PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

Metilda 50/850 mg
Film-coated tablets

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Composition:
Each tablet contains:
Metilda 50/850 mg:
Vildagliptin 50 mg and metformin hydrochloride 850 mg
Metilda 50/1000 mg:
Vildagliptin 50 mg and metformin hydrochloride 1,000 mg
Inactive ingredients: see section 6 "Additional information".
Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.
This medicine has been prescribed for treatment of your illness. Do not pass it on to others. It may harm them even if it seems to you that their illness is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?
Both active ingredients are oral antidiabetic medicines.
- Metilda is intended for treatment of type 2 diabetes. Metilda is intended for treatment in adults already receiving combined treatment with separate tablets of vildagliptin and metformin hydrochloride, or whose diabetes is not adequately controlled with metformin hydrochloride alone.

The doctor will prescribe treatment with Metilda either alone or in combination with another diabetes medicine, depending on your condition. Metilda is also intended for treatment in adults in combination with insulin or with a medicine from the sulfonylurea group, together with diet and exercise.
Therapeutic class:
Vildagliptin – dipeptidyl-peptidase-4 (DPP-4) inhibitor.
Metformin – biguanides.
Type 2 diabetes develops when the body does not produce enough insulin, 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, causing the blood glucose level to rise. Both of these substances are produced in the pancreas. Both active ingredients in the medicine Metilda help to control the level of glucose in the blood.
Metilda 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, to metformin hydrochloride or to any of the other ingredients this medicine contains (see section 6 "Additional information"). If you think you may be allergic to any of these ingredients, talk to the doctor before taking Metilda.
- Your diabetes is uncontrolled with, for example, 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. Symptoms include abdominal pain, rapid and deep breathing, somnolence 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 breathing difficulties, 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 about to have an x-ray (a specific type of x-ray involving injection of an iodine-containing contrast agent) (see sub-section "Drug interactions").
- You have liver function problems.
- You drink alcohol excessively (whether every day or only from time to time).
- You are breastfeeding (see also "Pregnancy, breastfeeding and fertility").

Special warnings regarding the use of the medicine
Risk of lactic acidosis
Metilda 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 further 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 your doctor to receive further instructions.
Stop taking Metilda for a short time if you experience a condition that is 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 Metilda and refer immediately to the doctor or the nearest hospital if you suffer from some of the symptoms of lactic acidosis, as this condition may lead to coma.
The symptoms of lactic acidosis include:
- Vomiting
- Abdominal pain
- Muscle cramps
- A general feeling of not being well with severe tiredness
- Breathing difficulties
- Reduced body temperature and heart rate

Lactic acidosis is a medical emergency and must be treated in a hospital.
Metilda is not a substitute for insulin. Therefore, you should not receive Metilda for the treatment of type 1 diabetes.
Before treatment with Metilda, tell the doctor if:
- You suffer or have suffered in the past from a disease of the pancreas.
- You are taking a medicine to treat diabetes from the sulfonylurea group. Your doctor may want to reduce the dose of the medicine from the sulfonylurea group when it is given together with Metilda in order to prevent a low level of glucose in the blood (hypoglycemia).
- You have previously taken vildagliptin and had to stop because of liver disease; in this case do not take this medicine.
- You suffer from reduced kidney function. Your doctor may prescribe you a lower dose of Metilda, depending on your kidney function.

During treatment with Metilda:
- Skin lesions are a common complication of diabetes. It is advised to follow the recommendations for skin and foot care given by the doctor or nurse. It is also advised to pay particular attention to new onset of blisters or ulcers while taking Metilda. If these occur, you should immediately consult the doctor.
- If you are about to undergo surgery, you must stop taking Metilda during and for some time after the surgery.
  Your doctor will decide when you should stop and when you should restart the treatment with Metilda.

Children and adolescents
Use of Metilda is not intended for children and adolescents under 18 years of age.
Tests and follow-up
- Before starting treatment with Metilda, the doctor will refer you for a liver function test. During the first year of treatment with this medicine a test should be performed every three months, and afterwards, periodic tests should be performed, in order to detect an increase in liver enzymes at an early stage.
- During treatment, the doctor will monitor the levels of glucose in your blood and urine from time to time.
- During treatment with Metilda, the doctor will check your kidney function at least once a year, and at a higher frequency if you are elderly and/or if there is a worsening of your kidney function.

Drug interactions
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist.
If you need to have an injection of a contrast agent that contains iodine into your blood stream, for example during an x-ray or scan, you must stop taking Metilda before or at the time of the injection. Your doctor will decide when you should stop and when you should restart the treatment with Metilda.
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 dose of Metilda accordingly.
Especially mention if you are taking medicines from the following groups:
- Glucocorticoids generally used to treat inflammation
- Beta-2 agonists usually used to treat respiratory disorders
- Other anti-diabetic medicines
- 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 for treatment of angina (such as ranolazine)
- Certain medicines for treatment of HIV infection (such as dolutegravir)
- Certain medicines for treatment of a specific type of thyroid cancer (medullary thyroid cancer) (such as vandetanib)
- Certain medicines for treatment of heartburn and peptic ulcers (such as cimetidine)

Use of Metilda and food
It is advisable to take the tablets either with or just after the meal. This will reduce the risk of abdominal discomfort.
Use of Metilda and alcohol consumption
Avoid excessive consumption of alcohol during treatment with Metilda, since alcohol consumption may increase the risk of lactic acidosis (see sub-section: "Special warnings regarding the 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 Metilda during pregnancy. There is insufficient information regarding the use of Metilda during pregnancy, so do not use Metilda if you are pregnant.
Breastfeeding
Do not use the medicine Metilda if you are breastfeeding (see also "Do not use the medicine if:").
Fertility
No information is available from clinical studies.
Driving and operating machinery
If you feel dizzy while taking Metilda, avoid driving a vehicle or using tools or machinery.

