NICE National Institute for Health and Care Excellence

Supporting information

Highly specialised technologies NICE prioritisation board routing criteria

19 December 2024

What has changed?

The key changes that are proposed are:

- Directly linking each criterion to the HST vision; this should ensure that NICE meets the HST programmes aims
- Adding definitions to support the application of the criteria; this should support more objective routing decisions, improving the transparency and predictability of outcomes
- Adding a criterion on innovation

Illustrations of how the refined HST criteria are applied in practice, using historical technology appraisals and highly specialised technologies, or other illustrative examples.

Routing criterion 1:

The disease is ultra-rare and debilitating, that is, it:

- is defined as having a point prevalence of 1:50,000 or less in England (**NICE strategic principles for rare disease**)
- is lifelong after diagnosis with current treatment, and
- has an exceptional negative impact and burden on people with the disease.

Example where a genetic subtype is not clinically meaningful:

NOD2 mutation in Crohn's disease is a genetic subtype of Crohn's disease which adds no prognostic value to treatment decisions and outcomes (the genetic mutations do not change the response to specific treatment).

Routing criterion 2:

The technology is an innovation for the ultra-rare disease.

Historical example of a repurposed technology:

Anhydrous sodium thiosulfate for preventing ototoxicity induced by cisplatin chemotherapy in patients 1 month to less than 17 years of age with localised solid tumour. Sodium thiosulfate has been available for a long time for treating acute cyanide poisoning and therefore it is not an innovation. It was routed to the TA programme.

Historical example of where a technology had more than one indication with the same IDH1 R132 mutation:

Ivosidenib for treating advanced cholangiocarcinoma with an IDH1 R132 mutation, and ivosidenib with azacitidine for untreated acute myeloid leukaemia with an IDH1 R132 mutation. This did not meet the HST routing criteria, and both were routed to TA programme and received positive recommendations after evaluation - (TA948) and (TA979).

Routing criterion 3:

No more than 300 people in England are eligible for the technology in its licensed indication and the technology is not an individualised medicine.

Historical example of an extension of an existing indication:

Burosumab for treating X-linked hypophosphataemia in children and young people is an HST (HST8). Then, burosumab also extended its indication to adults. The extended indication for adults did not meet the HST routing criteria because this is an extension of an existing indication for another subgroup of

people with the ultra-rare disease and was routed to TA programme with a positive recommendation (TA993).

Example of an individualised medicine:

Patient-customized oligonucleotide therapy for a child with neuronal ceroid lipofuscinosis 7 (CLN7, a form of Batten's disease).

Routing criterion 4:

The technology is likely to offer substantial additional benefit for people over existing established clinical management, and the existing established clinical management is considered inadequate.

Example of a symptom unique to an ultra-rare disease:

A symptom unique to the ultra-rare disease is not a symptom like pain, wounds, seizures, weight gain (i.e., where other treatment options are available from other diseases with the same symptoms.

Frequently Asked Questions (FAQs)

1. What are Highly Specialised Technologies (HST)?

The Highly Specialised Technologies (HST) Programme evaluates technologies for ultra-rare, very severe and debilitating diseases that need the specific considerations by the programme.

The HST Programme aims to:

- encourage research on, and innovation for, ultra-rare diseases when there are challenges in generating an evidence base that is robust enough to bring the product to market
- secure fairer and more equitable treatment access for very small populations with ultra-rare diseases
- recognise that an approach that maximises health gain for the NHS may not always be acceptable: it could deliver results that are not equitable.

The HST routing criteria describe the exceptional circumstances in which technologies should be routed to highly specialised technologies guidance.

2. Why are you refining the HST criteria?

While substantial improvements were made to the existing HST routing criteria in 2021/2022, these criteria still leave some room for differing interpretations and are subjective. We are refining the HST criteria to ensure fairer, more justifiable, and predictable decisions. New definitions will aid in consistent, transparent assessments, aligning more closely with the HST programme's vision.

The refined criteria will also align with our transformation aims of being more timely, useable, more relevant and with greater demonstrable impact.
When will the refined criteria be implemented?

