PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

GLUCOPHAGE XR 500 mg (prolonged release tablet)

GLUCOPHAGE XR 1000 mg (prolonged release tablet)

Metformin hydrochloride

Sugar-free

Read all of this leaflet carefully before you start taking GLUCOPHAGE XR

- Keep this leaflet. You may need to read it again.
- If you have more questions, please ask your doctor, pharmacist, nurse or other health care provider.
- **Glucophage XR** 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 **Glucophage XR** is and what it is used for
2. What you need to know before you take **Glucophage XR**
3. How to take **Glucophage XR**
4. Possible side effects
5. How to store **Glucophage XR**
6. Contents of the pack and other information

1. What Glucophage XR is and what it is used for:

Glucophage XR is a prolonged release tablet which contains the active ingredient metformin hydrochloride and belong to a group of medicines called biguanides, used in the treatment of Type 2 (non-insulin dependent) diabetes mellitus.

Glucophage XR is used together with diet and exercise to lower the risk of developing Type 2 diabetes in overweight adults, when diet and exercise alone for 3 to 6 months have not been enough to control blood glucose (sugar). You are at high risk of developing Type 2 diabetes if you have additional conditions like high blood pressure, age above 40 years, an abnormal amount of lipids (fat) in the blood or a history of diabetes during pregnancy.

Glucophage XR is used for the treatment of type 2 diabetes mellitus in adults, when dietary management and exercise alone have not been enough to control blood glucose (sugar). Insulin is a hormone that enables body tissues to take glucose from the blood and to use it for energy or for storage for future use. People with Type 2 diabetes do not make enough insulin in their pancreas or their body does not respond properly to the insulin it does make. This causes a build-up of glucose in the blood which can cause a number of serious long-term problems so it is important that you continue to take your medicine, even though you may not have any obvious symptoms. Glucophage XR makes the body more sensitive to insulin and helps return to normal the way the body uses glucose.

Glucophage XR is associated with either a stable body weight or modest weight loss.
Glucophage XR tablets are specially made to release the medication slowly in your body and therefore are different to many other types of tablets containing metformin.

2. What you need to know before you take GLUCOPHAGE XR

Do not take Glucophage XR if

- You are hypersensitive (allergic) to metformin hydrochloride or any of the other ingredients (listed in section 6). An allergic reaction may cause a rash, itching or shortness of breath.
- You have liver problems.
- You have severely reduced kidney function

- You have uncontrolled diabetes, with, for example, severe hyperglycaemia (high blood glucose), nausea, vomiting, diarrhea, rapid weight loss, lactic acidosis 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.
- You have lost too much water from your body (dehydration). Dehydration may lead to kidney problems, which can put you at risk of lactic acidosis.
- You have a severe infection, such as an infection affecting your lung or bronchial system or your kidney. Severe infections may lead to kidney problems, which can put you at risk for lactic acidosis.
- You have been treated for acute heart problems or have recently had a heart attack or have severe circulatory problems or breathing difficulties. This may lead to a lack of oxygen supply to tissue which can put you at risk for lactic acidosis.
- You are a heavy drinker of alcohol.

Take special care with GLUCOPHAGE XR

Risk of Lactic acidosis:

Glucophage XR may cause lactic acidosis a very rare, but serious and life-threatening complication that can occur when lactic acid builds up in the blood stream faster than it can be removed.

The risk of developing 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 a reduced supply of oxygen (such as acute severe heart disease).

If any of the above apply to you, talk to your doctor for further information.

Stop taking Glucophage XR 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.

Stop taking Glucophage XR and contact your doctor or the nearest hospital immediately if you experience some of the symptoms of lactic acidosis, as this condition may lead to a 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.

Surgery

If you need to have major surgery you must stop taking Glucophage XR during and for some time after the procedure. Your doctor will decide when you must stop and when to restart your treatment with Glucophage XR. You may need to use soluble insulin while your Glucophage XR is stopped for your operation. Your doctor will discuss this with you.

During treatment with Glucophage XR, 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.

If you are older than 75 years, treatment with Glucophage XR should not be started to lower the risk of developing type 2 diabetes.

You may see some remains of the tablets in your stools. Do not worry – this is normal for this type of tablet.

You should continue to follow any dietary advice that your doctor has given you and you should make sure that you eat carbohydrates regularly throughout the day.

Do not stop taking this medicine without speaking to your doctor.

Pregnancy and breastfeeding:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other health care professional for advice before taking Glucophage XR.

The use of Glucophage XR during pregnancy is not advised. There is no information available concerning the safety of Glucophage XR during breastfeeding.

Driving and using machinery:

Glucophage XR range therapy on its own has no effect on the ability to drive or to use machines. Care should however be taken when Glucophage XR range is combined with other anti-diabetic medicines such as sulphonylureas or insulin, as this may cause low blood glucose levels and might interfere with your driving ability.

Other medicines and GLUCOPHAGE XR

Always tell your healthcare professional if you are taking any other medicine (this includes complementary or traditional medicines.)

