Technology Appraisals

Optimising Success for Access to Rare Disease Treatments

Rare Disease Research Partners

Serving rare disease communities

Welcome

Dr Tom Kenny
Chief Executive Officer

Rare Disease Research Partners and is a wholly owned, not for profit subsidiary of the Society for Mucopolysaccharide Diseases (the MPS Society), Registered Charity in England and Wales No 1143472.

Rare Disease Research Partners social objectives are to reinvest any surplus to support the mission of the MPS Society to transform the lives of patients through specialist knowledge, support, advocacy and research.

Rare Disease Research Partners

Alex Morrison
Head of Research and Medical Communications

Sam Wiseman
Managed Access Agreement Coordinator

Technology appraisals webinar

- Please do not record this webinar
- Please do not take screenshots
- Please do not reproduce slides without the speaker's consent
- We will have a Q&A session at the end, please send in your questions via the Q&A function
- This webinar is being recorded and will be available on our website rd-rp.com

Technology appraisals webinar

Our aim is to support access to treatments in rare diseases through the collection of high quality patient and caregiver experience data

Agenda

- The technology appraisal landscape
- Overcoming hurdles in the NICE process
- Considerations for a successful Managed Access Agreement
- Beyond the company submission
- Questions

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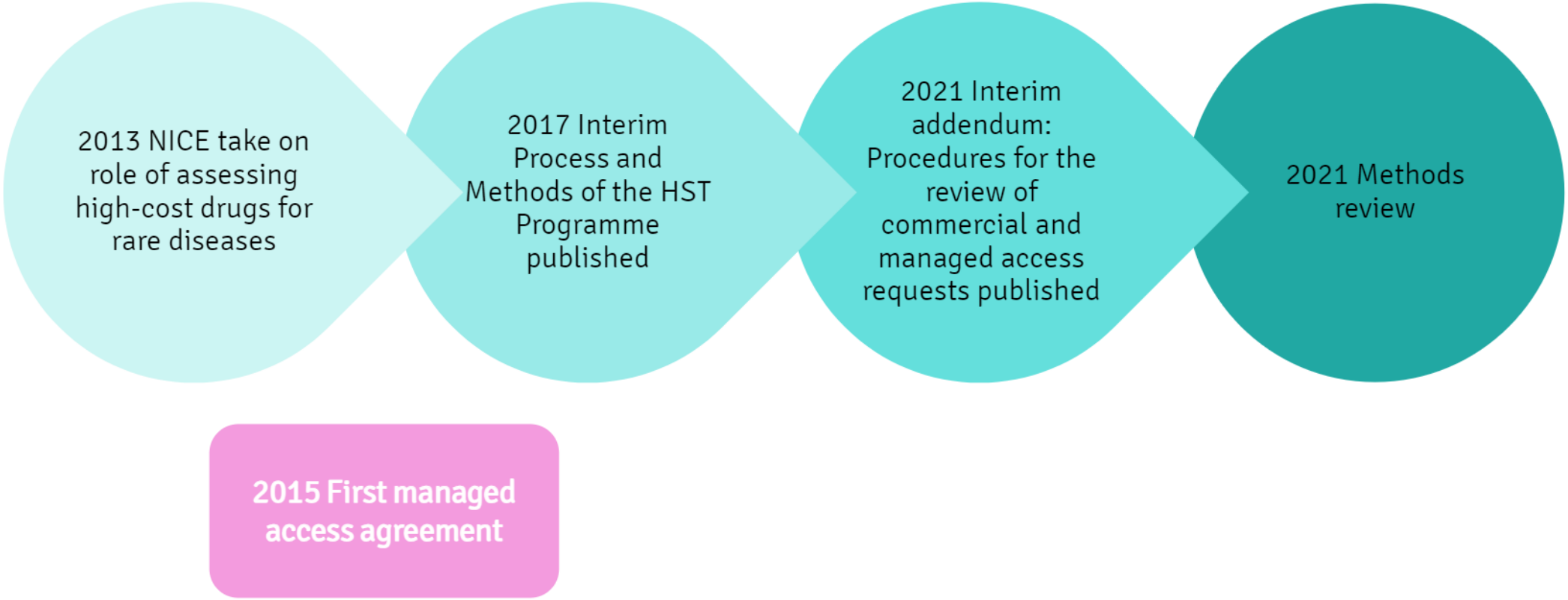
The Technology Appraisal Landscape

Overview of technology appraisal in rare disease

- Technology appraisals
  - This guidance assesses the clinical and cost effectiveness of health technologies
- Highly specialised technologies (HST)
  - This guidance contains recommendations on the use of new and existing highly specialised medicines and treatments

NICE. Highly specialised technologies guidance. [Internet]. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-highly-specialised-technologies-guidance. [Accessed on 27th September 2021].

The evolving HST appraisal landscape



Current criteria for a HST

All must apply:[1]

- The target patient group for the technology in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS
- The target patient group is distinct for clinical reasons
- The condition is chronic and severely disabling
- The technology is expected to be used exclusively in the context of a highly specialised service
- The technology is likely to have a very high acquisition cost
- The technology has the potential for life long use
- The need for national commissioning of the technology is significant

1. NICE. Interim Process and Methods of the Highly Specialised Technologies Programme Updated to reflect 2017 changes. April 2017. Available from: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf. [Accessed on 27th September 2021]

Methods review: proposed new HST criteria

To be considered for HST, 4 criteria must be met:

- The condition is very rare: defined by 1:50,000 in England
- Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications
- The very-rare condition significantly shortens life or severely impairs its quality
- No satisfactory treatment options exist, or, if it does, the technology is likely to be of significant benefit to those affected

Identification of HST topics

- NICE only consider drugs for very rare conditions
- Most topics identified by the National Institute for Health Research Innovation Observatory
- They aim to notify the Department of Health and Social Care of key, new and emerging healthcare technologies that might need to be referred to NICE against the following timeframes:
  - New drugs, in development, at 20 months to marketing authorisation
  - New indications, at 15 months to marketing authorisation
- A single highly specialised technology evaluation can only cover a single technology for a single indication

NICE. Highly specialised technologies guidance. [Internet]. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-highly-specialised-technologies-guidance. [Accessed on 27th September 2021]

Current HST process

1 Provisional evaluation topics chosen

The Department of Health and Social Care (DHSC) produces a list of provisional evaluation topics.