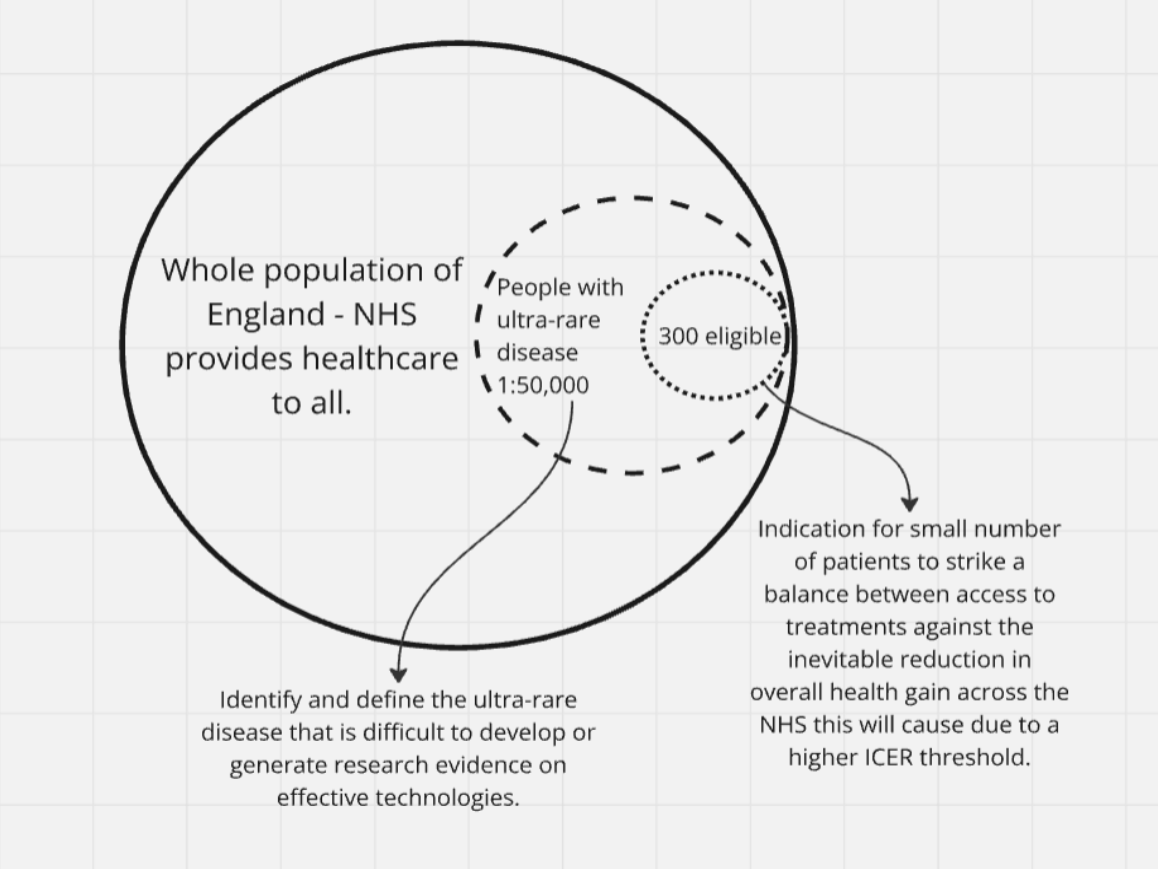
Subject to consultation, NICE proposes to implement the refined criteria from 1st April 2025. This is dependent on any changes following consultation being signed off by the NICE board in March 2025. The consultation will run from 19 December 2024 to 30 January 2025.

3. What does this mean for technologies that are due a routing decision in Q4 2024/5 and Q1 2025/6?

We know that some technologies are potentially due for a routing decision in these 2 quarters. For those where a routing decision happens after the publication of the refined criteria (anticipated to be April 2025) we will assess using the refined criteria. For technologies due a routing decision in Q4 2024/25 we will assess using existing criteria. If the refined criteria are not finalised for April 2025 the existing ones will be used until the refined criteria are finalised, published and implemented.

4. Why is criterion 1 defining ultra rare as 1 in 50,000 or less and criteria 3 limiting the population to no more than 300. A prevalence of 1 in 50,000 would equate to approximately 1100

people in England, yet criteria 3 limits the eligible population for treatment to 300 people.



