A comparison of the NICE highly specialised technology (HST) programme with assessment by the National Authority for Health (HAS; France) and the Federal Joint Committee (G-BA; Germany)

Georgia Hann[1], James Wordsworth[1], Stephen Ralston[2], **David Cork[1]**

[1]SIRIUS Market Access, Newcastle Upon Tyne, United Kingdom

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

PSY143

Introduction

- NICE (England, UK) defines ultra-orphan drugs as those treating life-threatening or seriously debilitating conditions affecting ≤1:50,000 people[1,2].
- The NICE HST programme was introduced in 2013 to assess these drugs, which are unlikely to meet standard cost-effectiveness criteria due to high acquisition costs required to recoup research and development costs for innovative technologies in small patient populations[3].
- Prior to the introduction of a cost-effectiveness evaluation in April 2017 (threshold £100,000 per QALY), the HST programme considered the following criteria in forming guidance:
  - Nature of the condition.
  - Impact of the new technology.
  - Cost to the NHS and personal social services.
  - Value for money.
  - Impact beyond direct health benefits.
  - Impact on the delivery of the specialised service.
- HAS (France) and the G-BA (Germany) also apply special criteria to the assessment of drugs for treatment of rare diseases[4,5].
- Table 1 summarises key criteria considered in the assessment of ultra-orphan technologies by NICE HST, HAS, and G-BA.

Table 1: Criteria for assessment of ultra-orphan drugs by NICE HST, HAS, and G-BA

Criteria	NICE HST (England)	HAS (France)	G-BA (Germany)
Clinical benefit	Considered for patients and where relevant, carers.	SMR and ASMR considered proven at MA (if BI threshold met).	Additional benefit considered proven at MA (if BI threshold met). Extent of medical benefit assessed.
Costs to the health service	BI and value for money considered.	BI threshold <€30 million per year.	BI threshold <€50 million per year.
Innovation	Considered.	Accelerated procedure.	Not mentioned.
Follow-up research	May be requested as part of MAA.	May be requested.	May be requested.

BI, budget impact; MA, market authorisation; MAA, managed access arrangement; PAS, patient access scheme; SMR, medical benefit; ASMR, additional medical benefit

- If the budget impact (BI) threshold is exceeded:
  - HAS assess the medical benefit (SMR; ranked substantial, moderate, mild, or insufficient) and additional medical benefit (ASMR; ranked I to V [major, important, moderate, minor, or no clinical improvement]).
  - The G-BA assess additional benefit over the relevant comparator, and the extent of additional benefit (rated major, considerable, minor, not quantifiable, no additional benefit, or less benefit).

Objectives

- Compare the outcomes of assessments of ultra-orphan drugs made by NICE HST with assessments of the same technologies by HAS in France and the G-BA in Germany.
- Explore the decision-making processes behind the recommendations made for ultra-orphan drugs by the three HTA organisations.

Methods

- A search was conducted on the NICE website (https://www.nice.org.uk/) for all HSTs that had guidance or final evaluation determinations (FEDs) published by 29th September 2017 (n=7).
- Searches were then conducted for evaluations of the same technologies by HAS (France; https://www.has-sante.fr/portail) and G-BA (Germany; (https://www.g-ba.de) (accessed 29th September 2017).

Results

- Seven ultra-orphan drugs had published guidance or FEDs from NICE HST by September 2017[6]. Each of these assessments was initiated prior to introduction of cost-effectiveness criteria to the HST programme.
- The outcome of assessment by NICE HST, HAS, and the G-BA for these drugs is presented in Table 2.
- All seven drugs received positive recommendations from NICE HST, HAS, and the G-BA, with the exception of sebelipase alfa, which was not recommended by NICE HST.
- Many of the recommendations are subject to re-evaluation after further data becomes available.

Table 2: Outcome of assessment of ultra-orphan drugs by NICE HST, HAS, and G-BA

Drug	Indication	NICE HST (England, UK)[6]	HAS (France)[7]	G-BA (Germany)[8]
Eculizumab	Atypical haemolytic uraemic syndrome	Recommended.	Recommended with request for supplementary data. SMR: substantial; ASMR: II	Accepted prior to routine benefit assessments.
Elosulfase alfa	Mucopolysaccharidosis type IVa	Recommended with MAA.	Recommended with re-evaluation within 5 years. SMR: substantial; ASMR: III	Recommended. Extent of additional medical benefit: minor
Ataluren	Duchenne muscular dystrophy	Recommended with PAS and MAA.	Recommended with re-evaluation in 2021. SMR: mild; ASMR: V	Recommended. Extent of additional medical benefit: minor
Migalastat	Fabry disease	Recommended with PAS.	Recommended with re-evaluation within 5 years. SMR: substantial; ASMR: IV	Recommended. Extent of additional medical benefit: not quantifiable
Eliglustat	Type 1 Gaucher disease	Recommended with PAS.	Recommended. SMR: substantial; ASMR: V	Recommended. Extent of additional medical benefit: not quantifiable
Asfotase alfa	Paediatric-onset hypophosphatasia	Recommended with MAA.	Recommended with re-evaluation within 3 years. SMR: substantial; ASMR: II	Recommended with validity until 1st December 2018. Extent of additional medical benefit: not quantifiable
Sebelipase alfa	Lysosomal acid lipase deficiency	Not recommended (appeal underway).	Recommended with request for supplementary data. SMR: substantial; ASMR: III (infantile), V (juvenile)	Recommended with validity until 1st December 2018. Extent of additional medical benefit: not quantifiable

