

GLUCOVANCE FILM COATED TABLET

Metformin Hydrochloride/Glibenclamide (500/2.5mg, 500/5mg)

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What is Glucovance used for

Glucovance is made up of two antidiabetic medicines, which belong to the groups of medicines called biguanide (metformin hydrochloride) and sulphonylurea (glibenclamide). Glucovance is taken orally for the treatment of type 2 diabetes mellitus in adult patients. It is used to replace the combination of the two active substances, metformin hydrochloride and glibenclamide given separately in patients previously treated with this combination.

How Glucovance works

Insulin is a hormone that enables body tissues to take up glucose (sugar) from the blood and to use it for producing energy or to store it for future use. Patients with type 2 diabetes mellitus (i.e. non-insulin dependent diabetes) do not produce enough insulin in their pancreas or their body does not respond properly to the insulin it produces. This causes an increased level of glucose in the blood. Glucovance helps to reduce their blood sugar towards a normal level.

Before you use Glucovance

When you must not use it

Do not take Glucovance

- if you are allergic (hypersensitive) to metformin hydrochloride, glibenclamide or other sulphonamides or any of the other ingredients of Glucovance
- if you have severely reduced kidney function
- if you have liver function problems
- if you suffer from type 1 diabetes mellitus (i.e. insulin-dependent)
- if you have uncontrolled diabetes, with, for example, severe

hyperglycaemia (high blood glucose), nausea, vomiting, diarrhoea, 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 which can lead to diabetic pre-coma. Symptoms include stomach pain, fast and deep breathing, sleepiness or your breath developing an unusual fruity smell.

- if you have a severe infection (for example an infection of the air passages or an urinary tract infection)
- if you are dehydrated (for example due to persistent or severe diarrhoea, recurrent vomiting)
- if you are treated for acute heart failure or have recently had a heart attack, have severe problems with your circulation (such as shock) or have breathing difficulties. This may lead to a lack in oxygen supply to tissue which can put you at risk for lactic acidosis (see 'Warnings and precautions').
- Patients with known or suspected mitochondrial diseases such as Mitochondrial Encephalopathy with Lactic Acidosis and Stroke-like episodes (MELAS) syndrome and Maternal inherited diabetes and deafness (MIDD) must avoid Metformin due to risk of lactic acidosis exacerbation.
- if you suffer from porphyria (a rare, hereditary disease due to an enzyme deficiency causing the body to produce and excrete too much porphyrin, a component used to make the part of blood pigment that carries oxygen)
- if you use miconazole (a medicine to treat certain yeast infections) even for local use
- if you drink alcohol excessively (either every day or only from time to time)
- if you are breast-feeding.

Before you start to use it

Make sure you ask your doctor for advice,

- if you need to have an examination such as X-ray or scan involving the injection of contrast medicines

that contain iodine into your bloodstream

- if you need to have a surgery under general, spinal or peridural anaesthesia
- if you must stop taking Glucovance for a certain period of time before and after the examination or the surgery. Your doctor will decide whether you need any other treatment for this time. It is important that you follow your doctor's instructions precisely.
- if you experience symptoms of low blood sugar (hypoglycaemia). The warning signs may occur suddenly and can include cold sweat, cold and pale skin, dizziness, headache, rapid heart beat, feeling sick, feeling very hungry, temporary changes in vision, drowsiness, unusual tiredness and weakness, nervousness or tremor, feeling anxious, feeling confused, difficulty in concentrating. If you notice any of these signs:
 - first eat glucose tablets or a high sugar snack (honey, sweets, biscuits, fruit juice),
 - Stop taking this medicine immediately and tell your doctor straight away as you may need to be hospitalised to bring your blood glucose back under control,
 - then rest.

Take special care with Glucovance

Risk of lactic acidosis.

Glucovance may cause a very rare, but very serious side effect called lactic acidosis, particularly if your kidneys are not working properly. The risk of lactic acidosis is also increased with uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, dehydration, liver problems and any medical conditions in which a part of the body has reduced supply of oxygen (such as acute severe heart disease). If any of the above apply to you, talk to your doctor for further instructions.

