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## **Indiana Medicaid Therapeutics Committee** **Therapeutic Class Review Summary**

### **Therapeutic Class:**

Injectable Hypoglycemics

### **Overview:**

Insulin is a pancreatic hormone that regulates carbohydrate metabolism in the body. It also increases lipogenesis and protein synthesis, while inhibiting lipolysis. Insulin can be provided exogenously as temporary replacement when the endogenous insulin supply is inadequate as in diabetes mellitus. The first insulin products were FDA approved in 1939, with biosynthetic insulin approved in 1982. Bovine insulin products were removed from the U.S. market in 1999 due to concern over the transmission of bovine spongiform encephalopathy (“mad-cow disease”). In addition, the use of porcine formulations has diminished greatly due to increased use of the recombinant human insulin preparations, and, as a result, manufacturers of porcine formulations in the US (Iletin<sup>®</sup> brand) have discontinued their production.

Insulin preparations are classified as rapid-, short-, intermediate-, and long-acting based on their onsets of activity and durations of action. Rapid-acting insulins, insulin lispro (Humalog<sup>®</sup>), insulin aspart (NovoLog<sup>®</sup>) and insulin glulisine (Apidra<sup>®</sup>) should be administered at mealtime due to their immediate onsets of action (5-20 minutes). Regular insulin (Humulin<sup>®</sup> R, Novolin<sup>®</sup> R) is classified as short-acting. These agents have an onset of action of 30-60 minutes and should be administered 30 minutes prior to meals. Intermediate-acting insulins include NPH insulin (Humulin<sup>®</sup> N, Novolin<sup>®</sup> N) and lente insulin (Humulin<sup>®</sup> L, Novolin<sup>®</sup> L). These agents are usually administered twice daily due to their longer durations of action. Insulin lispro protamine and insulin aspart protamine are also intermediate-acting, but are only available as premixed insulins (Humalog<sup>®</sup> Mix 75/25<sup>™</sup>, NovoLog<sup>®</sup> Mix 70/30) in the U.S. Ultralente insulin (Humulin<sup>®</sup> U), insulin glargine (Lantus<sup>®</sup>) and insulin detemir (Levemir<sup>®</sup>) are long-acting insulins with durations of action ranging from 14-28 hours. Due to limited use, however, manufacturers in the US have discontinued lente insulin and ultralente insulin production.

The different types of insulin can be used concomitantly to form an individual regimen, or premixed combinations (Humulin<sup>®</sup> 70/30, Humulin<sup>®</sup> 50/50, Novolin 70/30) may be used. Insulin pen dosage forms (NovoLog<sup>®</sup> Penfill<sup>®</sup>) provide an option for patients who have difficulty measuring the correct insulin dose in a syringe. Insulin pumps are also available for continuous insulin infusion. Exubera<sup>®</sup>, an insulin powder for oral inhalation, has been discontinued.

Exenatide (Byetta<sup>®</sup>) and pramlintide (Symlin<sup>®</sup>) are two non-insulin medications that can contribute to the regulation of carbohydrate metabolism in diabetes. Exenatide, an incretin mimetic agent, mimics the enhancement of glucose-dependent insulin secretion



and several other antihyperglycemic actions of incretins. It is administered twice daily within 60 minutes before morning and evening meals. Pramlintide is administered immediately prior to major meals; and mimics the hormone amylin by modulating gastric emptying, preventing postprandial rise in plasma glucagon, and causing satiety. Both exenatide and pramlintide are indicated as adjunctive therapy and are available in pre-filled pens for convenient dosing. Symlin is also available in a vial.

<b>Generic Name</b>	<b>Brand Name</b>	<b>Manufacturer</b>
Insulin	<b>Recombinant-</b> Humulin® R, Humulin® N, Humulin® L, Humulin® U, Humulin® 50/50, Humulin® 70/30, Humalog®, Humalog® Mix 50/50™, Humalog® Mix 75/25™ <b>Pork-</b> Iletin® II NPH, Iletin® II Regular	Eli Lilly
Insulin	<b>Recombinant-</b> Novolin® R, Novolin® N, Novolin® L, Novolin® 70/30, NovoLog®, NovoLog® Mix 70/30	Novo Nordisk
Insulin glargine	Lantus®	Aventis
Insulin detemir	Levemir®	Novo Nordisk
Insulin glulisine	Apidra®	Aventis
Exenatide	Byetta®	Amylin
Pramlintide	Symlin®	Amylin

**Summary:**

Several types of insulin products are available in four basic forms, each with a different time of onset and duration of action. These forms include rapid-acting insulin, short-acting insulin, intermediate-acting insulin, and long-acting insulin. The different types of insulin can be used concomitantly to form an individual regimen, or premixed combinations may be used. The orally inhaled insulin, Exubera®, was recently discontinued. Exenatide and pramlintide are two non-insulin medications that can contribute to the regulation of carbohydrate metabolism in diabetes. The most appropriate treatment should be based on the individual. Selection for the preferred drug list should depend upon efficacy, safety, availability, and cost.