Assessing criteria for NICE recommendation with the HST programme

Caroline Upton[1], James Wordsworth[1], David Cork[1], Alistair Curry[2], Stephen Ralston[2]

[1]SIRIUS Market Access, Newcastle-upon-Tyne, United Kingdom. email: info@siriusmarketaccess.com

[2]SIRIUS Market Access, London, United Kingdom. email: info@siriusmarketaccess.com

PHP255

Introduction

- Standard NICE technology appraisals (TAs) have strict criteria for cost-effectiveness, sometimes resulting in a negative recommendation despite clinical efficacy being demonstrated.
- In the case of rare conditions, cost-effectiveness can be even more difficult to demonstrate, due to the high acquisition costs required to recoup the costs of research and development, and the small population that will be eligible for treatment.
- Treatments for rare conditions are important to improve the prognosis of patients who otherwise experience low quality of life, morbidity, or early death.
- These medicines are often novel and innovative to target the rarity of the disease.
- In the UK, there are three main routes by which treatments for such interventions can be assessed for reimbursement; the Highly Specialised Technology Programme (HSTP), the Cancer Drugs Fund (CDF) and End of life (EoL) criteria (Table 1).

Table 1: Summary of HSTP, CDF, and end of life schemes ,in the UK

	HSTP	CDF	EoL
Life expectancy	-	-	< 24 months
Life extension threshold	-	-	> 3 months
Cost effectiveness threshold	£100,000/ QALY. Weighting applies to drugs with higher ICERs (>£100,000) but a higher QALY gain.	£20-30,000/ QALY if EoL criteria not met. £50,000/ QALY if EoL criteria met.	£50,000/ QALY
Required follow-up research	Managed access agreement (MAA) may be agreed between key stakeholders, manufacturer, NHS and patient groups to collect more data.	2 year MAA must demonstrate cost-effectiveness.	-

- The HSTP has existed since 2013 and takes into account factors specific to the technology such as:
  - Nature of the condition.
  - Impact of the new technology.
  - Cost (budget impact) to the NHS and personal social services.
  - Value for money, defined by the productive, technical and allocative efficiency of the treatment (not cost-utility analysis).
  - Impact of the technology beyond direct health benefits.
  - Impact of the technology on delivery of the specialised service.
- As of April 2017, cost-effectiveness evaluation was introduced, with the threshold for automatic funding set at £100,000/ QALY.
- Incremental weighting is applied based on the extent of the QALY gain for HSTs that cost > £100,000/ QALY (Table 2).

Table 2: Incremental weighting for HSTs > £100,000/ QALY

Incremental QALYs gained (per patient, lifetime horizon)	Weight versus 100k/ QALY
≤ 10	1
10 - 30	Between 1 and 3 (using equal increments)
> 30	3

Objectives

This work aimed to review the criteria by which HSTP assesses treatments for rare conditions, and to understand which key factors impacted on reimbursement decisions.

Abbreviations:
CDF, Cancer Drugs Fund; EoL, End of life; FED, Final evaluation determination; HST(P), Highly specialised technology (programme); ICER, Incremental cost effectiveness ratio; MAA, Managed access agreement; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; PAS, Patient access scheme; QALY, Quality-adjusted life year; QoL, Quality of life; RCT, Randomised controlled trial; TA, Technology appraisal

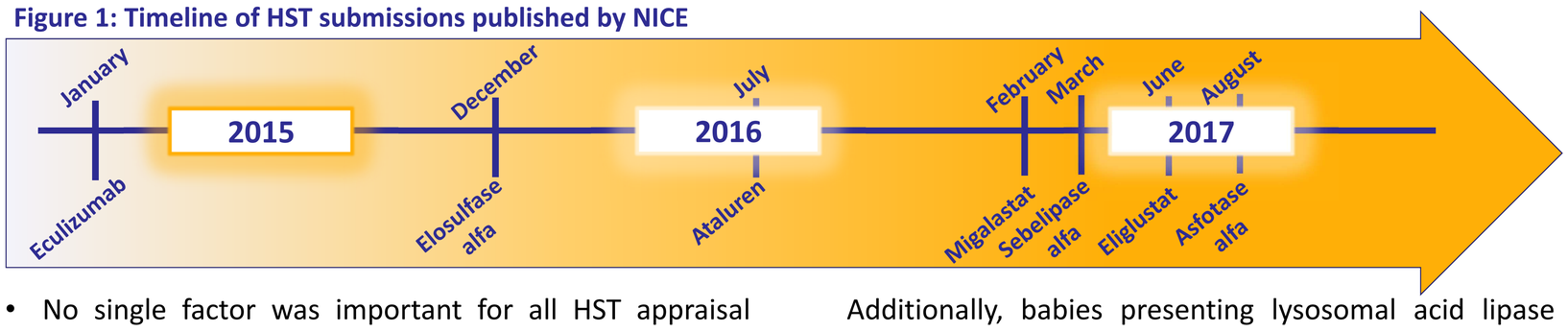
Methods

A search was conducted on the NICE website (www.nice.org.uk: accessed 24th May, 2017) for all HSTs that had final evaluation determinations (FEDs) due in 2017[1,2]. Those that were identified were reviewed to assess the impact of factors such as budget impact, cost per patient, QALY gains, innovation, unmet need, and others associated with NICE recommendation.

