GLUCOPHAGE XR 1000 mg prolonged release tablets

Active ingredient: metformin hydrochloride

Composition

Each Glucophage XR 1000 mg prolonged release tablet contains as active ingredient 1000 mg metformin hydrochloride (equivalent to 780 mg of metformin base).

Excipients:

Magnesium stearate, sodium carboxymethylcellulose, hypromellos

Properties

Glucophage XR is an antidiabetic medicine that belongs to the group of biguanides. Metformin, the active ingredient in Glucophage XR, reduces hepatic glucose production, increases insulin sensitivity in muscles and delays intestinal glucose absorption.

A reduction of diabetic complications has been shown in overweight type 2 diabetic adult patients treated with Glucophage immediate-release as first-line therapy after diet therapy.

Indication

Glucophage XR is used for the treatment of type 2 diabetes in adults as an adjunct to adequate diet and exercise. Glucophage XR may be given alone, or with other oral antidiabetic agents, or with insulin.

Contraindications

Glucophage XR must not be used in the following cases:

- hypersensitivity to metformin hydrochloride or any of the excipients
- severe destabilisation of diabetes with either pre-coma or ketoacidosis (a condition caused by substances called 'ketone bodies' accumulating in the blood; symptoms include stomach pain, fast and deep breathing, sleepiness or unusual fruity odour of the breath)
- renal insufficiency, even if moderate (impairment of kidney function with increased blood creatinine levels or decreased creatinine clearance < 60 ml/mn)
- infectious diseases (for example respiratory tract infection, urinary tract infection)
- X-ray examination involving the use of iodinated contrast media (for example intravenous urography, angiography), see section 'Special warnings and precautions'
- Elective major surgery, see section 'Special warnings and precautions'
- disease which may cause tissue hypoxia (heart failure, recent myocardial infarction, respiratory insufficiency, shock)
- hepatic insufficiency (impaired liver function)
- dehydration (for example due to persistent or severe diarrhoea, recurrent vomiting)
- excessive consumption of alcoholic beverages
- during breast-feeding.

Pregnancy and lactation

Glucophage XR is not the appropriate treatment of type 2 diabetes during pregnancy. Women who are pregnant or plan to become pregnant have to consult their doctor for replacement of Glucophage XR by insulin. Glucophage XR is contra-indicated during breast-feeding. As a general rule, women who are pregnant or breast-feeding should always ask their doctor for advice before taking a medicine.

Special warnings and precautions

Lactic acidosis

Symptoms of lactic acidosis are vomiting, abdominal pain with muscle cramps, a general feeling of not being well with severe fatigue and difficulty in breathing.

If these symptoms occur, patients must stop taking Glucophage XR immediately and consult their doctor straight away. Lactic acidosis can occur due to metformin accumulation, especially in diabetic patients with significant renal insufficiency. Other associated risk factors are poorly controlled diabetes, ketosis, prolonged fasting, alcoholism, hepatic insufficiency and any condition associated with hypoxia. **Lactic acidosis is a medical emergency and must be treated in a hospital. The most effective way to remove lactate and metformin from the blood is haemodialysis.**

Kidney function

Since metformin (active ingredient in Glucophage XR) is excreted mainly by the kidneys, your kidney function (creatinine clearance and/or serum creatinine levels) must be determined before treatment initiation and regularly thereafter:

- at least annually in patients with normal kidney function
- at least two to four times a year in patients with serum creatinine levels at the upper limit of normal and in elderly patients. Special caution should be exercised in situations where kidney function may become impaired, for example in the elderly or when initiating antihypertensive treatment or diuretic treatment or treatment with a non-steroidal anti-inflammatory medicine (NSAID).

Iodinated contrast media

If a patient is scheduled to undergo X-ray examinations involving the use of iodinated contrast media, such as intravenous urography or angiography, treatment with Glucophage XR must be discontinued 48 hours before the test or at the time of the test. Glucophage XR may not be reinstituted until 48 hours afterwards, and only after kidney function has been tested and found to be normal.

Surgery

If a patient is going to have an elective major surgery, treatment with Glucophage XR must be discontinued 48 hours before the surgery. Glucophage XR will not be re-instituted until 48 hours after the surgery, and only after ensuring that kidney function is normal.

Other precautions

- Avoid consumption of alcoholic beverages.
- Patients have to inform their doctor of any other treatment they are receiving and of any infectious illnesses such as influenza, respiratory tract infection or urinary tract infection.
- The usual laboratory tests for diabetes monitoring should be performed regularly.
- Patients should continue to follow dietary advice given by their doctor.

Effect on ability to drive and use machines

When used alone, Glucophage XR does not cause hypoglycemia. Consequently, there is no particular risk when driving or using machines. However, caution is advised if certain antidiabetic medicines are taken together with Glucophage XR, such as sulphonylurea, insulin, glinides or other hypoglycemic agents. Symptoms of hypoglycaemia include weakness, dizziness, increased sweating, fast heart beating, vision disorders of difficulty in concentration. When a patient starts to feel these symptoms, he should not drive or use machines.

