B.C. Ministry of Health Services Drug Coverage Decisions

About PharmaCare	B.C. PharmaCare helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.
PharmaCare Coverage	The Ministry of Health Services (Ministry) makes PharmaCare coverage decisions by considering existing PharmaCare policies, programs and resources and the evidence-based recommendations of an independent advisory body called the Drug Benefit Council (DBC). The DBC's advice to the Ministry is based upon a review of many considerations, including available clinical and pharmacoeconomic evidence, clinical practice and ethical considerations, and the recommendations of the national Common Drug Review, when applicable.
Inside	**Page 1** includes the Ministry's decision and reasons in wording that is easier for readers without a medical background to understand. **Page 2** summarizes the DBC recommendation, the Ministry's decision and the reasons for the Ministry's decision.

Insulin glulisine (Apidra™) for diabetes

Understanding the DBC Recommendation and PharmaCare Coverage Decision

Background

- **Insulin** is a substance made by the pancreas. It allows the body to use sugar for energy.
- **Type 1 diabetes** occurs when the pancreas stops making insulin. **Type 2 diabetes** occurs when the body cannot use insulin properly or it does not make enough insulin. For both types of diabetes, high blood sugar results.
  - Symptoms include increased thirst, urinating often, weight loss, blurry vision, increased hunger or tiredness.
  - Depending on the type of diabetes, it may be treated with diet, exercise and drugs including insulin injections.
  - **Blood sugar** and **glycosylated haemoglobin (HbA1c)** are tests used to determine how well the diabetes is controlled. Of the two tests HbA1c is a better way to measure how well the disease is being controlled over time.
- **Insulin glulisine** has the brand name **Apidra™**.
  - Insulin glulisine is similar to the insulin produced by the body. It is a rapid acting insulin and is given by needle under the skin **(subcutaneous injection**). It is called an antidiabetic agent.

Why was this drug reviewed?

- Drug company request.

What did the review find?

- Studies in **type 1 diabetes** show that insulin glulisine works as well as insulin lispro or regular insulin (synthetic human) based on HbA1c levels. The number of patients having side effects is the same.
  - The effect of insulin glulisine on blood sugar levels measured 2 hours after a meal was similar to insulin lispro.
- Studies in type 2 diabetes show that insulin glulisine works as well as regular insulin (synthetic human) based on HbA1c or the difference is too small to be important. The number of patients having side effects is the same.
- Insulin glulisine lowers blood sugar levels 2 hours after a meal more than regular human insulin does. It is not known if this difference is important.
- One study in type 2 diabetes shows that insulin glulisine is better at decreasing HbA1c compared to antidiabetic agents taken by mouth; however, there are more times when the blood sugar levels drop below normal during the day and night with insulin glulisine.
- The cost of insulin glulisine is less than the cost of other rapid-acting insulins that are already covered by PharmaCare, but more than regular insulin (synthetic human).

What decision was made?

- Insulin glulisine will be **covered** by PharmaCare up to the average cost claimed by pharmacies for regular insulin products.

Key Term(s)

- No key term(s).

Please visit us online to find out more about the Pharmaceutical Services Division and the PharmaCare program at www.health.gov.bc.ca/pharmacare. To find out more about how drugs are considered for PharmaCare coverage, visit www.health.gov.bc.ca/pharmacare/formulary.

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Insulin glulisine (Apidra™) for type 1 or type 2 diabetes mellitus

Drug Class

- Antidiabetic agent

Available Dosage Forms

- 100 IU/mL - 10 mL vial
- 100 IU/mL - 3 mL SoloSTAR pre-filled pens

Sponsor/Requestor

- Sanofi-Aventis Canada Inc.

Submission (Request) to PharmaCare

- Health Canada has approved insulin glulisine for the treatment of adult patients with type 1 or type 2 diabetes mellitus where treatment with insulin is required.

Drug Benefit Council (DBC) Recommendations

- Insulin glulisine (Apidra™) be listed as a benefit similar to other rapid-acting insulin analogues as long as there is no incremental budget impact to PharmaCare.

Reasons for the Ministry of Health Services Decision

Type 1 Diabetes Mellitus

- A literature search identified four open-label, randomized controlled trials (RCTs), from 12 to 52 weeks in duration. In the three RCTs, insulin glulisine was compared to insulin lispro or regular human insulin, using insulin glargine as basal insulin. In one RCT, insulin glulisine was compared to insulin aspart. All RCTs were designed as non-inferiority trials.
- In the RCTs, insulin glulisine was found non-inferior, but not superior, to insulin lispro and regular human insulin in the mean change in HbA1C.
- There was no statistically significant difference in the mean two-hour postprandial plasma glucose (PPG) between insulin glulisine and insulin lispro.
- There were no clinically important differences in the proportion of patients experiencing serious adverse events, withdrawals due to adverse events, total adverse events, episodes of hypoglycemia, or monthly rates of severe and nocturnal hypoglycemia with insulin glulisine compared to other rapid-acting insulin analogues or regular human insulin.

Type 2 Diabetes Mellitus

- A literature search identified three open-label RCTs. Two non-inferiority RCTs, 26 and 52 weeks in duration, compared insulin glulisine to regular human insulin, using NPH insulin as basal insulin. One RCT was a superiority trial, 16 weeks in duration, that compared insulin glulisine in combination with oral antidiabetic drugs to insulin glulisine alone, and to oral antidiabetic drugs alone.
- Insulin glulisine was non-inferior to regular human insulin in the mean change in HbA1c. In one RCT, there was a statistically significant, but not clinically important, improvement in HbA1c among patients who received insulin glulisine compared to regular human insulin (mean difference in change in HbA1c = -0.16%, 95% confidence interval = -0.26 to -0.05).
- In the superiority RCT, there was statistically significant lowering of HbA1c with insulin glulisine with or without oral antidiabetic medications compared to oral antidiabetic medications alone, but there was also a higher incidence of overall and nocturnal hypoglycemia.
  - There was statistically significant lowering of the mean two-hour PPG in insulin glulisine compared to regular human insulin, but the clinical significance of this is unknown.
- There were no clinically important differences in the proportion of patients experiencing serious adverse events, withdrawals due to adverse events, total adverse events, episodes of severe and nocturnal hypoglycemia, or in the monthly rate of severe and nocturnal hypoglycemia with insulin glulisine compared to regular human insulin.

Other Issues

- The impact of insulin glulisine on clinical outcomes of diabetes is unknown.
- All RCTs used insulin glulisine vials or cartridges and no RCTs were identified that studied insulin glulisine pre-filled pens.
- The cost of insulin glulisine appears less than the cost of other rapid-acting insulin analogues, which are, at the time of review, reimbursed by PharmaCare up to the average cost claimed by pharmacies for regular insulin.

Decision and Status

- Insulin glulisine will be **covered** up to the average cost claimed by pharmacies for regular insulin products.
- Effective June 1, 2009.

Key Term(s)

- No key term(s).