If you need to have an injection of a contrast medium that contains iodine into your bloodstream, in the context of an X-ray or scan, you must stop taking Glucophage XR before or at the time of

injection. Your doctor will decide when you must stop and when to restart your treatment with Glucophage XR.

You may need more frequent blood glucose and kidney function tests, or your doctor may need to adjust the dosage of Glucophage XR. It is especially important to mention the following:

- Medicines which increase urine production (diuretics (water tablets) such as furosemide).
- Medicines used to treat pain and inflammation (NSAID and COX-2 inhibitors, such as ibuprofen and celecoxib)
- Certain medicines for the treatment of high blood pressure (ACE inhibitors and angiotensin II receptor antagonists)
- Steroids such as prednisolone, mometasone, beclomethasone.
- Sympathomimetic medicines including epinephrine and dopamine used to treat heart attacks and low blood pressure. Epinephrine is also included in some dental anaesthetics.
- Medicines that may change the amount of Glucophage XR in your blood, especially if you have reduced kidney function (such as verapamil, rifampicin, cimetidine, dolutegravir, ranolazine, trimethoprim, vandetanib, isavuconazole, crizotinib, olaparib).

Avoid excessive alcohol intake while taking Glucophage XR since this may increase the risk of lactic acidosis.

3. How to take GLUCOPHAGE XR

Your individual dose will be decided by your doctor after laboratory tests and examinations. Always take this medicine as the doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.
Swallow the tablets whole with a glass of water, do not chew.

Glucophage XR 500 mg:

The usual starting dose is one tablet daily taken with the evening meal. Your doctor may adjust your dose after 10 to 15 days.

The maximum recommended dosage is usually not more than 4 tablets daily.

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

Glucophage XR 1000 mg:

The usual starting dose is one tablet daily taken with the evening meal at a maximum recommended dose of 2 tablets per day.

Glucophage XR 1000mg is intended as maintenance therapy for patients currently treated with either 1000mg or 2000mg of metformin hydrochloride.

If you forget to take GLUCOPHAGE XR

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

IF YOU TAKE MORE GLUCOPHAGE XR THAN YOU SHOULD

If you take extra tablets by mistake you need not worry, but if you have unusual symptoms, contact, your doctor. If the overdose is large, lactic acidosis is more likely. Symptoms of lactic acidosis are non-specific, such as vomiting, bellyache with muscle cramps, a general feeling of not being well with severe tiredness, and difficulty in breathing. Further symptoms are reduced body temperature and heartbeat. If you experience some of these symptoms, you should immediately seek medical attention, as lactic acidosis may lead to coma.

In the event of over-dosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Your doctor will tell you how long your treatment with Glucophage XR will last. Do not stop treatment early without consulting your doctor or pharmacist. If you have the impression that the effect of Glucophage XR is too strong or too weak, tell your doctor or pharmacist.

4. Possible side effects

Glucophage XR can have side effects.

The following side effects occur less frequently:

Decrease of vitamin B_{12} absorption with decrease of serum levels during long-term use of Glucophage XR consideration of this decrease in absorption is recommended if you present with megaloblastic anaemia (a deficiency of folic acid or Vit. B_{12}).

Lactic acidosis (A condition where lactic acid build up in the bloodstream faster than it can be removed) (See Take Special Care).

Skin reactions such as erythema, a type of hypersensitivity reaction with fever, itching and skin lesions, pruritus (itching) and urticaria (hives or rash of the skin).

The following side effects occur frequently:

Taste disturbance.

The following side effects occur very frequently:

Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite. These side-effects occur most frequently during initiation of therapy and resolve spontaneously in most cases. A slow increase of the dose may also improve gastro-intestinal tolerability.

Less frequent: When liver function is tested by your doctor your liver function test may be abnormal or you might experience hepatitis (swelling of the liver), resolving on Glucophage XR discontinuation.

Not all side-effects reported for Glucophage XR are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking, please consult your doctor, pharmacist or other healthcare professional for advice.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects:

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publication: http://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of Glucophage XR.

5. How to store GLUCOPHAGE XR

Store all medicines out of reach of children.

Store at or below 30 °C.

Do not remove from carton until ready for use.

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

6. Contents of the pack and other information

What GLUCOPHAGE XR contains

The active substance is Metformin hydrochloride.

Each prolonged release Glucophage XR 500 mg tablet contains 500 mg metformin hydrochloride.

Each prolonged release Glucophage XR 750 mg tablet contains 750 mg metformin hydrochloride.

Each prolonged release Glucophage XR 1000 mg tablet contains 1000 mg metformin hydrochloride.

The other ingredients are: magnesium stearate, sodium carboxymethylcellulose; hydroxypropyl methylcellulose; microcrystalline cellulose.

What GLUCOPHAGE XR looks like and contents of the pack

Glucophage XR 500 mg: White to off-white, round, biconvex tablet debossed on one side with '500'.

Glucophage XR 1000 mg: White to off-white, capsule-shaped, biconvex tablet, debossed with '1000' on one face and 'Merck' on the other side.

Glucophage XR are packed in transparent PVC or PVC/PVDC blisters with an aluminium backing of 60, 90 or 120 tablets.

Holder of the certificate of registration

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