2 Consultees and commentators identified

3 Scope prepared

NICE works with the DHSC to develop a scope. The scope defines the disease, the patients and the technology covered by the evaluation and the questions it aims to answer. Consultees and commentators are requested to comment on the draft scope.

4 Evaluation topics referred

The DHSC refers HST evaluation topics to NICE.

5 Evidence submitted

The manufacturer or sponsor of the technology is invited to provide an evidence submission. NICE also invites all non-manufacturer consultees to submit a statement on the potential clinical effectiveness and value for money of a treatment.

6 Evidence Review Group (ERG) report prepared

NICE commissions an independent academic centre to technically review the evidence submission and prepare an ERG report.

7 Evaluation report prepared

This includes all of the evidence that will be looked at by the Evaluation Committee. This evidence includes:

- the ERG report and any comments received on it
- written submissions
- personal statements from patient experts and clinical specialists.

NICE. Highly specialised technologies guidance. [Internet]. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-highly-specialised-technologies-guidance. [Accessed on 27th September 2021]

Current HST process

8 Evaluation Committee

An independent advisory committee considers the evaluation report and hears evidence from nominated clinical experts, patients and carers. Evaluation Committee discussions are held in public.

9 Evaluation consultation document (ECD) produced if needed

The Evaluation Committee makes its provisional recommendations in the ECD. An ECD will be produced only if the recommendations from the Evaluation Committee are restrictive. A restrictive recommendation will be one that is more limited than the instructions for use that accompany the technology. Consultees and commentators have four weeks to comment on the ECD. The ECD is also made available on our website so health professionals and members of the public can comment on it.

10 Final evaluation determination (FED) produced

The Evaluation Committee considers the comments on the ECD if produced, then makes its final recommendations in the FED on how the technology should be used in the NHS in England. Consultees can appeal against the final recommendations in the FED.

11 Guidance issued

If there are no appeals, or an appeal is not upheld, the final recommendations are issued as NICE guidance.

NICE. Highly specialised technologies guidance. [Internet]. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-highly-specialised-technologies-guidance. [Accessed on 27th September 2021]

Supporting evidence generation

Horizon scanning

Evidence generation and advice

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- Managed access agreements
- Caregiver and patient surveys
- Patient organisation support
- Clinical forums

Stakeholder submissions

- Patient experts
- Clinical experts

Company submissions

- Clinical trials and supporting evidence
- Managed access data

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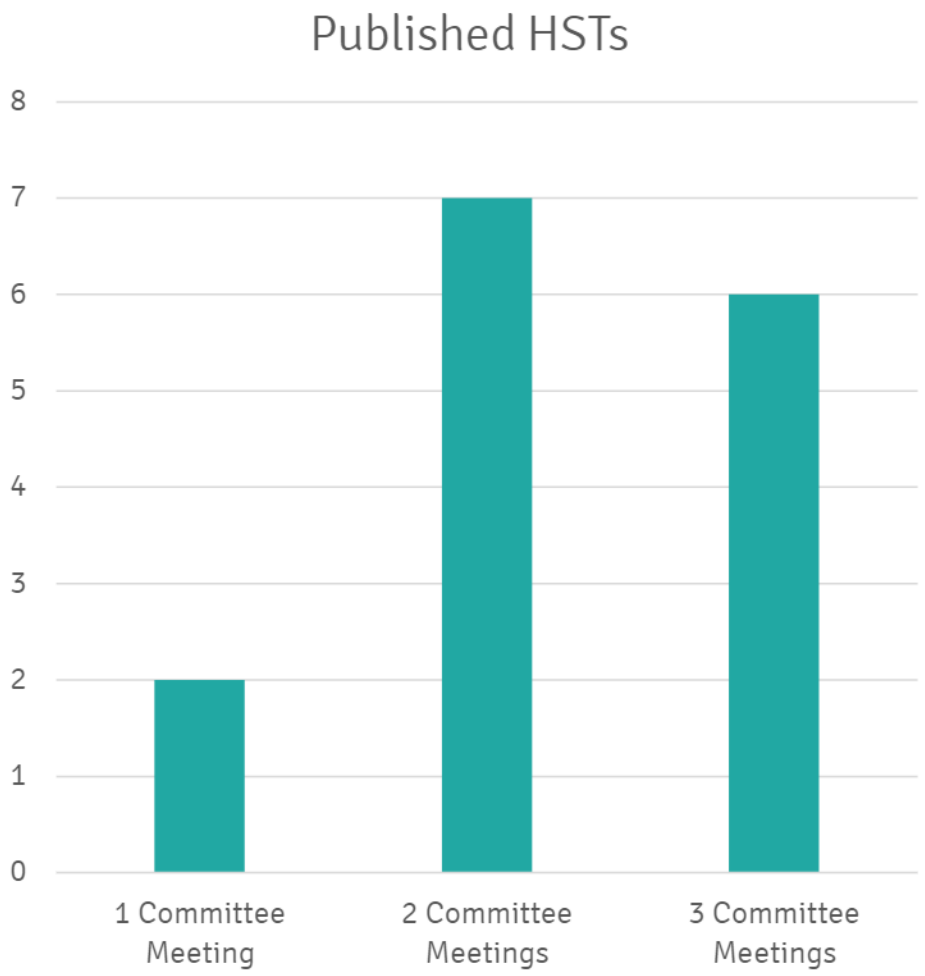
Overcoming hurdles in the NICE process

