Trends Underlying Positive and Negative Decision-Making for New Treatments Targeting Rare Diseases Appraised by NICE in 2023

Stothard, CA; Bodke, A; Crossley, O; Knott, C; Samuels, E; Tang, M. Nexus Values, United Kingdom

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Introduction

- NICE provides recommendations through TA and HST assessments. However, value demonstration in RD is complex due to challenges in data collection, impacting patient access to potentially effective treatments.[1]
- This research aimed to identify recent trends underlying positive and negative decisions for treatments targeting RD in England to anticipate potential challenges in future submissions.

Methods

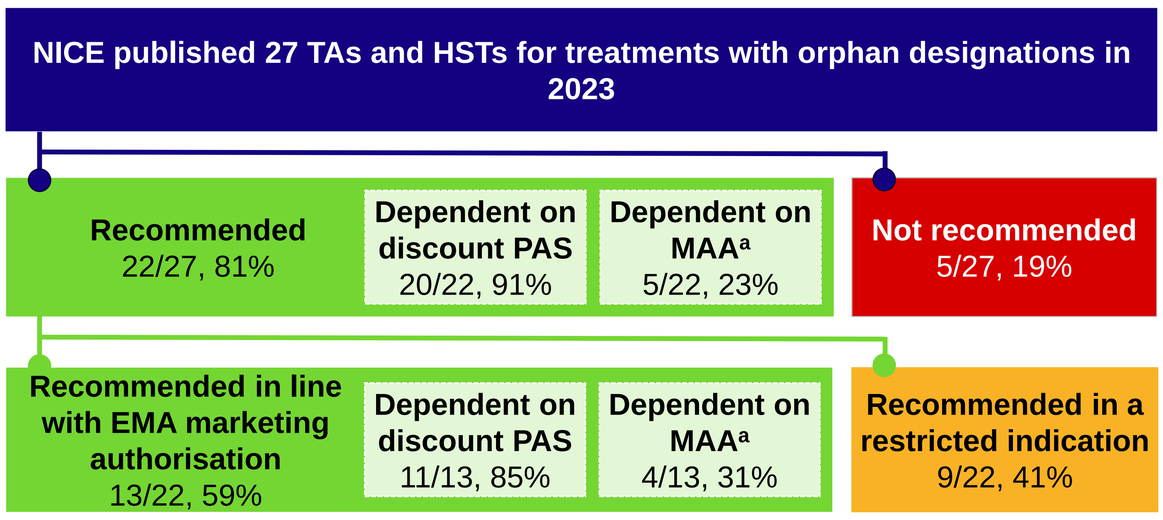
- NICE TAs and HSTs for medicines with orphan designation published in 2023 were identified. Terminated/withdrawn submissions were excluded.
- The EMA website was searched to identify marketing authorisation of the treatments assessed in the identified TAs and HSTs.
- Pre-defined topics, including NICE recommendation, clinical and economic evidence submissions, and decision drivers, were extracted from the TA, with 7% quality checked by a second reviewer.

Results

Overview of NICE recommendations for treatments in RD

- NICE published 27 TA and HST for treatments with orphan designation in 2023 (Figure 1).
- 81% of these treatments received a positive recommendation.
- However, only 59% (13/22) of positive recommendations were in line with EMA marketing authorisation.
- In addition, 23% (5/22) of positive recommendations were dependent on a MAA or funding within the CDF. MAA (4/5) were mostly used for treatments recommended in line with EMA marketing authorisation.
- While 69% (9/13) of treatments recommended in line with EMA marketing authorisation did not require an MAA, most of these (67%, 6/9) were supported with RWE.

