GLUCOPHAGE XR RANGE PACKAGE INSERT

SCHEDULING STATUS S3

PROPRIETARY NAME (AND DOSAGE FORM)

Glucophage XR 500 mg (prolonged release tablet)

Glucophage XR 750 mg (prolonged release tablet)

Glucophage XR 1000 mg (prolonged release tablet)

COMPOSITION

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.

Inactive ingredients: magnesium stearate, sodium carboxymethylcellulose; hydroxypropyl methylcellulose.

PHARMACOLOGICAL CLASSIFICATION

A 21.2 Oral hypoglycaemics

PHARMACOLOGICAL ACTION

Pharmacodynamic Properties

Metformin is a biguanide with anti-hyperglycaemic effects, lowering both basal and postprandial plasma glucose. It does not stimulate insulin secretion and therefore does not produce hypoglycaemia.

Metformin may act *via* three mechanisms:

- reduction of hepatic glucose production by inhibiting gluconeogenesis and glycogenolysis;
- in muscle, by increasing glucose sensitivity, improving peripheral glucose uptake and utilisation; and
- delay of intestinal glucose absorption.

Metformin stimulates intracellular glycogen synthesis by acting on glycogen synthase. Metformin increases the transport capacity of all types of membrane glucose transporters.

Pharmacokinetic Properties

Absorption

Following a single oral dose of Glucophage XR 500 mg peak plasma levels (C_{max}) are achieved with a median value of 7 hours.

Following a single oral dose of 1500 mg of Glucophage XR 750 mg, a mean plasma concentration of 1193 ng/ml is achieved after a median value of 5 hours (range of 4 to 12 hours).

Glucophage XR 750 mg was shown to be bioequivalent to Glucophage XR 500 mg, at a total daily dose of 1500 mg, with respect to C_{max} and AUC in healthy fed and fasted subjects.

Following a single oral administration in the fed state of one tablet of Glucophage XR 1000 mg, a mean peak plasma concentration of 1214 ng/ml is achieved after a median time of 5 hours (range of 4 to 10 hours). Glucophage XR 1000 mg was shown to be bioequivalent to Glucophage XR 500 mg, at a dose of 1000 mg, with respect to C_{max} and AUC in healthy fed and fasted subjects.

At steady-state, both C_{max} and AUC of metformin do not increase proportionally to the administered dose.

Although the AUC is decreased by 30 % when the metformin prolonged release tablet is given under fasting conditions, the peak is neither modified nor delayed by fasting conditions.

When the 1000 mg metformin prolonged release tablet is administered in fed conditions the AUC is increased by 77 % (C_{max} is increased by 26 % and T_{max} is slightly prolonged by about 1 hour) relative to intake in the fasting state. Although there is no information on the exposure after the 750 mg and 500 mg prolonged release tablets. It is presumed that similar increased exposure occurs with these formulations when given in the fed-state.

Distribution

Plasma protein binding is negligible. Metformin partitions into erythrocytes. The blood peak concentration is less than the plasma peak and appears approximately at the same time. The mean volume of distribution (Vd) ranged between 63 – 276 l.

Metabolism

Metformin is eliminated unchanged in the urine. No metabolite has been identified in humans. There is no biliary excretion.

Elimination

Metformin renal clearance (>400 ml/min) shows elimination by glomerular filtration and by tubular secretion. After oral intake, the apparent terminal elimination half-life is approximately 6,5 hours.

INDICATIONS

Treatment of type 2 diabetes mellitus in adults, particularly in overweight patients, when dietary management and exercise alone do not result in adequate glycaemic control. Glucophage XR can be given alone as initial therapy or can be administered in combination with other oral antidiabetic agents or with insulin.

CONTRA-INDICATIONS

- Hypersensitivity to metformin hydrochloride or any of the other ingredients.
- Diabetic ketoacidosis, diabetic pre-coma.
- Renal failure or renal dysfunction (creatinine clearance < 60 ml/min).

- Acute conditions with the potential to alter renal function e.g. dehydration, severe infection, shock, intravascular administration of iodinated contrast media.
- Acute or chronic disease which may cause tissue hypoxia such as cardiac or respiratory failure, pancreatitis, recent myocardial infarction, shock.
- Hepatic insufficiency, acute alcohol intoxication, alcoholism (acute or chronic).
- The use of Glucophage XR during pregnancy is not advised.

WARNINGS AND SPECIAL PRECAUTIONS

Lactic acidosis

Lactic acidosis is associated with the use of Glucophage XR range.