Part 1

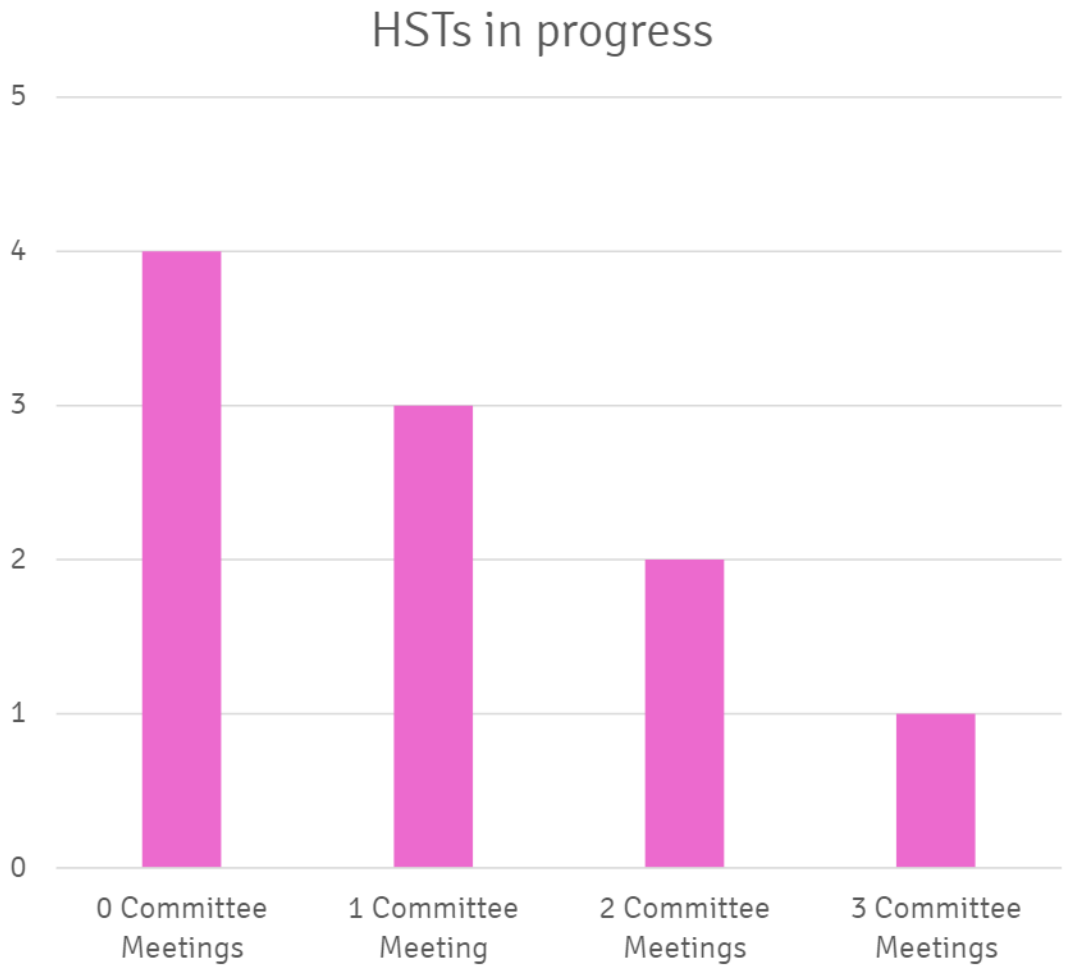
HST outcomes



- 15 HSTs are published
- All are recommended
- 4 in Managed Access Agreements
- 6 had 3 committee meetings
- 3 involved appeals

NICE. Guidance and advice list. [Internet]. https://www.nice.org.uk/guidance/published?type=hst. [Accessed on 27th September 2021]

