Comparator misalignment as a contributor to negative reimbursement decisions for pharmaceuticals in Sweden

HTA80

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Background

The Swedish Dental and Pharmaceutical Benefits Agency (TLV) evaluates health technology assessment (HTA) submissions to determine whether pharmaceutical products should be included in the national reimbursement scheme. A critical aspect of these evaluations is the choice of a relevant comparator, as it directly affects the assessment of clinical and economic outcomes. As TLV's a general rule, the most cost-effective of the clinically relevant treatment alternatives available in Sweden should be used as the comparator [1]. Companies propose a relevant comparator in their reimbursement submissions, but TLV may decide that an alternative comparator better reflects standard care in Sweden. This may influence the assessment of cost-effectiveness and impact the reimbursement decision.

This study aims to assess how often TLV requests changing the comparator in HTA submissions, and whether such changes contribute to the rejection of the reimbursement applications.

Methods

A search was conducted in the NMA*i* tool [2] to identify all TLV reimbursement rejections issued in a 10-year period (between 2015-01-01 to 2025-01-01), filtered by category (decisions), and subcategory (rejections and exclusions). For each case, the decision and the supporting assessment report were retrieved and reviewed. Key information was extracted, such as the comparator selected by the company TLV's suggested comparator, or the company's effort to comply. Missing assessment reports were requested from TLV. Data were analysed to assess how often TLV identifies a different relevant comparator and if this contributed to rejections.

1. **Search** – NMA*i* tool, filtered for rejections/exclusions
2. **Collect** – Final decisions + reimbursement documents
3. **Extract** – Company comparator, TLV comparator, arguments, outcomes
4. **Verify** – Request missing documents from TLV
5. **Analyse** – Assess frequency and reason of comparator changes

Results

A total of 105 hits were identified, including both TLV decisions and assessment reports. From these, 76 unique assessments were identified.

TLV did not agree with the suggested comparator in 19 of the 76 rejected assessments (25%), representing 17 unique medicines (including two reassessed for the same indication). These covered diverse disease areas, most frequently neurology (4) and oncology (3), with nine other areas represented by two or fewer assessments each.

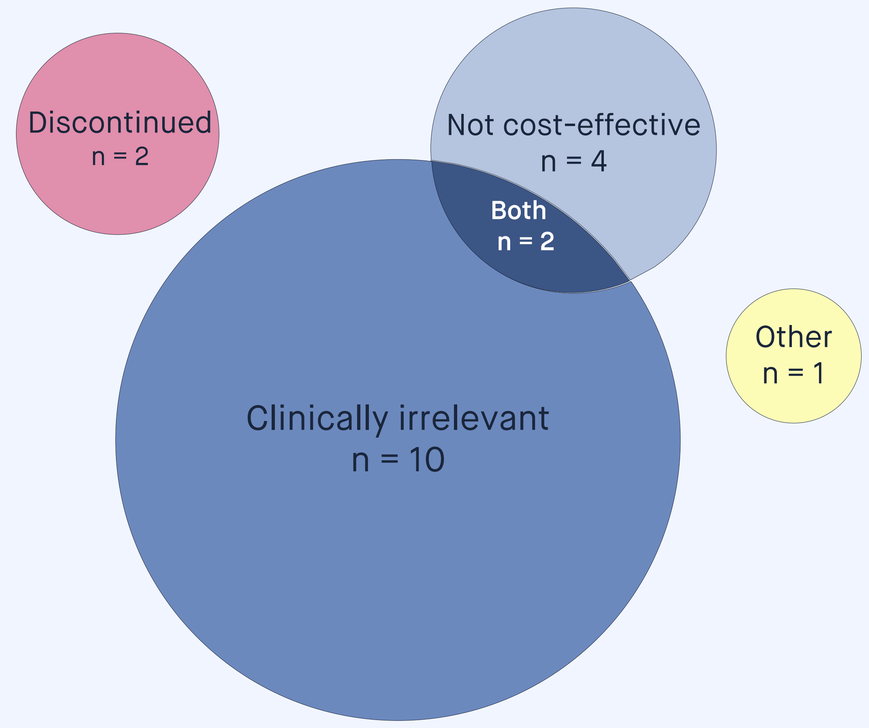
TLV's rationale for suggesting an alternative comparator fell into four categories. The largest category, observed in 10 assessments, was that the chosen comparator was not the most clinically relevant treatment option, based on clinical guidelines and/or expert opinion. In 4 assessments, the comparator was deemed not to be the most cost-effective alternative, either because it had not been previously assessed in Sweden or had been rejected for failing to meet criteria for inclusion in the reimbursement scheme. In two assessments, the comparator was considered both clinically irrelevant and not cost-effective. Two smaller categories were also identified. In two assessments, TLV rejected the comparator because they were soon to be discontinued. In one assessment, TLV acknowledged that the comparator was clinically relevant but could not conduct an analysis due to a confidential price agreement between the company and the regions. TLV therefore determined that no addition to best supportive care (BSC) was the most appropriate comparator in this case. This assessment was from 2021, since then TLV has access to confidential net prices.

In most assessments, the change in comparator affected the outcome of the submission. Companies were either unable to provide the necessary analysis (73.7%) or failed to demonstrate cost-effectiveness against the new comparator (26.3%).

Of the 17 unique medicines, 13 (76.5%) were reassessed at a later date, and 8 out of these (61.5%) subsequently received reimbursement for the same indication as previously submitted.

Six resubmitted with TLV's preferred comparator. In one case the submission was reassessed, and the company's comparator was accepted. In the last one, the company kept their comparators from their previously submitted but restricted the reimbursement to the treatment line following TLV's suggested comparator.

Figure 1. TLV's reason for not accepting comparator chosen by the company



Discussion and conclusion

In the assessments where TLV disagreed with the company's selected comparator, TLV's general advice (Allmänna råd TLVAR 2003:2) on economic evaluations [1] was cited as the guiding framework. It specifies that the most cost-effective of the clinically relevant treatment alternatives available in Sweden should be used as the comparator. These may include not only other medications but also non-pharmacological treatments, medications outside the pharmaceutical benefits scheme, or medicines approved for other indications. When no clinically relevant and cost-effective alternatives exist, "no treatment" may be used as a comparator.

Our findings show that TLV most often changed the comparator because the company's proposed option was considered either clinically irrelevant or not cost-effective. No cases were identified in which medicines outside the reimbursement scheme were accepted as comparators. When TLV suggested BSC or generic drugs as comparators, companies frequently struggled to demonstrate cost-effectiveness. One assessment was identified as an outlier, where TLV could not accept the clinically most relevant comparator due to a confidential net price agreement between the company and the regions. Thus, BSC was used as a common comparator.

As this study included only published rejected applications, no conclusions can be drawn about the overall rejection rate following a change in comparator or the proportion of companies that successfully demonstrated cost-effectiveness upon resubmission. Companies also have the possibility to withdraw applications that risk a negative outcome. Regardless, the findings indicate that in one-quarter of rejections during this period, comparator mismatch played an important role.

References

1. TLV:s allmänna råd (TLVAR 2003:2) om ekonomiska utvärderingar, updated 2015 and reprinted 2017. 2. Palomar M, et al. Using the NMA*i* tool to ease comparative analyses of HTAs in the Nordics. ISPOR Europe 2024 Conference; 2024 Nov 10–13; Barcelona