国立保健医療科学院 保健医療経済評価研究センター
Center for Outcomes Research and Economic Evaluation for Health (C2H), National Institute of Public Health (NIPH) | URL: http://c2h.niph.go.jp

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# [C2H2110] Summary of cost-effectiveness evaluation of Teduglutide (Revestive)

## 1. Indications

Short Bowel Syndrome (SBS)

## 2. Price of the drug

Teduglutide has been reimbursed since November 2021 at JPY 79,302 (as of March 2023). The price was calculated using a method that included a usefulness premium (II) of 5%. This product was designated as the H2 item for cost-effectiveness evaluation.

## 3. Scope of the cost-effectiveness evaluation

This product is indicated for the treatment of SBS. The scope of evaluation agreed upon during the first session of the Expert Committee of Cost-Effectiveness Evaluation (ECCEE) is described below.

| | |
|---|---|
| Population | (a) Adult SBS patients<br>(b) Pediatric SBS patients |
| Comparator | Standard care<br>(Selected technology: Teduglutide + Standard care) |

## 4. Evaluation of additional benefits

In the systematic review, the manufacturer detected a clinical trial for SBS in populations (a) and (b) and found that teduglutide had an additional benefit over comparator technologies, significantly improving the response rate. In response, the academic group added other relevant publications. Additional benefits in population (a) were primarily evaluated in the CL0600-020 trial (STEPS trial), a randomized controlled trial (RCT) involving adult patients with SBS.

The results of the STEPS trial demonstrated that the teduglutide arm was significantly superior to the standard care arm in terms of the proportion of patients who experienced a reduction of at least one day of PS per week, improving the response rate and PS change.

Moreover, additional benefits in population (b) were evaluated primarily in the TED-C14-006 trial (006 trial), an RCT involving pediatric patients with SBS. The 006 trial was an open-label trial, which may have led to an imbalance in patient backgrounds. However, teduglutide's benefit was evaluated in a post-hoc analysis that reported a statistically significant increase in the number of responders in the teduglutide arm than in the standard care arm. Moreover, there was a trend toward the superiority of the teduglutide arm in terms of the number of days of PS performed per week and decreasing the amount of PS needed.

Based on these results, the post-hoc analysis determined additional benefits for teduglutide in both populations (a) and (b).

5. Results of the cost-effectiveness analysis

The manufacturer conducted a cost-effectiveness analysis using a Markov model comprising nine health states for population (a) and five health states for population (b), based on the number of days per week of PS administered.

In response, the academic group added a long-term setting based on the long-term observational results of the CL0600-004 trial (004 trial), in which some PS withdrawals continued teduglutide treatment. This was because of the the assumption that patients who withdrew from PS would maintain their discontinued teduglutide treatment is clinically inappropriate.

Additionally, the manufacturer assumed that the long-term effects on the reduction in PS implementation days would continue for over two years for children and five years for adults. However, the rationale and validity of this setting were unclear. Therefore, the academic group conducted an analysis assuming that no state transitions occurred after the observation period in the STEPS-2 or 006 trials for populations (a) and (b), respectively.

C2H deemed further reanalysis necessary because we should consider the large uncertainty can not be avoided in rare pediatric diseases. Therefore, C2H continued to review the analytical model, and inquire about the manufacturer.

As a result, populations (a) and (b) were analyzed in a setting where a certain percentage of all SBS patients in the model would continue teduglutide treatment in the long term, based on the results of the long-term observational

study of the 004 trial and unpublished information. However, regarding the long-term effects on the reduction, manufactures' suggestion was accepted. C2H submitted the resulting ICERs mentioned below for final analysis.

| Population | ICER (JPY/QALY) |
|---|---|
| Adult SBS patients | 88,522,201 |
| Pediatric SBS patients | 9,533,412 |