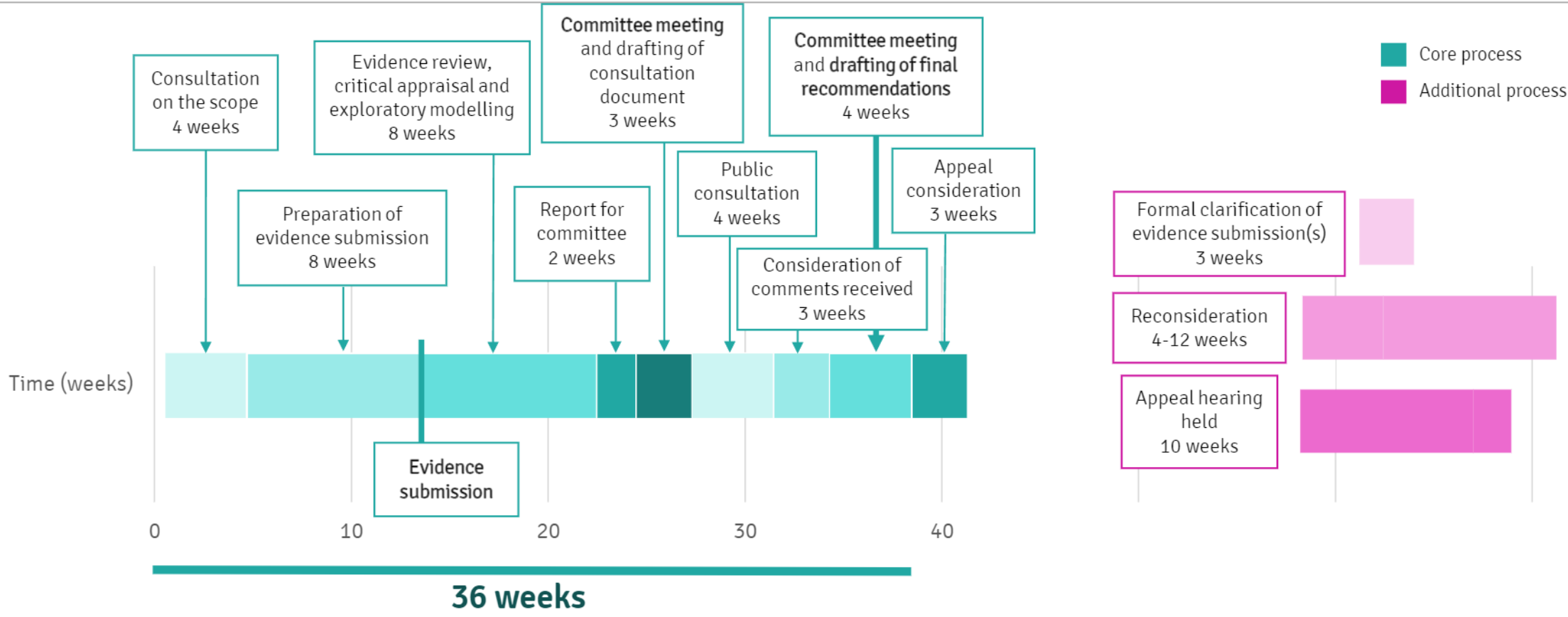
HST outcomes



- 10 HSTs in progress
- 1 involved an appeal
- In addition:
  - Sebelipase alfa for LAL-D – several committee meetings and an appeal, re-entered the process for Wolman's disease
  - Elosulfase alfa evaluation following a period of managed access
  - 3 treatments did not receive marketing approval
  - 1 withdrawn from EMA

NICE. Guidance and advice list. [Internet]. https://www.nice.org.uk/guidance/indevelopment?type=hst. [Accessed on 27th September 2021]

HST timeline



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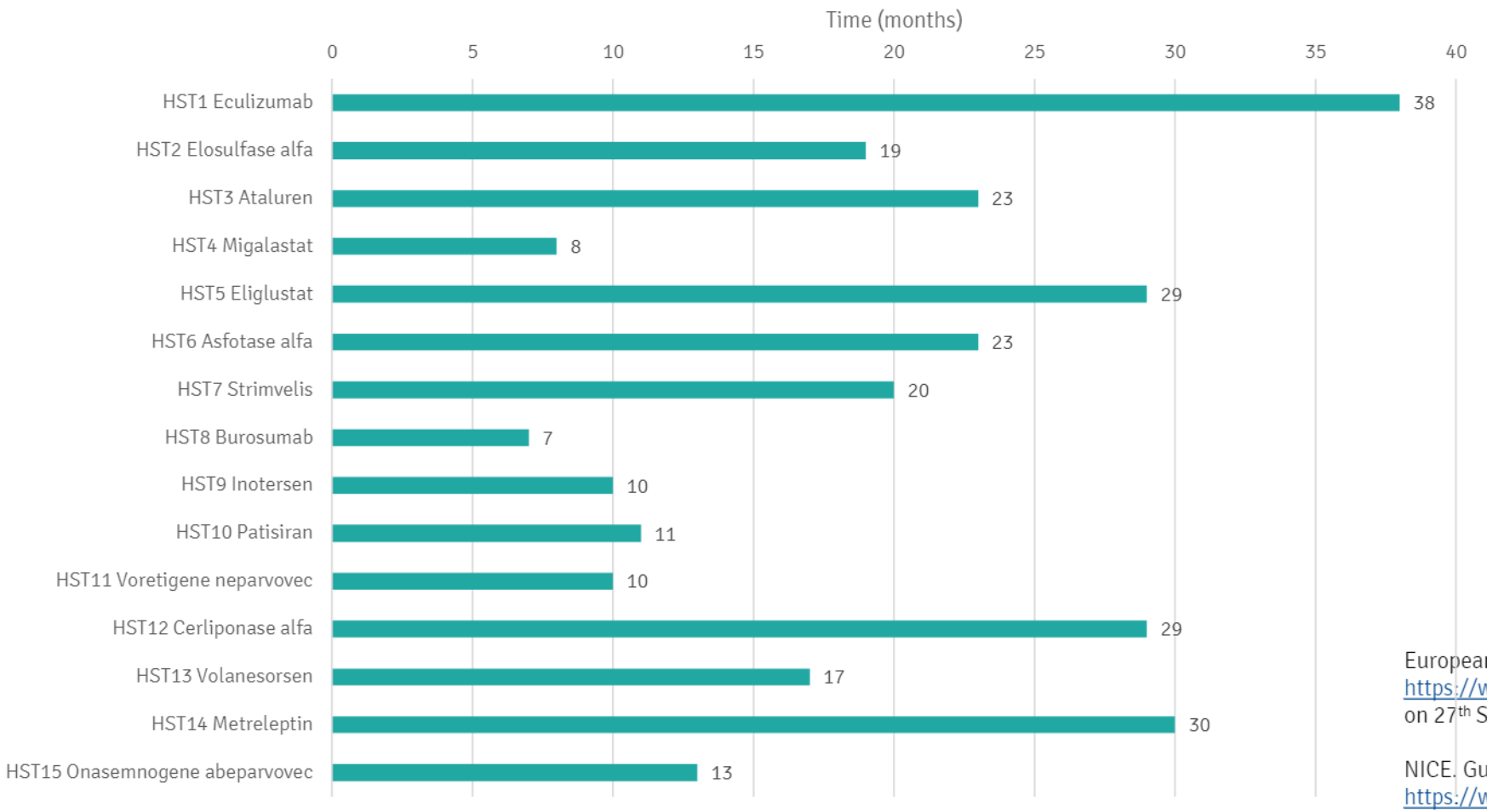
HST timeline

- Draft recommendations cannot be published without receipt of marketing authorisation for the technology
- They are anticipated to be issued within 4 months of confirmation from the European Commission that a marketing authorisation has been granted

NICE. Interim Process and Methods of the Highly Specialised Technologies Programme Updated to reflect 2017 changes. April 2017. Available from: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf. [Accessed on 27th September 2021]

