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EPAR summary for the public

Xelevia

sitagliptin

This is a summary of the European public assessment report (EPAR) for Xelevia. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Xelevia.

What is Xelevia?

Xelevia is a medicine that contains the active substance sitagliptin. It is available as tablets (25, 50 and 100 mg).

What is Xelevia used for?

Xelevia is used in patients with type 2 diabetes to improve the control of blood glucose (sugar) levels. It is used in addition to diet and exercise in the following ways:

- on its own, in patients who are not satisfactorily controlled on diet and exercise and in whom metformin (an antidiabetes medicine) is not suitable;
- in combination with metformin or a PPAR-gamma agonist (a type of antidiabetes medicine) such as a thiazolidinedione, in patients who are not satisfactorily controlled on metformin or the PPAR-gamma agonist used on its own;
- in combination with a sulphonylurea (another type of antidiabetes medicine) in patients who are not satisfactorily controlled with a sulphonylurea used on its own and in whom metformin is not suitable;
- in combination with both metformin, and a sulphonylurea or a PPAR-gamma agonist, in patients who are not satisfactorily controlled on the two medicines;

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- in combination with insulin, with or without metformin, in patients who are not satisfactorily controlled on a stable dose of insulin.

The medicine can only be obtained with a prescription.

How is Xelevia used?

Xelevia is taken at a dose of 100 mg once a day. If Xelevia is taken with a sulphonylurea or insulin, the dose of the sulphonylurea or insulin may need to be lowered to reduce the risk of hypoglycaemia (low blood sugar levels).

In patients with moderately or severely reduced kidney function the dose of Xelevia should be reduced.

How does Xelevia work?

Type 2 diabetes is a disease in which the pancreas 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 active substance in Xelevia, sitagliptin, 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 increasing levels of incretin hormones in the blood, sitagliptin stimulates the pancreas to produce more insulin when blood glucose levels are high. Sitagliptin does not work when the blood glucose is low. Sitagliptin also reduces the amount of glucose made by the liver, by increasing insulin levels and decreasing the levels of the hormone glucagon. Together, these processes reduce blood glucose levels and help to control type 2 diabetes.

How has Xelevia been studied?

Xelevia was studied in nine studies, involving almost 6,000 patients with type 2 diabetes whose blood glucose levels were not adequately controlled:

- four of the studies compared Xelevia with placebo (a dummy treatment): Xelevia or placebo were used on their own in two studies involving 1,262 patients, as an add-on to metformin in one study involving 701 patients, and as an add-on to pioglitazone (a PPAR-gamma agonist) in one study involving 353 patients;
- two studies compared Xelevia with other antidiabetes medicines. One study compared Xelevia with glipizide (a sulphonylurea), when they were used as an add-on to metformin in 1,172 patients. The other study compared Xelevia with metformin, used on their own, in 1,058 patients;
- three additional studies compared Xelevia with placebo when they were added to other antidiabetes medicines: glimepiride (another sulphonylurea), with or without metformin, in 441 patients; the combination of metformin and rosiglitazone (a PPAR-gamma agonist) in 278 patients; and a stable dose of insulin, with or without metformin, in 641 patients.

In all of the studies, the main measure of effectiveness was the change 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.

What benefit has Xelevia shown during the studies?

Xelevia was more effective than placebo when it was taken alone or in combination with other antidiabetes medicines. In patients taking Xelevia on its own, HbA1c levels fell from around 8.0% at the start of the studies by 0.48% after 18 weeks and 0.61% after 24 weeks. In contrast, they rose by 0.12% and 0.18%, respectively, in the patients taking placebo. Adding Xelevia to metformin reduced

HbA1c levels by 0.67% after 24 weeks, compared with a fall of 0.02% in the patients adding placebo. When added to pioglitazone, Xelevia reduced HbA1c levels by 0.85% after 24 weeks, compared with a fall of 0.15% in the patients adding placebo.

In the studies comparing Xelevia with other medicines, the effectiveness of adding Xelevia to metformin was similar to that of adding glipizide. When taken on their own, Xelevia and metformin produced similar reductions in HbA1c levels, but the effectiveness of Xelevia seemed to be slightly lower than that of metformin.

In the additional studies, adding Xelevia to glimepiride (with or without metformin) led to a reduction in HbA1c levels of 0.45% after 24 weeks, compared with an increase of 0.28% in those adding placebo. HbA1c levels were reduced by 1.03% after 18 weeks in patients adding Xelevia to metformin and rosiglitazone, compared with a fall of 0.31% in those adding placebo. Finally, they were reduced by 0.59% in patients adding Xelevia to insulin (with or without metformin), compared with a fall of 0.03% in those adding placebo.

What is the risk associated with Xelevia?

Serious side effects reported with Xelevia (generally seen in more than 5% of patients) include pancreatitis (inflammation of the pancreas) and hypersensitivity (allergic reactions). Hypoglycaemia has been reported in combination with a sulphonylurea in 4.7-13.8% of patients and with insulin in 9.6% of patients. For the full list of all side effects reported with Xelevia, see the package leaflet.

Xelevia must not be used in people who are hypersensitive (allergic) to sitagliptin or any of the other ingredients.

Why has Xelevia been approved?

The CHMP decided that Xelevia's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Xelevia

The European Commission granted a marketing authorisation valid throughout the European Union for Xelevia on 21 March 2007.

The full EPAR for Xelevia 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 Xelevia, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 08-2012.