritising and selecting the topic
- summarising the best available evidence
- critically reviewing the strengths and weaknesses of the selected evidence
- placing any new and existing evidence in the context of the wider evidence base for managing the condition, particularly NICE guidance, if available
- highlighting any potential implications for local decision-making or clinical practice.

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

3 Who is involved in producing evidence summaries?

3.1 The medicines and technologies programme

The medicines and technologies programme (MTP) is part of NICE's Health and Social Care Directorate. The MTP is a team of healthcare professionals, and technical, project and administrative staff who are responsible for:

- developing and reviewing processes and methods for producing evidence summaries
- identifying potential topics for evidence summaries in collaboration with the NICE topic selection group
- developing and preparing evidence summaries for publication in line with the agreed process and standards (this includes selecting and critically appraising the evidence)
- identifying and liaising with external specialist commentators and pharmaceutical companies to ensure the content of evidence summaries is relevant and useful
- providing quality assurance of the content of evidence summaries
- ensuring timelines and processes for quality assurance are followed
- reviewing uptake of published NICE guidance (technology appraisals, guidelines, and medical and diagnostic technologies)
- estimating savings and costs of implementing guidance
- helping organisations to overcome perceived barriers to implementing guidance through practical support.

3.2 Other NICE teams

The MTP works closely with other teams at NICE to develop evidence summaries. These include:

- the public involvement programme (PIP) – providing advice on involving patients, carers and members of the public
- the topic selection team – assisting in identifying and prioritising topics
- guidance information services – assisting with topic selection and conducting literature searches

- the technology appraisals team – ensuring there is no conflict or overlap with published, planned or proposed NICE technology appraisals
- NICE guidelines team – suggesting topics for prioritisation and ensuring that there is synergy with published or planned NICE guidelines, including the review and updating of NICE guidelines
- the publishing team – publishing the evidence summaries.

3.3 The NICE medicines and prescribing associate programme

NICE medicines and prescribing associates are a network of healthcare 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 or service and in their wider local health economy to support high-quality, cost-effective prescribing and medicines optimisation. Four regional technical advisers working within the MTP support the associates in their roles. Details of the regional technical advisers are published on the NICE website. NICE medicines and prescribing associates assist with identifying topics (see section 5.1), and external specialist commentators.

3.4 NHS England

NHS England provides commissioning decisions for medicines through specialised commissioning or clinical commissioning groups. NHS England refers priority medicines topics to NICE for developing into evidence summaries.

3.5 Pharmaceutical companies

When a topic is selected for an evidence summary, NICE informs the pharmaceutical company that manufactures the medicine that it intends to produce an evidence summary and the expected time frame. NICE invites the company to provide information to support the production of the evidence summary.

The pharmaceutical company is also invited to provide comments on a draft evidence summary within an agreed time frame. The company can comment on factual accuracy and respond to any specific questions from NICE about the information they submitted to inform the development of the evidence summary.

3.6 External specialist commentators

Specialist commentator(s) and/or specialist agencies (for example, Public Health England for an infectious disease topic) are identified by the organisation commissioning the evidence summary, existing NICE networks, national professional organisations or NICE medicines and prescribing associates (see section 3.3), and asked to review the evidence summary before publication. Specialists are identified early in the production process and provide comments within an agreed time frame. They have significant expertise in the therapeutic area for which the medicine is to be used. Their role is to clarify any issues about the reviewed evidence and the practical implications of the information contained in the evidence summary.

3.7 Prioritisation panel and topic selection group

For unlicensed and off-label use of medicines, the prioritisation panel is made up of standing members who advise NICE on topics that should be prioritised for development as an evidence summary. The panel meets twice a year. Members include lay members, representatives from the Association of the British Pharmaceutical Industry (ABPI), Royal College of Paediatrics and Child Health (RCPCH), and NHS pharmacists. Details of panel members can be found on the NICE website.

For all other medicines, a topic selection group meets monthly to discuss the topics that have been identified through the topic identification process. These meetings include representatives from several teams at NICE (such as the MTP, guidance information services and technology appraisals team) as well as representatives from the UK Medicines Information (UKMi) Service, Specialist Pharmacy Services and National Institute for Health Research (NIHR). Advice from the NICE medicines and prescribing associates network and the prioritisation panel is also taken into account. Topics are selected where a demand for information has been identified.