Lactic acidosis is a rare, but serious (high mortality in the absence of prompt treatment), metabolic complication that can occur due to Glucophage XR administration.

In patients presenting with a metabolic acidosis and not having evidence of ketoacidosis (ketonuria and ketonaemia), lactic acidosis should be suspected and Glucophage XR range therapy should be stopped.

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

Glucophage XR range is excreted by the kidney and regular monitoring of renal function is advised in all diabetic patients with type 2 diabetes mellitus.

The incidence of lactic acidosis may be reduced by assessing also other associated risk factors such as poorly controlled diabetes mellitus, type 2: ketosis, prolonged fasting, excessive alcohol intake, hepatic insufficiency and any condition associated with hypoxia.

Diagnosis

Lactic acidosis is characterised by acidotic dyspnoea, abdominal pain and hypothermia followed by a coma. Diagnostic laboratory findings include a decreased blood pH, plasma lactate levels above 5 mmol/l, and an increased anion gap and lactate/pyruvate ratio. If metabolic acidosis is suspected, Glucophage XR should be discontinued and the patient should be hospitalised immediately.

Renal function

As Glucophage XR is excreted by the kidney, serum creatinine levels should be determined before initiating treatment and regularly thereafter:

- At least annually in patients with normal renal function,
- At least two to four times a year in patients with serum creatinine levels at the upper limit of normal and in elderly subjects.

Decreased renal function in elderly subjects is frequent and asymptomatic. Special caution should be exercised in situations where renal function may become impaired, for example when initiating antihypertensive therapy or diuretic therapy and when starting therapy with a NSAID.

Glucophage XR range therapy should be stopped 2-3 days before surgery and before clinical investigations such as intravenous urography and intravenous angiography, and reinstated only after control of renal function has been regained.

The use of Glucophage XR formulations is not advised in conditions which may cause dehydration, or in patients suffering from serious infections, trauma or on low calorie intake.

Patients on long-term treatment with Glucophage XR formulations should have an annual estimation of vitamin B_{12} levels, since Glucophage XR range may cause mal-absorption of vitamin $B_{12,}$ which may result in megaloblastic anaemia.

Administration of iodinated contrast agent

As the intravascular administration of iodinated contrast materials in radiological studies (such as intravenous urography and intravenous angiography) can lead to renal failure, Glucophage XR should be discontinued prior to, or at the time of the test and not reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal.

Surgery

Glucophage XR should be discontinued 48 hours before elective surgery with general anaesthesia and should not be resumed earlier than 48 hours afterwards.

During concomitant treatment with a sulphonylurea, blood glucose should be monitored because combination therapy may cause hypoglycaemia. Stabilisation of diabetic patients with Glucophage XR and insulin should be carried out in hospital because of the possibility of hypoglycaemia until the ratio of the two medicines has been obtained (see Contra-Indications).

Contraindications should be carefully observed.

- All patients should continue their diet with a regular distribution of carbohydrate intake during the day. Overweight patients should continue their energy-restricted diet.
- The usual laboratory tests for diabetes monitoring should be performed regularly.

The tablet shells may be present in the faeces. Patients should be advised that this is normal.

Effects on ability to drive and use machinery

Glucophage XR monotherapy does not cause hypoglycaemia and therefore is not expected to have an effect on the ability to drive or to use machines.

However, patients should be alerted to the risk of hypoglycaemia when Glucophage XR range is used in combination with other antidiabetic agents such as (sulphonylureas, insulin, repaglinide).

INTERACTIONS

Inadvisable combinations

Alcohol

Increased risk of lactic acidosis in acute alcohol intoxication, particularly in case of:

- fasting or malnutrition,
- hepatic insufficiency.

Avoid consumption of alcohol and alcohol-containing medications.

Iodinated contrast agents

Intravascular administration of iodinated contrast agents may lead to Glucophage XR accumulation and a risk of lactic acidosis.

Glucophage XR should be discontinued prior to, or at the time of the test and not reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal.

Associations requiring precautions for use

Glucocorticoids (systemic and local routes), beta-2-agonists, and diuretics have intrinsic hyperglycaemic activity. Medical practitioners should inform the patient and perform more frequent blood glucose monitoring, especially at the beginning of treatment. If necessary, the dosage of the antidiabetic medicines should be adjusted during therapy with the other medicine and upon its discontinuation.

ACE-inhibitors may decrease the blood glucose levels. If necessary, the dosage of the antidiabetic medicine should be adjusted during therapy with the other medicine and upon its discontinuation.

