# Cost-Effectiveness of Insulin Degludec vs. Insulin Glargine U100 in Type 1 Diabetes Mellitus in a Swedish Setting after One Year

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## Background and aims

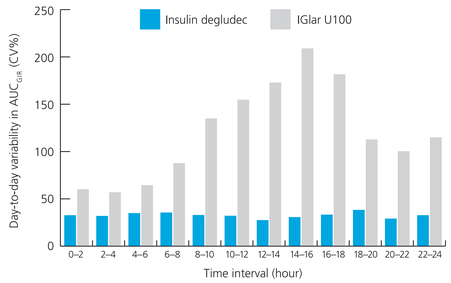
*Background*

- Insulin degludec is a basal insulin with a long duration of action and a flat glucose-lowering profile under steady-state conditions in type 1 diabetes (T1D).[1–3] Under these conditions insulin degludec has a four-fold lower day-to-day variability than insulin glargine 100 units/mL (IGlar U100, Figure 1).[3]
- According to randomised controlled trials, insulin degludec has a beneficial hypoglycaemia profile compared with IGlar U100.[4,5]
- Cost-effectiveness, as well as safety and efficacy, is an important factor in the decision to implement a new medication, and required for reimbursement in various countries, like Sweden.

*Aim*

This analysis was made to assess the cost-effectiveness of insulin degludec compared with original and biosimilar IGlar U100 in T1D in a Swedish health care setting, using evidence from SWITCH 1.

**Figure 1:** Lower day-to-day variability in glucose-lowering effect for degludec versus IGlar U100[3]




AUC, area under the curve; CV, coefficient of variation; GIR, glucose infusion rate; IGlar U100, insulin glargine U100

## Methods

- Evidence from the total data set of SWITCH 1[4] was used in this cost-effectiveness study.

*SWITCH 1*

- SWITCH 1 was a treat-to-target, multinational, double-blinded, two-armed, randomised, cross-over clinical trial (RCT) with two full treatment periods of 32 weeks respectively, with 16 weeks titration period and 16 weeks maintenance period.[4]
- Patients were randomised 1:1 to insulin degludec or IGlar U100 once daily, with insulin aspart 2–4 times daily as bolus insulin.
- At randomisation and at crossover, the starting dose of basal insulin was reduced by 20% in both treatment arms. The basal insulin dose was then titrated once weekly according to the trial algorithm.[4]
- Patients included in the study were at least 18 years old and had at least one risk factor of hypoglycaemia.
- Endpoints were difference blood glucose-confirmed symptomatic hypoglycaemic episodes (< 3.1 mmol/L; total, nocturnal and severe), reported after 16 weeks of maintenance period and after full treatment period.[4]
- A post hoc analyses of SWITCH 1 data showed a difference in rates of non-severe diurnal hypoglycaemia (Rate Ratio (RR) 0.98 (95% Confidence Interval [CI]: 0.94; 1.03)), but a significant reduction in both non-severe nocturnal (RR 0.76 (95% CI: 0.69; 0.84)) and severe (RR 0.74 (95% CI: 0.61; 0.91)) hypoglycaemic events in favour of insulin degludec. (Table 1)
- Insulin doses at the end of trial: IGlar U100 basal dose was 40.58 units/day. Insulin degludec/IGlar U100 basal dose ratio was 0.97 [95% CI: 0.94–0.99]. The bolus dose used in the IGlar U100 arm was 31.93 U/day and the bolus dose ratio for the two arms (insulin degludec/IGlar U100) was 0.97 [0.94–1.01]. (Table 1)

**Table 1:** Hypoglycaemic event rates, full treatment period, and end-of-trial insulin doses from SWITCH 1

| | IGlar U100 | Insulin Degludec* | Rate Ratio |
|---|---|---|---|
| Non-severe daytime hypoglycaemia | 1 718.08 | 1 683.72 | 0.98 (NS) |
| Non-severe nocturnal hypoglycaemia | 345.07 | 261.54 | 0.76 |
| Severe hypoglycaemia | 104.82 | 77.89 | 0.74 |
| Basal insulin dose (IUs per day) | 40.58 | 39.36 | 0.97 |
| Bolus insulin dose (IUs per day) | 31.93 | 30.97 | 0.97 (NS) |

*Calculated insulin degludec hypoglycaemic event ratio and dose ratio.