3.8 The Medicines and Healthcare products Regulatory Agency

The Medicines and Healthcare products Regulatory Agency (MHRA) is invited to comment on a draft evidence summary within an agreed time frame. The role of the MHRA is to comment on regulatory and safety issues.

4 Conflicts of interest

NICE staff and medicines and prescribing associates, members of the prioritisation panel and specialist commentators are required to comply with the NICE conflicts of interest policy. For more information, please see the policy.

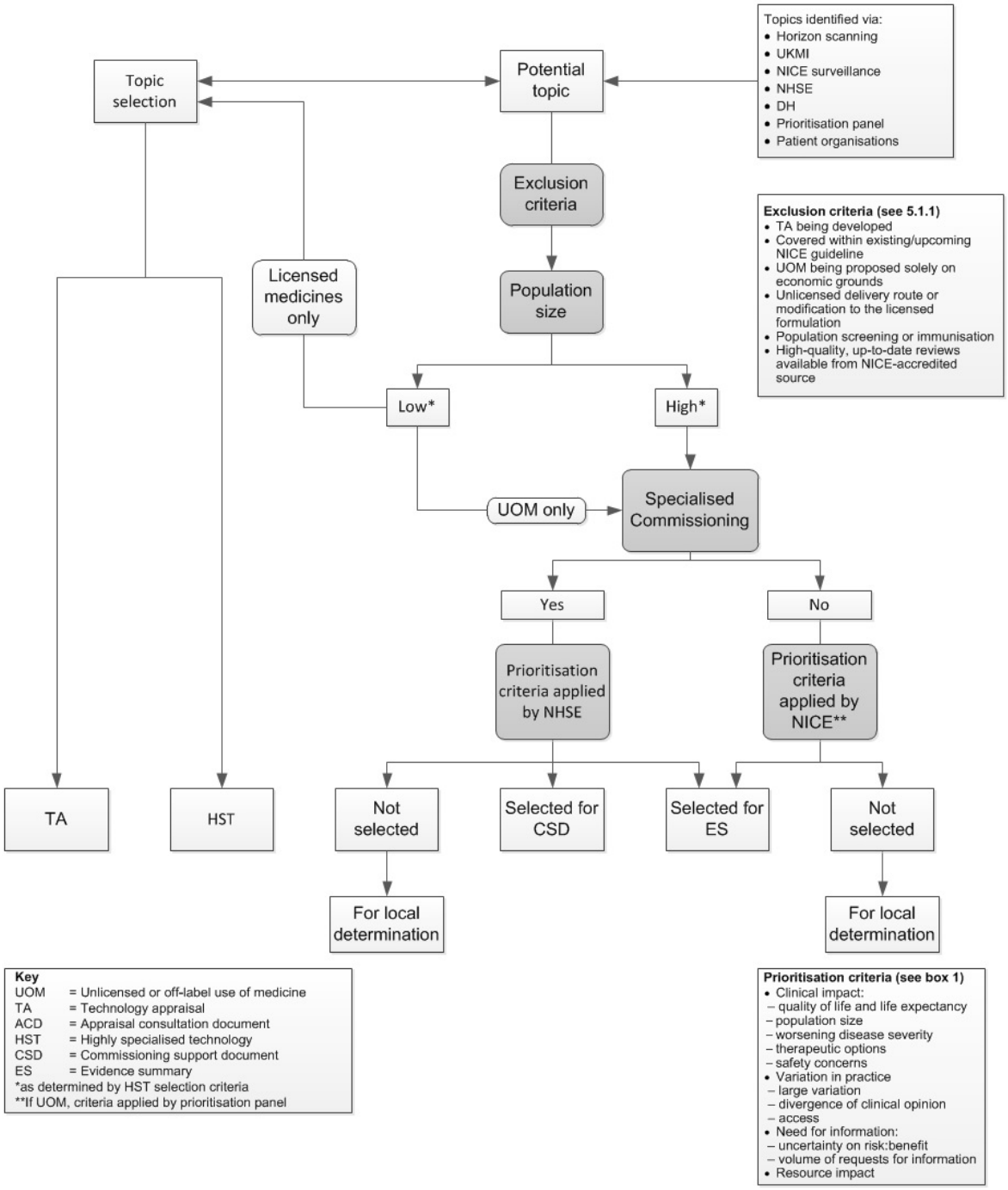
5 Topic identification, prioritisation and selection

NICE's medicines and technologies programme (MTP) is responsible for managing topic identification, prioritisation and selection for evidence summaries.

