SCHEDULING STATUS

S3

GLUCOVANCE 500 mg/2,5 mg (film-coated tablet)

GLUCOVANCE 500 mg/5 mg (film-coated tablet)

Metformin hydrochloride and glibenclamide

Contains sugar: lactose

Read this entire leaflet carefully before you start taking GLUCOVANCE.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- Glucovance has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What Glucovance is and what it is used for
2. What you need to know before you take Glucovance
3. How to take Glucovance
4. Possible side effects
5. How to store Glucovance
6. Contents of the pack and other information

1. What Glucovance is and what it is used for

Glucovance is made up of two antidiabetic medicines, which belong to the groups of medicines called biguanide (metformin hydrochloride) and sulphonylurea (glibenclamide).

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.

Glucovance is used for the oral treatment (via the mouth) of type 2 diabetes in adults:

- As second-line therapy when diet and exercise, and initial treatment with a sulphonylurea or metformin do not result in adequate blood glucose level control.
- As replacement for previous combination therapy with metformin and glibenclamide in patients whose glycaemia is stable and well-controlled.

2. What you need to know before you take

Do not take Glucovance

- if you are allergic (hypersensitive) to metformin hydrochloride, glibenclamide or other sulphonamides or any of the other ingredients of Glucovance (listed in section 6)
- if you have kidney or liver function problems
- if you suffer from type 1 diabetes mellitus (i.e. insulin-dependent) or if you have severe loss of diabetes control with either pre-coma or ketosis (a condition caused by substances called ‘ketone bodies’ accumulating in the blood; you may notice that your breath has an unusual, fruity odour)
- if you have a severe infection (for example an infection of the air passages or a 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')
- 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 breastfeeding.

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 major surgery

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.

Warnings and precautions

Take special care with Glucovance

- if you experience symptoms of a condition called lactic acidosis, i.e. vomiting, bellyache with muscle cramps and a general feeling of discomfort with severe fatigue and difficulty in

breathing (see, “Very rare side effects”). **If these symptoms occur, stop taking this medicine immediately and tell your doctor straight away.**

- 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 heartbeat, 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.

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 section “Other medicines and Glucovance”).

Discuss with your doctor whether Glucovance is the appropriate treatment for your diabetes if you often experience severe symptoms of low blood sugar or if you find it hard to recognise them.

- 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). Tell your doctor if you have this condition, as Glucovance may not be suitable for you.
- 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.

Children and adolescents

Glucovance not recommended for use in children.

Other medicines and Glucovance

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

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

- miconazole even for local use (see section 2, "Do not take Glucovance")

- if you need to have an injection of a contrast medium that contains iodine into your bloodstream, for example in the context of an X-ray or scan, you must stop taking Glucovance before or at the time of the injection. Your doctor will decide when you must stop and when to restart your treatment with Glucovance. (see section 2, “Do not take Glucovance”)

Special precautions may be required if you take Glucovance and any of the following medicines at the same time:

- angiotensin-converting enzyme inhibitors (used to treat a variety of cardiovascular conditions, such as high blood pressure, and some other diseases)
- diuretics (used to remove water from the body by increasing urine production)
- medicines used to treat pain and inflammation (NSAID and COX-2-inhibitors, such as ibuprofen and celecoxib)
- beta-blockers, clonidine, reserpine, guanethidine or sympathocomimetics (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 treat 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. non-steroidal anti-inflammatory drugs, such as phenylbutazone)
- 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 such as cholestyramine, colestipol, colesevelam (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, trimethoprime, vandetanib, isavuconazole, crizotinib, olaparib).

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

Avoid medicines containing alcohol (see section “Glucovance with food, drink and alcohol”).

Glucovance with food, drink and alcohol

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 section 2 “Warnings and precautions”). This also applies to medicines containing alcohol.

Pregnancy and breastfeeding

Pregnancy

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.

Breast-feeding

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

Driving and using machines

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.

Important information about some of the ingredients of Glucovance:

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.

3. How to take Glucovance

Do not share medicines prescribed for you with any other person.

Dosage

Always take Glucovance exactly as your doctor or pharmacist has instructed you. You should check with your doctor or pharmacist if you are unsure.

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.

If you have the impression that the effect of Glucovance is too strong or too weak, talk to your doctor or pharmacist.

The usual starting dose is equivalent to the individual doses of metformin hydrochloride and glibenclamide you received before being treated with Glucovance. If you are an elderly person, the usual starting dose is one tablet of Glucovance 500 mg/2,5 mg per day.

