Comparing Ultra-Rare Disease Pathways within the United Kingdom: Can Different Processes Lead to Market Access Variations?

HTA317

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Introduction

- The National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC) are assessing the clinical- and cost-effectiveness of new health technologies in England, Wales, and Scotland.
- Recently, both agencies have updated their approaches for the assessment of medicines used to treat ultra-rare diseases (i.e., a disease that affects 1 in 50,000 patients[1,2]) **(Figure 1).**
- Differences in NICE and SMC processes may lead to variations in patient access to medicines treating ultra-rare diseases, known as ultra-orphan (U-O) medicines, across the UK.

Figure 1. NICE and SMC process diagrams[1-4]

Abbreviations: ACD, Appraisal Consultation Document; EAG, External Assessment Group; FED, Final Evaluation Determination; NICE, National Institute for Health and Care Excellence; SMC, Scottish Medicines Consortium.

Methods

- Medicines assessed through the revised SMC U-O pathway between October 2019 and May 2023 were identified and cross-referenced to NICE Highly Specialised Technologies (HST) appraisals **(Figure 2).**
- Relevant evidence including marketing authorisation (MA) and health technology assessment (HTA) dates was extracted from NICE, SMC, the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) websites.

Objective: To evaluate how HTA processes for medicines targeting ultra-rare diseases differ in England and Scotland in terms of (i) timely access and (ii) reimbursement recommendations.

Figure 2. Sample selection process

Abbreviations: HST, Highly Specialised Technology; NICE, National Institute for Health and Care Excellence; SMC, Scottish Medicines Consortium.

Results

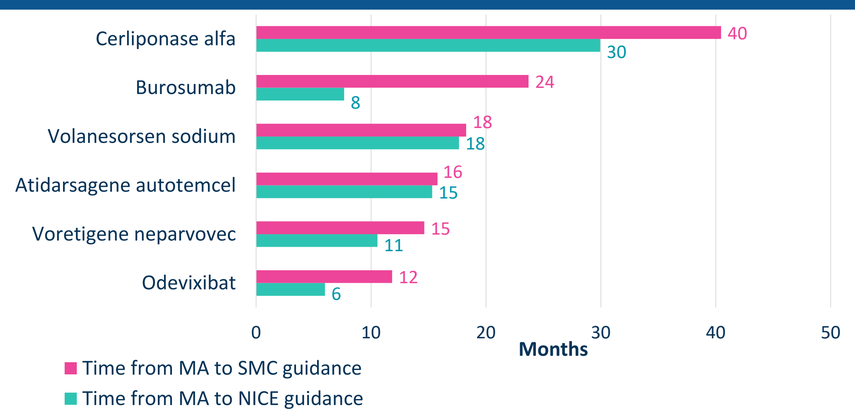
Sample characteristics

- Five out of the six U-O medicines in our sample had a paediatric indication.
- Two had a conditional MA, two were approved under exceptional circumstances, and two had a standard MA by EMA.
- The treatment cost of all U-O drugs was high with annual costs varying from £77,792 to £2,875,000.

Time to market and patient access

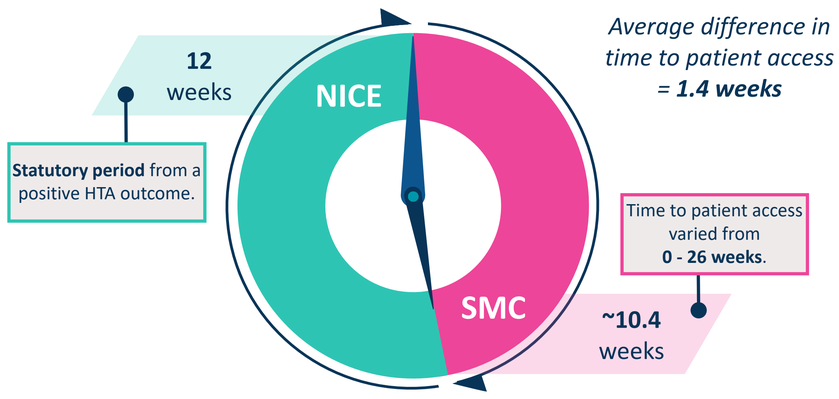
- The average time from MA to HTA recommendation by NICE and SMC was 27 and 39 months, respectively **(Figure 3)**. For all six medicines, HTA recommendations were issued later in Scotland than in England.
- Inconsistencies were observed in the time from HTA recommendation to patient access in Scotland. Two of the U-O medicines could be prescribed in Scotland on average four months later than in England, while three were made available in Scotland almost immediately after HTA recommendations **(Figure 4).** For one medicine, such information was not available.

