

Package leaflet: Information for the patient

Komboglyze 2.5 mg/850 mg film-coated tablets
saxagliptin/metformin hydrochloride

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Komboglyze is and what it is used for
2. What you need to know before you take Komboglyze
3. How to take Komboglyze
4. Possible side effects
5. How to store Komboglyze
6. Contents of the pack and other information

1. What Komboglyze is and what it is used for

This medicine contains two different substances called:

saxagliptin, part of a class of medicines called DPP-4 inhibitors (dipeptidyl peptidase-4 inhibitors), and metformin, part of a class of medicines called biguanides.

Both belong to a group of medicines called oral anti-diabetics.

What Komboglyze is used for

This medicine is used to treat a type of diabetes called 'type 2 diabetes'.

How Komboglyze works

Saxagliptin and metformin work together to control your blood sugar. They increase the levels of insulin after a meal. They also lower the amount of sugar made by your body. Along with diet and exercise, this helps lower your blood sugar. This medicine can be used alone or together with other antidiabetic medicines, including insulin.

To control your diabetes, you still need to diet and exercise, even when you are taking this medicine. So it is important to keep following the advice about diet and exercise from your doctor or nurse.

2. What you need to know before you take Komboglyze

Do not take Komboglyze

- If you are allergic to saxagliptin, metformin or any of the other ingredients of this medicine (listed in section 6);
- If you have had a serious allergic (hypersensitive) reaction to any other similar medications that you take to control your blood sugar.

Symptoms of a serious allergic reaction may include:

- Rash
- Raised red patches on your skin (hives)
- Swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing.

If you have these symptoms, stop taking this medicine and call your doctor or nurse right away.

- If you have ever had a diabetic coma;
- If you have uncontrolled diabetes, with, for example, severe hyperglycaemia (high blood glucose), nausea, vomiting, diarrhoea, rapid weight loss, lactic acidosis (see “Risk of lactic acidosis” below) or ketoacidosis. Ketoacidosis is a condition in which substances called ‘ketone bodies’ accumulate in the blood and which can lead to a diabetic pre-coma. Symptoms include stomach pain, fast and deep breathing, sleepiness or your breath developing an unusual fruity smell;
- If you have severely reduced kidney function or problems with your liver;
- If you have recently had a heart attack or if you have heart failure or serious problems with your blood circulation or difficulties in breathing which could be a sign of heart problems;
- If you have a severe infection or are dehydrated (have lost a lot of water from your body);
- If you are breast-feeding (see also “Pregnancy and breast-feeding”);
- If you drink a large amount of alcohol (either every day or only from time to time) (please see section “Komboglyze with alcohol”);

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking this medicine.

Warnings and precautions:

Risk of lactic acidosis

Komboglyze may cause a very rare, but very serious side effect called lactic acidosis, particularly if your kidneys are not working properly. The risk of developing lactic acidosis is also increased with uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, dehydration (see further information below), liver problems and any medical conditions in which a part of the body has a reduced supply of oxygen (such as acute severe heart disease).

If any of the above apply to you, talk to your doctor for further instructions.

Stop taking Komboglyze for a short time if you have a condition that may be associated with dehydration (significant loss of body fluids) such as severe vomiting, diarrhoea, fever, exposure to heat or if you drink less fluid than normal. Talk to your doctor for further instructions.

Stop taking Komboglyze and contact a doctor or the nearest hospital immediately if you experience some of the symptoms of lactic acidosis, as this condition may lead to coma.

Symptoms of lactic acidosis include:

- vomiting
- stomach ache (abdominal pain)
- muscle cramps
- a general feeling of not being well with severe tiredness
- difficulty in breathing
- reduced body temperature and heartbeat

Lactic acidosis is a medical emergency and must be treated in a hospital.

