EMA/68074/2013
EMEA/H/C/002059

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 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 Komboglyze.

What is Komboglyze?

Komboglyze is a medicine that contains the active substances saxagliptin and metformin. It is available as tablets (2.5 mg / 850 mg or 2.5 mg / 1,000 mg).

What is Komboglyze used for?

Komboglyze is used in adults 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:

- 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 insulin in patients whose blood glucose is not adequately controlled by insulin and metformin alone;
- in combination with a sulphonylurea in patients whose blood glucose is not adequately controlled with the highest possible doses of a combined metformin and sulphonylurea treatment.

The medicine can only be obtained with a prescription.

How is Komboglyze used?

Komboglyze is taken as one tablet twice a day at mealtimes. The strength of tablet to use depends on the dose of the other antidiabetes medicines that the patient was taking before. Patients not

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adequately controlled on metformin alone who start taking Komboglyze should continue to receive the same dose of metformin they were previously taking. Patients already adequately controlled with saxagliptin and metformin as separate tablets who switch to Komboglyze should use the tablet containing the same component doses. If Komboglyze is taken with insulin or a sulphonylurea, the dose of insulin or the sulphonylurea may need to be lowered, to reduce the risk of hypoglycaemia (low blood sugar levels).

How does Komboglyze 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 substances in Komboglyze, saxagliptin and metformin, each have a different mode of action 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.

As a result of the action of both active substances, blood glucose levels are reduced and this helps to control type 2 diabetes.

How has Komboglyze been studied?

One study examined the effects of saxagliptin added to metformin in 160 patients. Another five looked at the effects of saxagliptin alone or in combination with metformin, compared either with placebo (a dummy treatment) or another medicine (a sulphonylurea or sitagliptin) in over 4,000 patients. A study in 455 patients compared saxagliptin with placebo when added to insulin, with or without metformin and the eighth study (in 257 patients) compared saxagliptin with placebo when added to metformin and a sulphonylurea.

The main measure of effectiveness in all the studies was the change in the levels of glycosylated haemoglobin (HbA1c), which is the percentage of haemoglobin in the blood that has glucose attached. HbA1c gives an indication of how well the blood glucose is controlled.

The company also presented the results of a study in 32 healthy people looking at the levels of saxagliptin in the blood when saxagliptin is taken at 2.5 mg twice daily compared with when it is taken at 5 mg once daily.

What benefit has Komboglyze shown during the studies?

Combinations of saxagliptin and metformin as used in Komboglyze were shown to be effective in lowering patients' blood glucose.

In the study of 160 patients, patients taking saxagliptin with metformin had a reduction of 0.6% in their HbA1c levels, compared with a reduction of 0.2% in patients taking placebo with metformin. The

five studies on the effects of saxagliptin alone or in combination with metformin also showed that adding saxagliptin to metformin was effective in lowering HbA1c levels.

In the study where saxagliptin was taken in addition to insulin (with or without metformin), HbA1c levels fell by around 0.7%, compared with a decrease of around 0.3% in patients who took placebo with insulin.

In the eighth study, a reduction of 0.7% was seen in patients who received triple therapy with saxagliptin, metformin and a sulphonylurea compared with a reduction of 0.1% in patients who were given placebo in place of saxagliptin.

The study in healthy people showed that when saxagliptin is taken at 2.5 mg twice daily it produces the same levels of active substance in the blood over a 24 hour period as when it is taken at 5 mg once daily.

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 (cold), 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 cause tissue hypoxia (where the tissue is deprived of adequate oxygen supply) 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?

The CHMP concluded that Komboglyze helps to reduce blood glucose levels in patients whose blood glucose levels are not adequately controlled by metformin alone, while the combination of saxagliptin and metformin in one tablet may help patients who already take both to follow their treatment correctly. The CHMP also noted that the combination does not cause any unexpected side effects. The Committee therefore concluded that the benefits of Komboglyze outweigh its risks and recommended that it be given marketing authorisation.

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 02-2013.