Stop taking Glucovance for a short time if you have a condition that may be associated with dehydration (significant loss of body fluids) such as severe vomiting, diarrhoea, fever, exposure to heat or if you drink less

fluid than normal. Talk to your doctor for further instructions. Stop taking Glucovance 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, stomach ache (abdominal pain), muscle cramps, a general feeling of not being well with severe tiredness, difficulty in breathing, reduced body temperature and heartbeat.

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

If you need to have major surgery you must stop taking Glucovance during and for some time.

Risk of Hypoglycaemia

If you experience symptoms of low blood sugar (hypoglycaemia). The warning signs may occur suddenly and can include cold sweat, cold and pale skin, dizziness, headache, rapid heart beat, feeling sick, feeling very hungry, temporary changes in vision, drowsiness, unusual tiredness and weakness, nervousness or tremor, feeling anxious, feeling confused, difficulty in concentrating.

Patients aged 65 years and older are particularly sensitive to hypoglycemic action of glibenclamide and are therefore more risk of hypoglycaemia. In the elderly, low blood sugar maybe somewhat difficult to recognise. The initial dose and maintenance of glibenclamide must be set by your doctor carefully in order to avoid hypoglycemic reactions.

If you notice any of these signs:

- first eat glucose tablets or a high sugar snack (honey, sweets, biscuits, fruit juice),
- Stop taking this medicine immediately and tell your doctor straight away as you may need to be hospitalised to bring your blood glucose back under control, then rest.

During treatment with Glucovance, your doctor will check your kidney function at least once a year or more frequently if you are elderly and/or if you have worsening kidney function.

General advice: Inform your family, friends and colleagues to turn you on your side and get medical aid straight away if you become unconscious. They should not give you any food or drink when you are unconscious. It could choke you.

A low blood sugar level might occur if:

- you eat too little or miss a meal
- your diet contains insufficient or unbalanced levels of sugar
- you drink alcohol
- you exercise more than usual
- you have liver, kidney or certain hormone problems
- the dosage of your medicine is too high
- you are an elderly person
- you are taking certain medicines and Glucovance at the same time (see ‘Taking other medicine’).
- if you suffer from any infectious illnesses such as flu, infection of the air passages or urinary tract infection.
- if you have an inherited condition where your red blood cells don’t produce enough of the enzyme G6PD (G6PD deficiency), taking Glucovance may cause your red blood cells to be destroyed too quickly (haemolytic anaemia).
- continue to follow any dietary advice your doctor has given you and get some regular exercise while you are taking this medicine.
- consult your doctor regularly to test your blood sugar levels and your kidney function.
- Consult your doctor, if any of the above-mentioned situations applies to you and if you feel unsure about using this medicine.

During treatment with Glucovance, your doctor will check your kidney function at least once a year or more frequently if you are elderly and/or if you have worsening kidney function.

Taking other medicines

While taking Glucovance, you must not use any of the following medicines:

- miconazole even for local use (see ‘When you must not take it’)
- iodinated contrast agents (see ‘When you must not take it’)

- Tell your doctor if you are taking, have recently taken or might take any other medicines. You may need more frequent blood glucose and kidney function tests or your doctor may need to adjust the dosage of Glucovance. It is especially important to mention the following:
 - ACE inhibitors and angiotensin II receptor antagonists (for the treatment of high blood pressure)
 - diuretics (increases urine production)
 - beta-blockers (used to treat a variety of cardiovascular conditions, such as high blood pressure, and some other diseases)
 - beta-2 agonists (used to treat asthma, such as ritodrine, salbutamol or terbutaline)
 - bosentan (used to pulmonary hypertension)
 - corticosteroids and tetracosactide (a class of hormones used to treat a variety of conditions, e.g. severe inflammation of the skin or in asthma)
 - certain painkillers (i.e. NSAIS and COX-2 inhibitors such as ibuprofen and celecoxib)
 - fluconazole (used to treat certain yeast infections)
 - chlorpromazine (a neuroleptic medicine, which affects how your brain works)
 - desmopressin (generally used to reduce urine production)
 - danazol (used to treat endometriosis, a condition where the tissue lining of the uterus is found outside the uterus)
 - bile acid sequestrants (cholesterol-lowering medicines used to reduce the amount of cholesterol in the blood)
 - medicines that may change the amount of Glucovance in your blood, especially if you have reduced kidney function (such as verapamil, rifampicin, cimetidine, dolutegravir, ranolazine, trimethoprim, vandetanib, isavuconazole, crizotinib, olaprib)

