How Much Does TLV Value Rarity? A Review of Reimbursement Decisions on Orphan Drugs in Sweden From 2017 Through 2022

Lanne G,[1] Kinderås M,[1] Brodtkorb TH,[1] Ling C[2]

[1]RTI Health Solutions, Ljungskile, Sweden; [2]RTI Health Solutions, Manchester, United Kingdom

BACKGROUND

- To facilitate the development of medicines for rare diseases, the European Medicines Agency grants orphan drug designation to medicines that are intended for life-threatening or chronically debilitating diseases with a prevalence of 5 or fewer in 10,000 in the European Union (EU).[1]
- Although it addresses conditions with high unmet need, reimbursement of orphan drugs continues to pose significant challenges for decision-makers given frequent high costs and limited evidence, such as small studies that are often single-armed and may include surrogate outcomes.
- In Sweden, the Dental and Pharmaceutical Benefits Agency (TLV) is responsible for deciding on the reimbursement of outpatient drugs, and historically, its decision-making was not influenced by the rarity of a condition.
- However, with the pricing decision for imiglukeras and velaglukeras alfa for the treatments of Gaucher's disease in 2016, TLV accepted for the first time a higher cost per quality-adjusted life-year gained due to the rarity of the targeted condition. The accepted incremental cost-effectiveness ratio (ICER) was twice as high—2,000,000 SEK—as the previous unofficial willingness-to-pay (WTP) threshold of 1,000,000 SEK for very high disease severity, which did not account for the rarity of the condition.[2,3]
- However, it is unclear whether this decision is a one-time increase in WTP or the start of a new decision rule for TLV in rare diseases. Thus, we still do not know how TLV values rarity or the implications for future appraisals.

OBJECTIVES

- To explore whether the rarity of the conditions has impacted the ICERs accepted by TLV from 2017 through 2022.

METHODS

- We identified all TLV decisions on reimbursement applications of medicinal products from 1 January 2017 through 31 December 2022 that had orphan drug status according to EU regulations[1] at the time of TLV evaluation and included a TLV ICER as a basis for decision.
  - When TLV evaluated subpopulations with separate ICERs, each subpopulation was categorized as a separate decision.
- Extracted variables for each decision included:
  - Decision date
  - ICER in TLV base case or TLV scenario analyses (For decisions that only included TLV scenario analyses, the mean was used because the scenario analyses were the basis for decision in those cases.)
  - TLV's assessment of disease severity (from low to very high)
  - TLV's assessment of the uncertainty in the health economic analysis (from low to very high)
- For each of the products, the number of patients affected per 10,000 in the EU was derived from the European Medicines Agency orphan drug designation to determine the rarity of the condition. The figure was multiplied by the total population of Sweden[4] to estimate the number of patients with the condition in Sweden.

RESULTS

- There were TLV decisions on 33 different products with orphan drug status in the 6 years from 2017 to 2022 at the time of each product's TLV evaluation.
  - 41 TLV decisions on 21 different products met the inclusion criteria (i.e., had a TLV ICER as basis for decision).
  - In 22 of the 41 decisions, the ICER was accepted, with an estimated mean number of 1,842 patients with each condition in Sweden (range, 105-4,209), and a mean TLV ICER of 753,628 SEK (range, 96,784 SEK-1,450,696 SEK).
  - In 19 cases, the ICER was not accepted, with an estimated mean number of 1,713 patients with each condition in Sweden (range, 105-5,261) and a mean TLV ICER of 4,987,857 SEK (range, 935,968 SEK-11,474,123 SEK).
- Only 2 positive decisions had ICERs above the previous unofficial WTP threshold of 1,000,000 SEK for very high disease severity, not accounting for the rarity of the condition.
- 5 negative decisions had ICERs between 1,000,000 SEK and 2,000,000 SEK, of which 3 addressed conditions that were assessed as very high disease severity and 2 as high disease severity.
- No clear trend was observed between the rarity of the conditions and the accepted TLV ICERs (Spearman rank correlation, −0.009). Instead, accepted ICERs seem to be mostly impacted by the disease severity, as is the case also for non-orphan drugs.