*Cost-effectiveness analysis*

- Cost-effectiveness was analysed over a 1-year time horizon with a Swedish health care perspective.
- The health economics model (DOSE) has been described elsewhere[6], and was used in the reimbursement application for insulin degludec in Sweden.
- Only differences with p<0.05 were included in the analysis.
- Costs were estimated based on the different rates of hypoglycaemic events and actual doses of insulin from SWITCH 1. (Table 1)
- Analyses were made for two different scenarios:
  - Insulin degludec vs IGlar U100 with a price = original IGlar U100. (Table 2)
  - Insulin degludec vs IGlar U100 with a price = biosimilar IGlar U100. (Table 3)
- The cost of pharmaceuticals was based on the Pharmacy Selling Price, PSP (Apotekens utpris, AUP) in April 2019.
- The cost of hypoglycaemic events was derived from studies measuring the cost of severe[7] and non-severe[8] events in Sweden (adjusted to the current price level by the consumer price index for health).
  - Costs are expressed in 2019 Swedish krona (SEK). (€ 1 = SEK 10.47, 19MAR2019)
- Difference in Quality-Adjusted Life-Years (QALYs) was calculated by applying a disutility value (which measures the impact of a health state on quality of life) to each type of hypoglycaemic event.[9]

## Results

- Costs, QALYs and Incremental Cost-Effectiveness Ratios (ICERs) for insulin degludec compared with original and biosimilar IGlar U100 are shown in Table 2 and 3, respectively. Pharmacy costs were higher for insulin degludec, but were partly offset by the costs of non-severe nocturnal and severe hypoglycaemia.
- Total cost difference was SEK 575–1 219.
- Insulin degludec was highly cost-effective compared with IGlar U100, with an incremental cost-effectiveness ratio (ICER) of SEK 25 000–52 000.

**Table 2:** Cost-effectiveness of insulin degludec compared with IGlar U100 (price=original)

| | Insulin Degludec | IGlar U100 (Original) | Incremental Cost (Insulin Degludec-IGlar) |
|---|---|---|---|
| **Pharmacy costs** | **13 095** | **12 097** | **998** |
| Insulin | 8 316 | 7 318 | 998 |
| Needles | 1 010 | 1 010 | 0 |
| SMBG tests | 3 769 | 3 769 | 0 |
| **Hypoglycaemic events** | **1 626** | **2 049** | **-423** |
| Non-severe diurnal events | 398 | 398 | 0 |
| Non-severe nocturnal events | 61 | 80 | -19 |
| Severe events | 1 167 | 1 571 | -404 |
| **Total costs** | **14 721** | **14 146** | **575** |
| **Effects** | | | |
| QALYs | 0.782 | 0.759 | 0.023 |
| **ICER (cost per QALY)** | | | **24 752** |

(€ 1 = SEK 10.47, 19MAR2019)

**Table 3:** Cost-effectiveness of insulin degludec compared with IGlar U100 (price=biosimilar )

| | Insulin Degludec | IGlar U100 (Biosimilar) | Incremental Cost (Insulin Degludec-IGlar) |
|---|---|---|---|
| **Pharmacy costs** | **13 095** | **11 453** | **1 642** |
| Insulin | 8 316 | 6 674 | 1 642 |
| Needles | 1 010 | 1 010 | 0 |
| SMBG tests | 3 769 | 3 769 | 0 |
| **Hypoglycaemic events** | **1 626** | **2 049** | **-423** |
| Non-severe diurnal events | 398 | 398 | 0 |
| Non-severe nocturnal events | 61 | 80 | -19 |
| Severe events | 1 167 | 1 571 | -404 |
| **Total costs** | **14 721** | **13 502** | **1 219** |
| **Effects** | | | |
| QALYs | 0.782 | 0.759 | 0.023 |
| **ICER (cost per QALY)** | | | **52 480** |

(€ 1 = SEK 10.47, 19MAR2019)

## Discussion

- Insulin degludec was highly cost-effective compared with IGlar U100 since a diabetes treatment is considered cost-effective in Sweden if cost/QALY is below SEK 500 000.
- The rigorous design of the SWITCH 1 trial1, including a hypoglycaemic sensitive T1D patient population and a relevant definition of hypoglycaemia, makes the results of this trial generalisable.
- The result was driven by reduced risk of hypoglycaemia and lower insulin doses.

## Conclusion

In this cost-effectiveness analysis, insulin degludec was highly cost-effective as compared to original and biosimilar IGlar U100 in patients with T1D in a Swedish health care setting after one year.

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**References:** (**1**) Heise et al. Diabetes Obes Metab 2012;14:944–50. (**2**) Heise et al. J Diabetes 2016;8:132–138. (**3**) Heise et al. Diabetes Obes Metab 2012;14:859–64. (**4**) Lane W et al. JAMA 2017;318(1):33—44. (**5**) Marso et al. The New England Journal of Medicine 2017;377(8):723–32. (**6**) Evans M et al. Diabetes Ther 2018;9:1919–30. (**7**) Jonsson L et al. Value Health 2006;9(3):193–8. (**8**) Geelhoed-Duijvestijn PHLM et al. Value Health 2012;15(7):A502. (**9**) Evans M et al. Health and Quality of Life Outcomes 2013;11:90–9.