A comprehensive review of NICE Highly Specialised Technology appraisals

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01 BACKGROUND

- The Highly Specialised Technology (HST) evaluation programme, introduced in April 2013, provides recommendations on the use of innovative and specialised medicines and treatments for rare conditions within the NHS in England.[1]
- The programme is designed to foster research and innovation for very rare diseases where developing a robust evidence base can be challenging. It also aims to ensure fair and equitable access to treatments for small patient populations.
- HST evaluations recognise that focusing solely on maximising health outcomes for the NHS may not always be equitable.[2]
- Technologies considered for HST evaluation must meet specific criteria. There were originally seven HST criteria, which were changed to four in 2021:

1. The disease is very rare – defined as 1:50,000 population in England

2. 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

3. The very rare disease for which the technology is indicated significantly shortens life or severely impairs quality of life

4. There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options

02 OBJECTIVE

- This study aimed to review all published HST submissions made to NICE from the introduction of the HST process.

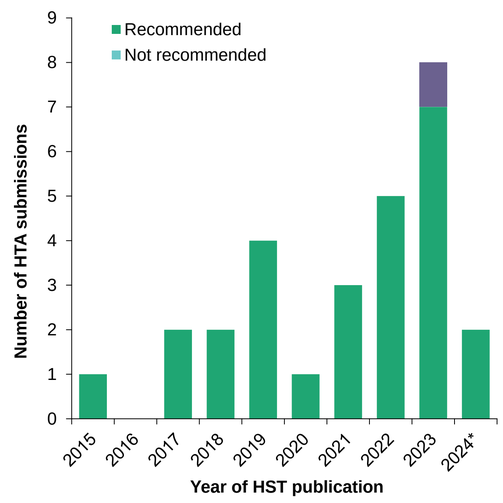
03 METHODS

- HST guidance published by NICE between January 2015 and 25 June 2024 were identified from nice.org.uk.
- Information on the submitted evidence and the NICE committee decision was extracted, including the indication, eligible patients, type of health technologies, clinical evidence, application of quality-adjusted life year (QALY) weights, cost-effectiveness estimates, and committee decision.

04 RESULTS

- All assessed technologies were for treatment of genetic conditions.
- The number of submissions has been increasing with a drop in 2020 (**Figure 1**). The only HST to not be recommended by NICE was published in 2023.

Figure 1: Annual number of HST submissions



*Submissions were only recorded for the first half of 2024 (up to June 2024)

- A summary of the 28 HST submissions are presented in **Table 1**.
- A high proportion (78.5%) of the assessed technologies were clearly stated by the evaluating committee to be innovative or represent step-change innovation.
- Despite challenges in conducting clinical trials for extremely rare diseases, 53.6% of appraisals included evidence from randomized controlled trials, with additional evidence from open-label studies, dose-escalation studies, real-world data, and retrospective natural history studies.