Cimetidine: Reduced renal clearance of Glucophage XR has been reported during cimetidine therapy, so a dose reduction should be considered.

Anticoagulants: Glucophage XR has been reported to diminish the activity of warfarin, and so dose adjustments and increased frequency of INR determinations should be considered.

Sulphonylurea: Concomitant therapy of Glucophage XR with sulphonylurea may cause hypoglycaemia.

Vitamins: Long-term treatment with Glucophage XR may cause vitamin B_{12} mal-absorption in the gastro-intestinal tract, thus a dose reduction of Glucophage XR should be considered.

PREGNANCY AND LACTATION:

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

DOSAGE AND DIRECTIONS FOR USE:

Glucophage XR 500 mg:

The usual starting dose is one tablet daily given with the evening meal.

After 10 to 15 days the dose should be adjusted on the basis of blood glucose measurements. A slow increase of dose may improve gastro-intestinal tolerability. The maximum recommended dosage is 4 tablets daily.

Dosage increases should be made in increments of 500 mg every 10 to 15 days, up to a maximum of 2000 mg once daily with an evening meal. If glycaemic control is not achieved with Glucophage XR 500 mg 4 tablets once daily, Glucophage XR 500mg 2 tablets twice daily should be considered, with both doses given with food. If glycaemic control is still not achieved, patients may be switched to standard metformin tablets to a maximum dose of 3000 mg daily.

Glucophage XR 750 mg

The usual starting dose is one tablet daily given with the evening meal.

After 10 to 15 days the dose should be adjusted on the basis of blood glucose measurements. A slow increase of dose may improve gastro-intestinal tolerability. The recommended dosage is 2 tablets once daily, with the evening meal.

If glycaemic control is not achieved with Glucophage XR 750 mg 2 tablets once daily Glucophage XR 750 mg may be increased to a maximum dose of 3 tablets once daily with the evening meal.

If glycaemic control is not achieved on Glucophage XR 750 mg 3 tablets once daily, one tablet of Glucophage XR 750 mg in the morning and two tablets of Glucophage XR 750 mg in the evening should be considered, with both doses being given with food.

If glycaemic control is still not achieved, patients may be switched to standard metformin tablets to a maximum dose of 3000 mg daily.

Glucophage XR 1000 mg

Glucophage XR 1000 mg is intended as maintenance therapy for patients already treated with either 1000 mg (2 tablets of Glucophage XR 500) or 2000 mg (4 tablets of Glucophage XR 500) of sustained release metformin hydrochloride. If glycaemic control is not achieved, patients may be switched to standard metformin hydrochloride tablets to a maximum daily dose of 3000 mg daily.

Switching patients already treated with metformin tablets

In patients already treated with metformin tablets, the starting dose of Glucophage XR prolonged release tablets should be equivalent to the daily dose of metformin immediate release tablets. In patients treated with metformin at a dose above 2000 mg daily, switching to Glucophage XR prolonged release tablets is not recommended.

Switching patients from other oral antidiabetic agents

If transfer from another oral antidiabetic agent is intended, discontinue the other agent and initiate Glucophage XR prolonged release tablets at the doses indicated above.

Combination therapy with insulin

Glucophage XR prolonged release tablets and insulin may be used in combination therapy to achieve better blood glucose control. The usual starting dose is Glucophage XR 500 mg once daily with the evening meal, while insulin dosage is adjusted on the basis of blood glucose measurements. After titration, switch to Glucophage XR 1000 mg may be considered.

Other combination therapy

See Warnings and special precautions.

Elderly

Due to the potential for decreased renal function in elderly subjects, the dosage for the Glucophage XR range should be adjusted based on renal function. Regular assessment of renal function is necessary. (See Warnings and special precautions.)

Children

In the absence of available data, the Glucophage XR range should not be used in children.

SIDE-EFFECTS

Side-effects

Adverse reactions reported are listed below by system organ class and by frequency.

Frequencies are defined as: very common (> 1/10), common (> 1/100, ≤ 1/10), uncommon (> 1/1000, ≤ 1/100), rare (≤ 1/10 000), very rare (< 1/10 000) and isolated reports.

Metabolism and nutrition disorders:

Very rare

Decrease of vitamin B_{12} absorption with decrease of serum levels during long-term use of the Glucophage XR range.

Consideration of such aetiology is recommended if a patient presents with megaloblastic anaemia.

