Impact of the Introduction of the NICE Severity Modifier on HTA Outcomes of Oncology and Non-oncology Orphan Drugs

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Introduction

- NICE introduced the severity modifier in 2022 aiming to broaden the range of severe conditions that qualify for an additional weighting, effectively raising the cost-effectiveness threshold while managing the finite budget of the NHS[1].
- This replaced the previous 'end-of-life' modifier, which provided a higher weight to treatments that improved patient outcomes at the later stages of a disease[1] but was criticised for being too narrow and not considering QoL improvements[2].
- The new severity modifier defines severity more broadly, accounting for both QoL and severity.[2] However, the 'opportunity cost neutral approach' of the severity modifier may inadvertently limit patient access to late-stage treatments for severe diseases[3].
- We evaluated the impact of the severity modifier on HTA outcomes of orphan drugs and whether there is variation in patient access to oncology vs. non-oncology orphan drugs.

Methods

- Since abstract publication, the methodology of this research has been refined to exclude HST appraisals. The severity modifier weighting of 1.2 or 1.7 is calculated based on shortfall in discounted QALYs between those with the conditions and the general population[2], whereas the weighting applied in HST appraisals (between 1.0-3.0) is determined by undiscounted QALY gains[4].

NICE TAs for drugs with EMA and/or MHRA orphan designation (published between January 2022 - December 2024) were identified

Exclusions

- Terminated appraisals
- HST appraisals
- MTAs

Pre-defined topics were extracted

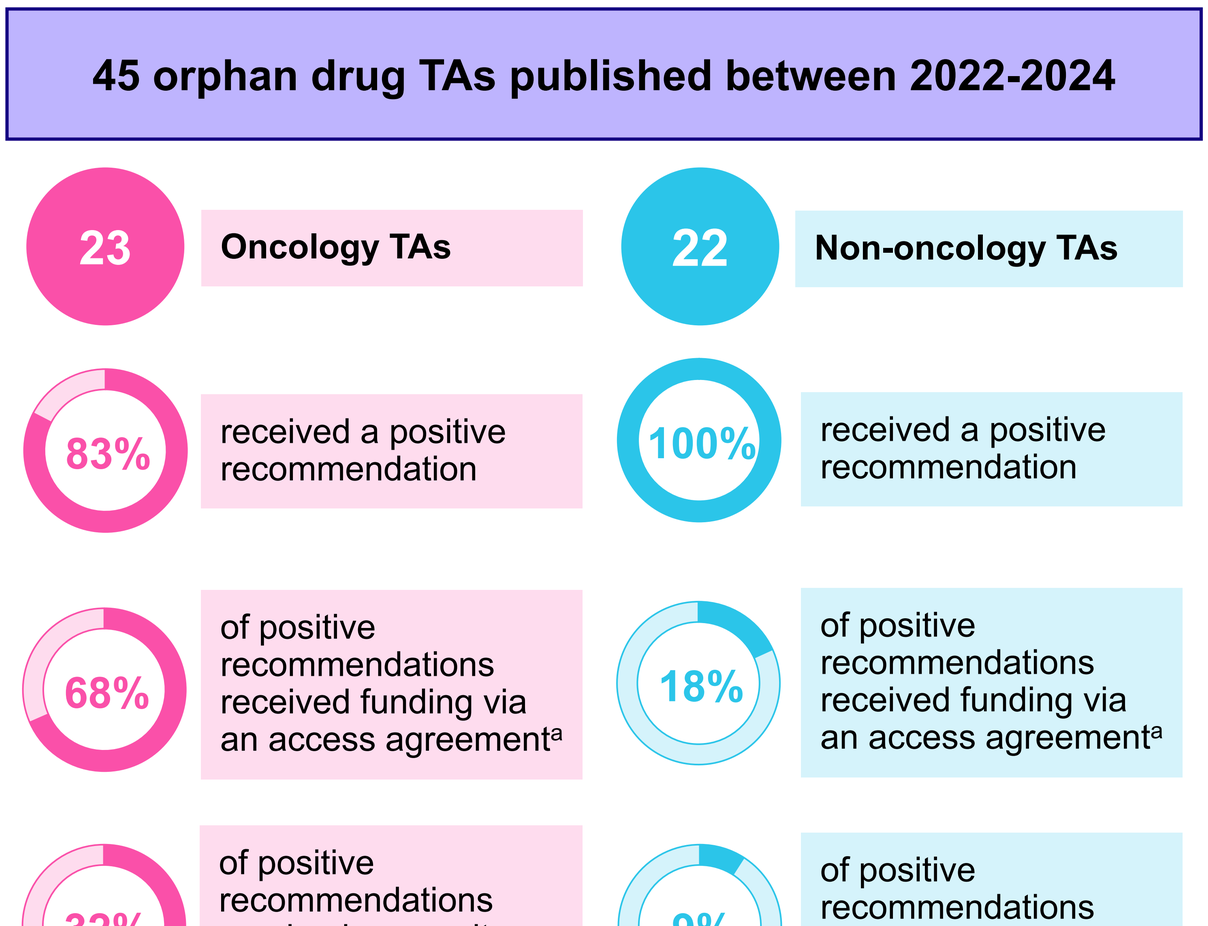
- Indication
- NICE recommendation
- Key decision drivers
- Application of a severity modifier
- Severity modifier weighting
- Use of access agreements