5.1 Topic identification

Topics for evidence summaries can be identified through several different routes (see figure 1).

Figure 1 Overview of evidence summary topic identification and selection



Suggestions for topics are invited from NHS England, the wider NHS, partner organisations, patient groups and groups identified through the MTP surveillance activities. Potential topics must not meet any of the exclusion criteria for topic identification (see section 5.1.1). A long list of potential evidence summary topics is compiled.

5.1.1 Exclusion criteria for topic identification

Exclusion criteria are designed to filter out topics that are not suitable for developing into an evidence summary and to ensure that each topic selected will add value. The exclusion criteria are applied to the long list of potential topics.

Exclusion criteria

If a potential topic meets any of the following criteria, an evidence summary will not be developed:

- The topic has been prioritised and referred for development into technology appraisal guidance and the appraisal consultation document will be published within 6 months of the medicine's launch.
- The topic is already covered by an existing NICE guideline or one that is currently in development and will be published in the next year.
- The use of the unlicensed or off-label medicine instead of licensed alternatives is being proposed solely on economic grounds.
- The topic relates to the use of a licensed medicine for a licensed indication but by an unlicensed delivery route or in a modification to the licensed formulation.
- The topic covers population screening or immunisation (these are normally evaluated by organisations other than NICE).
- High-quality, up-to-date reviews are already available from a NICE-accredited source, for example, the Scottish Intercollegiate Guidelines Network (SIGN).

5.2 Topic prioritisation

Topics referred directly from NHS England will be prioritised. Topics identified through other routes will be prioritised using the following criteria:

Box 1 Criteria for prioritising topics for NICE evidence summaries

The following indicate when a topic will be prioritised:

Clinical impact:

- high potential that the medicine (if effective) will significantly improve the quality of life and life expectancy for the people in whom it might be used
- likely large population size affected
- worsening disease severity without the medicine
- few existing therapeutic options
- potential safety concerns with the medicine

Variation in practice:

- large variation in clinical practice
- significant divergence of clinical opinion
- reports of difficulty of access to the unlicensed medicine or off-label use of the medicine

Need for information:

- considerable uncertainty exists on the risk:benefit balance of the medicine
- high volume of requests from the NHS for information on the topic

Resource impact:

- likely significant resource impact of using the medicine

Prioritisation criteria (see box 1) are applied by either NICE's MTP topic selection group or, for unlicensed or off-label use of medicines, by NICE's MTP prioritisation panel. The purpose of this stage is to engage with those who have a role in managing the introduction of medicines to healthcare communities, with their advice informing the selection of a topic for development into an evidence summary. A final, prioritised list of topics is then compiled by NICE's MTP.

5.3 Approval of topic for evidence summary

NICE's Director of Health and Social Care reviews the final list of potential evidence summaries and approves the topics which NICE should develop into evidence summaries. Once approved, the pharmaceutical companies that manufacture the medicines are informed of the intention to

develop the evidence summaries and the topics are added to the NICE guidance and advice in development list on the NICE website.

6 Development

NICE's medicines and technologies programme (MTP) develops an evidence summary for each of the approved topics.

6.1 Equality and diversity considerations

Evidence summaries are developed in accordance with NICE's equality and diversity and conflict of interest policies.

6.2 Process and timescales

Table 1 shows the key steps in the development of evidence summaries. The rapid development process reflects their status as advice products as well as the timescale in which the advice is needed.