Time from EMA approval to publication of NICE guidance

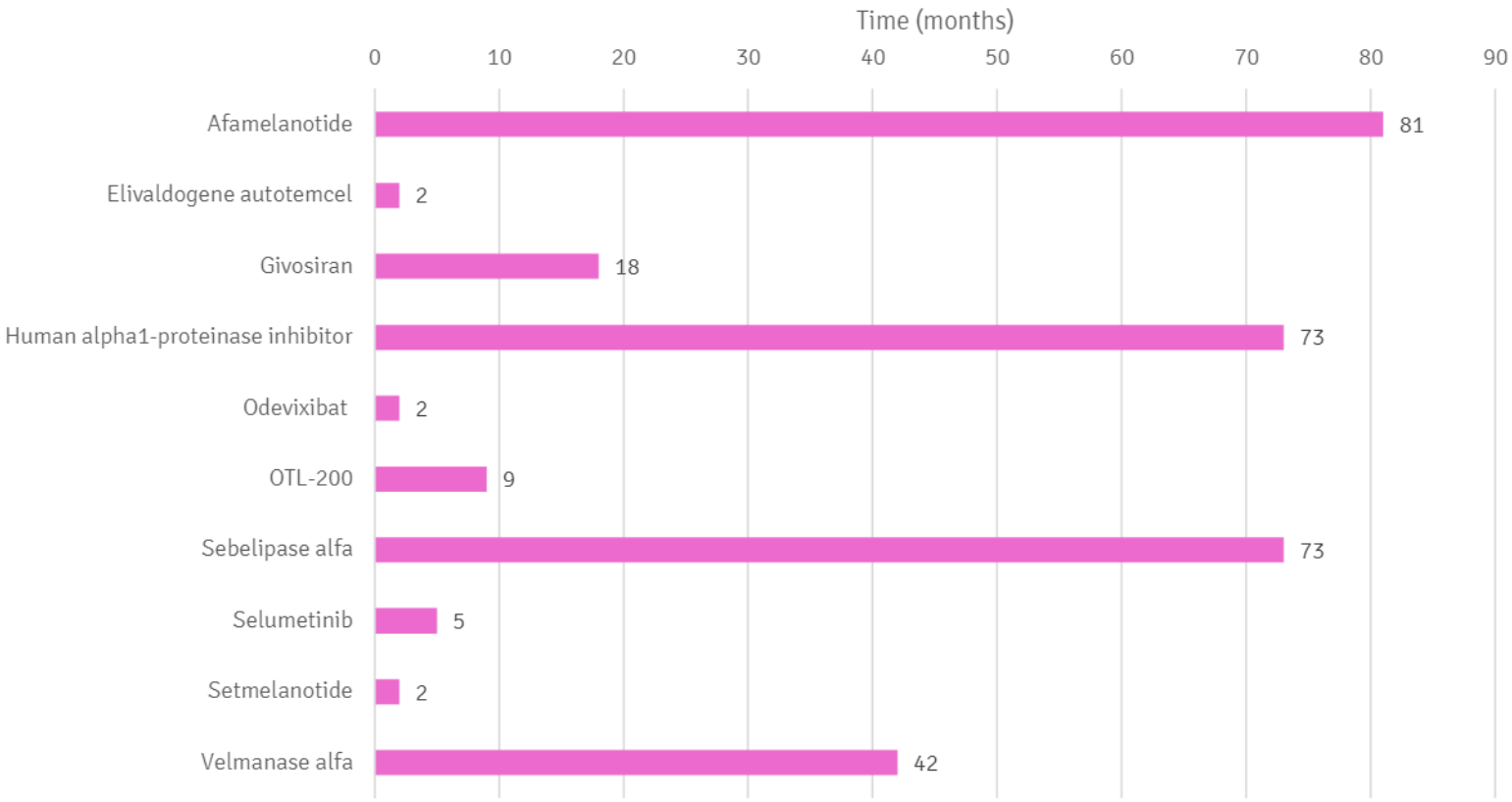


Mean: 19 months

European Medicines Agency. Medicines. [Internet]. https://www.ema.europa.eu/en/medicines. [Accessed on 27th September 2021]

NICE. Guidance and advice list. [Internet]. https://www.nice.org.uk/guidance/published?type=hst. [Accessed on 27th September 2021]

Time from EMA approval – HSTs in progress



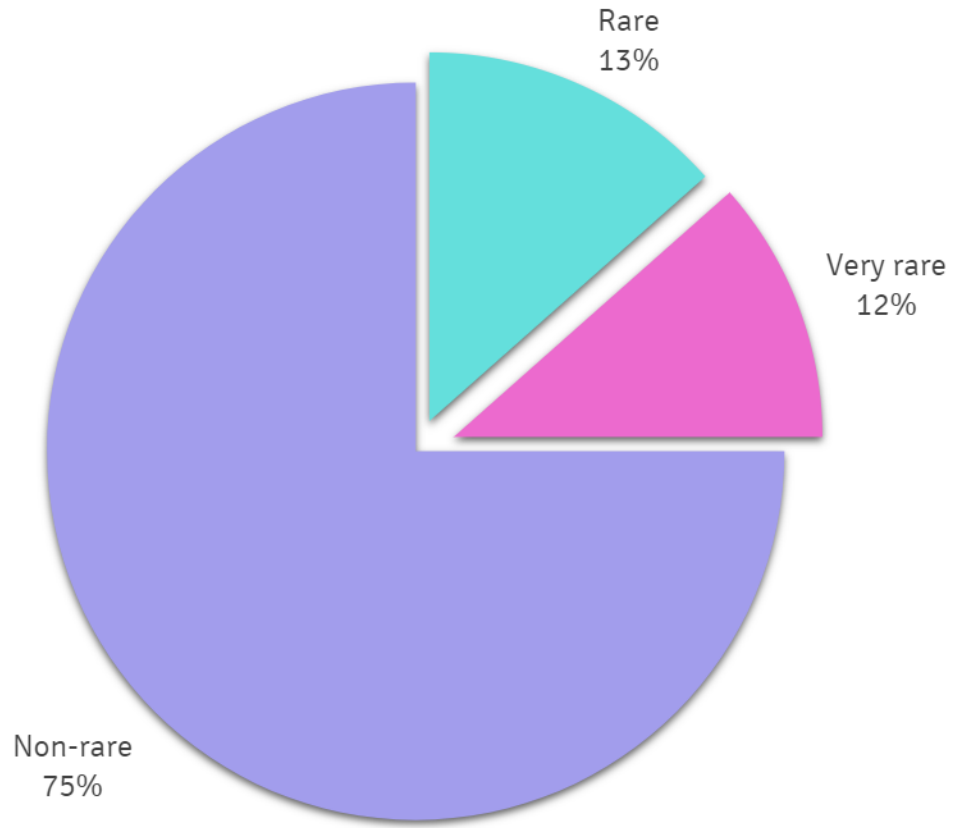
Mean: 31 months

European Medicines Agency. Medicines. [Internet]. https://www.ema.europa.eu/en/medicines. [Accessed on 27th September 2021]
NICE. Guidance and advice list. [Internet]. https://www.nice.org.uk/guidance/indevelopment?type=hst. [Accessed on 27th September 2021]