Figure 1: Outcomes for treatments targeting RD assessed by NICE in 2023



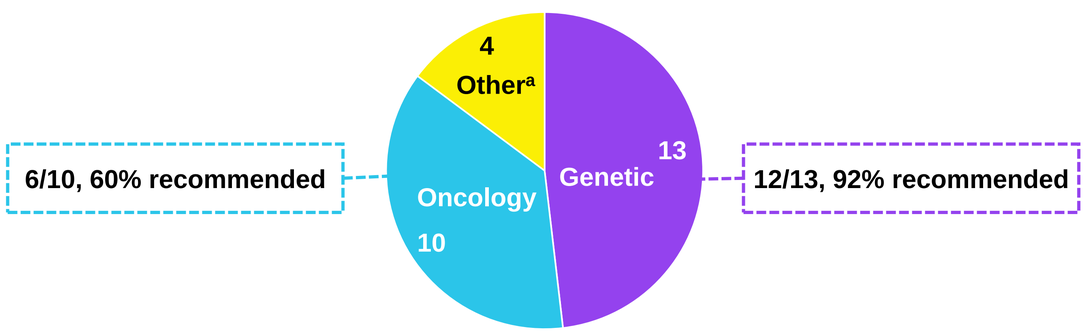
Note: [a]Or funded via the CDF.

- Only 1 treatment was recommended in line with EMA marketing authorisation without the use of a MAA or discount PAS. This submission included evidence from 5 Phase 2-3 studies demonstrating a similar benefit to SoC while offering a comparable cost and reduced administration burden.[2]

Overview of RD indications

- Most TAs and HSTs were for genetic conditions (48%), followed by oncology indications (37%; Figure 2); genetic conditions had the largest proportion of positive recommendations (92%).

Figure 2: Number of treatments by disease type



Note: [a]Infections, renal, respiratory, systemic conditions (all n=1). Groups are mutually exclusive.

Restrictions compared to marketing authorisation

- Of the treatments recommended in a restricted indication, most (78%) were restricted to a patient subgroup (Table 1).

Table 1: Indication restrictions applied compared to marketing authorisation

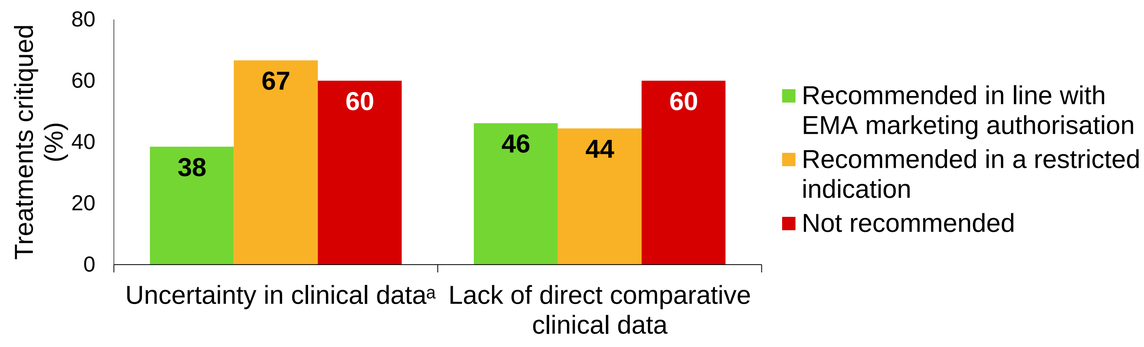
Restriction applied	Number of treatments (%)
Patient subgroup[a]	7 (78)
Treatment line	2 (22)
Add-on to SoC only	1 (11)

Note: Groups not mutually exclusive. Percentages represent a proportion of the TA and HST recommended in a restricted indication (out of 9). [a]Age, disease stage, performance indicators, treatment history/contraindications.

Key decision drivers – Clinical evidence

- Of the treatments recommended in a restricted indication, 67% were critiqued for clinical data uncertainty compared to only 38% of treatments recommended in line with EMA marketing authorisation (Figure 3).
- Many of the treatments recommended in line with EMA marketing authorisation that were critiqued for clinical data uncertainty were dependent on a MAA (3/5, 60%).
- Most treatments with a negative recommendation were critiqued for data uncertainty (3/5) or lack of direct comparative clinical data (3/5).

