NOVARTIS

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

EUCREAS® 50/500 mg Film-coated Tablets

EUCREAS® 50/850 mg Film-coated Tablets

EUCREAS® 50/1000 mg Film-coated Tablets

Composition:
Each tablet contains:

Eucreas 50/500 mg:
vildagliptin 50 mg and metformin hydrochloride 500 mg.

Eucreas 50/850 mg:
vildagliptin 50 mg and metformin hydrochloride 850 mg.

Eucreas 50/1000 mg:
vildagliptin 50 mg and metformin hydrochloride 1000 mg.

Inactive ingredients: See section 2 "Before using the medicine" and section 6 "Further information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Both active ingredients are oral antidiabetic agents.

Eucreas is intended for treatment of type 2 diabetes; Eucreas is intended for treatment of adults already receiving combined treatment with vildagliptin and metformin hydrochloride in separate tablets, or whose diabetes is not controlled with metformin hydrochloride alone.

The doctor will prescribe Eucreas either alone or in combination with another diabetes medicine depending on your condition. Eucreas, together with diet and exercise, is also intended to be taken in combination with insulin or with a medicine of the sulfonylurea group, for adults.

Therapeutic group:
Vildagliptin – dipeptidyl peptidase-4 (DPP-4) inhibitor.
Metformin – biguanides.

Type 2 diabetes develops when the body does not produce enough insulin, or when the insulin that the body produces does not work properly, or when the body produces too much glucagon.

Insulin is a substance which helps to lower the level of glucose in the blood, especially after meals. Glucagon is a substance that stimulates the liver to produce glucose and causes the blood glucose levels to rise. These two substances are produced in the pancreas. The two active ingredients in the Eucreas preparation help to control the level of glucose in the blood.

Eucreas causes the pancreas to produce more insulin and less glucagon (effect of vildagliptin), and also helps the body to make better use of the secreted insulin (effect of metformin hydrochloride).

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to vildagliptin, metformin hydrochloride or to any of the additional ingredients contained in the medicine (see section 6 "Further information"). If you think you may be allergic to one of these ingredients, speak to the doctor before taking Eucreas.
- Your diabetes is uncontrolled and includes, e.g., severe hyperglycemia (high blood glucose level), nausea, vomiting, diarrhea, 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 may lead to diabetic pre-coma. The symptoms include abdominal pain, fast and deep breathing, sleepiness or breath with an unusual fruity smell.
- You have recently had a heart attack or if you suffer from heart failure or serious problems with the blood circulation or difficulties in breathing which could be a sign of heart problems.
- You suffer from severely reduced kidney function.
- You have a severe infection or are seriously dehydrated (you have lost a lot of water from your body).
- You are going to have an X-ray (a specific type of imaging involving injection of an iodine-containing contrast agent) (see section "Drug interactions").
- You have liver function problems.
- You drink alcohol excessively (whether it is every day or only from time to time).
- You are breastfeeding (see also "Pregnancy, breastfeeding and fertility").

Special warnings regarding use of the medicine
Risk of lactic acidosis

Eucreas 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 in cases of uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, dehydration (see additional information below), liver function problems and any medical condition in which a part of the body has a reduced supply of oxygen (such as acute severe heart disease).

If one or more of the above conditions apply to you, talk to the doctor to receive further instructions.

Stop taking Eucreas for a short time if you have a condition associated with dehydration (significant loss of body fluids), such as severe vomiting, diarrhea, fever, exposure to heat or if you are drinking less fluids than normal. Talk to the doctor for further instructions.

Stop taking Eucreas 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
- abdominal pain
- muscle cramps
- malaise with severe tiredness
- difficulty in breathing
- reduced body temperature and heartbeat

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

Refer to a doctor immediately for additional instructions if:
- You are known to suffer from a genetically inherited disease that affects the mitochondria (energy-producing components within cells) such as MELAS syndrome (mitochondrial encephalopathy, myopathy, lactic acidosis and stroke-like episodes) or maternal-inherited diabetes and deafness (MIDD).
- You experience any of the following symptoms after starting treatment with metformin: seizures, declined cognitive abilities, difficulty with body movements, symptoms indicating nerve damage (e.g., pain or numbness), migraine and deafness.

Eucreas is not a substitute for insulin. Therefore, you should not receive Eucreas for the treatment of type 1 diabetes.