Special precautions may include self-monitoring of blood glucose, blood tests and modification of dosage.

Avoid excessive alcohol intake while taking Glucovance since this may increase the risk of lactic acidosis (see Take Special Care of Glucovance).

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

How to take Glucovance

How much to use

Always take Glucovance exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Only adults may take this medicine. Your doctor will adapt the dosage of your treatment depending on its effect on your blood tests. Continue to follow any dietary advice your doctor has given you. Glucovance cannot replace the benefits of a healthy lifestyle.

Have a regular meal schedule with a sufficient and balanced sugar intake. This will decrease the risk of low blood sugar. The usual starting dose is equivalent to the individual doses of metformin hydrochloride and glibenclamide you received before being treated with Glucovance.

Maximum daily dose:
2000 mg metformin/20 mg
glibenclamide

Dosage adjustment in elderly patients:

Take special care if you are an elderly person. The dose of Glucovance will be carefully increased depending on your blood sugar levels and your kidney function. Make sure that you consult your doctor regularly.

When to use it

Take the tablets with a meal. Swallow each tablet whole with a glass of water. Do not crush or chew them before swallowing.

Take the tablets

- once a day, in the morning (breakfast) if you take 1 tablet per day
- twice a day, in the morning (breakfast) and evening (dinner) if you take 2 per day

- three times a day, in the morning (breakfast), noon (lunch) and evening (dinner), if you take 3 tablets per day.

How long to take it

Continue taking your medicine for as long as your doctor or pharmacist tells you. It does not cure your condition. Therefore you must continue to take it as directed by your doctor if you expect to keep your glucose levels controlled.

If you forget to take it

Do not take a double dose to make up for a forgotten dose. Take the next dose at the usual time.

If you take too much (overdose)

If you have taken more Glucovance tablets than you should have, you may experience lactic acidosis or low blood sugar. Inform your doctor immediately

While you are using Glucovance

Things you must do

Tell your doctor if you are, you think you might be or are planning to become pregnant. During pregnancy, diabetes should be treated with insulin. If you find out that you are pregnant while taking Glucovance, consult your doctor so that he/she may change your treatment.

Things you must not do

Avoid alcohol when you take this medicine as alcohol can increase certain side-effects such as lactic acidosis and a low blood sugar level (see 'side-effects'). This also applies to medicines containing alcohol.

Breast-feeding:

You must not take Glucovance, if you are breast-feeding or if you are planning to breast-feed your baby.

Things to be careful of

Do not drive or use machines:

- if your vision is blurred. This may happen at the beginning of the treatment because of a lower level of sugar in your blood.
- if you feel that symptoms of low blood sugar begin to appear.

Each Glucovance tablet contains lactose. If your doctor has told you that you have an intolerance to certain sugars, contact your doctor before taking this medicine.

Side effects

Like all medicines, Glucovance can cause side effects, although not everybody gets them. The following side effects were observed in clinical studies or in routine patient management.

Vision disorders: When you start taking this medicine, it may disturb your vision due to a lower level of sugar in your blood. However, this reaction usually disappears after a while.

Low blood sugar: For symptoms of low blood sugar, see 'Take special care with Glucovance'.

Very common side effects (may affect more than 1 in 10 patients)

- gastrointestinal disorders such as nausea, vomiting, diarrhoea, bellyache and loss of appetite.

