Sitagliptin

Product:
SITAGLIPTIN (Januvia®) 100mg tablet

Class of drugs:
Oral anti-diabetic agent

Indication:
Treatment of diabetes mellitus, Type 2

Manufacturer:
Merck Frosst Canada Inc.

Date of CED Review:
July 2008 & February 2009

CED Recommendation

The CED recommended that sitagliptin (Januvia®) not be funded through the Ontario Public Drug Programs. There is currently no long-term data to show that sitagliptin prevents diabetes-related complications. Furthermore, only limited data are available on long-term safety.

Executive Officer Decision

Taking into consideration the CED's recommendation and based on a subsequent cost and utilization agreement with the manufacturer, the Executive Officer decided to list sitagliptin (Januvia®) on the Ontario Drug Benefit Formulary as General Benefit with therapeutic notes.

Status

Funded as a General Benefit on the Ontario Drug Benefit Formulary with therapeutic notes.

Highlights of Recommendation:

- Sitagliptin is an oral medication indicated for the treatment of Type 2 diabetes mellitus.
- Short-term studies have shown that sitagliptin is effective at reducing blood sugar and improving blood glucose control.
- At present, there are no long-term data to indicate that sitagliptin reduces the complications of diabetes, including heart attacks, strokes, blood vessel disease, blindness, kidney failure and death.
- Also, long-term safety data on sitagliptin are limited. This is a concern because diabetes is a chronic condition and drug treatments would be used on a long-term basis.
- The manufacturer submitted a listing proposal for sitagliptin to the Ontario Public Drug Programs.
- **Overall, the Committee recommended that sitagliptin not be funded because data on long-term health benefits and safety are lacking.**

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

Several oral anti-diabetes medications are available for the management of Type 2 diabetes. These include sulfonylureas, metformin, and thiazolidinediones (glitazones). Metformin is the only oral anti-diabetes medication which has been proven to reduce the incidence of diabetes-related complications and mortality. Sitagliptin belongs to a new class of oral anti-diabetes drugs called dipeptidyl peptidase-4 (DPP-4) inhibitors.

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Detailed Discussion:

- The CED reviewed sitagliptin on two occasions, in July 2008 and February 2009.
- The CED considered several randomized controlled studies evaluating sitagliptin in patients with Type 2 diabetes whose blood glucose levels were not well controlled with existing therapies.
- In patients whose diabetes was inadequately controlled with metformin alone, adding sitagliptin to metformin was shown to improve blood glucose control, as measured by reduction in HbA1c levels.
- Combination therapy with sitagliptin plus metformin provided similar improvements in blood glucose control as combination treatment with sulfonylurea plus metformin and combination glitazone plus metformin.
- Only short-term studies evaluating sitagliptin are currently available. There are no long-term data to indicate that sitagliptin improves clinical outcomes. It is unknown whether sitagliptin reduces heart disease, kidney disease, eye damage, or death.
- A clinical study examining the effects of sitagliptin on cardiovascular outcomes is currently underway. Results are expected in approximately 2014.
- Long-term safety data on sitagliptin are limited. To date, there have been no major safety signals on the use of this drug.
- The manufacturer submitted a listing proposal for sitagliptin to the Ontario Public Drug Programs. Sitagliptin is more expensive than other oral anti-diabetic agents available on the Ontario Drug Benefit Formulary.
- **Overall, the CED noted that sitagliptin has been shown to improve blood glucose control. However, emerging evidence suggests that controlling blood sugar levels represents only one aspect of the total health effects of oral anti-diabetes medications. Given that long-term data on health outcomes and safety are lacking, the CED recommended that sitagliptin not be funded.**

Funding Status:

Taking into consideration the CED's recommendation and based on a subsequent cost and utilization agreement with the manufacturer, the Executive Officer decided to list sitagliptin on the Ontario Drug Benefit Formulary as General Benefit with the following therapeutic notes:

Treatment of Type 2 diabetes in patients on maximal doses of metformin (2000mg/day)who have:

- Inadequate glycemic control (defined as HbA1c>0.07) and intolerance or contraindication to a sulfonylurea; or
- An HbA1c less than or equal to 0.07 and elevated 2 hour post prandial glucose (PPG > 10mmol/L) or fasting plasma glucose (FPG > 7mmol/L) levels and intolerance or contraindication to a sulfonylurea; or
- Inadequate glycemic control (HbA1c>0.07) and on maximal doses of a sulfonylurea and for whom insulin is not an option.

An adequate trial of diet and exercise therapy alone is essential before any hypoglycaemic agent is prescribed in non-insulin dependent diabetes mellitus. When indicated (i.e., fasting plasma glucose remains > 10mmol/L), drug therapy should be considered as a supplement to continuing caloric restriction and exercise.

Ontario

Ministry of
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