Before treatment with Eucreas, tell the doctor if:
- You suffered or are suffering from a disease of the pancreas.
- You are taking a medicine from the sulfonylurea group to treat diabetes. Your doctor may want to reduce the dosage of the medicine from the sulfonylurea group when it is given together with Eucreas in order to prevent a low level of glucose in the blood (hypoglycemia).
- You have taken vildagliptin in the past and had to stop because of a liver disease; do not take this medicine.
- You suffer form decreased kidney function. The doctor may prescribe you a lower dosage of Eucreas, in accordance with your kidney function.

During treatment with Eucreas:
- Skin lesions are a common complication of diabetes. It is advised to follow the doctor's or nurse's recommendations for skin and foot care. In addition, it is recommended to pay particular attention to new onset of blisters or ulcers during the course of treatment with Eucreas. If these occur, consult the doctor immediately.
- If you are due to undergo surgery, stop taking Eucreas during and for some time after the surgery. Your doctor will decide when you must stop and when to restart treatment with Eucreas.

Children and adolescents
Use of Eucreas is not intended for children and adolescents under 18 years of age.

Tests and follow-up
- Before starting treatment with Eucreas, you will be referred by the doctor to perform a liver function test. During the first year of treatment with the medicine, a test should be performed every three months and periodically thereafter, for early diagnosis of an increase in liver enzyme levels.
- During treatment, the doctor will monitor blood and urine glucose levels from time to time.
- Before starting and during the course of treatment with Eucreas, the doctor will check your kidney function at least once a year, and more frequently if you are elderly and/or have worsening in your renal function.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

If you need to have an iodine-containing contrast agent injected into the bloodstream, for example, during an X-ray or scan, stop taking Eucreas before or at the time of the injection. Your doctor will decide when you must stop and when to restart Eucreas treatment.

If you are taking other medicines, the doctor may refer you for more frequent testing of blood glucose levels and kidney function, or the doctor may need to adjust the dosage of Eucreas accordingly.

Especially note if you are taking medicines from the following groups:
- Glucocorticoids generally used to treat inflammation;
- Beta-2 agonists usually used to treat respiratory disturbances;
- Other medicines used to treat diabetes;
- Medicines which increase urine production (diuretics);
- Medicines used to treat pain and inflammation (non-steroidal anti-inflammatory drugs [NSAIDs] and COX-2 inhibitors, such as ibuprofen and celecoxib);
- Certain medicines for the treatment of high blood pressure (angiotensin-converting enzyme [ACE] inhibitors and angiotensin II receptor antagonists);
- Certain medicines affecting the thyroid;
- Certain medicines affecting the nervous system;
- Certain medicines used to treat angina (e.g., ranolazine);
- Certain medicines used to treat HIV infection (e.g., dolutegravir);
- Certain medicines used to treat a specific type of thyroid cancer (medullary thyroid cancer) (e.g., vandetanib);
- Certain medicines used to treat heartburn and peptic ulcer (e.g., cimetidine).

Use of Eucreas and food
It is recommended to take the tablets either with or immediately after a meal. This will reduce the risk of stomach upset.

Use of Eucreas and alcohol consumption
Avoid excessive consumption of alcohol during the course of treatment with Eucreas, since alcohol consumption may increase the risk of lactic acidosis (see section "Special warnings regarding use of the medicine").

Pregnancy, breastfeeding and fertility
Pregnancy
Report to the doctor if you are pregnant, think you might be pregnant, or are planning to become pregnant. The doctor will discuss with you the potential risk of taking Eucreas during pregnancy. There is no sufficient information about use of Eucreas during pregnancy; therefore, do not use Eucreas if you are pregnant.

Breastfeeding
Do not use Eucreas if you are breastfeeding (see also "Do not use this medicine if:").

Fertility
There is no information from clinical studies.

Driving and operating machinery
If you feel dizzy while taking Eucreas, avoid driving a vehicle or operating tools or machinery.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally one tablet, twice a day. If your kidney function is abnormal or you are taking a medicine from the sulfonylurea group, the doctor may prescribe you a lower dosage of Eucreas.

The medicine may be prescribed for you as a monotherapy or as part of a combination treatment with other medicines for lowering blood glucose level.

Do not exceed the recommended dose.

If you have a question regarding the duration of treatment with Eucreas, refer to a doctor.

Do not chew! The tablets are film-coated. Swallow the tablets whole with a glass of water.

It is recommended to take the tablets either with or immediately after a meal. This will reduce the chance of stomach upset.

