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EPAR summary for the public

Komboglyze

saxagliptin / metformin

This is a summary of the European public assessment report (EPAR) for Komboglyze. 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 Komboglyze.

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

What is Komboglyze and what is it used for?

Komboglyze is a diabetes medicine used with diet and exercise to treat adults with type 2 diabetes to improve control of blood glucose (sugar) levels. It is used in the following ways:

- in patients whose blood glucose levels are not adequately controlled by metformin alone;
- in patients already being treated with saxagliptin and metformin as separate tablets;
- in combination with other diabetes medicines, including insulin, in patients whose blood glucose is not adequately controlled by these medicines and metformin.

Komboglyze contains the active substances saxagliptin and metformin.

How is Komboglyze used?

Komboglyze is available as tablets (2.5 mg/850 mg and 2.5 mg/1,000 mg) and can only be obtained with a prescription. It is taken as one tablet twice a day with meals. The strength of tablet to use depends on the dose of the other diabetes medicines that the patient was taking and the patient's kidney function. Patients not adequately controlled on metformin alone who start taking Komboglyze should continue to receive the same dose of metformin as they were taking. If Komboglyze is taken with a sulphonylurea (medicines that make the body produce insulin) or insulin, the dose of these medicines may need to be lowered, to avoid hypoglycaemia (low blood sugar levels).

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How does Komboglyze work?

In type 2 diabetes, the pancreas does not make enough insulin to control the level of glucose in the blood or the body is unable to use insulin effectively. This leads to high levels of glucose in the blood. The active substances in Komboglyze, saxagliptin and metformin, work in a different way to help reduce blood glucose levels and control type 2 diabetes.

Saxagliptin is a dipeptidyl peptidase 4 (DPP4) 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, saxagliptin stimulates the pancreas to produce more insulin when blood glucose levels are high. Saxagliptin does not work when the blood glucose is low. Saxagliptin also reduces the amount of glucose made by the liver, by increasing insulin levels and decreasing the levels of the hormone glucagon. Saxagliptin has been authorised in the EU as Onglyza since 2009.

The active substance metformin works mainly by blocking glucose production and reducing its absorption in the gut. Metformin has been available in the EU since the 1950s.

What benefits of Komboglyze have been shown in studies?

Several studies in patients with type 2 diabetes have shown that the combination of the active substances in Komboglyze, saxagliptin and metformin, is effective in lowering patients' blood glucose. In all the studies the main measure of effectiveness was the reduction in blood levels of a substance called glycosylated haemoglobin (HbA1c) after 24 weeks of treatment. This gives an indication of how well the blood glucose is controlled.

- One study examined the effects of saxagliptin added to metformin in 160 patients. Results showed that in patients taking saxagliptin with metformin HbA1c levels fell by around 0.6 percentage points, compared with a fall of 0.2 percentage points in patients taking placebo (a dummy treatment) with metformin.
- Another five studies looked at the effects of saxagliptin alone or in combination with metformin, compared either with placebo or another diabetes medicine (a sulphonylurea or sitagliptin) in over 4,000 patients. Results showed that adding saxagliptin to metformin was effective in lowering HbA1c levels.
- A study in 455 patients compared saxagliptin with placebo when added to insulin, with or without metformin. HbA1c levels fell by around 0.7 percentage points in patients adding saxagliptin, compared with a fall of around 0.3 percentage points in patients who added placebo.
- A study in 257 patients compared saxagliptin with placebo when added to metformin and a sulphonylurea. A reduction of 0.7 percentage points was seen in patients who received saxagliptin, metformin and a sulphonylurea compared with a reduction of 0.1 percentage points in patients who received placebo in place of saxagliptin.
- A study in 534 patients whose blood glucose levels were not satisfactorily controlled with metformin alone showed that when saxagliptin and dapagliflozin were taken together with metformin, they decreased HbA1c levels by 1.5 percentage points, compared with a reduction of 0.9 percentage points with saxagliptin and metformin and 1.2 percentage points with dapagliflozin and metformin. HbA1c levels were on average around 9% at the start of the study.
- A study in 315 patients whose blood glucose levels were not satisfactorily controlled with metformin and dapagliflozin showed that adding saxagliptin to dapagliflozin and metformin reduced HbA1c levels by 0.5 percentage points, compared with a reduction of 0.2 percentage points when

placebo was added to treatment with dapagliflozin and metformin. HbA1c levels were around 8% at the start of the study.

- A study in 320 patients not controlled with metformin and saxagliptin, showed that adding dapagliflozin to treatment with saxagliptin and metformin reduced HbA1c levels by 0.8 percentage points, compared with a reduction of 0.1 percentage points when placebo was added to saxagliptin and metformin.

What is the risk associated with Komboglyze?

The most common side effects seen with saxagliptin used together with metformin (seen in between 1 and 10 patients in 100) are upper respiratory infection (nose and throat infection), urinary tract infection (infection of the structures that carry urine such as the bladder), gastroenteritis (diarrhoea and vomiting), sinusitis (inflammation of the sinuses), nasopharyngitis (inflammation of the nose and throat), headache and vomiting. For the full list of all side effects reported with saxagliptin and metformin, see the package leaflet.

Komboglyze must not be used in patients who are hypersensitive (allergic) to saxagliptin and metformin or any of the other ingredients, or who have ever had a serious allergic reaction to any DPP4 inhibitor. It must not be used in patients with diabetic ketoacidosis or diabetic pre-coma (a dangerous condition that can occur in diabetes), patients with moderately to severely reduced kidney function or with acute (sudden) conditions which can affect kidney function, patients with diseases which can deprive tissue of oxygen such as heart failure or difficulty breathing, patients with reduced liver function, alcohol poisoning or alcoholism. It must not be used in women who are breastfeeding.

Why has Komboglyze been approved?

Komboglyze has been shown to help reduce blood glucose levels and it does not cause any unexpected side effects. The European Medicines Agency therefore concluded that the benefits of Komboglyze outweigh its risks and recommended that it be given marketing authorisation.

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

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

Other information about Komboglyze

The European Commission granted a marketing authorisation valid throughout the European Union for Komboglyze on 24 November 2011.

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

This summary was last updated in 06-2017.