

Please read this leaflet carefully in full before taking this medicine.

COMPOSITION

Glucophage XR 750 mg prolonged release tablets contain as active ingredient 750 mg metformin hydrochloride (equivalent to 585 mg of metformin base)

Excipients:

Glucophage XR 750 mg: Magnesium stearate, sodium carboxymethylcellulose, hypromellose.

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.

INDICATIONS

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.

CONTRA-INDICATIONS

Glucophage XR **must not be used** in the following cases:

- hypersensitivity to metformin hydrochloride or any of the ingredients,
- severe destabilisation of diabetes (ketoacidosis or pre-coma),
- renal insufficiency, even if moderate (impairment of kidney function with increased blood creatinine levels or decreased creatinine clearance < 60 ml/min),
- infectious diseases (for example respiratory tract infection, urinary tract infection),
- following an X-ray examination involving the use of iodinated contrast media (for example intravenous urography, angiography),
- disease which may cause tissue hypoxia (heart failure, recent myocardial infarction, respiratory insufficiency, shock),
- hepatic insufficiency (impaired liver function),
- 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

- Vomiting, abdominal pain with muscle cramps and/or a general feeling of malaise with severe fatigue occurring during therapy may be signs of serious destabilisation of diabetes (diabetic ketoacidosis or lactic acidosis) requiring specific treatment.

If this occurs, patients must stop taking Glucophage XR immediately and consult their doctor promptly. 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.

- Periodic laboratory tests have to be prescribed to assess blood glucose level and kidney function (creatinine levels or creatinine clearance) before treatment initiation and regularly thereafter since metformin is excreted mainly by the kidneys.

- 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 and when starting treatment with a non-steroid anti-inflammatory.

- Certain illnesses or medicines such as corticosteroids, diuretics, beta2 agonists (e.g. salbutamol, terbutaline) and angiotensin-converting enzyme inhibitors may cause more or less severe destabilisation of diabetes. 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.

- 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 prior to or at the time of the test and will not resume treatment until 48 hours after the test, after ensuring that kidneys are functioning normally.

- In the event of a hospitalisation for tests, a surgical procedure, or for any other reason, patients have to inform their doctor that they are taking Glucophage XR.

- Consumption of alcoholic beverages has to be avoided.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

When used alone, Glucophage XR does not cause hypoglycaemia and therefore has no influence on the ability to drive and use machines.

However, if certain antidiabetic medicines are taken together with Glucophage XR, such as sulphonylurea, insulin, glinides or other hypoglycaemic agents, the mental concentration may be impaired in the event of hypoglycaemia.

UNDESIRABLE EFFECTS

As all medicines, Glucophage XR can cause undesirable effects. The following undesirable effects observed in patients treated with Glucophage XR were similar

in nature and severity to those observed in patients treated with Glucophage immediate release. Frequencies are defined as follows: very common: $\geq 10\%$; common $\geq 1\%$, $< 10\%$; uncommon: $\geq 0.1\%$, $< 1\%$; rare $\geq 0.01\%$, $< 0.1\%$; very rare: $< 0.01\%$ and isolated cases).

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 symptoms persist, **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 must stop taking Glucophage XR** immediately and consult their doctor promptly

- Skin reactions such as erythema (red skin), itching or urticaria (eruption with itching).

- Decreased vitamin B₁₂ levels (to take into consideration in case of megaloblastic anaemia).

Isolated cases: 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, non-steroid anti-inflammatory agents, antihypertensive agents of the angiotensin-converting enzyme inhibitors class, diuretics, beta₂ agonists such as salbutamol or terbutaline, or alcohol containing medicines.

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

DOSAGE AND ADMINISTRATION

The dosage of Glucophage XR is determined by the doctor on an individual basis according to the results of laboratory blood glucose measurement.

Usual starting dose: Glucophage XR 750 mg: 1 tablet once daily, given with the evening meal.

After treatment with Glucophage immediate release tablets, the starting dose of Glucophage XR is equivalent to the daily dose of Glucophage immediate release.

In case Glucophage XR is used in combination with insulin, the usual starting dose of Glucophage XR is also one tablet once daily, 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 one tablet depending on blood glucose measurements.

Maximum daily dose: Glucophage XR 750 mg: 3 tablets 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:

Glucophage XR 750 mg: 1 tablet during breakfast and 2 tablets 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 feces, which is not linked with 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 and sight of children.

PHARMACEUTICAL FORM

Glucophage XR 750 mg prolonged release tablets are white capsule-shaped, biconvex, debossed on one side with '750' 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

GLUCOPHAGE XR 750 mg: boxes of 30 prolonged release tablets in blister pack.

Reg. N° Lebanon 24930

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GENERAL RECOMMENDATIONS FOR PATIENTS

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.

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