Technology appraisals (TA)

- 52 TAs published in 2021
  - 6 very rare
  - 7 rare
  - 39 non-rare

- Very rare 1:50,000*
- Rare 1:2,000**

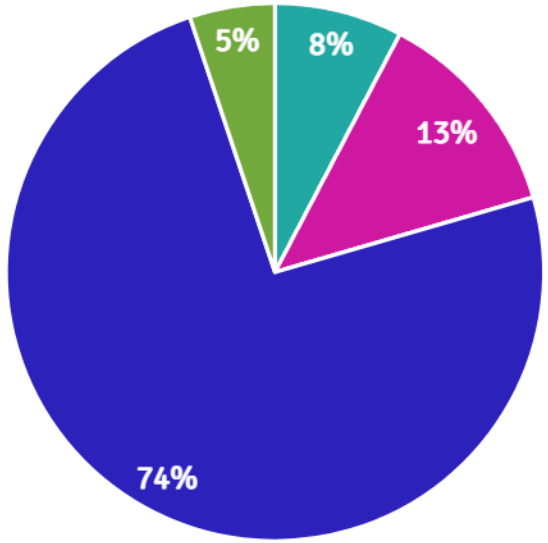


*definition from NICE Methods Review 2021, **European Commission definition

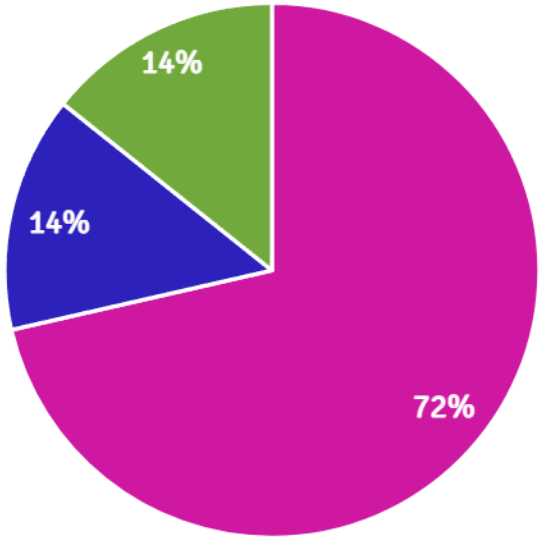
NICE. Guidance and advice list. [Internet]. https://www.nice.org.uk/guidance/published?type=ta. [Accessed on 27th September 2021]

TA outcomes in 2021

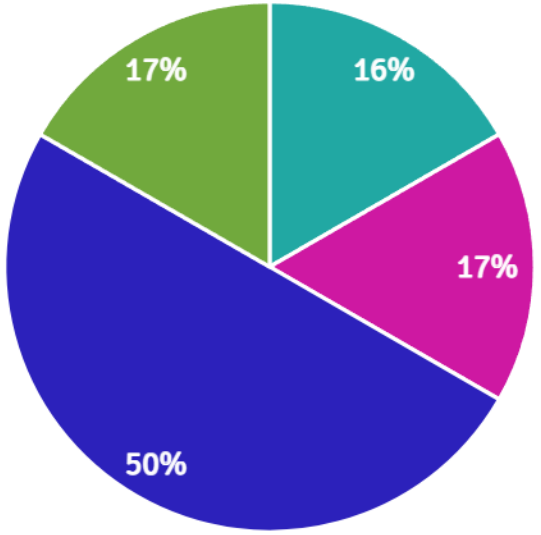
Non-rare (n=39)



Rare (n=7)



Very rare (n=6)



- Not Recommended
- Terminated Appraisal
- Recommended (NHS)
- Recommended (Cancer Drugs Fund)

- Not Recommended
- Terminated Appraisal
- Recommended (NHS)
- Recommended (Cancer Drugs Fund)

- Not Recommended
- Terminated Appraisal
- Recommended (NHS)
- Recommended (Cancer Drugs Fund)

NICE. Guidance and advice list. [Internet]. https://www.nice.org.uk/guidance/published?type=ta. [Accessed on 27th September 2021]

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Overcoming hurdles in the NICE process

Part 2

Published HSTs – outcome of first committee meeting

Reasons given for not recommending

Evidence of benefit

- 1.3 The Committee recommends that NICE requests further clarification from the company on the size of the benefit for patients, carers and family members .
- However, the Committee believed that, given the designs of the trials and several issues with the natural history data, there was considerable uncertainty around the robustness of the results and the precise size of the benefit
- The committee noted the clinical-effectiveness evidence, and considered that a robust comparison with conventional therapy could not be made based on the evidence presented

Sub-population evidence

- in people with poor metaboliser status, but was mindful of the very limited evidence base for this population.
- It was not convinced that the potential of benefit with asfotase alfa was the same for all people with juvenile-onset hypophosphatasia. This was supported by the clinical experts, who stated that they were not certain about how this population would be treated in clinical practice.

