Patient Package Leaflet in Accordance With
the Pharmacists' Regulations (Preparations) –1986

This medicine is dispensed with a doctor's prescription only

Kombiglyze® XR 5 mg/1000 mg

Extended-Release Tablets

Composition:

Each tablet contains:

5 mg saxagliptin

1000 mg metformin hydrochloride

Kombiglyze® XR 2.5 mg/1000 mg

Extended-Release Tablets

Composition:

Each tablet contains:

2.5 mg saxagliptin

1000 mg metformin hydrochloride

For inactive ingredients please see section 6 – "Further Information".

Read the leaflet carefully in its entirety before using the medicine.

Keep this leaflet; you may need it again. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

This medicine is not intended for children and adolescents under the age of 18 years.

Very important information to know before using Kombiglyze XR:

Lactic acidosis and pancreatitis – please see section 2 below, "Special warnings regarding use of this medicine".

1. WHAT IS THE MEDICINE INTENDED FOR?

Kombiglyze XR is intended to balance blood sugar levels in adult patients (from 18 years and above) with type 2 diabetes in combination with diet and exercise.

2. BEFORE USING THE MEDICINE

X Do not use the medicine if:

- you have type 1 diabetes
- you have severe decreased renal function (your doctor will define your renal disfunction level)
- you have kidney function problems
- you are sensitive to the active ingredients: metformin hydrochloride or saxagliptin or to any of the other ingredients of Kombiglyze XR (see section 6 "Further Information"). Signs of a severe allergic reaction (hypersensitivity) to Kombiglyze XR can include:
    - swelling of the face, lips, throat and other areas on the skin
    - difficulty breathing or swallowing
    - raised red marks on the skin (hives)
    - skin rash, itching, flaking or peeling of the skin

  If you have these signs, stop taking Kombiglyze XR and refer to the attending doctor or nurse immediately.
- you have metabolic acidosis or diabetic ketoacidosis (high levels of certain acids - ketones in your blood or urine).
- you are pregnant
- you are breastfeeding

! Special warnings regarding use of this medicine

Serious side effects can occur in patients taking Kombiglyze XR:

1. **Lactic Acidosis** (a build-up of lactic acid in the blood) - A rare but serious side effect that can be life threatening.

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

Stop the treatment and refer to the doctor immediately if you experience any of the symptoms of lactic acidosis that may include:

- feeling very weak and tired
- unusual muscle pain
- trouble breathing
- unusual sleepiness or sleeping longer than usual
- unexplained stomach or intestinal problems with nausea and vomiting or diarrhea
- feeling cold, especially in the arms and legs
- dizziness
- slow or irregular heartbeat

You have a higher risk of getting lactic acidosis if:

- have severe kidney function problems or your kidneys are affected by injectable dye or contrast agents for an x-ray procedure
- you have liver function problems.
- you have congestive heart failure that requires treatment with medicines.
- you drink a lot of alcohol, drink frequently, or drink large amounts of alcohol within a short time.
- you are dehydrated (loss of a large amount of body fluids). Dehydration can occur if you are sick with fever, diarrhea or vomiting. Dehydration can also occur when you sweat a lot with activity or exercise and do not drink enough.
- you are about to undergo certain x-ray tests with injectable dyes or contrast agents.
- you are about to undergo surgery.
- you have had a heart attack, severe infection, or stroke.
- you are 80 years of age or older and have not had your kidney function tested.

2. **Inflammation of the pancreas (pancreatitis)** which may be severe and life threatening.

Certain medical conditions increase the likelihood of getting pancreatitis.

3. Heart failure. Heart failure means your heart does not pump blood well enough. Before you start taking KOMBIGLYZE XR, tell your doctor if you have ever had:

    - heart failure or have problems with your kidneys.

    Contact your doctor right away if you have any of the following symptoms:

    - increasing shortness of breath or trouble breathing, especially when you lie down
    - swelling or fluid retention, especially in the feet, ankles or legs
    - an unusually fast increase in weight
    - unusual tiredness

    These may be signs of heart failure.

! Before treatment with Kombiglyze XR, tell the doctor if:

- you have type 1 diabetes. Kombiglyze XR is not intended to treat type 1 diabetes.
- you have a history of or risk for diabetic ketoacidosis (high levels of certain acids - ketones, in the blood or urine). Kombiglyze XR must not be used for the treatment of diabetic ketoacidosis.
- you have kidney function problems.
- you have liver function problems.
- you have heart function problems, including congestive heart failure.
- you are above 80 years of age. If you are over the age of 80 you should not take Kombiglyze XR unless kidney functions have been checked and were found to be normal.
- you drink alcohol frequently or drink large amounts of alcohol within a short time.
- you are about to undergo certain x-ray tests with injectable dyes or contrast agents. Or if you are about to undergo surgery and will not be able to eat or drink much. In these situations, it will be necessary to stop taking Kombiglyze XR for a short time. Consult your doctor about when you should stop taking Kombiglyze XR and when you should start taking Kombiglyze XR again.

- you have any other medical condition or ailment.

If you are taking other medicines

If you are taking, or have recently taken, other medicines, including non-prescription medicines and food supplements, tell the doctor or pharmacist. Especially inform the doctor or pharmacist if you are taking: antibiotics, anti-fungals or HIV/AIDS medications, because your dose of Kombiglyze XR might need to be changed.