Adverse effects

Like all medicines, Glucophage XR can cause adverse effects although not everybody gets them. The following adverse effects observed in patients treated with Glucophage XR were similar in nature and severity to those observed in patients treated with Glucophage immediate-release. They are presented by frequencies which are defined as follows: very common: 10%; common 1% ,<10%; uncommon: 0.1% ,<1%; rare 0.01% ,<0.1%; very rare: <0.01%; not known (cannot be estimated from available data). Very common: Gastrointestinal discomfort such as nausea, vomiting, diarrhoea, abdominal pain and loss of appetite may occur especially at the beginning of treatment. These symptoms are generally transient and can be reduced by taking the tablets with meals. **Should these symptoms continue, patients must stop taking the treatment and consult their doctor.**

Common: Taste disturbance

Very rare:

- Lactic acidosis is a very serious complication, which results in vomiting, abdominal pain with muscle cramps and/or a general feeling of malaise with severe fatigue and which requires specific treatment. If this occurs, patients should stop taking Glucophage XR immediately and consult their doctor promptly. Lactic acidosis is a medical emergency and must be treated in a hospital.
- Skin reactions such as erythema (red skin), itching or urticaria (eruption with itching).
- Decreased vitamin B12 levels (to take into consideration if the patient is suffering from megaloblastic anaemia).

Very rare: Isolated cases of liver function tests abnormalities or hepatitis resolving upon Glucophage XR discontinuation. **Patients must report any undesirable or distressing effect to their doctor or pharmacist.** To prevent serious reactions, they must speak to their doctor immediately, if an undesirable effect is severe, occurred suddenly or gets worse rapidly.

Interactions

While taking Glucophage XR, patients must not use:

- iodinated contrast agents (see section 'Contraindications').

Special precautions may be required if patients take Glucophage XR and any of the following medicines at the same time:

- corticosteroids, tetracosactides, beta2 agonists such as salbutamol or terbutaline, diuretics, danazol or chlorpromazine increase glycaemia. Blood glucose monitoring is recommended and dose adjustment of Glucophage XR should be considered.
- antihypertensive agents of the angiotensin-converting enzyme inhibitors class may have an hypoglycaemic action. If necessary, the dosage of Glucophage XR should be adjusted.
- diuretics (especially loop diuretics) may increase the risk of lactic acidosis. Kidney function monitoring is recommended.
- alcohol containing medicines. Alcohol increases the risk of lactic acidosis, especially in case of fasting or malnutrition or hepatic insufficiency.

As a general rule, patients have to tell their doctor or pharmacist, if they are taking or have recently taken another medicine, including over-the-counter medicines.

Dosage and administration

This medicine is only for adults. The dosage of Glucophage XR is determined by the doctor on an individual basis according to the results of laboratory blood glucose measurement. Glucophage XR 1000 mg is intended as a maintenance treatment for patients already treated with either 1000 mg or 2000 mg of metformin.

Initial treatment

For patients new to metformin, the initial dose is one tablet of Glucophage XR 500 mg once daily given with the evening meal. For patients already treated with metformin, the initial dose on switch should not exceed the daily dose of metformin already being taken. One tablet of Glucophage XR 1000 mg may be used to replace two tablets of metformin 500 mg. In case Glucophage XR is used in combination with insulin, the initial dose is one tablet of Glucophage XR 500 mg, while insulin dosage is adjusted on the basis of blood glucose measurements.

Titration

After 10 to 15 days, the dose may be slowly increased by increment of 500 mg depending on blood glucose measurements. After titration, switch to Glucophage XR 1000 mg may be considered in patients receiving 1000 mg or 2000 mg of metformin.

Maximum dose

Two tablets of Glucophage XR 1000 mg once daily, given with the evening meal.

If glycaemic control is not achieved on maximal daily dose given once daily, then the same dose may be considered but divided along the day according to the following scheme: one tablet during breakfast and one tablet during evening meal.

Elderly and decreased renal function

In elderly and in patients with decreased renal function, the dosage should be adjusted based on renal function.

Administration

Swallow the tablets without chewing during your evening meal (once daily dosage) or with breakfast and evening meal (twice daily dosage). Always take the tablets with food. The tablet shells may appear in the faeces, which is not linked to a decrease of therapeutic activity.

Duration of treatment

Glucophage XR must be taken daily without interruption. Patients who have stopped the treatment must contact their doctor.

Missed dose

In case of missed dose, patients have to take the next dose at the usual time. Patients must not double the dose of Glucophage XR.

Overdose

In case of overdose, patients must contact their doctor immediately. High overdose or concomitant risks may lead to lactic acidosis. Lactic acidosis is a medical emergency and must be treated in hospital. The most effective method to remove lactate and metformin is haemodialysis.

Storage

Store below 30°C. Do not use after the expiry date shown on the outer packaging.

KEEP OUT OF THE REACH OF CHILDREN

Pharmaceutical form

Glucophage XR 1000 mg tablets prolonged release tablets are white to off-white, capsule-shaped, biconvex and debossed on one side with '1000' and on the other side with 'Merck'. Glucophage XR tablets are made to provide a "prolonged release" formulation. The active ingredient metformin is slowly released and thus enables to take the tablets once or twice a day (see under section 'Dosage and administration').

Presentations

Boxes of 30 or 60 prolonged release tablets in blister pack.

Not all pack sizes may be registered or marketed.

GENERAL RECOMMENDATIONS

This medicine has been prescribed by your doctor for the treatment of diabetes, a disease characterized by hyperglycaemia, i.e. an excess of glucose in the blood. Glucose appears in the urine only when it exceeds a certain level in the blood.

There are two types of diabetes:

- the most common type (type 2) can be treated by medicines taken by the oral route (oral antidiabetics),
- the other type (type 1) requires the administration of insulin injections.

It is essential that medical tests be performed to determine the type of diabetes, as insulin injections and oral antidiabetics cannot be freely interchanged.

Important:

- in all cases, strictly adhere to the diet and exercise recommended by your doctor.
- carry a card or bracelet saying you are diabetic
- visit your doctor regularly
- read this leaflet carefully in full before taking this medicine

THIS IS A MEDICAMENT

Medicament is a product, which affects your health and its consumption contrary to instructions is dangerous for you. Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers, Union of Arab Pharmacists.

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