Start and stop criteria

- The Committee requests that the company and NHS England provide further details of the criteria for starting and stopping treatment in clinical practice

Excerpts from evaluation consultation documents HSTs 2–8.
NICE. Guidance and advice list. [Internet]. https://www.nice.org.uk/guidance/published?type=hst. [Accessed on 27th September 2021]

Published HSTs – outcome of first committee meeting

Reasons given for not recommending

Cost

- The Committee requests that the company provides a further explanation of the cost
- However, the Evaluation Committee has not yet been presented with an adequate justification for its considerable cost, in light of the available evidence of its effect on health outcomes relevant for patients, carers and family members
- The Committee also recommends that NICE requests the company to provide further justification for the cost
- The committee was mindful, however, of the substantial additional costs compared with ERT
- The committee was not convinced that these [costs] could be justified solely based on the benefits of an oral treatment
- The committee had concerns about the true value for money
- . The Committee highlighted that it had not been given enough justification for the high cost per person of asfotase alfa, or for the overall cost of asfotase alfa in terms of what could be expected to be reasonable in the context of a highly specialised service

Economic analysis

- The Committee requests that the company provides additional economic analyses
- The Committee thought that the company's budget impact and cost–consequence model substantially underestimated the costs associated with asfotase alfa compared with best supportive care given the uncertainty around the model structure and several of the company's assumptions
- the ICERs were above the range that can be considered an effective use of NHS resources for highly specialised technologies, and emphasised that they were also uncertain

Excerpts from evaluation consultation documents HSTs 2–8.
NICE. Guidance and advice list. [Internet]. https://www.nice.org.uk/guidance/published?type=hst. [Accessed on 27th September 2021]

The challenges of evidence generation

- Evidence from small populations
- Choosing the right QoL measures
  - Is a validated disease specific tool available?
- What impacts of treatment are most meaningful to patients?
  - Ask the patient
  - How can you measure these benefits?
- Is there sufficient evidence for entering a managed access agreement?
- The importance of patient and clinical expert evidence

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Considerations for a successful managed access agreement

What is a Managed Access Agreement (MAA)

- Data collection agreement of clinical and PRO data to address concerns raised by NICE Evaluation Committee when reviewing the data

- Allows patients to access the technology while additional data is gathered to facilitate a re-evaluation of the technology at the end of the MAA

- Considered when a technology is evaluated through the Highly Specialised Technology pathway and the "evidence of clinical effectiveness or impact on other health outcomes is either is absent, weak or uncertain"[1]

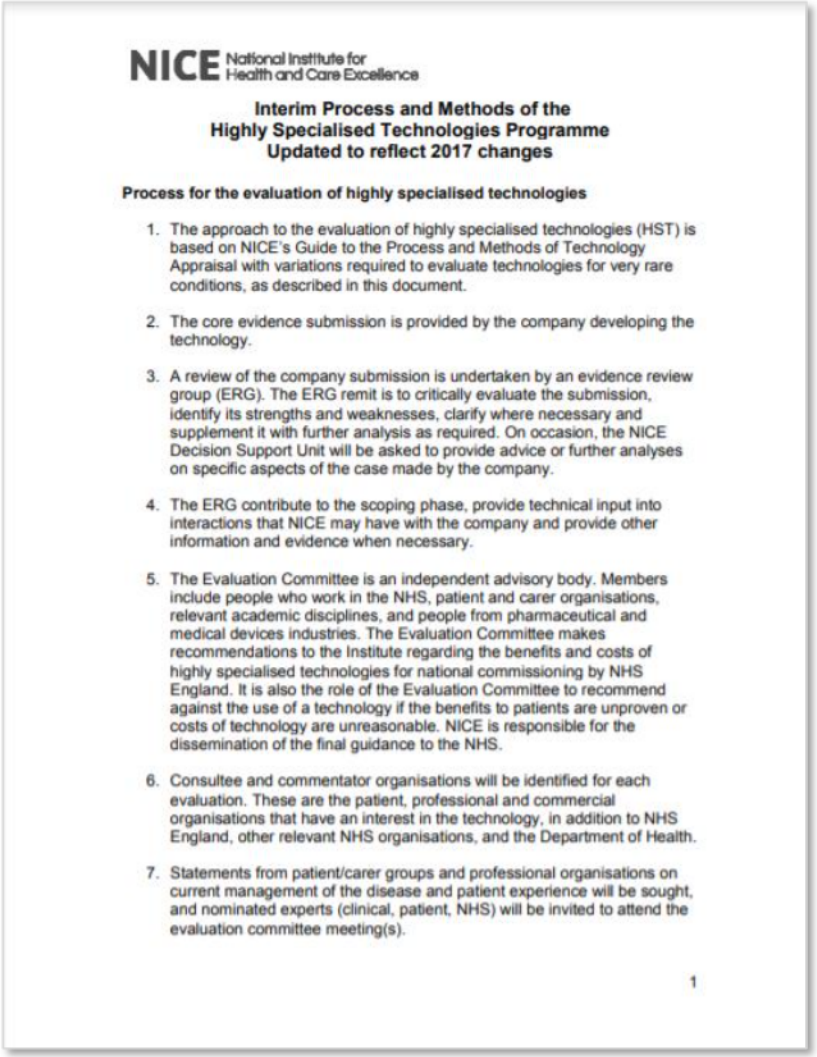
- 4 MAA's currently in progress
  - HST 2 - Elosulfase alfa – MPS IVA
  - HST 3 – Ataluren – Duchenne muscular dystrophy with a nonsense mutation
  - HST 6 - Asfotase alfa - Paediatric-onset hypophosphatasia
  - HST 12 - Cerliponase alfa – CLN2

1. NICE. Interim Process and Methods of the Highly Specialised Technologies Programme Updated to reflect 2017 changes. April 2017. Available from: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf. [Accessed on 27th September 2021]

What is a Managed Access Agreement (MAA)

A MAA contains the following elements:

- A proposal that addresses a significant uncertainty in the evidence base identified by the evaluation Committee
- A duration of the arrangement, with a rationale, that is agreed by the key stakeholders
- Clearly defined starting and stopping criteria
- A list of outcomes for which data will be collected
- How data will be collected and analysed
- An agreement on how regular the outcomes in the MAA will be reviewed
- A statement that describes what will happen to patients receiving treatment who are no longer eligible for treatment if a more restricted or negative recommendation is issued after the guidance has been reviewed following data collection



NICE National Institute for Health and Care Excellence

Interim Process and Methods of the Highly Specialised Technologies Programme Updated to reflect 2017 changes

