TAJ PHARMA
16 Years of Good Life

PACKAGE LEAFLET: INFORMATION FOR THE USER

GLIBENCLAMIDE AND METFORMIN HYDROCHLORIDE FILM-COATED TABLETS
500MG/5MG & 500MG/2.5MG
TAJ PHARMA

Metformin hydrochloride and Glibenclamide

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

WHAT IS IN THIS LEAFLET:

1. WHAT GLIBENCLAMIDE AND METFORMIN HYDROCHLORIDE IS AND WHAT IT IS USED FOR

Glibenclamide and Metformin Hydrochloride 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. Glibenclamide and Metformin Hydrochloride helps to reduce their blood sugar towards a normal level.

Glibenclamide and Metformin Hydrochloride is used for the oral treatment (via the mouth) of type 2 diabetes mellitus in adult patients.
It is used to replace the combination of the two active substances of Glibenclamide and Metformin Hydrochloride (metformin hydrochloride and glibenclamide) given separately in patients previously treated with this combination, if the combination was effective in controlling the patients' glucose level in the blood.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE GLIBENCLAMIDE AND METFORMIN HYDROCHLORIDE

Do not take Glibenclamide and Metformin Hydrochloride

- if you are allergic (hypersensitive) to metformin hydrochloride, glibenclamide or other sulphonamides or any of the other ingredients of Glibenclamide and Metformin Hydrochloride (listed in section 6)
- 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').
- 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.

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

You must stop taking Glibenclamide and Metformin Hydrochloride 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

Talk to your doctor before taking Glibenclamide and Metformin Hydrochloride.

Risk of lactic acidosis

Glibenclamide and Metformin Hydrochloride may cause a very rare, but very serious side effect called lactic acidosis, particularly if your kidneys are not working properly. The risk of developing lactic acidosis is also increased with uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, dehydration (see further information below), 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 Glibenclamide and Metformin Hydrochloride 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 Glibenclamide and Metformin Hydrochloride 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 Glibenclamide and Metformin Hydrochloride during and for some time after the procedure. Your doctor will decide when you must stop and when to restart your treatment with Glibenclamide and Metformin Hydrochloride.

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 at risk of hypoglycaemia. In the elderly, low blood sugar may be somewhat difficult to recognise. The initial dose and the maintenance dose 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.

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 Glibenclamide and Metformin Hydrochloride at the same time (see section 2, "Other medicines and Glibenclamide and Metformin Hydrochloride").

Discuss with your doctor whether Glibenclamide and Metformin Hydrochloride 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 Glibenclamide and Metformin Hydrochloride may cause your red blood cells to be destroyed too quickly (haemolytic anaemia). Tell your doctor if you have this condition, as Glibenclamide and Metformin Hydrochloride 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.

During treatment with Glibenclamide and Metformin Hydrochloride, 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.

Other medicines and Glibenclamide and Metformin Hydrochloride
While taking Glibenclamide and Metformin Hydrochloride, you must not use any of the following medicines:
miconazole even for local use (see section 2,"Do not take Glibenclamide and Metformin Hydrochloride")
If you need to have an injection of contrast medium that contains iodine into your bloodstream, for example in the context of an X-ray or scan, you must stop taking Glibenclamide and Metformin Hydrochloride before or at the time of the injection. Your doctor will decide when you must stop and when to restart your treatment with Glibenclamide and Metformin Hydrochloride.

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 Glibenclamide and Metformin Hydrochloride. It is especially important to mention the following:

- medicines which increase urine production (diuretics)
- 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)
- 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 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)
- 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 Glibenclamide and Metformin Hydrochloride 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.

Glibenclamide and Metformin Hydrochloride with alcohol
Avoid excessive alcohol intake while taking Glibenclamide and Metformin Hydrochloride since this may increase the risk of lactic acidosis (see section "Warnings and precautions"

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. During pregnancy, diabetes should be treated with insulin. If you find out that you are pregnant while taking Glibenclamide and Metformin Hydrochloride, consult your doctor so that he/she may change your treatment.
You must not take Glibenclamide and Metformin Hydrochloride, 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 Glibenclamide and Metformin Hydrochloride
Each Glibenclamide and Metformin Hydrochloride 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 GLIBENCLAMIDE AND METFORMIN HYDROCHLORIDE

Dosage
Always take this medicine exactly as your doctor has told you. 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. Glibenclamide and Metformin Hydrochloride 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 Glibenclamide and Metformin Hydrochloride. If you are an elderly person, the usual starting dose is one tablet of Glibenclamide and Metformin Hydrochloride 500 mg/2.5 mg per day.

Maximum daily dose
For Glibenclamide and Metformin Hydrochloride 500 mg/2.5 mg: 6 tablets.
For Glibenclamide and Metformin Hydrochloride 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 Glibenclamide and Metformin Hydrochloride 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 Glibenclamide and Metformin Hydrochloride if you have to take it in combination with a cholesterol-lowering medicine (bile acid sequestrant). Glibenclamide and Metformin Hydrochloride must be taken at least 4 hours prior to a cholesterol-lowering medicine (bile acid sequestrant).

If you take more Glibenclamide and Metformin Hydrochloride than you should
If you have taken more Glibenclamide and Metformin Hydrochloride tablets than you should have, you may experience lactic acidosis or low blood sugar (for symptoms of lactic acidosis and low blood sugar, see section 2, "Warnings and precautions"). **TALK to your DOCTOR IMMEDIATELY.**

If you forget to take Glibenclamide and Metformin Hydrochloride
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 Glibenclamide and Metformin Hydrochloride
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

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

Glibenclamide and Metformin Hydrochloride may cause a very rare (may affect up to 1 user in 10,000), but very serious side effect called lactic acidosis (see section "Warnings and precautions"). If this happens you must **stop taking Glibenclamide and Metformin Hydrochloride and contact a doctor or the nearest hospital immediately**, as lactic acidosis may lead to coma.
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 people)

- 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

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 Glibenclamide and Metformin Hydrochloride") 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 section "Warning and precautions")
- 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 Glibenclamide and Metformin Hydrochloride 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
- decreased vitamin B12 levels in the blood

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

5. HOW TO STORE GLIBENCLAMIDE AND METFORMIN HYDROCHLORIDE

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date, which is stated on the carton after "EXP". The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Glibenclamide and Metformin Hydrochloride contains
- The active substances are metformin hydrochloride and glibenclamide.
- One film-coated tablet of Glibenclamide and Metformin Hydrochloride 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 Glibenclamide and Metformin Hydrochloride 500 mg/5 mg contains 500 mg metformin hydrochloride corresponding to 390 mg metformin base and 5 mg glibenclamide.
- The other ingredients are microcrystalline cellulose, sodium croscarmellose, povidone K 30, magnesium stearate and Opadry OY-L-24808 (orange) [lactose monohydrate, hypromellose, titanium dioxide, macrogol, yellow iron oxide, red iron oxide, black iron oxide] in Glibenclamide and Metformin Hydrochloride 500 mg/2.5 mg or Opadry (yellow) [lactose monohydrate, hypromellose, titanium dioxide, macrogol, yellow iron oxide, red iron oxide, Quinoline Yellow Lake] in Glibenclamide and Metformin Hydrochloride 500 mg/5 mg.

What Glibenclamide and Metformin Hydrochloride looks like and contents of the pack
The tablets are supplied in clear or opaque blister packs containing 20, 28, 30, 50, 56, 60, 84, 90, 100, 120, 180 or 600 tablets (PVC/Aluminium). Not all pack sizes may be marketed.

7. MANUFACTURED IN INDIA BY:

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