

PACKAGE LEAFLET: Information for the user

METFORMINE

Film-coated tablets – 500 mg, 850 mg or 1000 mg

(Metformin hydrochloride)

Read this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets worse or if you notice any side effect not listed in this leaflet, please inform your doctor or pharmacist.

What is in this leaflet:

1. What Metformine is and what it is used for
2. What you should know before you take Metformine
3. How to take Metformine
4. Possible side effects
5. How to store Metformine
6. Other information

1. WHAT METFORMINE IS AND WHAT IT IS USED FOR

Metformine is an oral antidiabetic which is not chemically or pharmacologically related to sulfonylurea derivatives. Metformine improves glucose tolerance in non-insulin-dependent diabetes mellitus by reducing basal and after-meal blood glucose levels. Metformine also reduces hepatic glucose production, intestinal glucose absorption and improves insulin sensitivity (increases peripheral glucose uptake).

Metformine is indicated in non-insulin-dependent diabetes mellitus when treatment by diet modification alone has not been effective and when the patient is overweight. Metformine may be used alone as initial treatment or in combination with a sulfonylurea derivative.

In insulin-dependent diabetes mellitus, Metformine may be used as adjunctive treatment in patients whose symptoms are difficult to manage.

2. WHAT YOU SHOULD KNOW BEFORE YOU TAKE METFORMINE

Do not take Metformine:

- if you are hypersensitive to metformin hydrochloride, or to any of the excipients of Metformine tablets;
- in case of diabetic coma or ketoacidosis;
- if you have renal dysfunction;
- if you have chronic hepatic disease;
- if you have cardiac insufficiency or myocardial infarction;
- if you have history of lactic acidosis-associated conditions such as shock or pulmonary insufficiency, severe infections, dehydration, alcoholism (acute or chronic) and conditions associated with hypoxia.

Metformine should be discontinued prior to parenteral iodinated contrast media administration and should not be re-administered any sooner than 48 hours and should be withheld until renal function is determined to be normal.

Take special care with Metformine

- Metformine may cause a very rare but serious complication called lactic acidosis, especially if kidney dysfunction is present. Lactic acidosis symptoms are as follows: vomiting, abdominal pain with muscle cramps, malaise and respiratory distress, reduced body temperature and heartbeat. **If you experience one of these symptoms, you might need hospitalization, because lactic acidosis may lead to coma. Immediately discontinue Metformine use and contact a doctor or the nearest hospital.**
- Metformine is excreted by the kidneys so it is recommended that kidney function is checked in all patients taking this medicine.
- Discontinue Metformine treatment 2-3 day prior to surgical intervention.
- Metformine use is not recommended in conditions associated with dehydration (severe vomiting or diarrhoea, fever, exposure to heat or if you drink less fluid than normal) or in patients suffering from infection or trauma.

- In patients who continuously use Metformine, annual check of Vitamin B₁₂ levels is recommended, as evidence exists that this medicine may decrease Vitamin B₁₂ absorption.
- Blood glucose levels should be checked during concomitant use of Metformine with a sulfonylurea derivative and / or insulin as their combination may cause hypoglycemia.
- Due to risk of hypoglycemia, treatment with Metformine and insulin of a patient with diabetes mellitus should take place in hospital until optimal doses are determined.

Other medicines and Metformine

Use of Metformine with other medicines may influence Metformine or other medicines' effect. Please, contact your doctor or pharmacist if you are taking / using or have recently taken / used other medicines, including medicines without a prescription. Do not forget to inform your doctor that you are taking Metformine if any other medicines are prescribed to you.

It is particularly important to tell your doctor that you are taking the following medicines:

- cationic medicines, cimetidine, furosemide, parenteral iodinated contrast media, nifedipine, topiramate, rilpivirine, rifampicin, dolutegravir, ranolazine, trimethoprim, vandetanib, isavuconazole, crizotinib, olaparib as these medicines may affect metformine plasma concentration;
- furosemide, clomiphene, because Metformine may influence their effect;
- thiazide and loop diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking medicines and isoniazid because they antagonize the blood glucose lowering effect of metformin;
- other antidiabetic medicines, angiotensin converting enzyme (ACE) inhibitors, anabolic steroids, monoamine oxidase (MAO) inhibitors, and alcohol, because they could lead to loss of glycemic control. Careful patient monitoring is required to maintain an optimal glycemic control when these medicines are used concomitantly with Metformin;
- angiotensin II receptor antagonists (ARB);
- ketotifen, because of depressed thrombocyte count when it is used with Metformine;
- medicines used to treat pain and inflammation such as ibuprofen and celecoxib because the risk of lactic acidosis is increased.

Taking Metformine with food and drinks

Metformine may cause hypoglycemia if taken with alcohol.