PAS, patient access scheme; MAA, managed access arrangement; SMR, medical benefit; ASMR, additional medical benefit

- Key drivers in the decision-making process for each assessment are summarised in Table 3.
- NICE HST decisions were usually driven by BI, value for money, and unmet need. Clinical benefit, innovation, and quality of life (QoL) of patients and carers (where relevant) were also key factors in some assessments.
- HAS considered clinical benefit (SMR and ASMR ratings), unmet need, target population size, and innovation as key drivers for decision-making. Costs were not discussed.
- The G-BA assessed clinical benefit (in the context of extent of additional medical benefit), target population size, annual treatment costs, and unmet need in decision-making.

Table 3: Factors that were key drivers in the decision-making process for each assessment by NICE HST, HAS, and G-BA

Criteria	Eculizumab			Elosulfase alfa			Ataluren			Migalastat			Eliglustat			Asfotase alfa			Sebelipase alfa		
	UK	FR	DE	UK	FR	DE	UK	FR	DE	UK	FR	DE	UK	FR	DE	UK	FR	DE	UK	FR	DE
Clinical benefit	✓	✓	NA	✓	✓	✓	-	✓	✓	-	✓	✓	-	✓	✓	-	✓	✓	-	✓	✓
Patient QoL	✓	✓	NA	✓	-	-	✓	✓	-	✓	-	✓	✓	-	-	✓	-	-	-	✓	-
Carer QoL/ burden	✓	-	NA	-	-	-	✓	✓	-	-	-	-	-	-	-	✓	-	-	-	-	-
QALYs/ utilities	✓	-	NA	-	-	-	-	-	-	-	-	-	-	-	-	✓	-	-	-	-	-
Unmet need	✓	✓	NA	✓	✓	-	✓	✓	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	-	✓	-
Budget impact	✓	-	NA	✓	-	-	✓	-	-	✓	-	-	✓	-	-	✓	-	-	✓	-	-
Value for money	✓	-	NA	✓	-	-	✓	-	-	✓	-	-	✓	-	-	✓	-	-	✓	-	-
Treatment cost	✓	-	NA	-	-	✓	-	-	✓	-	-	✓	-	-	✓	-	-	✓	-	-	✓
Target pop. size	-	✓	NA	-	✓	✓	-	✓	✓	-	✓	-	-	✓	✓	-	✓	✓	-	✓	✓
Innovation	✓	✓	NA	-	-	-	✓	-	-	-	✓	-	-	✓	-	✓	-	-	-	-	-

✓ Key driver of decision; - Not a key driver of decision; NA No assessment available

Conclusion

- Clinical benefit and costs were key drivers of decision-making in the assessment of ultra-orphan drugs:
  - NICE HST considered BI and value for money more consistently than clinical benefit, likely reflecting uncertainty in available data due to small population sizes available for conducting clinical trials.
  - Although HAS assessments did not discuss costs, SMR and ASMR were assessed, indicating that the BI threshold of €30 million was exceeded in all cases.
  - The G-BA considered additional medical benefit proven at MA in all cases and assessed the extent of additional benefit, which suggests that the BI of each drug was not considered to exceed €50 million.
- Unmet need was a key driver in all countries, particularly in light of uncertain clinical evidence.
- Certainty around the target population size was frequently an important factor in decision-making, as it was considered a key driver of costs.
- Patient QoL was commonly a key driver for NICE HST and HAS, and infrequently for the G-BA. Carer QoL was a driving factor in some cases for NICE HST and HAS.
- All three bodies requested follow-up data and re-evaluations after a set timeframe in the majority of assessments, in order to manage uncertainty in available clinical data and costs to the health service.
- In conclusion, clinical benefit and unmet need are important drivers behind recommendations for ultra-orphan drugs by NICE HST, HAS, and the G-BA, but the uncertainty associated with clinical data commonly brings BI and other cost considerations to the forefront.
- As further high-cost ultra-orphan drugs are introduced, additional criteria may be necessary to manage combined BI e.g. the cost-effectiveness threshold recently introduced by NICE HST (£100,000 per QALY).

References:

1. NICE Citizens Council Report (2004). Ultra-orphan drugs. National Institute for Health and Care Excellence.
2. European Parliament and the Council of the European Union (2014). Regulation No. 536/2014 on clinical trials on medicinal products for human use, and repealing directive 2001/20/EC.
3. NICE (2013). Interim process and methods of the highly specialised technologies programme. National Institute for Health and Care Excellence.
4. Gammie, T., et al. (2015). *PLoS ONE* 10 (10), e0140002. doi:10.1371/journal.pone.0140002.
5. Kawalec, P., et al. (2016). Orphanet Journal of Rare Diseases 11 (122). doi:10.1186/s13023-016-0501-4.
6. NICE guidance and advice list: published (2017). Accessed 29th September 2017.
7. Haute Autorité de Santé search (2017). Accessed 29th September 2017.
8. Germeinsamer Bundesausschuss search (2017). Accessed 29th September 2017.

SIRIUS MARKET ACCESS