Use of the medicine and alcohol consumption

- Inform the doctor if you drink alcohol frequently or drink large amounts of alcohol within a short time.

Pregnancy and breastfeeding

- Before taking this medicine, report to your doctor if you are pregnant or planning to become pregnant. Do not use Kombiglyze XR if you are pregnant.
- If you are breastfeeding in or planning to breastfeed, report to your doctor. It is unknown whether this medicine is transferred to breast milk during breastfeeding. Do not take Kombiglyze XR if you are breastfeeding or planning to breastfeed.

Driving

- Use of this medicine may cause dizziness. If you experience dizziness while taking the medicine, do not drive a car, do not operate dangerous machinery or engage in any other activity that requires alertness.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. The dosage and manner of treatment will be determined by the doctor only. **Do not exceed the recommended dosage**.

If you have decreased renal function, your doctor may prescribe a lower dosage.

Check with the doctor or pharmacist if you are uncertain.

- Kombiglyze XR should be taken with food to help lessen an upset stomach side effect.
- Swallow the tablet whole with water. Do not halve, crush or chew Kombiglyze XR tablets.

- You may sometimes notice a soft mass in your stools that resembles a tablet. These are the remnants of the inactive ingredients in the tablet.

Tests and Follow-Up: Before starting treatment and throughout the treatment period, the doctor will refer you for blood tests to check kidney function.

During treatment with the medicine, the doctor will refer you for blood tests, blood sugar level and hemoglobin A1C tests to monitor your diabetes.

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.

If you forgot to take this medicine at the required time, do not take a double dose. Take the next dose at the scheduled time and consult the doctor.

Be sure to adhere to the treatment as recommended by the doctor.

How can you contribute to the success of the treatment?

Check blood sugar levels according to doctor's instructions.

Stay on your prescribed diet and exercise program while taking the medicine.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

4. SIDE EFFECTS

As with any medicine, use of Kombiglyze XR may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Kombiglyze XR can cause serious side effects. See section, **"Very important information to know before using Kombiglyze XR".**

Effects that require special attention - stop taking Kombiglyze XR and refer to a doctor immediately:

If you experience the following effects which result from an allergic (hypersensitivity) reaction:

- swelling of the face, lips, throat, and other areas on the skin
- difficulty breathing or swallowing
- raised, red marks on the skin (hives)
- skin rash, itching, flaking or peeling of skin

Refer to the doctor as soon as possible if you experience the following symptoms:

- Effects due to low blood sugar levels (hypoglycemia): this effect may become worse in people who also take another medication to treat diabetes, such as sulfonylureas or insulin. Tell your doctor if you take other diabetes medicines. If you have symptoms of low blood sugar level, you should check your blood sugar and treat if low, then call your doctor. Symptoms of low blood sugar include**:** shaking, sweating, rapid heartbeat, change in vision, hunger, headache, change in mood.
- Joint pain. Some people who take medicines called DPP-4 inhibitors, one of the medicines in Kombiglyze XR, may develop joint pain that can be severe. Contact your doctor if you have severe joint pain.
- Skin reaction. Some people who take medicines called DPP-4 inhibitors, one of the medicines in KOMBIGLYZE XR, may develop a skin reaction called bullous pemphigoid that can require treatment in a hospital. Tell your doctor right away if you develop blisters or the breakdown of the outer layer of your skin (erosion). Your doctor may tell you to stop taking Kombyglyze XR.
- Unexplained stomach problems (stomach problems that begin late in treatment can sometimes be a sign of a more serious matter).

Common side effects that occur frequently:

- upper respiratory tract infection
- stuffy or runny nose and sore throat
- urinary tract infection
- headache
- diarrhea
- nausea and vomiting

If one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, must be kept in a safe place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package.

  The expiry date refers to the last day of that month.

- Storage conditions: Do not store at a temperature above 30°C.

  Store in the original packaging.

  Use within 12 months of first opening the package.

6. FURTHER INFORMATION

- **Composition of the preparation:**

  In addition to the active ingredients, Extended-Release Kombiglyze also contains:

  Tablet contents:

  carboxymethylcellulose sodium, hypromellose 2208, magnesium stearate.

  The tablet film coat contains:

  polyvinyl alcohol, polyethylene glycol 3350, titanium dioxide, talc and iron oxides.

- **How does the medicine look and what are the contents of the package:**

  Kombiglyze XR 5 mg/1000 mg Tablets are pink, capsule shaped, with “5/1000” printed on one side and “4223” printed on the other side, in blue ink.

  Package content: A bottle containing 30 or 90 or 500 tablets.

  Kombiglyze XR 2.5 mg/1000 mg Tablets are pale to light yellow, capsule shaped, with “2.5/1000” printed on one side and “4222” printed on the other side, in blue ink.

  Package content: A bottle containing 60 or 500 tablets.

Manufacturer:

AstraZeneca Pharmaceuticals LP, Mount Vernon, Indiana, USA.

License Holder and Importer:

AstraZeneca (Israel) Ltd.,

P.O.B 1455, Hod Hasharon 4524075.

- This leaflet was checked and approved by the Ministry of Health in July 2015, and was updated according to Ministry of Health guidelines in August 2019.
- Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:

  Kombiglyze XR 5 mg/1000 mg 33930

  Kombiglyze XR 2.5 mg/1000 mg 33929