The impact of the NICE disease severity modifier on the willingness-to-pay threshold

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Background and objectives

On 31 January 2022, NICE published an updated manual on the process and methods for HTAs.

As part of this update, EOL criteria—introduced in 2009—were replaced with a new severity modifier (1). These EOL criteria allowed NICE to recommend therapies indicated for patients with a short life expectancy even if these treatments had a higher than usually accepted ICER.

The severity modifier aims to encompass a broader range of disease areas, as well as formally, quantitatively, and transparently allowing additional weightings to be applied to incremental QALYs for patients with severe diseases (2). This is accomplished via the use of 2 measures of severity: the AS and PS. The severity modifier allows for flexibility in the WTP threshold above the standard £20,000-£30,000/QALY gained for technology appraisals (1). The method by which these values are calculated and their impact on the WTP threshold are outlined in Table 1.

This research aims to critically analyse the use of the severity modifier as opposed to EOL criteria in HTA submissions between June 2022 and June 2023. A case study analysis of appraisal TA852, which was resubmitted with additional evidence following the introduction of the severity modifier, is also provided.

Table 1. Absolute and proportional shortfall calculations and WTP threshold values

QALY weight	AS[a]	PS[b]	WTP threshold
x1	<12	<0.85	£20,000 to £30,000
x1.2	12 to 18	0.85 to 0.95	Up to £36,000
x1.7	≥18	≥0.95	Up to £51,000

[a]Remaining QALY expectation in the absence of disease – remaining QALY expectation with disease
[b]Disease-related QALY loss (AS) ÷ remaining QALY expectation in the absence of disease

Results

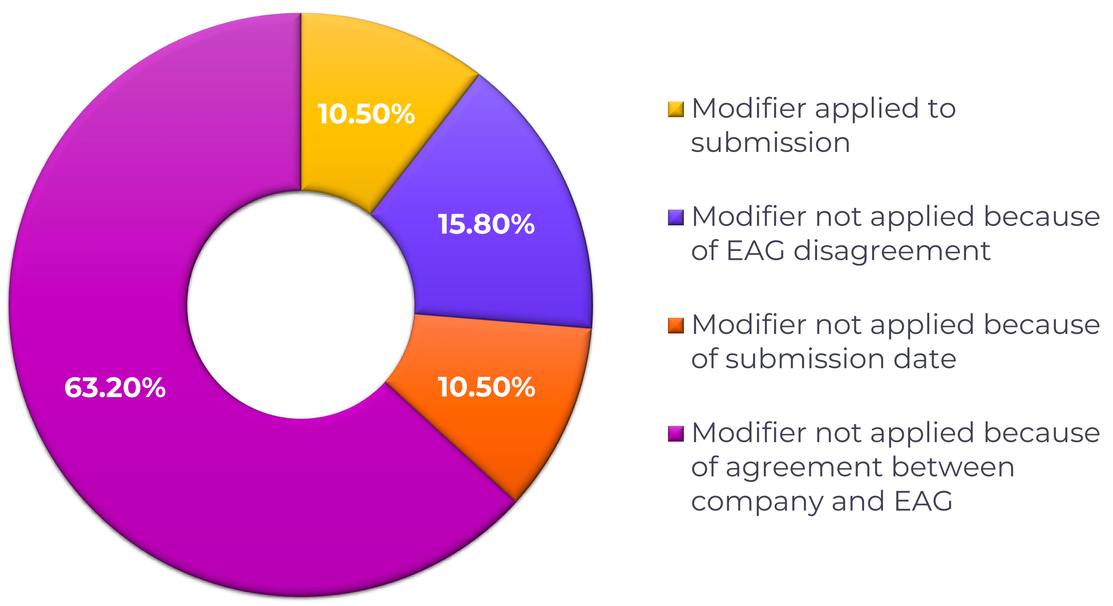
Between June 2022 and June 2023, 96 single-technology and 1 multiple-technology appraisal submissions were published. Terminated appraisals (n=25) were excluded, leaving 72 appraisals that were suitable for analysis.

Among these 72 appraisals, the severity modifier was considered/calculated by the submitting company in 19 submissions (26.4%; see Figure 1).

- Severity modifier applied to submission = 2/19 (10.5%)
- Severity modifier not applied because of an agreement between the company and EAG = 12/19 (63.2%)
- Severity modifier not applied because of EAG disagreement = 3/19 (15.8%)
- Severity modifier not applied because of submission date = 2/19 (10.5%)

Based on our analysis of the 20 appraisals that included sufficient data to calculate the AS and PS values, the WTP thresholds of 6 appraisals may have been altered using the severity modifier rather than any of the EOL criteria. An increased WTP threshold may have been applied to 2 appraisals; 4 may have had a reduced threshold applied.