Lactic acidosis (see Warnings and Special Precautions).

Nervous system disorders

Common: Taste disturbance.

Gastro-intestinal disorders

Very common: Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite.

Hepato-biliary disorders

Isolated reports: Liver function test abnormalities or hepatitis resolving on Glucophage XR range discontinuation.

Skin and subcutaneous tissue disorders

Very rare: Skin reactions such as erythema, pruritus and urticaria.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Hypoglycaemia can occur when Glucophage XR range is given concomitantly with a sulphonylurea, insulin or alcohol. In excessive dosage, and particularly if there is a possibility of accumulation, lactic acidosis may develop. Intense symptomatic and supportive therapy is recommended which should be particularly directed at correcting fluid loss and correcting blood glucose levels.

Treatment of overdosage

There is no specific antidote for overdose with Glucophage XR range. Treatment is supportive and symptomatic and should be directed at correcting fluid loss and metabolic disturbances. Haemodialysis is the most effective way to remove lactate and metformin.

IDENTIFICATION

Glucophage XR 500 mg:	White to off-white, capsules-shaped, biconvex tablet, debossed on one side with ‘’500”.
Glucophage XR 750 mg:	White capsule-shaped, biconvex tablet, debossed on one side with “750” and on the other side with “Merck”.
Glucophage XR 1000 mg:	White to off-white, capsule-shaped, biconvex tablet, debossed with “1000” on one face and “Merck” on the other side.

PRESENTATION

60 or 90 tablets packed in transparent PVC or PVC/PVDC blisters with an aluminium backing.

STORAGE INSTRUCTIONS:

KEEP OUT OF REACH OF CHILDREN.

Store at or below 30 °C.

Do not remove from carton until ready for use.

REGISTRATION NUMBER:

Glucophage XR 500 mg:	A39/21.2/0027
Glucophage XR 750 mg:	43/21.2/0185
Glucophage XR 1000 mg:	45/21.2/0066

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

Merck (Pty) Ltd
1 Friesland Drive
Longmeadow Business Estate South
Modderfontein
1645

NAME AND ADDRESS OF THE MANUFACTURER:

Merck Santé
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45400 Semoy,
France

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

27 November 2014

Botswana Registration Numbers:	
Glucophage XR 500 mg: BOT1101800	S2
Glucophage XR 750 mg: BOT1703119	S2
Glucophage XR 1000 mg: BOT1703120	S2
Namibia Registration Numbers:	
Glucophage XR 500 mg: 08/21.2/0201	NS2
Glucophage XR 750 mg: 17/21.2/0006	NS2
Glucophage XR 1000 mg: 15/21.2/0137	NS2
Kenya Registration Numbers:	
Glucophage XR 500 mg: 22094	POM
Glucophage XR 750 mg: 22095	POM
Tanzania Registration Numbers:	
Glucophage XR 500 mg: TZ17H0149	POM
Glucophage XR 750 mg: TZ17H0151	POM
Glucophage XR 1000 mg: TZ17H0150	POM

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

PROPRIETARY NAME AND DOSAGE FORM:

Glucophage XR 500 mg (prolonged release tablet)

Glucophage XR 750 mg (prolonged release tablet)

Glucophage XR 1000 mg (prolonged release tablet)

Read this entire leaflet carefully before you start taking

Glucophage XR 500 mg

Glucophage XR 750 mg

Glucophage XR 100 mg

- Keep this leaflet. You may need to read it again.
- If you have more questions, please ask your doctor or your pharmacist.
- Glucophage XR 500 mg /Glucophage XR 750 mg /Glucophage XR 1000 mg has been prescribed for you personally and you should not share it with other people. It may harm them, even if their symptoms are the same as yours.

WHAT GLUCOPHAGE XR 500 MG / GLUCOPHAGE XR 750 MG /GLUCOPHAGE XR 1000 MG CONTAINS:

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 formulation is sugar-free.

The other ingredients are hydroxypropyl methylcellulose, magnesium stearate, sodium carboxymethylcellulose.

WHAT GLUCOPHAGE XR 500 MG /GLUCOPHAGE XR 750 MG /GLUCOPHAGE XR 1000 MG IS USED FOR

Treatment of type 2 diabetes mellitus in adults, when dietary management and exercise alone do not result in adequate glycaemic control. Glucophage XR range can be given alone as initial therapy or can be administered in combination with other oral antidiabetic agents or with insulin.