Talk to your doctor or pharmacist before taking Komboglyze

- If you have type 1 diabetes (your body does not produce any insulin). This medicine should not be used to treat this condition;
- If you have or have had a disease of the pancreas;

- If you are taking insulin or an antidiabetic medicine known as ‘sulphonylurea’, your doctor may want to reduce your dose of insulin or the sulphonylurea when you take either of them together with this medicine, in order to avoid low blood sugar;
- If you have had allergic reactions to any other medicines that you take to control the amount of sugar in your blood;
- If you have a problem or take a medicine that can lower your body’s defence against infections;
- If you have ever had heart failure or you have other risk factors for developing heart failure such as problems with your kidneys. Your doctor will advise you of the signs and symptoms of heart failure. You should call your doctor, pharmacist or nurse immediately if you experience any of these symptoms. Symptoms can include, but are not limited to, increasing shortness of breath, rapid increase in weight and swelling of the feet (pedal oedema);

If you need to have major surgery, you must stop taking Komboglyze during and for some time after the procedure. Your doctor will decide when you must stop and when to restart your treatment with Komboglyze.

Diabetic skin lesions are a common complication of diabetes. Rash has been seen with saxagliptin and with certain anti-diabetic medicines in the same class as saxagliptin. Follow the recommendations for skin and foot care that your doctor or nurse gave you. Contact your doctor if you encounter blistering of the skin, as it may be a sign for a condition called bullous pemphigoid. Your doctor may ask you to stop Komboglyze.

If any of the above apply to you, or if you are not sure talk to your doctor or pharmacist before taking this medicine.

Kidney tests or checks

During treatment with this medicine, your doctor will check your kidney function at least once a year or more frequently if you are elderly and/or if you have worsening kidney function.

Children and adolescents

Komboglyze is not recommended for use in children and adolescents under 18 years. It is not known if this medicine is safe and effective when used in children and adolescents under 18 years of age.

Other medicines and Komboglyze

If you need to have an injection of contrast medium that contains iodine into your bloodstream, for example in the context of an X-ray or scan, you must stop taking Komboglyze before or at the time of the injection. Your doctor will decide when you can restart your treatment with Komboglyze.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. You may need more frequent blood glucose and kidney function tests, or your doctor may adjust the dosage of Komboglyze. It is especially important to mention the following:

- cimetidine, a medicine used to treat stomach problems
- ketoconazole which is used to treat fungal infections
- bronchodilators (beta-2 agonists) which are used to treat asthma
- diltiazem which is used for high blood pressure
- rifampicin, an antibiotic used to treat infections such as tuberculosis
- corticosteroids, which are used to treat inflammation in diseases like asthma and arthritis
- carbamazepine, phenobarbital or phenytoin, which are used to control fits (seizures) or long-term pain
- medicines which increase urine production (diuretics)
- medicines used to treat pain and inflammation (NSAID and COX-2-inhibitors, such as ibuprofen and celecoxib)
- certain medicines for the treatment of high blood pressure (ACE inhibitors and angiotensin II receptor antagonists).

If any of the above apply to you, or if you are not sure, talk to your doctor or pharmacist before taking this medicine.

Komboglyze with alcohol

Avoid excessive alcohol intake while taking Komboglyze since this may increase the risk of lactic acidosis (see “Warnings and precautions”).

Pregnancy and breast-feeding

Do not take this medicine if you are pregnant or might become pregnant. This is because it may affect the baby.

Do not take this medicine if you are breast-feeding or plan to breast-feed. This is because metformin passes into human milk in small amounts.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Saxagliptin and metformin have a negligible influence on the ability to drive and use machines. Hypoglycaemia may affect your ability to drive and use machines or work with safe foothold and there is a risk of hypoglycaemia when taking this medicine in combination with medicines known to cause hypoglycaemia such as insulin and sulphonylureas.

3. How to take Komboglyze

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

If your doctor prescribes this medicine together with a sulphonylurea or insulin, remember to take this other medicine as directed by your doctor to achieve the best results for your health.

How much to take

- The amount of this medicine that you will take varies depending on your condition and the doses you currently take of metformin and/or individual tablets of saxagliptin and metformin. Your doctor will tell you exactly the dose of this medicine to take.
- The recommended dosing is one tablet twice a day.

If you have reduced kidney function, your doctor may prescribe a lower dose.

How to take this medicine

- Take this medicine by mouth.
- Take with a meal to lower your chance of getting an upset stomach.

Diet and exercise

To control your diabetes, you still need to diet and exercise, even when you are taking this medicine. So it is important to keep following the advice about diet and exercise from your doctor or nurse. In particular, if you are following a diabetic weight control diet, keep on with this while you are taking this medicine.