Figure 1. TLV Base-Case ICERs in Decisions on Products With Orphan Drug Status, 2017-2022

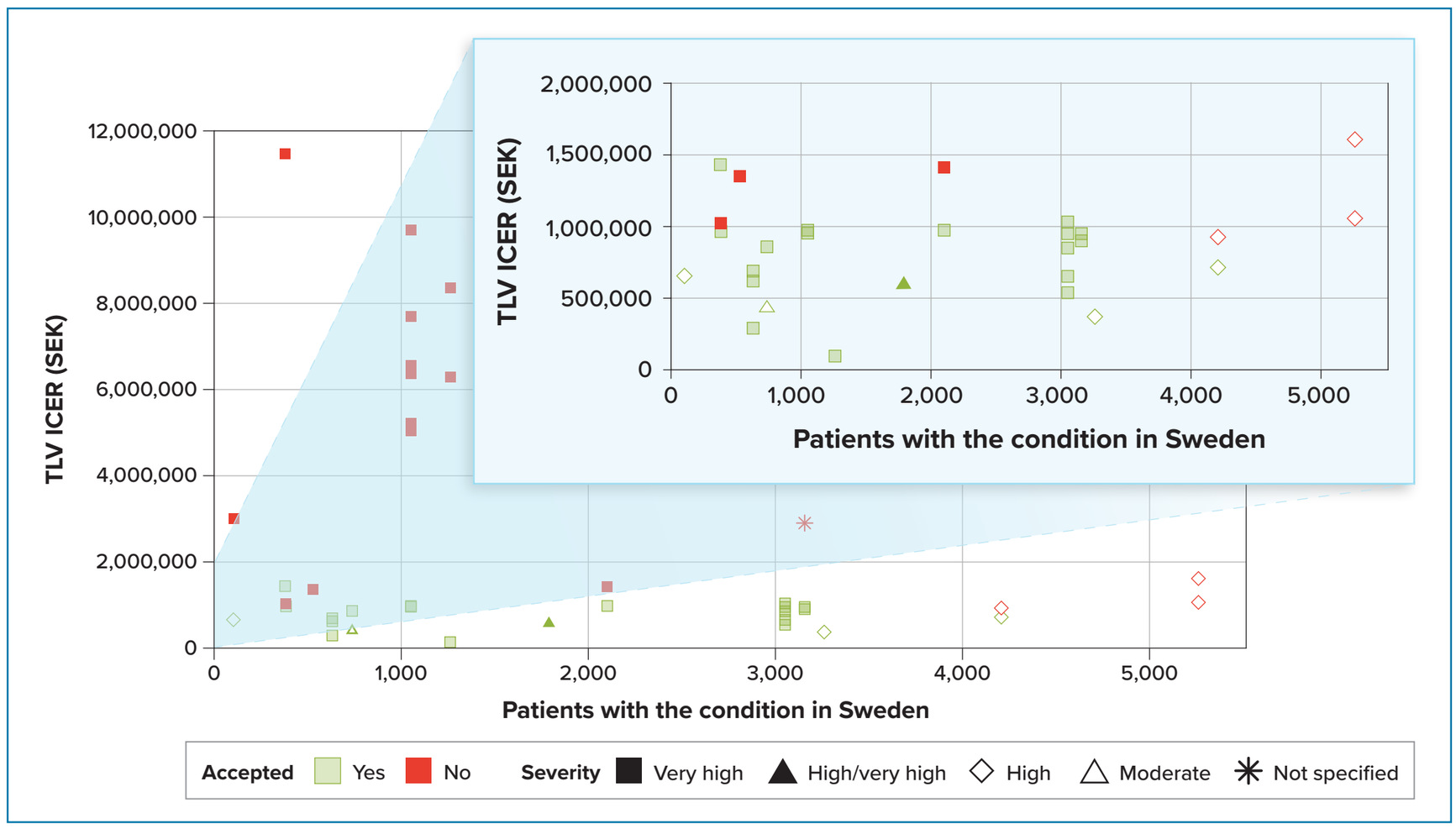


Table 1. Highest Accepted TLV ICERs (SEK) and Lowest Rejected TLV ICERs (SEK) by Severity and Uncertainty in Orphan Drugs

Severity	Uncertainty in the health economic analysis					
	Very high	High	Moderate to high	Moderate	Low	Not specified
Very high	1,450,696 1,028,000	984,776 11,474,123	968,247	901,883	960,884	983,000 3,000,000
Very high to high	—	586,35	—	—	—	—
High	—	720,412 935,968	—	—	—	376,581
Moderate	—	—	—	423,500	—	—
Not specified	2,903,946	—	—	—	—	—

Note: This table presents the highest accepted TLV ICERs (SEK) and lowest rejected TLV ICERs (SEK) in TLV decisions on products with orphan status in relation to TLV's assessments of disease severity and uncertainty in the health economic analysis.

CONCLUSION

- Although the decision made by TLV in 2016 on imiglukeras and velaglukeras alfa opened rarity for consideration in determining acceptable ICERs, the current review suggests that there has not been any clear shift in accepted ICERs as a function of rarity.

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CONTACT INFORMATION

Maria Kinderås, MSc
Senior Research Associate

RTI Health Solutions

Ljungskile Hälle Lider 2B SE 45932
Ljungskile, Sweden

Telephone: +1.919.485.1149
Email: mkinderas@rti.org

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