Pregnancy

Metformine should not be used during pregnancy.

Breastfeeding

Do not take Metformine if you are breastfeeding, because it may be distributed into breast milk.

Driving and using machinery

Car drivers and machinery users should be alerted to the symptoms of hypoglycemia and its effects on vigilance when Metformine is used in combination with a sulfonylurea derivative and/or insulin.

3. HOW TO TAKE METFORMINE

Always take Metformine tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you feel that Metformine effect is too strong or too weak.

There is no fixed dose of Metformine for diabetes mellitus treatment. The dose should be individualized based on its effectiveness and tolerance without exceeding maximum daily dose of 3 g. Treatment is initiated with a small dose, which is gradually increased in order to avoid gastrointestinal side effects and determine the minimal required dose for optimal glycemic control.

Dosage is as follows:

Adults: the usual initial dosage is 500 mg twice daily or 850 mg twice daily taken in the morning and evening with meals. The dose may be increased by 500 mg every week, given in separate doses up to a maximum of 3000 mg daily. Metformine may be used twice daily up to 1700 – 2000 mg daily (e.g. 1000 mg twice daily, morning and evening with meals). If a dose of 2500 - 2550 mg is required, it might be better tolerated if it is given three times daily with food.

Elderly: Metformine should be carefully used in elderly patients since aging is associated with

reduced renal function which may lead to medicine's accumulation in the body and consequent lactic acidosis. Thus, renal function should be monitored in this patient category in order to determine the exact dose.

Children:

In children 10 years of age or older the usual initial metformin dose is 500 mg twice daily. The dose may be increased by 500 mg daily at weekly intervals until the desired glycemic response is achieved or up to a maximum dosage of 2000 mg daily.

If you take more Metformine than you should

If you take more Metformine tablets than you should or if the children have taken this medicine by mistake, contact your doctor or the nearest hospital or call the emergency service to ask for the risks and advice on the actions that should be taken.

If you forget to take Metformine

If you forget to take one or more doses, take the next dose at the next prescribed time.

Do not take a double dose to make up for a forgotten dose.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody manifests them. Sometimes they are serious, sometimes not. Do not get alarmed by this list of possible side effects. You may not get any of them.

Metformine may cause a very rare (may affect up to 1 user in 10,000) but very serious side effect called lactic acidosis (see section 'Take special care with Metformine'). If this happens, you must stop taking Metformine and contact a doctor or the nearest hospital immediately, as lactic acidosis may lead to coma.

Other possible side effects are listed by frequency as follows:

Very common (affects more than 1 user in 10):

- Diarrhoea, nausea, vomiting, stomach ache or loss of appetite. If you get these, do not stop taking the tablets as these symptoms will normally go away in about 2 weeks. It helps if you take the tablets with or immediately after a meal.

Common (affects 1 to 10 users among 100):

- Taste disturbance.

Rare (affects up to 1 user in 10,000):

Metformine may cause abnormal liver function tests and hepatitis (inflammation of the liver) which may result in jaundice. If you develop yellowing of the eyes and/or skin contact your doctor immediately.

Very rare (affects less than 1 user in 10,000):

- Decreased vitamin B12 levels;
- Skin rashes including redness, itching and hives.

If any of the side effects gets worse or if you notice side effects not mentioned in this leaflet, please contact your doctor or pharmacist.

5. HOW TO STORE METFORMINE

Keep out of the reach and sight of children.

Do not use the tablets after the expiry date which is stated on the packaging.

Store below 25°C.

6. OTHER INFORMATION

What Metformine film-coated tablets contain

The active substance is metformin hydrochloride.

Each film-coated tablet contains 500 mg, 850 mg or 1000 mg metformin hydrochloride.

The excipients for the 500 mg film-coated tablet are:

tablet core: microcrystalline cellulose, povidone, sodium starch glycolate, magnesium stearate, talc;

film-coating: polyvinyl alcohol, titanium dioxide, macrogol, talc.

Excipients for the 850 mg film-coated tablet are:

tablet core: povidone, colloidal anhydrous silica, magnesium stearate;

film-coating: polyvinyl alcohol, titanium dioxide, macrogol, talc.

The excipients for the 1000 mg film-coated tablet are:

tablet core: povidone, colloidal anhydrous silica, sodium starch glycolate, magnesium stearate;

film-coating: polyvinyl alcohol, titanium dioxide, macrogol, talc.

Contents of the pack

500 mg film-coated tablet: carton box with 30 tablets.

850 mg film-coated tablet: carton box with 60 tablets.

1000 mg film-coated tablet: carton box with 30 tablets.

Marketing Authorisation Holder (MAH) and Manufacturer:

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Tirana, Albania.

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