[C2H2408] Summary of cost-effectiveness evaluation of Insulin Icodec (Awiqli)

1. Indications

Diabetes requiring insulin therapy

2. Price of the drug

The Awiqli Injection FlexTouch 300 Units has been reimbursed since November 2024, and its price as of June 2026 was JPY 2,081. The price was determined using the Similar Efficacy Comparison Method (I), with a usefulness premium (II) of 5%. The product was designated as an item for cost-effectiveness evaluation under the H1 classification.

3. Scope of cost-effectiveness evaluation

This product is used to treat patients with diabetes requiring insulin therapy. The scope of evaluation, as agreed upon at the first session of the Expert Committee of Cost-Effectiveness Evaluation (ECCEE), is described below:

Target population	(a) Type 1 diabetes (b) Insulin-naïve type 2 diabetes (c) Basal insulin-treated type 2 diabetes (d) Basal-bolus insulin-treated type 2 diabetes
Comparator	Insulin glargine U300

4. Evaluation of additional benefits

【Population (a)】

The manufacturer used the results of ONWARDS 6, a head-to-head trial comparing insulin icodec and insulin degludec U100, as no clear differences in efficacy or safety were identified between insulin glargine U300 and insulin degludec U100. The manufacturer concluded that insulin icodec was "inferior or could not be considered comparable," citing the difference in HbA1c change from baseline to week 26 (0.05% [95% CI −0.13 to 0.23]) and the estimated rate ratio (ERR) for clinically significant or severe hypoglycemia compared with degludec U100 (1.89 [95% CI 1.54 to 2.33]).

The academic group accepted the manufacturer's approach to evaluate both changes in HbA1c levels and the incidence of hypoglycemia. Regarding the

change in HbA1c, the academic group concluded that there were no additional benefits of insulin icodec over insulin glargine U300, as the difference in HbA1c change was within the non-inferiority margin and was not necessarily clinically meaningful. Regarding hypoglycemia, the academic group concluded that insulin icodec was "inferior or could not be considered comparable."

【Population (b)】

The manufacturer used the results of ONWARDS 3, a head-to-head trial comparing insulin icodec and insulin degludec U100. The manufacturer concluded that insulin icodec demonstrated additional benefit, citing the difference in HbA1c change compared with insulin degludec U100, which was statistically significantly lower for insulin icodec from baseline to week 26 (−0.2% [95% CI −0.3 to −0.1]).

The academic group evaluated both the changes in HbA1c levels and the incidence of hypoglycemia. Regarding the change in HbA1c, the academic group concluded that no additional benefits of insulin icodec over insulin glargine U300 were demonstrated, as ONWARDS 3 was designed as a non-inferiority trial and the differences in HbA1c change were not necessarily clinically meaningful. Regarding hypoglycemia, the academic group concluded that insulin icodec was "inferior or could not be considered comparable," citing the ERR for clinically significant or severe hypoglycemia compared with insulin degludec U100, which was statistically significantly higher for insulin icodec from baseline to week 26 (3.12 [95% CI 1.30 to 7.51]) and showed a trend toward being higher from baseline to week 31 (1.82 [95% CI 0.87 to 3.80]).

【Population (c)】

The manufacturer used the results of ONWARDS 2, a head-to-head trial comparing insulin icodec and insulin degludec U100. The manufacturer concluded that insulin icodec demonstrated additional benefit, citing the difference in HbA1c change compared with insulin degludec U100, which was statistically significantly lower for insulin icodec from baseline to week 26 (−0.22% [95% CI −0.37 to −0.08]).

The academic group evaluated both the changes in HbA1c levels and the incidence of hypoglycemia. Regarding the change in HbA1c, the academic group concluded that no additional benefits of insulin icodec over insulin glargine U300 were demonstrated, as ONWARDS 2 was designed as a non-inferiority trial and the differences in HbA1c change were not necessarily clinically meaningful.

Regarding hypoglycemia, the academic group concluded that insulin icodec was "inferior or could not be considered comparable," as the ERR for clinically significant or severe hypoglycemia was higher for insulin icodec than for insulin degludec U100 from baseline to week 31 (1.93 [95% CI 0.93 to 4.02]).

【Population (d)】
The manufacturer conducted a network meta-analysis because no head-to-head trials comparing insulin icodec and insulin glargine U300 or insulin degludec U100 were identified in a systematic review. The manufacturer found no significant differences in HbA1c change or the incidence of hypoglycemia and concluded that no additional benefits were demonstrated. The academic group largely confirmed this assessment.

5. Results of the cost-effectiveness analysis
The manufacturer did not conduct a cost-effectiveness analysis for population (a). The manufacturer conducted cost-effectiveness analyses for populations (b) and (c), and a cost-minimization analysis for population (d). The academic group conducted cost-minimization analyses for all populations because no additional benefits were demonstrated. The academic group used the manufacturer's model for population (d), but updated it with the latest drug prices and standardized proportions of concomitant medications using pooled data. In the ECCEE, the manufacturer asked the committee to consider the potential reduction in related medical costs for patients receiving home-visit nursing care, given that insulin icodec is administered once weekly compared to conventional once-daily insulin. The academic group conducted an additional analysis based on the committee's instructions. The results of the additional analyses were as follows:

Population	Comparator	ICER (JPY/QALY)
(a) Type 1 diabetes	Insulin glargine U300	Cost increase
(b) Insulin-naïve type 2 diabetes	Insulin glargine U300	Comparable cost
(c) Basal insulin-treated type 2 diabetes	Insulin glargine U300	Comparable cost
(d) Basal-bolus insulin-treated type 2 diabetes	Insulin glargine U300	Cost increase