Maximum daily dose

For Glucovance 500 mg/2,5 mg: 6 tablets.

For Glucovance 500 mg/5 mg: 3 tablets. In exceptional cases, your doctor may prescribe 4 tablets.

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.

Dosage adjustment in patients with reduced kidney function

If you have reduced kidney function, your doctor may prescribe a lower dose.

Administration

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 or 4 tablets per day
- three times a day, in the morning (breakfast), noon (lunch) and evening (dinner), if you take 3, 5 or 6 tablets per day.

Your doctor will tell you how to take Glucovance if you have to take it in combination with a cholesterol-lowering medicine (bile acid sequestrants such as cholestyramine, colestipol, colesevelam). Glucovance must be taken at least 4 hours prior to a cholesterol-lowering medicine (bile acid sequestrants such as cholestyramine, colestipol, colesevelam). See section 2, “Other medicines and Glucovance”.

If you take more Glucovance than you should

If you have taken more Glucovance tablets than you should have, you may experience low blood sugar (for symptoms of low blood sugar, see section 2, “Warnings and precautions”).

TALK to your DOCTOR IMMEDIATELY.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, seek help at the nearest hospital or poison control centre.

If you forget to take Glucovance

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

If you stop taking Glucovance

There are usually no side effects when you stop taking this medicine. However, as your diabetes is not treated any more, complications due to a lack of treatment can occur.

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

4. Possible side effects

Glucovance can have side effects

Not all side effects reported for Glucovance are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking Glucovance, please consult your health care provider for advice.

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 section 2, “Warnings and precautions”.

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 Glucovance and consult your doctor.**

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

- taste disturbance

Uncommon side effects (may affect up to 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: a very serious complication particularly if your kidneys are not working properly, which results in vomiting, bellyache with muscle cramps and a general feeling of discomfort with severe fatigue and difficulty in breathing and which requires specific treatment. **If these symptoms occur, stop taking this medicine immediately and tell your doctor straight away.**
- 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). In this case Glucovance must be discontinued.
- 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 heartbeat)
- low level of sodium, which can cause tiredness and confusion, muscle twitching, fits or coma decreased vitamin B12 levels in the blood

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.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse.
You can also report side effects to the South African Health Products Regulatory Authority (SAHPRA) via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of Glucovance.

5. How to store Glucovance

- Keep all medicines out of the reach and sight of children.
- Do not use Glucovance after the expiry date, which is stated on the carton after "EXP".
- Store below at or below 30 °C.

- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What Glucovance contains

- The active substances are metformin hydrochloride and glibenclamide.
- One film-coated tablet of Glucovance 500 mg/2,5 mg contains 500 mg metformin hydrochloride corresponding to 390 mg metformin base and 2,5 mg glibenclamide.
- One film-coated tablet of Glucovance 500 mg/5 mg contains 500 mg metformin hydrochloride corresponding to 390 mg metformin base and 5 mg glibenclamide.
- The other ingredients are croscarmellose sodium, magnesium stearate, microcrystalline cellulose, opadry, povidone, purified water and talc.

What Glucovance looks like and contents of the pack

Glucovance 500 mg/2,5 mg tablets are orange capsule-shaped, biconvex, embossed film-coated tablets with “2,5” engraved on one side.
Glucovance 500 mg/5 mg tablets are yellow capsule-shaped, biconvex, embossed film-coated tablets with “5” engraved on one side.

30 or 60 tablets in a clear or opaque white PVC/Aluminium blisters.

Holder of Certificate of Registration

Merck (Pty) Ltd

1 Friesland Drive

Longmeadow Business Estate South

Modderfontein, 1645

South Africa

Name and address of the manufacturer:

Merck Santé s.a.s

Centre de Production

2 Rue du Pressoir Vert

45400 Semoy, France

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Registration numbers

Glucovance 500 mg/2.5 mg tablets: 36/21.2/0412

Glucovance 500 mg/5 mg tablets: 36/21.2/0413

Glucovance 500 mg/2.5 mg		
	Schedule	**Reg. No.:**
Namibia	NS2	04/21.2/0812
Botswana	S2	BOT08014368
Kenya	POM	16537
Tanzania	POM	TZ13H218
Uganda	POM	7810/18/12

Glucovance 500 mg/5 mg		
	Schedule	**Reg. No.:**
Namibia	NS2	04/21.2/0813
Botswana	S2	BOT08014369
Kenya	POM	16538
Tanzania	POM	TZ13H217
Uganda	POM	7829/18/12