Table 1: Characteristics of HST submissions

HST	Drug name	Indication	Recommendation	Population	Technology	ICER (Company, EAG)	QALY weighting
HST1	Eculizumab	Atypical haemolytic uraemic syndrome	✓	Adults and children	Monoclonal antibody	🔒	NR
HST4	Migalastat	Fabry disease	✓	>16 yrs	Small molecule	🔒	0.34
HST5	Eliglustat	Type 1 Gaucher disease	✓	Adults	Enzyme inhibitor	🔒	NR
HST 7	Strimvelis	Adenosine deaminase deficiency–severe combined immunodeficiency	✓	Children	Ex-vivo gene therapy	£36,360/ £14,645 £494,255/ £170,668	1.4 and 1.96
HST 8	Burosumab	X-linked hypophosphataemia	✓	1-17 yrs	Monoclonal antibody	🔒	🔒
HST 9	Inotersen	Hereditary transthyretin amyloidosis	✓	Adults	Antisense oligonucleotide	🔒	None
HST 10	Patisiran	Hereditary transthyretin amyloidosis	✓	Adults	Ribonucleic acid interference agent	£80,730 £80,730-£125,256	None
HST 11	Voretigene neparvovec	Inherited retinal dystrophies caused by RPE65 gene mutations	✓	All	Virus vector-based gene therapy	£86,635 £60,908-£86,118	1.2
HST 12	Cerliponase alfa	Neuronal ceroid lipofuscinosis type 2	✓	Children	Enzyme replacement therapy	🔒	3.0
HST 13	Volanesorsen	Familial chylomicronaemia syndrome	✓	Adults	Antisense oligonucleotide	🔒	None
HST 14	Metreleptin	Lipodystrophy	✓	>2 yrs	Leptin receptor agonists	£60,611 £110,460	None
HST 15	Onasemnogene abeparvovec	Spinal muscular atrophy	✓	<12 mths	Gene therapy	🔒	>1.86
HST 16	Givosiran	Acute hepatic porphyria	✓	>12 yrs	RNA interference	🔒	1.8
HST 17	Odevixibat	Progressive familial intrahepatic cholestasis	✓	>6 mths	Sodium-bile acid cotransporter inhibitors	🔒	None
HST 18	Atidarsagene autotemcel	Metachromatic leukodystrophy	✓	Children	Gene therapy	🔒	🔒
HST 19	Elosulfase alfa	Mucopolysaccharidosis type 4A	✓	All ages	Protein replacements	🔒	🔒
HST 20	Selumetinib	Plexiform neurofibromas associated with type 1 neurofibromatosis	✓	>3 yrs	MAP kinase 1 inhibitors	£78,696 £99,770	None
HST 21	Setmelanotide	Obesity by LEPR or POMC deficiency	✓	>6 yrs	Melanocortin type 4 receptor agonists	£212,746 £324,925	🔒
HST 22	Ataluren	Duchenne muscular dystrophy	✓	>2 yrs	Protein synthesis stimulants	🔒	None
HST 23	Asfotase alfa	Paediatric-onset hypophosphatasia	✓	0-6 mths Conditional 6 mths-18 yrs	Enzyme replacement therapy	£74,980/ £88,410 £77,757/ £98,276	🔒
HST 24	Onasemnogene abeparvovec	Presymptomatic spinal muscular atrophy	✓	>12 mths	Gene therapy	🔒	None
HST 25	Lumasiran	Primary hyperoxaluria type 1	✓	All ages	RNA interference (RNAi) therapeutic	🔒	2.0
HST 26	Eladocagene exuparvovec	Aromatic L-amino acid decarboxylase deficiency	✓	>18 mths	Gene therapy	NR	🔒
HST 27	Afamelanotide	Erythropoietic protoporphyria	X	NR	Melanocortin 1 receptor agonist	£305,244 £1,892,822	None
HST 28	Birch bark	Epidermolysis bullosa	✓	>6 mths	Anti-inflammatory, antiviral and antibacterial	NR	None
HST 29	Velmanase alfa	Alpha-mannosidosis	✓	>18 yrs	Enzyme replacement therapy	£61,396 £112,623	None
HST 30	Sebelipase alfa	Wolman disease	✓	>2 yrs	Enzyme replacement therapy	NR	3.0
HST 31	Setmelanotide	Obesity and hyperphagia in Bardet-Biedl syndrome	✓	6-17 yrs	Melanocortin-4 receptor agonist	£169,658 £174,904	🔒

EAG, external assessment group; ICER, Incremental cost effectiveness ratio; QALY, quality-adjusted life year; yrs, years; mths, months; NR, not reported. 🔒 confidential

05 DISCUSSION AND CONCLUSIONS

- Technologies assessed by the HST pathway have a high rate of positive recommendation.
- Technologies appraised to date have focused on treatments for rare genetic conditions, with a significant proportion aimed at children and young people.
- In fifteen (53.6%) assessments, NICE applied QALY weighting due to significant health gains, recognizing that some of these treatments provide substantial benefits in terms of quality of life, justifying higher cost-effectiveness thresholds.
- NICE did not recommend afamelanotide due to significant uncertainties in its benefits and cost-effectiveness, with an ICER of £1,892,822/QALY far exceeding acceptable limits. Attempts to establish a commercial agreement, including a managed access arrangement, were also unsuccessful.
- NICE plan to revise the current HST criteria in 2024/25 to more explicitly reflect the over-arching HST vision. This will include qualifying statements for each criterion to enhance transparency and provide clearer guidance. The aim is to ensure that decisions are well-informed and less controversial without changing the number of therapies accepted through the HST route.

References

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