This is because the 2 criteria serve different purposes in the routing assessment process. The point prevalence of 1:50,000 or approximately 1100 people, is used to define and identify an ultra-rare disease that difficult to generate research evidence on effective technologies. After the ultra-rare disease is identified, further assessment of the size of the population the technology is indicated for within the ultra-rare disease is required to ensure the balance between access to treatment against the inevitable reduction in overall health gain across the NHS this will cause due to a higher ICER threshold for evaluation. The acceptable population size here is set to be 300.

5. Are the definitions really additional criteria?

We've heard that more clarity and predictability would be appreciated when applying the criteria. The aim of the definitions is to add detail to make decision-

making more objective and consistent, and to aid predictability, transparency and efficiency for all parties – patients, manufacturers and NICE.

6. Who has been involved in the refinement of the criteria?

This work has been led by an internal taskforce with engagement from across NICE. We have also engaged extensively with patient groups, industry, committee chairs who are and have been involved in HST guidance development, and policy and strategy leads at NHS England and DHSC. We are now holding a public consultation to gain broader views on the proposed refinement.

7. Why is the consultation happening over the Christmas period?

The timing of the consultation has been carefully considered. If the consultation took place any later, it would coincide with several others, and we are keen to avoid overloading stakeholders with multiple simultaneous consultations. Although consultation during December and January is not ideal, we have designated an extended consultation period to account for this and give extra time for stakeholders to respond. If the consultation runs to plan, we should be able to adopt the refined criteria at the start of the 2025/26 financial year.

8. Are cancer technologies considered for HST routing?

Although cancer treatments have not historically been routed to HST, they can be considered if they meet all the refined criteria, like any other technology for an ultra-rare disease.

9. Why have you excluded individualised medicine?

We excluded individualised medicine - treatments developed and customised for a specific individual (such as bespoke oligonucleotides) - from the HST criteria to keep the focus on ultra-rare, debilitating diseases that severely impact small patient populations and require HST programme support to drive research and equitable treatment access. NICE does not believe HST is the right approach to evaluating individualised medicine.

10. Why did you undertake a retrospective routing decision analysis?

We undertook a retrospective routing decision analysis to evaluate how past decisions would align with the refined HST criteria. This allows us to assess whether the refined criteria would have led to more or fewer technologies being routed to HST. The results (see appendix A below) showed that the same number of technologies would have been routed to HST under the proposed set of refined criteria and definitions as the existing ones.

11. Does that mean that previous decisions will be reviewed again using the refined criteria?

No. Previous decisions will remain unchanged and won't be reviewed again using the refined criteria.

12. What other steps are NICE talking to support swift access to innovative treatments for ultra rare diseases?

As well as improving the transparency and predictability of the HST routing criteria, we're seeking to realise a set of process improvements. We hope that an improvement in the criteria will support more timely evaluation. We know there are challenges in evidence needs for a HST evaluation and are being more proactive on horizon scanning and our offer to companies with products likely to be assessed by NICE. We also recognise the challenges in reviewing and estimating the prevalence of ultra rare conditions for the application of HST routing decisions and are exploring how we can support the development of methods for that.

13. What if we disagree with a HST routing decision?

Since the beginning of this business year (29 May 2024) responsibility for HST routing decisions rests with the NICE Prioritisation Board. All decisions made by the NICE Prioritisation Board are published on our website and clarification can be sought using the 'clarification process'. We consulted on this process in February 2024.

14. Is the aim of this change to either reduce or increase the number of technologies that go through the HST route?

No. The aim of the review is to provide extra clarity about the application of criteria to improve the transparency and consistency of the routing decisions. There is no intention to either increase or decrease the number of technologies routed to HST.

15. Are you changing the criteria to save costs?

No. The changes we are proposing will not impact on the number of technologies routed to HST and is therefore not intended to generate cost savings. It will instead provide greater clarity on NICE's decision-making criteria to ensure the process is more transparent and facilitates efficient decision-making during HST routing decisions.

Appendix A: Retrospective analysis of topics presented to TSOP/PB from 2022-2024

A retrospective analysis of previous decisions using the proposed refined HST routing criteria has been conducted to evaluate the impact of the proposed refined criteria. The summary of the retrospective analysis highlighted that there were only 2 changes to the previous routing decisions (see table for respective analysis).