Figure 1. NICE HTA submissions from June 2022 to June 2023 that considered the severity modifier



Methods

NICE single- and multiple-technology appraisal submissions between June 2022 and June 2023 were reviewed, with all terminated appraisals excluded from the analysis.

Key data required for the calculation of the AS and PS were extracted. This included the mean age at diagnosis, the male/female ratio of the target population, and the QALYs of patients, along with their current SOC. Further information on the company's submitted ICER value and whether the EOL criteria or severity modifier were applied to the submission was extracted.

Where appropriate and when sufficient data were available, the online QALY shortfall calculator (3) was utilised to calculate the severity modifier that may have been applied and the resulting WTP threshold for the treatment in question.

Case study analysis of TA852: Trifluridine-tipiracil for treating metastatic gastric cancer or gastro-oesophageal junction adenocarcinoma after 2 or more treatments

- The first NICE HTA submission to have the severity modifier applied
- Originally not recommended for use (TA699) because it did not meet the EOL criteria of extending survival by more than 3 months
- Upon the introduction of the severity modifier, the company was invited by NICE to resubmit evidence for review with the incorporation of the severity modifier
- Based on the mean age at diagnosis, sex distribution, and QALYs of the general population and patients with the disease (as well as their current SOC), the AS and PS values were 11.32 and 96.84%, respectively (Table 2)
    - Although the AS value was <12, which would imply no additional QALY weighting, the PS value was ≥0.95, meaning that a x1.7 QALY weighting was applied (Table 1)
- This meant that the company's base-case ICER value of £45,662/QALY gained was accepted as a result of the WTP threshold being increased from £20,000-30,000/QALY gained to £51,000/QALY gained

Table 2. TA852 AS and PS shortfall analysis

Mean age at diagnosis	Female % of target population	Severity modifier applied	WTP threshold	Expected QALY years		Shortfall	
				General population	With SOC	Absolute	Proportional
62 years	33.6%	x1.7	Up to £51,000	11.69	0.37	11.32	96.84%

Conclusions

Of the 72 technology appraisals analysed as part of this review, only 2 had the severity modifier applied following an EAG critique (TA866 and TA852).

Based on the methods outlined in Table 1, the WTP thresholds of 6 appraisals may have been altered using the severity modifier rather than by utilising any of the EOL criteria. Moreover, a greater WTP threshold of £36,000/QALY gained may have been applied to 2 of these appraisals as opposed to the standard threshold of £20,000-£30,000/QALY gained. Three of these appraisals originally met the EOL criteria, meaning that the WTP thresholds for these submissions were £50,000/QALY gained. However, our analysis revealed that had the severity modifier been applied in place of the EOL criteria, these appraisals may have had a lower WTP threshold compared with the original threshold of £50,000/QALY gained.

Appraisal TA852, replacing TA669, was resubmitted with additional evidence following the introduction of the severity modifier. This was because the EOL criteria were not originally met, and the product was therefore not recommended for use in January 2021. The introduction of the severity modifier—and the subsequent removal of the EOL criteria—increased the WTP threshold to £51,000/QALY gained, meaning the therapy was recommended for use.

Furthermore, approximately 16% (3/19) of the appraisal submissions for which the submitting company requested that the severity modifier be considered did not have it applied because of discrepancies in the absolute and/or shortfall values calculated by the company and the EAG.

Our analysis underscores the importance of awareness among submitting companies regarding the utilisation of severity modifiers in their evidence submissions. It also emphasises the necessity of carefully considering all alternative modelling scenarios in order to adequately prepare for appraisal outcomes.

Abbreviations: AS, absolute shortfall; EAG, external assessment group; EOL, end-of-life; HTA, health technology assessment; ICER, incremental cost-effectiveness ratio; NICE, National Institute for Health and Care Excellence; PS, proportional shortfall; QALY, quality-adjusted life year; SOC, standard of care; WTP, willingness to pay

References

1. National Institute for Health and Care Excellence. NICE technology evaluations: the manual (PMG36) [Internet]. London; 31 January 2022 [cited 23 October 2023]. Available from: https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741.
2. McNamara S, Schneider P, Love-Koh J, Doran T, Gutacker N. Quality-adjusted life expectancy norms for the English population. Value in Health. 2023;26(2):163-9.
3. Schneider P, McNamara S, Love-Koh J, Doran T, Gutacker N. QALY shortfall calculator [Internet]. York; 2021 [cited 23 October 2023]. Available from: https://shiny.york.ac.uk/shortfall.

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