Results

Seven treatments were identified which were due FEDs by June 2017. The number of HST submissions published by NICE increased between 2015 and June 2017, with more than half of the submissions being published during 2017 (Figure 1).

Figure 1: Timeline of HST submissions published by NICE



- No single factor was important for all HST appraisal outcomes; each case was considered individually according to the strengths and limitations of its own data. A summary of key drivers which contributed to the decision for each HST assessment is available in Table 3.
- Of the seven treatments with FEDs by June 2017, elosulfase alfa and ataluren were recommended with managed access agreements (MAAs); eculizumab, eliglustat, and migalastat were recommended without MAAs; asfotase alfa was recommended for a subpopulation with an MAA; and sebelipase alfa was provisionally not recommended.
- These outcomes did not reflect data quality; eculizumab offered only single-arm, non-randomised data, while sebelipase alpha was supported by RCTs.
- Recommendations also did not reflect QALY gains, as incremental QALYs gained with sebelipase alfa (6.64) were higher than for migalastat (0.34-0.98). Additionally, babies presenting lysosomal acid lipase deficiency did not survive longer than 12 months without sebelipase alfa, suggesting substantial unmet need.
- Cost-effectiveness was not reported, but the annual treatment cost (from list price) appears significant. Sebelipase alfa had the greatest reported annual cost per patient of £491,992 (for an 11-year-old child), compared with £211,000-£340,000 for eculizumab and £394,680 for elosulfase alfa.
- The annual budget impact, based on list prices, was also highest for sebelipase alfa (5-year net £59 million). However, the £13.4 million impact for the subgroups not recommended for asfotase alfa was less than the £17.3 million for elosulfase alfa, indicating the decision was made partially on efficacy grounds.
- The HSTs assessed for this research may not have met the threshold of £100,000/ QALY, as applied to HST submissions since April 2017.

Table 3: Factors which were key drivers of the decision for each HST assessment

Reference number (year)	HST1 (2015)[3]	HST2 (2015)[4]	HST3 (2016)[5]	HST4 (2017)[6]	HST5 (2017)[7]	HST6 (2017)[8]	ID737 (2017)[9]
Treatment	Eculizumab	Elosulfase alfa	Ataluren	Migalastat	Eliglustat	Asfotase alfa	Sebelipase alfa
Indication	Atypical haemolytic uraemic syndrome	Mucopolysacc-haridosis type IVa	Duchenne muscular dystrophy	Fabry disease	Type 1 Gaucher disease	Paediatric-onset hypophosphatasia	Lysosomal acid lipase deficiency
HST assessment decision	Recommended.	Recommended with MAA.	Recommended with PAS and MAA.	Recommended with PAS.	Recommended with PAS.	Recommended with MAA, discount and annual per-patient cost cap.	Not recommended.
Clinical trial data	✓	✓	-	-	-	-	-
Budget impact	✓	✓	✓	✓	✓	✓	✓
QALY gains (Committee's preferred estimate)	✓ (10.14)	- (5.04)	- (3.05)	- (0.34)	- (1.05 – 1.06)	✓ (14 – 25)	- (6.64)
Innovation	✓	-	✓	-	-	✓	✓
Other important factors considered during TA	• Patient and clinical expert opinion. • Patient quality of life (QoL). • QoL and cost burden on families. • Treatment duration.	• Patient and clinical expert opinion. • Patient QoL. • Confounding variables. • Surrogate endpoint.	• Patient and clinical expert opinion. • Patient QoL. • QoL and cost burden on families.	• Patient and clinical expert opinion. • Patient QoL.	• Patient and clinical expert opinion. • Patient and carer QoL.	• Patient and clinical expert opinion. • Patient and carer QoL. • Model design. • Patient subgroups (juvenile vs paediatric onset).	• Patient and clinical expert opinion. • Patient and carer QoL. • Limitations in the MAA.

✓ Key driver of the HST assessment decision; - Not a key driver of the HST assessment decision

Conclusions

- HST recommendations do not directly reflect treatment efficacy, which is frequently associated with substantial uncertainty. Annual treatment cost and budget impact are more likely to be the key drivers behind HST assessment decisions.
- Patient and clinical expert opinion are extremely important during HST reviews, as well as patient and carer quality of life.
- Clinical trial data, whilst important, is often not pivotal in HST decisions, due to small patient populations and the difficulties associated with conducting RCTs.
- Reimbursement of HSTs by NICE almost always depends on the implementation of an MAA or a PAS.
- HSTs are very expensive; HSTs assessed for this research may not have met the threshold of £100,000/ QALY, as applied to HST submissions since April 2017.
- Orphan diseases can be expensive to treat, potentially posing a significant risk to healthcare budgets. Therefore a budget impact threshold is important in order to ensure that cost-effective treatments are reimbursed.

References

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