These side effects occur most frequently after starting therapy. It helps if you spread the doses over the day and if you take the tablets with a meal. Should these symptoms continue, STOP taking this medicine and CONSULT your DOCTOR.

Common side effects (may affect up to 1 in 10 people)

- taste disturbance
- decreased or low vitamin B12 levels in the blood (symptoms may include extreme tiredness (fatigue), a sore and red tongue (glossitis), pins and needles (paresthesia) or pale yellow skin). Your doctor may arrange some tests to find out the cause of your symptoms because some of these may also be caused by diabetes or due to other unrelated health problems.

Uncommon side effects (may affect 1 in 100 people)

- abnormal urea and creatinine levels in the blood, which show changes in the way the kidneys are working.
- a crisis of certain forms of porphyria (porphyria hepatica or porphyria cutanea); for an explanation of porphyria, see section 2, "Do not take Glucovance") may occur in patients with certain enzyme deficiency.

Rare side effects (may affect up to 1 in 1,000 people)

- reduction in the number of white blood cells, which makes infections more likely
- reduction in blood platelets which increases risk of bleeding or bruising
- skin reactions including itching, hives, skin rash

Very rare side effects (may affect up to 1 in 10,000 people)

- lactic acidosis: "see 'Take special care with Glucovance' "
 - severe reduction in the number of white blood cells (agranulocytosis), anaemia due to a too extensive breakdown of the red blood cells (haemolytic anaemia), lack or insufficient number of new blood cells produced by the bone marrow (bone marrow aplasia) and very severe reduction in the number of blood cells (pancytopenia; this can make the skin look pale, can cause weakness or breathlessness, can increase the risk of bleeding or bruising or make infections more likely)
 - abnormalities in liver function tests or inflammation of the liver (hepatitis; this can cause tiredness, loss of appetite, weight loss, with or without yellowing of the skin or whites of the eyes). If this happens to you, **stop taking Glucovance and talk to your doctor.**
 - excessive skin sensitivity to sun, serious allergic reactions of the skin or blood vessels
 - intolerance to alcohol (with symptoms such as general feeling of discomfort, redness of face, rapid heart beat)
 - low level of sodium, which can cause tiredness and confusion, muscle twitching, fits or coma
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website portal.bpfk.gov.my (Consumers→Reporting).

Storage and disposal of Glucovance

Storage

Keep out of the reach and sight of children.
Do not use Glucovance after the expiry date, which is stated on the carton after "EXP". The expiry date refers to the last day of that month.
Store below 30°C

Disposal

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Product description

What it looks like

Glucovance 500mg/2.5mg:

Orange capsule-shaped, biconvex, film-coated tablets with "2.5" engraved on one side.
Pack sizes: 120 tablets in clear or opaque blister (PVC/PVDC/Aluminium).

Glucovance 500mg/5mg:

Yellow capsule-shaped, biconvex, film-coated tablets with "5" engraved on one side
Pack sizes: 120 tablets in clear or opaque blister (PVC/PVDC/Aluminium).

Ingredients

Glucovance 500 mg/2.5 mg contains 500 mg metformin hydrochloride and 2.5 mg of glibenclamide as active ingredients.

Glucovance 500 mg/5 mg contains 500 mg metformin hydrochloride and 5 mg of glibenclamide as active ingredients.

The other ingredients are:

Tablet core:

Microcrystalline cellulose, sodium croscarmellose, povidone K 30, magnesium stearate

Film-coating

Glucovance 500mg/2.5mg:Opadry OY-L-24808(orange)(lactose) monohydrate, hypromellose, titanium dioxide (E171), macrogol, yellow iron oxide (E172), red iron oxide (E172), black iron oxide (E172).

Glucovance 500mg/5mg:Opadry 31-F-22700(yellow)(lactose) monohydrate, hypromellose, titanium

dioxide (E171), macrogol, yellow iron oxide (E172), red iron oxide (E172), Quinoline Yellow Lake (E104).

MAL number:

Product	MAL number
Glucovance 500/2.5mg	MAL20051296A
Glucovance 500/5mg	MAL20051297A

Manufacturer

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