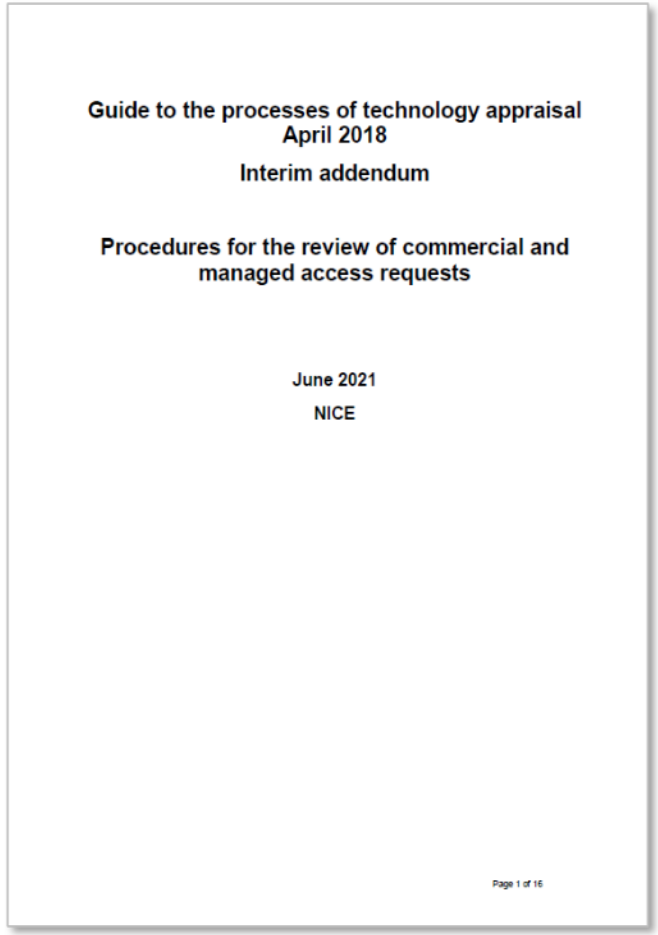
Process for the evaluation of highly specialised technologies

1. The approach to the evaluation of highly specialised technologies (HST) is based on NICE's Guide to the Process and Methods of Technology Appraisal with variations required to evaluate technologies for very rare conditions, as described in this document.
2. The core evidence submission is provided by the company developing the technology.
3. A review of the company submission is undertaken by an evidence review group (ERG). The ERG remit is to critically evaluate the submission, identify its strengths and weaknesses, clarify where necessary and supplement it with further analysis as required. On occasion, the NICE Decision Support Unit will be asked to provide advice or further analyses on specific aspects of the case made by the company.
4. The ERG contribute to the scoping phase, provide technical input into interactions that NICE may have with the company and provide other information and evidence when necessary.
5. The Evaluation Committee is an independent advisory body. Members include people who work in the NHS, patient and carer organisations, relevant academic disciplines, and people from pharmaceutical and medical devices industries. The Evaluation Committee makes recommendations to the Institute regarding the benefits and costs of highly specialised technologies for national commissioning by NHS England. It is also the role of the Evaluation Committee to recommend against the use of a technology if the benefits to patients are unproven or costs of technology are unreasonable. NICE is responsible for the dissemination of the final guidance to the NHS.
6. Consultee and commentator organisations will be identified for each evaluation. These are the patient, professional and commercial organisations that have an interest in the technology, in addition to NHS England, other relevant NHS organisations, and the Department of Health.
7. Statements from patient/carer groups and professional organisations on current management of the disease and patient experience will be sought, and nominated experts (clinical, patient, NHS) will be invited to attend the evaluation committee meeting(s).

1

Procedures for the review of commercial and managed access requests

- Published criteria in June 2021
- Describes the process that NICE will follow when considering a commercial and managed access (C&MA) request
- C&MA request containing a Managed Access Agreement include:
  - Data collection agreement
  - Commercial access agreement



Guide to the processes of technology appraisal
April 2018

Interim addendum

Procedures for the review of commercial and managed access requests

June 2021

NICE

Page 1 of 16

NICE. Guide to the processes of technology appraisal April 2018 Interim addendum. June 2021. Available from:https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/CMA-interim-process-addendum.pdf. [Accessed on 27th September 2021]

Considerations for a successful MAA

- Clear & robust data management process to handle data collected
- EQ-5D & other disease specific tools
- PRO & qualitative data collection
  - Don't underestimate the importance of PRO data and evidence collection
  - Completion via telephone rather than asking to self complete
- Patient friendly materials
  - Recommend producing guides/booklets on the MAA
  - Make translations available

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Beyond the company submission

Patient advocacy group submissions

- Submission template includes these questions
  - How did you gather information about the experiences of patients and carers to include in your submission?
  - What is it like to live with the condition? What do carers experience when caring for someone with the condition?
  - What do patients or carers think of current treatments and care available on the NHS?
  - Is there an unmet need for patients with this condition?
  - What do patients or carers think are the advantages of the technology?
  - What do patients or carers think are the disadvantages of the technology?
  - Are there any groups of patients who might benefit more or less from the technology than others? If so, please describe them and explain why.
  - Are there any other issues that you would like the committee to consider?

Patient advocacy group submissions

- Add context to the clinical trial data
- Can provide data not included in the company submission
- May need support to provide the expertise or resource to collect the information and report it

did not have treatment. Although many children who had OTL-200 were alive and well, siblings who had not had treatment had died or were very weak. The committee commended the patient organisations for the submissions providing detailed feedback from a survey on the effect of OTL-200 on quality of life. The company did not collect health-related quality-of-life data in its studies so some of these additional outcomes were not captured in the analyses. The ERG considered that the analyses

Excerpt from Evaluation consultation document. Available at: https://www.nice.org.uk/guidance/indevelopment?type=hst. [Accessed on 27th September 2021]

Clinical experts

- Two can provide submissions and attend committee meeting
- Value in gathering all the clinical experts together
- Can corroborate patient submission
- Additional insight to disease burden and patient outcomes with treatment

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Q&A

Please submit your questions using the Q&A function

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Thank you

28th September 2021