If you take more Komboglyze than you should

If you take more Komboglyze tablets than you should, talk to a doctor or go to a hospital straight away. Take the medicine pack with you.

If you forget to take Komboglyze

- If you forget to take a dose of this medicine, take it as soon as you remember. However, if it is time for your next dose, skip the missed dose and take your next dose at the usual time.
- Do not take a double dose of this medicine to make up for a forgotten dose.

If you stop taking Komboglyze

Keep taking this medicine until your doctor tells you to stop. This is to help keep your blood sugar under control.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop taking Komboglyze and contact a doctor immediately if you notice any of the following serious side effects:

- **Lactic acidosis**, Komboglyze may cause a very rare (may affect up to 1 user in 10,000), but very serious side effect called lactic acidosis (see section “Warnings and precautions”). If this happens you must **stop taking Komboglyze and contact a doctor or the nearest hospital immediately**, as lactic acidosis may lead to coma.
- **Severe and persistent pain in the abdomen** (stomach area) which might reach through to your back, as well as nausea and vomiting, as it could be a sign of an inflamed pancreas (pancreatitis).

You should call your doctor if you experience the following side effects:

- severe joint pain.

Other side effects of Komboglyze include:

Common (may affect up to 1 in 10 people)

- headache
- muscle pain (myalgia)
- being sick or indigestion (dyspepsia)
- infection of the structures that carry urine (urinary tract infection)
- infection of the upper airways
- inflamed nose or throat such as with a cold or sore throat
- inflamed stomach (gastritis) or gut, sometimes caused by an infection (gastroenteritis)
- infection of your sinuses, sometimes with a feeling of pain and fullness behind your cheeks and eyes (sinusitis)
- flatulence
- dizziness
- tiredness (fatigue).

Uncommon (may affect up to 1 in 100 people)

- joint pain (arthralgia)
- difficulties in getting or maintaining an erection (erectile dysfunction).

Side effects seen when taking saxagliptin alone:

Common

- dizziness
- tiredness (fatigue).

Side effects seen when taking saxagliptin alone or in combination:

Not known (frequency cannot be estimated from the available data):

- constipation
- blistering of the skin (bullous pemphigoid)

Some patients have had a small reduction in the number of one type of white blood cells (lymphocytes) shown in a blood test when saxagliptin was used alone or in combination. In addition, some patients have reported rash and skin reactions (hypersensitivity) while taking saxagliptin.

During post-approval use of saxagliptin, additional side effects have been reported that include serious allergic reactions (anaphylaxis), and swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing. If you have an allergic reaction, stop taking this medicine and call your doctor right away. Your doctor may prescribe a medicine to treat your allergic reaction and a different medicine for your diabetes.

Side effects seen when taking metformin alone:

Very common (may affect more than 1 in 10 people)

- nausea, vomiting
- diarrhoea or stomach pain
- loss of appetite.

Common

- a metallic taste in your mouth.

Very rare

- decreased vitamin B12 levels
- liver problems (hepatitis)
- redness of the skin (rash) or itching.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Komboglyze

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister and the carton after EXP. The expiry date refers to the last day of that month.

Store below 25°C.

Do not use this medicine if the package is damaged or shows signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Komboglyze contains

The active substances are saxagliptin and metformin hydrochloride. Each film-coated tablet contains 2.5 mg saxagliptin (as hydrochloride) and 850 mg metformin hydrochloride.

The other ingredients (excipients) are:

- Tablet core: povidone K30, magnesium stearate.
- Film-coating: polyvinyl alcohol, macrogol 3350, titanium dioxide (E171), talc (E553b), iron oxide red (E172), iron oxide yellow (E172).
- Printing ink: shellac, indigo carmine aluminium lake (E132).

What Komboglyze looks like and contents of the pack

- Komboglyze 2.5 mg/850 mg film-coated tablets ('tablets') are light brown to brown and round, with "2.5/850" printed on one side and "4246" printed on the other side, in blue ink.
- Komboglyze is available in aluminium foil blister. The pack-sizes are 14, 28, 56 and 60 film-coated tablets in non-perforated blisters, multipacks containing 112 (2 packs of 56) and 196 (7 packs of 28) film-coated tablets in non-perforated blisters and 60 x1 film-coated tablets in perforated unit dose blisters.

Not all pack sizes may be marketed in your country.

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Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>