

Recommendations and Reasons

Committee to Evaluate Drugs (CED)

Insulin detemir

Product:

Insulin detemir (Levemir® Penfill®)
100units/mL suspension for injection

Class of drugs: Insulin

Indication:

Treatment of diabetes mellitus

Manufacturer:

Novo Nordisk Canada Inc.

Highlights of Recommendation:

- ◆ Insulin detemir is a long-acting insulin analogue for the treatment of Type 1 and Type 2 diabetes mellitus.
- ◆ Studies in patients with Type 1 diabetes found that insulin detemir is similarly effective in controlling blood glucose (sugar) as NPH insulin.
- ◆ Studies in patients with Type 2 diabetes found mixed results. Some studies indicated that insulin detemir was not as good at controlling blood sugar levels as NPH insulin. There was no convincing evidence that insulin detemir provided better blood sugar control than NPH insulin.
- ◆ In terms of adverse effects, the totality of the evidence indicates there is a comparable risk of severe hypoglycemia (low blood sugar) with insulin detemir and NPH insulin for patients with Type 1 and Type 2 diabetes.
- ◆ Insulin detemir costs approximately three times as much as NPH insulin and is also more expensive than insulin glargine.
- ◆ **Overall, the CED noted that insulin detemir does not provide any important therapeutic benefits over NPH insulin, the less costly formulary alternative.**

Background:

Diabetes mellitus is a disease that occurs because the pancreas does not produce enough insulin (a hormone) and/or the cells in the body do not respond to insulin properly to help control the level of glucose (sugar) in the blood. With Type 1 diabetes, the body does not make insulin at all. With Type 2 diabetes, the body does not make or use insulin well.

Normally, when the body digests food, glucose enters the bloodstream as a fuel source, and insulin moves glucose from the bloodstream into cells. In diabetes, high levels of glucose remain in the bloodstream resulting in long-term health complications if left untreated. The long-term outcomes of poorly treated diabetes include heart attacks, strokes, blood vessel disease, nerve damage (neuropathy), kidney disease, blindness and foot infections/limb loss.

Patients with Type 1 diabetes are managed with insulin. Patients with Type 2 diabetes often require oral medications and/or insulin if weight loss and dietary changes on their own do not lead to improved blood glucose control.

Insulin detemir is a long-acting insulin for Type 1 and Type 2 diabetes mellitus. It is usually used once daily, in combination with short or rapid-acting insulin or oral anti-diabetic agents, but can also be used twice daily based on patients' needs.

NPH insulin, a long-acting human insulin, and insulin glargine, another long-acting insulin analogue, are listed on the ODB Formulary as General Benefits.

CED Recommendation-

The CED recommended that insulin detemir (Levemir® Penfill®) not be listed on the ODB Formulary unless there is a significant price reduction, on the basis that there is no compelling evidence demonstrating superiority over other lower cost insulin products already listed.

Executive Officer Decision

Taking the CED's recommendation into consideration and based on a subsequent listing agreement that addresses cost and utilization, the Executive Officer decided to list insulin detemir (Levemir® Penfill®) on the ODB Formulary.

Status

Funding through the Ontario Public Drug Programs as a General Benefit on the ODB Formulary.

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Detailed Discussion:

- ◆ The CED reviewed insulin detemir on three occasions, initially in September 2006, and again in July 2008 and January 2009.
- ◆ Five open-label randomized controlled trials were reviewed comparing insulin detemir to NPH insulin in patients with Type 1 diabetes. Only one trial showed a statistically significant reduction in hemoglobin A1c (HbA1c) for patients using insulin detemir. The other trials found insulin detemir to be similar to NPH insulin in controlling blood glucose.
- ◆ For Type 2 diabetes, two of the five randomized controlled trials found that insulin detemir did not control HbA1c as well as NPH insulin.
- ◆ Although the rate of minor hypoglycemic (low blood sugar) events was reduced with insulin detemir compared with NPH insulin, none of the trials reported statistically significant differences in the rate of major hypoglycemic or nocturnal hypoglycemic (low blood sugar in the middle of the night) events.
- ◆ No trials reported reduced loss of consciousness, ketoacidosis, seizures, or hospital admissions.
- ◆ In the [meta-analysis](#) the CED reviewed, there were no proven benefits for insulin detemir and the CED was uncertain whether there were any statistically or clinically significant differences in hard outcomes such as diabetes-related mortality and long-term complications.
 - ◇ Canadian Optimal Medication Prescribing and Utilization Service. *Long-acting insulin analogues for the treatment of diabetes mellitus: meta-analyses of clinical outcomes—Update of CADTH Technology Report No. 92 [Optimal therapy report]*. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2008 Mar. Available at http://www.cadth.ca/media/compus/reports/compus_Long-Acting-Insulin-Analogs-Report_Clinical-Outcomes.pdf
- ◆ There was no data on long-term risk and major diabetes-related complications as the trials were of short duration (4 to 12 months).
- ◆ Insulin detemir costs approximately three times more than NPH insulin. The CED noted that the price premium is not justified, given that insulin detemir has not been demonstrated to provide improved blood glucose control or

reduced risks of major hypoglycemic events.

- ◆ **Overall, the CED noted that insulin detemir does not provide any important therapeutic benefits over NPH insulin, the less costly formulary alternative.**

CEDAC Recommendation:

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that insulin detemir (Levemir®) not be listed at the submitted price.



Ministry of
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