3. HOW SHOULD YOU USE THE MEDICINE?
Always use the medicine according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the medicine.
The dosage and treatment regimen will be determined only by the doctor.
The generally accepted dosage is one tablet, twice daily. If your kidney function is abnormal or if you are taking a medicine from the sulfonylurea group, the doctor may prescribe you a lower dose of Metilda.
The medicine may be prescribed for you as a monotherapy or as part of a combined therapy with other medicines that lower the level of glucose in the blood.
Do not exceed the recommended dose.
If you have questions about the duration of the treatment with Metilda, refer to the doctor.
Do not chew! The tablets are film-coated. Swallow the tablets with a glass of water.
The score line is intended to make swallowing easier, not to allow the administration of half a dose.
There is no information regarding crushing.
It is advisable to take the tablets either with or just after the meal. This will reduce the chance of abdominal discomfort.
Take one tablet in the morning and one tablet in the evening.
During treatment, continue to follow the dietary recommendations given by the doctor, particularly if you are following a dietary regimen adjusted for diabetics.
If you accidentally took an overdose or if a child accidentally swallowed this medicine, **refer to the doctor or to a hospital emergency room immediately** and take the package of the medicine with you. Medical attention may be required.
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 the forgotten dose.
Adhere to the treatment as recommended by the doctor, so that the medicine continues 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 every time you take a medicine. Wear glasses if you need them.
If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. SIDE EFFECTS
As with any medicine, using Metilda may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.
Stop taking Metilda and refer to the doctor immediately if you have one or more of the following symptoms:
- **Lactic acidosis** (very rare: effects that occur in less than one user out of 10,000): Metilda may cause a very rare but very serious side effect called lactic acidosis (see section 2 under "Special warnings regarding the use of the medicine"). If this happens, you must **stop taking Metilda and refer to the doctor or to the nearest hospital immediately,** as lactic acidosis may lead to coma.
- Angioedema (rare: effects that occur in 1-10 users out of 10,000): symptoms include swollen face, tongue or throat, swallowing difficulties, breathing difficulties, sudden onset of rash or hives, which may indicate a reaction called angioedema.
- Liver disease (hepatitis) (uncommon: effects that occur in 1-10 users out of 1,000): symptoms include yellowing of the skin and eyes, nausea, loss of appetite, dark urine, which may indicate liver disease (hepatitis).
- Inflammation of the pancreas (pancreatitis) (uncommon: effects that occur in 1-10 users out of 1,000): symptoms include severe and persistent pain in the stomach area, which may radiate to the back, as well as nausea and vomiting.

Other side effects:
Some patients have experienced the following side effects while taking Metilda:
- Common side effects (effects that occur in 1-10 users out of 100): sore throat, rhinitis, fever, itchy rash, excessive sweating, joint pain, dizziness, headache, uncontrollable tremor, 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 users out of 1,000): tiredness, weakness, metallic taste, low glucose level, loss of appetite, swelling of the hands, ankles or feet (edema), chills, inflammation of the pancreas (pancreatitis), muscle pain.
- Very rare side effects (effects that occur in less than one user out of 10,000): signs of a high level of lactic acid in the blood (a condition called lactic acidosis) such as somnolence or dizziness, severe nausea or vomiting, abdominal pain, irregular heart rate or deep and rapid breathing; skin redness, itch; decreased vitamin B12 levels (signs such as pallor, tiredness, confusion or memory problems).

Since this medicine has been marketed, the following side effects have been reported:
Side effects with unknown frequency (cannot be estimated from the available data): localized peeling of the skin or blisters, blood vessel inflammation (vasculitis) which may cause skin rash or raised, flat, red, round spots under the skin's surface 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 this leaflet, consult your doctor.
Reporting side effects
Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il) which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?
- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from 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: store below 25°C, in the original package in order to protect from moisture.
- Do not discard medicines in wastewater or a domestic trash can. Ask the pharmacist how to dispose of medicines no longer in need. This will help protect the environment.

6. ADDITIONAL INFORMATION
In addition to the active ingredients, Metilda tablets contain:
Cellulose, Hydroxypropylcellulose, Magnesium Stearate, Hypromellose, Titanium Dioxide, Copovidone, Polydextrose, Macrogol, Yellow Iron Oxide, Triglycerides
What does the medicine look like and what are the contents of the package?
Metilda 50/850 mg: yellow, oval, film-coated tablet, marked with a line on one side and A8 on the other side.
Size of the package: 60 tablets.
Metilda 50/1000 mg: yellow-brown, oval, film-coated tablet, marked with a line on one side and A1 on the other side.
Size of the package: 60 tablets.
Name and address of the manufacturer and marketing authorization holder:
Teva Israel Ltd.,
124 Dvora HaNevi'a St., Tel Aviv 6944020.
The leaflet was revised in June 2023 in accordance with the Ministry of Health guidelines.
Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
Metilda 50/850 mg: 173-24-36319-00
Metilda 50/1000 mg: 173-25-36320-00

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