



## **CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION**

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### **INSULIN GLARGINE (Lantus® - Aventis Pharma Inc.)**

**Description:**

Insulin glargine is an insulin analog indicated for once-daily subcutaneous administration for patients over 17 years of age with Type 1 or Type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia.

**Recommendation:**

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that insulin glargine not be listed.

**Dosage Forms:**

100 IU/mL, 10 mL vial

**Reasons for the recommendation:**

1. The committee considered 20 open-label randomized controlled trials (RCTs) lasting from 4 to 52 weeks that compared insulin glargine with NPH insulin, of which 11 were conducted in Type 1 diabetes and 9 in Type 2 diabetes. One trial compared insulin glargine with insulin ultralente in Type 1 diabetes. The studies did not find statistically or clinically significant differences between insulin glargine and NPH (or ultralente) in serious morbidity or glycemic control (as measured by mean HgA1c at endpoint or fasting blood sugar) in patients with either Type 1 or Type 2 diabetes.
2. No significant differences between insulin glargine and NPH (or ultralente) insulin were observed in the incidence of severe symptomatic hypoglycemia in either Type 1 or Type 2 diabetes.
3. Variable results were found for the incidence of overall and nocturnal hypoglycemia for both Type 1 and Type 2 diabetes. For symptomatic nocturnal hypoglycemia (confirmed and unconfirmed), 4 of 6 trials in Type 1 diabetes showed a significantly reduced number of events in the insulin glargine arm compared with NPH, yet two large trials failed to observe this difference after 1 to 7 months of follow-up. Eight of 9 studies reported the incidence of nocturnal hypoglycemia in Type 2 diabetes. Two trials did not detect a statistically significant difference between insulin glargine and NPH at 4 weeks. Six studies (from 4 to 52 weeks) found that significantly fewer patients in the insulin glargine group had hypoglycemic events.
4. Quality of life was measured with validated instruments such as the Treatment Satisfaction and the General Well-being scales. Results were inconsistent for the Type 1 diabetes trials. There was no significant difference between groups in the type 2 diabetes trials.

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### **Common Drug Review**



5. The pharmacoeconomic model submitted by the manufacturer was based on the assumption that patients treated with insulin glargine achieved a lower level of haemoglobin A1c without increasing the incidence of hypoglycemic events compared to NPH insulin; this assumption was not supported by the results of the RCTs. Insulin glargine costs \$5.50 per 100 units, while NPH insulin costs \$1.60 per 100 units (the dose equivalency ratio of insulin glargine to NPH insulin is approximately 1:1), and the committee did not feel that the reported differences in clinically important outcomes in favour of insulin glargine over NPH insulin justified the three-fold difference in cost.

**Of Note:**

1. Methods for identifying and counting hypoglycemic episodes were poorly reported in the RCTs. Hypoglycemia that is not biochemically confirmed is a subjective outcome (open to reporting bias) and clinical trial adjudicators were not blinded to treatment allocation (open to ascertainment bias).
2. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.