BEFORE YOU TAKE GLUCOPHAGE XR 500 MG/ GLUCOPHAGE XR 750 MG /GLUCOPHAGE XR 1000 MG

Do not take Glucophage XR range if

- You are hypersensitive (allergic) to metformin hydrochloride or any of the other ingredients.
- You have severe complications of your diabetes such as diabetic ketoacidosis, a metabolic state resulting from a profound lack of insulin.
- Your kidneys do not work properly or do not work at all.
- You have ~~a~~ short term conditions that may affect your kidney function e.g. dehydration, severe infection, shock, administration of iodinated contrast media through the veins.
- You have short or long term conditions that may cause a lack of oxygen to your tissues such as heart or breathing failure, a recent heart attack, shock.
- You suffer from a liver condition, or use excessive amounts of alcohol.
- You have or have a history of inflammation of your pancreas.
- You are pregnant or breastfeeding.

Take special care with GLUCOPHAGE XR 500 MG /GLUCOPHAGE XR 750 MG /GLUCOPHAGE XR 1000 MG if you have the following:

Lactic acidosis

Lactic acidosis is a 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. Symptoms include nausea and vomiting. This complication could happen when Glucophage XR accumulates in your blood, especially if you have serious kidney dysfunction. Glucophage XR treatment should be stopped and you should be hospitalised.

Surgery

Glucophage XR should be discontinued 48 hours before surgery with general anaesthesia and should not be usually resumed earlier than 48 hours afterwards.

Other precautions:

- All patients should continue their diet with a regular distribution of carbohydrate intake during the day. Overweight patients should continue their energy-restricted diet.
- The usual laboratory tests for diabetes monitoring should be performed regularly.
- Although Glucophage XR alone never causes hypoglycaemia, caution is advised when it is used in combination with insulin or sulphonylureas.
- The tablet shells may be present in the faeces. Patients should be advised that this is normal.

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.

Taking other medicines with GLUCOPHAGE XR 500 MG /GLUCOPHAGE XR 750 MG /GLUCOPHAGE XR 1000 MG:

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

Combinations that should be avoided, such as

- Drinking alcohol and alcohol-containing medications.
- Administration of iodinated contrast agents in your veins as this may lead to kidney failure, resulting in Glucophage XR accumulation and a risk of lactic acidosis, where lactic acid builds up in the bloodstream faster than it can be removed causing nausea and vomiting. Glucophage XR should be discontinued prior to, or at the time of the test and not reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal.

Take special care when using any of the following medications together with Glucophage XR:

- Glucocorticoids (systemic and local routes) that are used to treat conditions that involve inflammation, beta-2-agonist medicines that opens the airways especially in patients with asthma, and diuretics (medication that helps your body get rid of extra fluid)
- ACE-inhibitors (medicines used to treat high blood pressure)
- Cimetidine (medicines used to treat stomach ulcers)
- Anticoagulants (medicines used to thin the blood)
- Sulphonylurea (medicines that control your blood glucose levels)
- Vitamins

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.

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.

Glucophage XR 750 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 recommended dosage is 2 tablets daily.

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 500 MG /GLUCOPHAGE XR 750 MG /GLUCOPHAGE XR 1000 MG:

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

IF YOU TAKE MORE GLUCOPHAGE XR THAN YOU SHOULD

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

POSSIBLE SIDE-EFFECTS

Glucophage XR can have side effects.

The following side effects occur less frequently:

Decrease of vitamin B12 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. B12).

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 500 MG /GLUCOPHAGE XR 750 MG /GLUCOPHAGE XR 1000 MG are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, 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.

STORAGE AND DISPOSAL INFORMATION

Store all medicines out of reach of children.

Store at or below 25 °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.

PRESENTATION

20, 30, 50, 60, 80, 90, 100 or 120 tablets are packed in transparent PVC or PVC/PVDC blisters with an aluminium backing.

IDENTIFICATION OF THE MEDICINE

Glucophage XR 500 mg:	White to off-white, capsules-shaped, biconvex modified release tablet, debossed on one side with '500'.
Glucophage XR 750 mg:	White capsule-shaped, biconvex tablet, debossed on one side with '750' and on the other side with 'Merck'.
Glucophage XR 1000 mg:	White to off-white, capsule-shaped, biconvex tablet, debossed with '1000' on one face and 'Merck' on the other side.

REGISTRATION NUMBERS

Glucophage XR 500 mg:	A39/21.2/0027
Glucophage XR 750 mg:	43/21.2/0185
Glucophage XR 1000 mg:	45/21.2/0066

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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