Table 1 Key steps for developing an evidence summary (with timelines)

Key step	Project time allocated	Calendar week
Agree final scope, send search request to guidance information services and contact the pharmaceutical company for data	5 days	1
Searching for evidence	10 days*	3
Sifting and selecting the evidence Appraising and categorising the evidence Produce initial draft	15 days*	6
Internal check of initial draft	5 days*	7
Review comments received and produce revised draft for external/ specialist review	3 days*	8
Revised draft sent for review to pharmaceutical company or companies, specialist commentators, NICE guidelines team, NICE technology appraisals team and MHRA (for unlicensed or off-label use of medicines only)	10 days*	10

Review comments received and produce revised draft for technical check	2 days	10
Technical check of content by medicines adviser	4 days	11
Review comments received and produce revised draft for sign-off	3 days	12
Sign-off of content by Associate Director/ Clinical Adviser/Programme Director	5 days	13
Review comments received and produce revised draft for NICE's Guidance Executive. Pharmaceutical company invited to check for any remaining factual errors and informed of date that the evidence summary will be published	1 day	13
Final sign-off and publication of the evidence summary		
Guidance Executive sign-off	3 days	14
Review Guidance Executive's comments and produce final draft for publication	5 days	15
Publication on NICE website	5 days	16
Total	**76 days**	

Occasionally commissioners may need the evidence summary to be prioritised and developed over a more rapid time frame; key steps of the process may be carried out more quickly (*denotes where time frames may differ).

6.3 Scoping of individual topics

NHS England provides the scope for any topics they refer to NICE; the scope is then agreed by NICE.

For those topics selected by other routes, the MTP scopes each topic, supported by NICE's guidance information services. The scoping process confirms the following:

- key contacts at the pharmaceutical company
- key contacts at the MHRA (for unlicensed or off-label use of licensed medicines only)

- external specialist commentators (through NICE's medicines and prescribing associates and other existing NICE networks, see section 3.3)
- terms for a literature search to identify published data from clinical trials that reflect the indication or possible indication for the medicine
- arrangements for identifying:
    - regulatory status
    - indication or likely indication
    - likely licensing and marketing timeline, if appropriate
    - evidence of clinical effectiveness for the condition under consideration
    - safety issues, encompassing key adverse drug reactions, precautions and contraindications with an indication of frequency of the adverse effects if possible
    - likely place in therapy
    - incidence and prevalence of condition (or likely indication), what treatment alternatives exist and an estimate of current medicine usage
    - cost of the medicine and course of treatment, and the cost of alternative treatment options.

6.4 Contacting the pharmaceutical company

NICE asks the pharmaceutical company to support the production of the evidence summary by providing any of the following data it holds:

- key published clinical trials relating to the indication being reviewed in the evidence summary and information about ongoing or recently completed studies
- key clinical trials that are ongoing or that have been completed but not yet published in full
- approved name and brand name
- the licence status within the European Union or the UK, including whether or not the pharmaceutical company expects to hold a UK marketing authorisation for the medicine for this indication within the next 2 years or knows that another pharmaceutical company is likely to have a medicine licensed in the UK for this indication within 2 years

- the usual dose, if known, or best estimate from the available data
- the presentation of the medicine, including form, strength and pack size.

In addition for new medicines:

- licensed (or likely) indication
- estimated usage
- expected cost (for medicines not yet available).

6.5 Literature search

6.5.1 Searching for evidence

A literature search is conducted by NICE's guidance information services according to the agreed scope and strategy. The search strategy and quality assurance of the search process is documented for audit purposes.

The purpose of the literature search is to find the best available (highest quality) published evidence relating to the efficacy, safety and cost effectiveness of the medicine. In addition, explicit reference is made to information in the summary of product characteristics (if there is one) relating to precautions, warnings and undesirable effects and also to published advice from the medicine regulators. Cost information is obtained from:

- NHS Drug Tariff (price at which NHS reimburses medicines, updated monthly)
- Drugs and pharmaceutical electronic market information (eMIT; for medicines predominantly used in secondary care)
- Dictionary of medicines and devices (DM+D; lists medicines and devices with information from the same sources as the Drug Tariff [NHS Business Services Authority] so mainly useful for devices, updated weekly)
- MIMS (may be needed for new medicines, where costs are not available elsewhere)
- British national formulary (BNF) or BNF for children (BNFc).

6.5.2 Selecting the evidence

Evidence identified from the literature search is reviewed to find relevant primary research that addresses the use of the medicine within the defined indication and population under review. If robust randomised controlled trials or systematic reviews are available, they form the basis of the review. However, given the nature of the work, the best available evidence on which to produce the evidence summary may include evidence other than randomised controlled trials.

First sift

The first sift reviews the title and abstract of the study against the search terms and removes evidence of low relevance.

