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EPAR summary for the public

Glyxambi

Empagliflozin / linagliptin

This is a summary of the European public assessment report (EPAR) for Glyxambi. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Glyxambi.

For practical information about using Glyxambi, patients should read the package leaflet or contact their doctor or pharmacist.

What is Glyxambi and what is it used for?

Glyxambi is a diabetes medicine used in adults with type 2 diabetes to improve control of their blood glucose (sugar) levels. It contains two active substances, empagliflozin and linagliptin.

Glyxambi is used in the following groups:

- patients whose blood glucose levels are not controlled well enough by a combination of one of Glyxambi's active substances (empagliflozin or linagliptin) with other diabetes medicines (metformin and/or a sulphonylurea);
- patients who are already taking empagliflozin and linagliptin as separate tablets.

How is Glyxambi used?

Glyxambi is available as tablets containing 10 or 25 mg of empagliflozin with 5 mg of linagliptin, and can only be obtained with a prescription. The recommended dose is one tablet once a day. Patients switching from empagliflozin and linagliptin to Glyxambi should receive the strength of Glyxambi that corresponds to the doses of empagliflozin and linagliptin in the separate tablets they were taking.

If Glyxambi is used in combination with insulin or a sulphonylurea, their doses may need to be reduced to decrease the risk of hypoglycaemia (low blood sugar levels). The doctor may need to reduce the

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dose of Glyxambi or discontinue its use in patients with reduced kidney function. For further information, see the package leaflet.

How does Glyxambi work?

Type 2 diabetes is a disease in which the body does not make enough insulin to control the level of glucose in the blood or when the body is unable to use insulin effectively. The result is a high level of glucose in the blood. The two active substances in Glyxambi work in different ways to lower glucose levels:

- Empagliflozin works by blocking a protein in the kidneys called sodium-glucose co-transporter 2 (SGLT2). Normally, as blood is filtered by the kidneys, SGLT2 stops glucose in the blood from being passed out into the urine. By blocking the action of SGLT2, empagliflozin causes more glucose to be removed in the urine, thereby reducing the levels of glucose in the blood. Empagliflozin has been authorised in the European Union (EU) as Jardiance since 2014.
- Linagliptin is a dipeptidyl-peptidase-4 (DPP-4) inhibitor. It works by blocking the breakdown of incretin hormones in the body. These hormones are released after a meal and stimulate the pancreas to produce insulin. By prolonging the action of incretin hormones in the blood, linagliptin stimulates the pancreas to produce more insulin when blood glucose levels are high. Linagliptin also reduces the amount of glucose made by the liver, by increasing insulin levels and decreasing the levels of the hormone glucagon. Linagliptin has been authorised in the EU as Trajenta since 2011.

Together, these actions reduce blood glucose levels and help to control type 2 diabetes.

What benefits of Glyxambi have been shown in studies?

Empagliflozin in combination with linagliptin (the same combination as in Glyxambi) was evaluated in 3 main studies involving 1,221 adults with type 2 diabetes. The main measure of effectiveness was the change after 24 weeks of treatment in the level of a substance in the blood called glycosylated haemoglobin (HbA1c), which gives an indication of how well the blood glucose is controlled.

The first study included patients whose blood glucose levels were not satisfactorily controlled with metformin and linagliptin. Patients were then given either empagliflozin or placebo (a dummy treatment) in addition to their existing treatment. Results showed that when empagliflozin was added to linagliptin and metformin, HbA1c levels decreased by 0.7-0.8 percentage points after 24 weeks, compared with no reduction when placebo was added. HbA1c levels were just below 8% at the start of the study.

The second study included patients whose blood glucose levels were not satisfactorily controlled with metformin and empagliflozin. Adding linagliptin to treatment with empagliflozin and metformin for 24 weeks reduced HbA1c levels from 7.8% to 7.2%, compared with a reduction from 7.9% to 7.7% when placebo was added.

A further study compared a fixed dose combination of empagliflozin and linagliptin (given in addition to metformin) with treatment with metformin plus either empagliflozin or linagliptin in patients who were not sufficiently controlled with metformin alone. The HbA1c levels were around 8% before treatment. After 24 weeks treatment the fixed dose combination reduced HbA1c levels to under 6.9% whereas they were around 7.3% with empagliflozin and linagliptin used alone.

What are the risks associated with Glyxambi?

The most common side effects with Glyxambi (which may affect more than 7 in 100 people) are urinary infections. The most serious side effects are ketoacidosis (high blood levels of acids called 'ketoacids'), pancreatitis (inflammation of the pancreas), hypersensitivity (allergic reactions) and hypoglycaemia (low blood sugar levels). For the full list of all side effects reported with Glyxambi, see the package leaflet.

Glyxambi must not be used in people who are hypersensitive (allergic) to empagliflozin, linagliptin, any of the other ingredients or who have ever had a serious allergic reaction to any DPP-4 or SGLT2 inhibitor. For the full list of restrictions, see the package leaflet.

Why is Glyxambi approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Glyxambi's benefits are greater than its risks and recommended that it be approved for use in the EU.

The CHMP considered that Glyxambi is effective at controlling blood glucose levels, with both components contributing to the effect. Regarding its safety profile, Glyxambi was well tolerated with side effects being characteristic of SGLT2 and DDP-4 inhibitors.

What measures are being taken to ensure the safe and effective use of Glyxambi?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Glyxambi have been included in the summary of product characteristics and the package leaflet.

Other information about Glyxambi

The European Commission granted a marketing authorisation valid throughout the European Union for Glyxambi on 11 November 2016.

The full EPAR for Glyxambi can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Glyxambi, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 11-2016.