Take one tablet in the morning and one tablet in the evening.

During treatment, continue to follow the dietary recommendations that the doctor has given you, particularly if you are following a diabetic weight control diet.

If you accidently 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. Medical treatment might be necessary.

If you forgot to take the medicine at the scheduled time, take a dose with the next meal. If you are due to take a dose at the next meal anyway, skip the forgotten dose. Do not take a double dose (two tablets at once) to compensate for a forgotten dose.

Adhere to the treatment as recommended by the doctor, so that the medicine will continue to control your blood glucose levels.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Eucreas 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.

Stop taking Eucreas and refer to a doctor immediately if you experience one or more of the following symptoms:
- **Lactic acidosis** (very rare: effects that occur in less than one user in 10,000):
  Eucreas may cause a very rare, but very serious side effect called lactic acidosis (see section "Special warnings regarding use of the medicine"). If this happens, **stop taking Eucreas and refer to a doctor or the nearest hospital immediately,** as lactic acidosis may lead to coma.
- **Angioedema** (rare: effects that occur in 1-10 in 10,000 users): Symptoms include swelling of the face, tongue or throat, difficulty swallowing, difficulty breathing, sudden onset of rash or hives, which may indicate a reaction called angioedema.
- **Liver disease (hepatitis)** (uncommon: effects that occur in 1-10 in 1,000 users): Symptoms include yellowing of the skin and eyes, nausea, lack of appetite, dark urine, which may indicate liver disease (hepatitis).
- **Inflammation of the pancreas (pancreatitis)** (uncommon: effects that occur in 1-10 in 1,000 users): Symptoms include severe and persistent pain in the stomach area that may radiate to the back, as well as nausea and vomiting.

Other side effects:
Some patients have experienced the following side effects while taking Eucreas:
- Common side effects (effects that occur in 1-10 in 100 users): sore throat, runny nose, fever, itchy rash, excessive sweating, joint pains, dizziness, headache, trembling that cannot be controlled, constipation, nausea, vomiting, diarrhea, accumulation of gas in the digestive system, heartburn, pain in and around the stomach (abdominal pain).
- Uncommon side effects (effects that occur in 1-10 in 1,000 users): tiredness, weakness, metallic taste, low glucose level, loss of appetite, swollen hands, ankles or feet (edema), chills, inflammation of the pancreas, muscle pain.
- Very rare side effects (effects that occur in less than one user in 10,000): signs of a high level of lactic acid in the blood (a condition known as lactic acidosis) such as drowsiness or dizziness, severe nausea or vomiting, abdominal pain, irregular heart rate or deep, rapid breathing; redness of the skin, itching; decreased vitamin B12 levels (paleness, tiredness, signs of confusion or memory problems).

Since the preparation has been marketed, the following side effects have been reported:
Frequency unknown (cannot be estimated from the available data): localized peeling of the skin or blisters, blood vessel inflammation (vasculitis) that may result in skin rash or raised, flat, red, round spots under the surface of the skin or bruising.

If a side effect occurs, 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
Side effects can also be reported to Novartis company via the email address: safetydesk.israel@novartis.com.

Revised in June 2025.

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight 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) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions:
- Store below 25°C and store in the original package to protect from moisture.
- Do not discard medicines in the wasterwater or household waste bin. Ask the pharmacist how to dispose of medicines that are no longer needed. This will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredients, Eucreas tablets also contain:
Hydroxypropyl cellulose, magnesium stearate, hypromellose, titanium dioxide (E 171), polyethylene glycol 4000, talc, iron oxide yellow (E 172), iron oxide red (E 172) (50/500 mg only).

What the medicine looks like and the contents of the package:
Eucreas 50/500 mg: film-coated, light yellow, oval, beveled-edge tablets with NVR written on one side and LLO on the other side.

Package size: 60 tablets.

Eucreas 50/850 mg: film-coated, yellow, oval, beveled-edge tablets with NVR written on one side and SEH on the other side.

Package size: 60 tablets.

Eucreas 50/1000 mg: film-coated, dark yellow, oval, beveled-edge tablets with NVR written on one side and FLO on the other side.

Package size: 60 tablets.

Registration holder and importer and address: Novartis Israel Ltd., P.O. Box 9240, Tel Aviv, Israel.

Revised in June 2025.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
Eucreas 50/500 mg: 147 89 33623
Eucreas 50/850 mg: 143 88 32042
Eucreas 50/1000 mg: 147 90 33627

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