Indiana Medicaid Therapeutics Committee
Therapeutic Class Review Summary

Therapeutic Class:
Dipeptidyl Peptidase-4 Inhibitors

Overview:
Type 2 diabetes is the most common form of diabetes, and accounts for approximately 90 percent to 95 percent of all diagnosed cases. In type 2 diabetes, either the body does not produce enough insulin or the cells are resistant to the insulin. Insulin is required to transport sugar, the basic fuel for cells, from the blood into cells. As time progresses, high blood sugar levels can increase the risk for serious complications, including heart disease, blindness, nerve damage, and kidney damage.

Sitagliptin (Januvia™) is the first diabetes treatment approved in a new class of drugs called the dipeptidyl peptidase-4 (DPP-4) inhibitors. It is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes. Sitagliptin is believed to exert its actions in patients with type 2 diabetes by slowing the inactivation of incretin hormones, which results in increased concentrations and prolonged actions of these hormones. Incretin hormones, including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), are released by the intestine throughout the day, and levels are increased in response to a meal. In addition, these hormones are rapidly inactivated by the enzyme DPP-4. When blood glucose concentrations are normal or elevated, GLP-1 and GIP increase insulin synthesis and release from pancreatic beta cells by intracellular signaling pathways involving cyclic AMP. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. By increasing and prolonging active incretin levels, sitagliptin increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner.
Sitagliptin may be used as monotherapy or as combination therapy with metformin or a peroxisome proliferator-activated receptor gamma agonist (e.g., thiazolidinediones) when either of these drugs alone, along with diet and exercise, does not provide adequate glycemic control.
The recommended dose is 100mg once daily as both monotherapy and combination therapy.
The most common adverse reactions reported were upper respiratory tract infection, nasopharyngitis, and headache.

Generic Name	Brand Name	Manufacturer	Generic Available
Sitagliptin	Januvia™	Merck	N

Summary:
Sitagliptin is the first diabetes treatment approved in a new class of drugs known as DPP-4 inhibitors that enhances the body's own ability to lower elevated blood sugar. The FDA approved sitagliptin for use with diet and exercise to improve blood sugar levels in patients with type 2 diabetes, the most common form of the disease. The preferred drug list should be based upon FDA-approved indications, efficacy, safety, and cost.