Table: retrospective analysis

Treatment	Old Criteria	New Criteria	Comments due to differences	Old decision	New decision
1.Ganaxolone for treating seizures caused by CDKL5 deficiency disorder in people 2 years and over	1. Met	1. Met		Not routed to HST	Not routed to HST
	2. Met	2.Met			
	3. Met	3. Met			
	4. Not met	4.Not met			
2.Etranacogene dezaparvovec for treating moderately severe or severe haemophilia B	1. Unclear	1. Not met	'Disease' in new criteria doesn't include subgroups	Not routed to HST	Not routed to HST
	2. Met	2. Not met	Would not meet HST vision – numerous centres dedicated to Haemophilia research		
	3. Not met	3. Met	>300 eligible for treatment		
	4. Not met	4. Not met			
3.Omburtamab I-131 for treating neuroblastoma with central nervous system or leptomeningeal metastasis	1.Met	1.Met		Not routed to HST	Not routed to HST
	2.Met	2. Not met	FDA have also not granted approval for lack of demonstrable benefit to OS		
	3.Met	3. Not met	No MHRA		

Treatment	Old Criteria	New Criteria	Comments due to differences	Old decision	New decision
	4. Not met	4. Not met			
4.Burosumab for treating FGF23-related hypophosphataemia in tumour-induced osteomalacia	1. Met	1. Met		Not routed to HST	Not routed to HST
	2. Not Met	2. Not met	Also has MA for X-linked hypophosphatemia		
	3. Unclear	3. Not met			
	4. Met	4. Met			
5.Setmelanotide for treating obesity and hyperphagia in Bardet-Biedl syndrome	1. Met	1. Met		Routed to HST	Not Routed to HST
	2. Met	2.Met			
	3. Met	3.Not met	Not the first indication for the medication. Has been approved HST (HST21)		
	4. Met	4. Met			
6.Belumosudil for chronic graft versus host disease after two or more lines of systemic therapy	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Met	2. Not met	Not a first line therapy, health gains not brought to all patients with GvH		
	3.Not met	3.Met	>300 eligible		
	4. Not met	4.Not met			
7.Tabelecleucel for treating post-transplant lymphoproliferative disorder caused by the Epstein-Barr virus	1. Unclear	1. Met	Based on checklist (with higher estimate) PTLD should be <1:50000	Not routed to HST	Not routed to HST
	2. Unclear	2.Not met	Magnitude of effect not defined in checklist and first line therapy with rituximab may result in remission		
	3.Not met	3.Met	Would be met as <300 people eligible for treatment in current indication		

Treatment	Old Criteria	New Criteria	Comments due to differences	Old decision	New decision
	4.Not met	4. Not met			
8.Maralixibat for treating cholestasis and pruritus in Alagille syndrome	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Not met	2.Met			
	3.Met	3. Not met	>300 people eligible for treatment		
	4.Met	4.Met			
9.Pegzilarginase for treating arginase-1 deficiency	1.Met	1. Met		Routed to HST	Routed to HST
	2. Met	2. Met			
	3. Met	3. Met			
	4. Met	4. Met			
10.Beremagene geperpavec for treating skin wounds associated with dystrophic epidermolysis bullosa	1. Met	1.Met		Not routed to HST	Not routed to HST
	2.Not met	2. Met			
	3.Met	3.Not met	TSOP decided more than 300 patients eligible. In addition, as per new criteria - HST 28 used in treatment of epidermolysis bullosa, so this would be a second HST for same disease condition		
	4.Met	4.Not met	Other HST available for DEB		
11.Vamorolone for treating inflammation associated with Duchenne muscular dystrophy	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Not met	2.Not met	Relative effectiveness compared to corticosteroids uncertain – would not meet HST vision		
	3.Met	3.Not met	>300 eligible		