Figure 3. Time from MA to HTA recommendation



Abbreviations: HTA, health technology assessment; MA, market authorisation; NICE, National Institute for Health and Care Excellence; SMC, Scottish Medicines Consortium.

Figure 4. Time from HTA recommendation to patient access



Abbreviations: HTA, health technology assessment; NICE, National Institute for Health and Care Excellence; SMC, Scottish Medicines Consortium.

HTA recommendations and critique

- Five U-O medicines assessed by NICE were recommended without requiring additional data collection, though four of them were critiqued for having only proven short-term clinical evidence. In contrast, all U-O medicines assessed by SMC were approved on the condition of additional evidence collection **(Table 1).**
- In Scotland, none of the medicines were considered cost-effective, while in England five were considered cost-effective through the HST programme. In both countries, all sampled medicines were subject to a price discount.
- Other social value judgments including disease severity and rarity, unmet medical need, innovation and impact on quality of life of patients and their carers positively influence the HTA recommendation in both agencies. The mode of administration and adverse events were found to negatively impact the HTA recommendation in three U-O medicines.
- In three U-O medicines, manufacturers submitted more clinical evidence to NICE than SMC, while the submitted economic models were the same in both agencies. Nevertheless, uncertainties raised by the committees related to the economic evidence differed, with the exception of odevixibat.

Table 1. Overview of HTA recommendations and committee's criticism

	Cerliponase alfa		Burosumab		Volanesorsen sodium		Atidarsagene autotemcel		Voretigene neparvovec		Odevixibat	
	NICE HST12	SMC SMC2286	NICE HST8	SMC SMC2240	NICE HST13	SMC SMC2299	NICE HST18	SMC SMC2413	NICE HST11	SMC SMC2228	NICE HST17	SMC SMC2411
Outcome	●	●	●	●	●	●	●	●	●	●	●	●
Main reasons for recommendation?												
Clinically effective?	◍	✓	◍	◍	◍	◍	◍	◍	◍	◍	✓	◍
Cost-effective?	✓		✓		✓		✓				✓	
Clinical uncertainties flagged?												
Study design		✓	✓	✓	✓	✓	✓	✓		✓	✓	✓
Clinical benefit	✓		✓		✓	✓	✓	✓		✓	✓	✓
Outcomes							✓	✓	✓	✓		
ITC	✓											
Quality of life		✓		✓		✓	✓	✓	✓	✓		
Lack of (long-term) data		✓	✓	✓	✓		✓	✓	✓	✓	✓	✓
Safety concerns					✓	✓		✓				✓
Economic uncertainties flagged?												
Model used	✓	✓				✓	✓	✓		✓	✓	✓
Model assumptions	✓		✓	✓	✓	✓	✓		✓	✓	✓	✓
Clinical evidence used	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Utilities	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Costs				✓	✓	✓		✓	✓		✓	✓

● Recommended ● Recommended with additional data collection required ✓ Yes ◍ Only in the short-term

Abbreviations: HTA, health technology assessment; ITC, indirect treatment comparison; NICE, National Institute for Health and Care Excellence; SMC, Scottish Medicines Consortium.

Conclusions

Access implications

- NICE offers a more consistent process for U-O medicines in terms of time-to-patient access due to legislation (i.e., the National Health Service [NHS] has to make available medicines approved by NICE within 3 months).
- The SMC process offers more managed access through a three-year conditional approval which could lead to downstream benefits in terms of gatekeeping the budget for the Scottish NHS by minimising uncertainties through additional data collection.
- Such differences could potentially lead to access variations within the UK. To eradicate such issues, a harmonised process for U-O medicines could be adopted.

Study limitations

Our results should be interpreted with caution due to the following limitations:

- Small sample size due to a limited number of SMC appraisals through the new and revised U-O process;
- Reliance only on publicly available data;
- NICE has a statutory three-month period from positive HTA recommendations to availability of the medicines in the NHS; thus, the actual time to patient access is unknown.

References: *(1) National Institute for Health and Care Excellence. Interim Process and Methods of Highly Specialised Technologies Programme. May 2017. (2) National Institute for Health and Care Excellence. Single technology appraisal (STA) timeline. April 2018. (3) National Institute for Health and Care Excellence. Highly specialised technologies guidance. April 2019. (4) Scottish Government. A Guide to the Ultra-Orphan Pathway. May 2019.* ***Declaration of funding:*** *This project has been funded in full by Symmetron Limited.*