

CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

INSULIN DETEMIR (Levemir[®] - Novo Nordisk Canada Inc.)

Description:

Insulin detemir is a basal insulin analog that is approved for treatment of adult patients with Type 1 or 2 diabetes mellitus who require a long acting (basal) insulin for maintenance of normal glucose homeostasis. It is recommended that insulin detemir be used in combination with short or rapid-acting meal time insulin.

Dosage Forms:

100 Units /mL solution for subcutaneous injection (available as vials and cartridges)

Recommendation:

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

Reasons for the Recommendation:

1. The Committee considered 12 open-label randomized controlled trials (RCTs) of 4 to 12 months duration with once- or twice-daily insulin detemir, of which six were in Type 1 diabetes, five in Type 2 diabetes and one in a mixed population of Type 1 and 2 diabetes. With the exception of two RCTs using insulin glargine as a comparator (one each in Type 1 and 2 diabetes), all RCTs compared insulin detemir with NPH insulin.
2. In Type 1 diabetes, four of five RCTs showed no statistically significant differences in control of Hemoglobin A1c (Hb A1c) between insulin detemir and NPH insulin while one RCT reported a difference in favour of insulin detemir. None of the RCTs reported statistically significant differences between insulin detemir and NPH insulin in the incidence of major hypoglycemic or major nocturnal hypoglycemic episodes. Statistically significant reductions in the incidence of minor hypoglycemic and minor nocturnal hypoglycemic episodes in favour of insulin detemir were reported by two and three of the RCTs, respectively. In the RCT comparing twice daily insulin detemir with once daily insulin glargine, there was no difference in the control of Hb A1c but the incidence of major hypoglycemic episodes was lower in the insulin detemir group.

In Type 2 diabetes, two of the five RCTs found that insulin detemir was inferior to NPH insulin in the control of Hb A1c. None of the five RCTs found differences between insulin detemir and NPH insulin in the incidence of major hypoglycemic and major nocturnal hypoglycemic episodes although statistically significant reductions in the incidence of minor hypoglycemic and minor nocturnal hypoglycemic episodes in favour of insulin detemir were reported by two and three of the RCTs,

respectively. In the RCT comparing twice daily insulin detemir with once daily insulin glargine, there was no difference in the control of Hb A1c nor the incidence of hypoglycemic events.

3. Hb A1c and hypoglycemic episodes need to be considered together when evaluating insulin therapy. In considering the results of all RCTs, the Committee found no convincing evidence that insulin detemir consistently led to a reduced Hb A1c with an accompanying equal or lower incidence of major hypoglycemia than other comparator insulins.
4. Insulin detemir costs \$7.32 per 100 units while NPH insulin costs \$2.44 per 100 units in cartridge form (the dose equivalency ratio of insulin detemir to NPH insulin is approximately 1:1). The economic model submitted by the manufacturer was in Type 1 diabetes only and assumed that insulin detemir was associated with a reduction in Hb A1c and hypoglycemia compared to NPH insulin. The Committee felt that these assumptions were not supported by the results from the RCTs and that the three-fold increase in cost of insulin detemir relative to NPH insulin was excessive.

Of Note:

1. Both published and unpublished information were reviewed and taken into consideration in making this recommendation.
2. The Committee noted that all 12 RCTs were of open-label design. This makes the outcomes of minor hypoglycemic episodes subject to potential reporting bias. In addition, the confounding effect of the concomitant use of bolus short-acting insulin was not clarified in these trials.

Common Drug Review