Figure 3: Treatments critiqued for clinical evidence submission

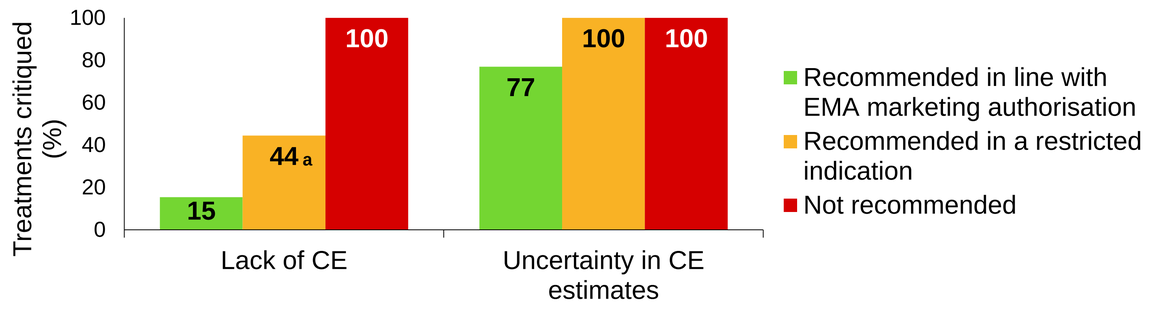


Note: Percentages represent a proportion of the TA and HST that received each recommendation (recommended in line with EMA marketing authorisation: 13; recommended in a restricted indication: 9; not recommended: 5). [a]Uncertainty in long-term benefit, quantifying size of treatment benefit, potential bias or confounding, small patient population.

Key decision drivers – Cost-effectiveness

- All 5 negative recommendations were driven by lack of CE and uncertainty in CE estimates (Figure 4).
- Only 2 treatments (15%) recommended in line with EMA marketing authorisation were not CE. Both indications have high disease burden and recommendations depended on a MAA or CDF funding.[3,4]

Figure 4: Treatments critiqued for lack of CE and uncertainty in CE estimates



Note: Percentages represent a proportion of the TA and HST that received each recommendation (recommended in line with EMA marketing authorisation: 13; recommended in a restricted indication: 9; not recommended: 5). [a]Treatments were only considered CE in the restricted indication.

Conclusions

- Aspects inherent to RD such as poorly defined populations and small population size create challenges in data collection. The consequent uncertainty in clinical data and the impact on reliability of CE estimates affects the likelihood of a positive, unrestricted recommendation.
- England is a CE-driven market, and, unsurprisingly, lack of CE was a key driver in all negative decisions. However, 2 treatments were recommended in line with EMA marketing authorisation despite lack of CE. These positive recommendations depended upon further data collection via a MAA/CDF to address uncertainty, and the committee considered the substantial disease burden experienced by patients and caregivers in their decision.
- Population restrictions alongside MAA and discounts allow payers to accommodate a degree of uncertainty, thereby supporting patient access. Following the demonstration of patient benefit, there is also a need to optimise the evidence base to reduce uncertainty on key CE model inputs, thereby reducing payer risk and increasing the likelihood of unrestricted patient access at a price reflective of the product's value.

Abbreviations: CDF: Cancer Drugs Fund; CE: cost-effectiveness; EMA: European Medicines Agency; HST: highly specialised technology; MAA: managed access agreement; NICE: National Institute for Health and Care Excellence; PAS: patient access scheme; RD: rare diseases; RWE: real-world evidence; SoC: standard of care; TA: technology appraisal.

References: 1. Horscroft, J. et al. *Demonstrating the Value of Drugs for Rare Diseases – 8 Common Challenges and How to Address Them Before They Arise* [White paper]. 2.TA863, NICE (2023). 3. TA755, NICE (2023). 4. TA895, NICE (2023). Included TA and HST are detailed in supplementary materials.

For further details contact: catherine.stothard@nexusvalues.com

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