Second sift

The second sift excludes articles that are out of scope, such as:

- non-English language studies
- articles with no abstract or full text freely available online
- conference abstracts[3]
- studies that have not been published in full[3].

The best available evidence is then selected (usually no more the 3 studies) by prioritising according to the following:

- whether patient-oriented outcomes[4] 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 (such as number of study participants)
- date of publication.

Brief details of lower priority evidence may be included in the evidence summary to add context.

The MTP records those studies that are excluded in the first and second sift. Reasons for non-inclusion of evidence from the second sift are published in the evidence summary.

6.5.3 Appraising and categorising the prioritised evidence

The MTP appraises the prioritised evidence using a NICE quality assessment checklist suitable for the type of evidence being reviewed. If a European public assessment report (EPAR) or other national public assessment report (PAR) has been published, it is used to supplement the information included in published study reports, if needed.

All included studies are appraised using a grading process where appropriate. Alternatively, a narrative of the relative quality of the evidence is provided.

6.6 Writing the evidence summary

The MTP drafts the evidence summary using a standard template, which includes sections relating to the following:

- overview, including:
    - regulatory status
    - key points
    - framework to inform local decision-making
- introduction and current guidance
- product overview
    - mode of action
    - regulatory status
    - dosing information
    - cost
- evidence review
    - clinical effectiveness

  - safety and tolerability
  - evidence strength and limitations
- estimated impact for the NHS
  - alternative treatment(s) or medicine(s)
  - costs of alternative treatment(s) or medicines(s)
  - current or estimated usage
  - likely place in therapy
- information for the public
- relevance to other programmes
  - NICE guidance programmes
  - NHS England commissioning policies
- references
- evidence tables
- excluded studies
- search strategy
- development of this evidence summary
  - expert advisers
  - declarations of interest.

6.7 Review of the draft evidence summary

The draft evidence summary is sent by the MTP to the identified external specialist reviewers, the pharmaceutical company or companies, NICE's guidelines team, NICE's technology appraisals team and the MHRA for review. The summaries are also sent to the commissioner for comment.

Any comments received are considered when revising the draft. Actions are also recorded. Feedback to commentators is available on request to NICE.

6.8 Quality assurance of the evidence summary

The evidence summary is quality assured by the MTP. This involves a detailed check of all content, to ensure all sections contain statements and conclusions that are fair and balanced. The evidence summary must accurately reflect the evidence reviewed and be substantiated by an explicit and appropriate source of evidence.

Once sign-off is received from the MTP Programme Director, Clinical Adviser or Associate Director, the pharmaceutical company is given the opportunity to review the near-final draft to check for any factual errors (1 working day) and any necessary corrections are made by the MTP.

NICE's Guidance Executive reviews the evidence summary and, if appropriate, approves the evidence summary for publication, ensuring that due process has been followed in its development. The pharmaceutical company is informed of the scheduled publication date, and may request an embargoed copy of the evidence summary to be sent to them 24 hours before publication.

6.9 Publication of the evidence summary

The final evidence summary is disseminated through the medicines and prescribing alert service, and uploaded and made available online through the guidance and advice list on the NICE website.

[3] 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 evidence summary may indicate if key clinical trials are ongoing or have been completed but not yet published in full.

[4] 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.

7 Review and update

Every evidence summary includes the date of publication and a link to the British national formulary, summary of product characteristics, and NICE website with a reminder to consult these sources for up-to-date information on the topic. The need to withdraw an evidence summary is considered by the MTP on an ongoing basis as part of its current awareness activities (see Medicines and Prescribing Alerts on the NICE website). In addition, guidance information services will conduct an annual search for licence changes that relate to unlicensed or off-label use of medicines. Examples of circumstances when an evidence summary may be withdrawn include:

- If a NICE technology appraisal or guideline that relates to the medicine and indication reviewed in the evidence summary is published.
- A product obtains a licence for the indication that the evidence summary has reviewed where previously this was an unlicensed or off-label use. The medicine will then be considered as a potential topic for NICE technology appraisal guidance in line with the NICE topic selection process.

8 About this process guide

This process guide provides an overview of the process for developing evidence summaries and is supported by Developing NICE guidelines: the manual, which outlines the processes and methods used to develop and update NICE guidelines.

For published evidence summaries, see the NICE website.

ISBN: 978-1-4731-2329-8