Results

Overview of NICE Technology Appraisals for Orphan Drugs

- Of the 213 TAs published between January 2022-December 2024, 45 were drugs designated orphan by either the EMA or MHRA.
- 41 orphan drugs were recommended with or without restrictions compared to its marketing authorisation (oncology: 19/23; non-oncology: 22/22; Figure 1).
- Of the positive orphan drug recommendations:
  - 17 depended on funding via an access agreement (oncology: 13; non-oncology: 4).
  - 8 received a severity modifier weighting (oncology: 6; non-oncology: 2). All TAs that received a severity modifier were recommended.

Figure 1: Outcomes of NICE TAs for orphan drugs published in 2022-2024



Notes: [a]Access agreements include MAAs or funding via the CDF.

Application of Severity Modifiers

- Of the recommended treatments with a severity modifier applied, more in oncology received the higher weighting of 1.7 compared to non-oncology indications (3/6 oncology vs. 0/2 non-oncology; Table 1).
- Of the recommended oncology treatments with a severity modifier applied, most were in a previously treated indication with 50% for patients who are heavily pre-treated (3L+; 3/6).

Table 1: Summary of NICE TAs that received a positive recommendation with a severity modifier applied

FAD	Treatment	Indication	LOT	⚖	🤝	%
Oncology						
TA977	Dabrafenib plus trametinib	BRAF V600E mutation-positive glioma in children	LGG: 1L+ HGG: 2L+[a]	LGG: 1.2 HGG: 1.7	N	Y
TA975	Tisagenlecleucel	R/R B-ALL	2L+	1.7	N	Y
TA954	Epcoritamab	R/R DLBCL and high-grade BCL	3L+	1.2[b]	Y	Y
TA947	Loncastuximab tesirine	R/R DLBCL and high-grade BCL	3L+	1.2[b]	Y	Y
TA948	Ivosidenib	Advanced cholangiocarcinoma with an IDH1 R132 mutation	2L+	1.7	Y	Y
TA927	Glofitamab	R/R DLBCL	3L+	1.2[b]	Y	Y
Non-oncology						
TA1011	Belzutifan	VHL disease[d]	Unspecified	1.2	Y	N
TA896	Bulevirtide	Hepatitis D	Unspecified	1.2	N	Y

Key: ⚖ Severity modifier weighting; 🤝 Dependent on an access agreement[c]; % Received a simple discount PAS

Notes: [a]After at least one radiation or chemotherapy treatment post-surgical resection. [b]When compared to a specific comparator. [c]Access agreements include MAAs or funding via the CDF. [d]For the treatment of tumours associated with VHL

Positive Recommendations Dependent on Access Agreements

- Of the recommended oncology treatments, 68% (13/19) were dependent on funding via the CDF, with 4/6 of the recommended treatments with a severity modifier dependent on funding via the CDF.
- Of the recommended non-oncology treatments, 18% (4/22) were dependent on a MAA, with 1/2 of the recommended treatments with a severity modifier dependent on a MAA.
- All TAs that received a positive recommendation and a severity modifier weighting included a simple discount PAS apart from one non-oncology approval in VHL disease.

Conclusions

- Despite non-oncology orphan drugs receiving a higher proportion of positive recommendations compared with oncology drugs, the limited applications of the severity modifier indicate that positive recommendations in rare diseases are not solely reliant on the severity modifier.
- The increased use of severity modifiers in oncology indications may reflect that half of the recommended treatments were in later lines of therapy.
- Other factors such as receiving funding via an access agreement or receiving a simple patient access discount also impact whether a drug is likely to be considered cost-effective and made available for use on the NHS.

Abbreviations: 1L+: first line plus; 2L+: second-line plus: 3L+: third-line plus; B-ALL: B-cell acute lymphoblastic leukaemia; BCL: B-cell lymphoma; BRAF: B-Raf; CDF: Cancer Drugs Fund; DLBCL: diffuse large B-cell lymphoma; EMA: European Medicines Agency; FAD: final appraisal document; HGG: high-grade glioma; HST: highly specialised technology; HTA: health technology assessment; IDH1: isocitrate dehydrogenase 1; LGG: low-grade glioma; LOT: line of therapy; MAA: Managed Access Agreement; MHRA: Medicines and Healthcare products Regulatory Agency; MTA: multiple technology appraisal; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; PAS: patient access scheme; QoL: quality of life; R/R: relapsed or refractory; TA: technology appraisal; VHL: von Hippel-Lindau.

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1. NICE. What is NICE's severity modifier? [Available from: https://indepth.nice.org.uk/what-is-nices-severity-modifier/index.html]
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4. NICE highly specialised technology appraisals. [Available from: https://www.nice.org.uk/guidance/published?ngt=Highly+specialised+technologies+guidance]

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