Treatment	Old Criteria	New Criteria	Comments due to differences	Old decision	New decision
	4.Met	4.Met			
12. Tofersen for treating amyotrophic lateral sclerosis caused by SOD1 gene mutations	1.Not met	1. Met	Genetically identified subtype with different clinical outcome	Not routed to HST initially as per TSOP decision. Decision later revised	Routed to HST
	2.Met	2.Met			
	3.Met	3.Met			
	4.Met	4.Met	Based on statement – no other treatment available – riluzole available (but not very effective in SOD1 mutation)		
13. Ivosidenib for treating advanced cholangiocarcinoma with an IDH1 mutation after at least 1 therapy	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2. Met	2. Not met	Multiple indications for ivosidenib (e.g., AML, see prospective analysis)		
	3.Met	3. Met			
	4.Not met	4. Not met			
14. Ravulizumab for treating AQP4 antibody-positive neuromyelitis optica spectrum disorder	1.Met	1.Met		Not routed to HST	Not routed to HST
	2.Not met	2.Not met	Drug licensed under multiple indications		
	3.Met	3.Not met	>300 eligible		
	4.Not met	4.Not met			
15. Odevixibat for treating cholestasis and pruritus in Alagille Syndrome	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Not met	2.Not met			
	3. Met	3.Not met	Approved for use in familial intrahepatic cholestasis syndrome with similar mechanism of action to maralixibat		

Treatment	Old Criteria	New Criteria	Comments due to differences	Old decision	New decision
	4. Met	4.Met			
16.Maralixibat for treating progressive familiar intrahepatic cholestasis	1.Met	1.Met		Not routed to HST	Not routed to HST
	2.Met	2.Not met	Not in line with HST vision, alternate drug available with similar mechanism of action- odevixibat		
	3.Met	3.Met			
	4.Not met	4.Not met			
17. Idebenone for treating visual impairment in Leber's hereditary optic neuropathy in people 12 years and over	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Not met	2.Met	In line with HST vision of distinct mechanism of action for syndrome		
	3.Met	3.Not met	>300 eligible		
	4.Met	4.Not met			
18. Leniolisib for activated phosphoinositide 3-kinase delta syndrome in people 12 years and over	1.Met	1. Met		Routed to HST	Routed to HST
	2. Met	2. Met			
	3. Met	3. Met			
	4. Met	4. Met			
19. Belzutifan for treating tumours associated with von Hippel-Lindau disease	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Met	2. Met			
	3.Met	3.Met			
	4.Not met	4.Not met			
	1.Not met	1.Not met			

Treatment	Old Criteria	New Criteria	Comments due to differences	Old decision	New decision
20. Evinacumab for treating homozygous familial hypercholesterolaemia in people aged 12 years and over	2.Met	2. Not met	Other treatment options available with evinacumab being investigated for usage in other disease conditions	Not routed to HST	Not routed to HST
	3.Not met	3. Met			
	4.Not met	4.Not met			
21. Leriglitazone for treating adrenoleukodystrophy	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Not met	2.Met			
	3.Met	3.Not met	>300 eligible		
	4.Met	4. Met			
22. Sodium thiosulfate for preventing ototoxicity in people aged 1 month to 17 years with localised cancer having cisplatin chemotherapy	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Met	2.Not met	Repurposed indication (used in cyanide poisoning)		
	3.Not met	3.Not met	As above		
	4.Met	4.Met			
23. Givinostat for treating Duchenne muscular dystrophy in people 6 years and over ID6323	1.Not met	1.Not met		Not routed to HST	Not routed to HST
	2.Not met	2.Met	Meets HST vision – not in use for other indications		
	3.Met	3.Not met	>300 eligible		
	4.Met	4.Met			
24. Omaveloxolone for treating Friedreich's ataxia in people 16 years and over	1.Met	1.Met		Not routed to HST	Not routed to HST
	2.Not met	2. Met			
	3.Met	3.Not met	>300 eligible		

Treatment	Old Criteria	New Criteria	Comments due to differences	Old decision	New decision
	4.Met	4.Met			
25. Vorasidenib for Astrocytoma, Oligodendroglioma (IDH1 or IDH2 mutations, aged 12 and over)	1. Met	1. Met		Not routed to HST	Not routed to HST
	2. Not met	2. Not met	Would be either eligible for Astrocytoma or Oligodendroglioma as not considered as the same disease condition of “Glioma”. This is how criteria 1 has been met		
	3. Met	3. Not met	>300 eligible		
	4. Met	4. Met			