30XXXXX

METFORMIN HCl GLICLAZIDE

Rx GLYZERIC®

500mg / 80mg Film-Coated Tablet
850mg / 80mg Film-Coated Tablet

ORAL HYPOGLYCEMIC

FORMULATION

Each film-coated tablet contains :

Metformin hydrochloride, BP .....500 mg
Gliclazide, BP.....80 mg
Metformin hydrochloride, BP .....850 mg
Gliclazide, BP.....80 mg

DESCRIPTION

500mg/80mg - Light pink to pink colored, capsule shaped, biconvex, film-coated tablets, plain on both sides.
850/80mg - Light orange to orange colored, capsule shaped, biconvex, film-coated tablets with breakline on one side and plain on other side.

PHARMACODYNAMICS

Gliclazide

Gliclazide is a hypoglycaemic sulfonylurea antidiabetic active substance differing from other related compounds by an N-containing heterocyclic ring with an endocyclic bond.
Gliclazide reduces blood glucose levels by stimulating insulin secretion from the β-cells of the islets of Langerhans. Increase in postprandial insulin and C-peptide secretion persists after two years of treatment.
In addition to these metabolic properties, gliclazide has haemovascular properties.

Metformin

Metformin is a biguanide with antihyperglycaemic effects, lowering both basal and postprandial plasma glucose. It does not stimulate insulin secretion and therefore does not produce hypoglycaemia.
Metformin may act via 3 mechanisms:
- Reduction of hepatic glucose production by inhibiting gluconeogenesis and glycogenolysis.
- In muscle, by increasing insulin sensitivity, improving peripheral glucose uptake and utilization.
- 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 (GLUTs) known to date.

PHARMACOKINETICS

Gliclazide

Absorption

Plasma levels increase reaching maximal concentrations between 2 and 6 hours. Gliclazide is well absorbed. Food intake does not affect the rate or degree of absorption.

Distribution

Plasma protein binding is approximately 95%. The volume of distribution is around 19 litres.

Biotransformation

Gliclazide is mainly metabolised in the liver and excreted in the urine; less than 1% of the dose is excreted unchanged in the urine. No active metabolites have been detected in plasma.

Elimination

The elimination half-life of gliclazide is between 10 and 12 hours.

Metformin

Absorption

After an oral dose of metformin hydrochloride tablet, maximum plasma concentration (Cmax) is reached in approximately 2.5 hours (tmax). Absolute bioavailability of a 500 mg or 850 mg metformin hydrochloride tablet is approximately 50-60% in healthy subjects. After an oral dose, the non-absorbed fraction recovered in faeces was 20-30%. After oral administration, metformin absorption is saturable and incomplete. It is assumed that the pharmacokinetics of metformin absorption is non-linear.

At the recommended metformin doses and dosing schedules, steady state plasma concentrations are reached within 24 to 48 hours and are generally less than 1 microgram/ml. In controlled clinical trials, maximum metformin plasma levels (Cmax) did not exceed 5 microgram/ml, even at maximum doses.
Food decreases the extent and slightly delays the absorption of metformin. Following oral administration of 850 mg tablet, a 40% lower plasma peak concentration, a 25% decrease in AUC (area under the curve) and a 35 minute prolongation of the time to peak plasma concentration were observed. The clinical relevance of these findings is unknown.

Distribution

Plasma protein binding is negligible. Metformin partitions into erythrocytes. The blood peak is lower than the plasma peak and appears at approximately the same time. The red blood cells most likely represent a secondary compartment of distribution. The mean volume of distribution (Vd) ranged between 63-276 l.

Metabolism

Metformin is excreted unchanged in the urine. No metabolites have been identified in humans.

Elimination

Renal clearance of metformin is > 400 ml/min, indicating that metformin is eliminated by glomerular filtration and tubular secretion. Following an oral dose, the apparent terminal elimination half-life is approximately 6.5 hours.
When renal function is impaired, renal clearance is decreased in proportion to that of creatinine and thus the elimination half-life is prolonged, leading to increased levels of metformin in plasma.

INDICATION

As an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus who are already treated with Gliclazide and Metformin or whose diabetes is not adequately controlled with Metformin alone, or for those patients who have initially responded to Gliclazide alone and require additional glycemic control.

CONTRAINDICATIONS

This medicine is contraindicated in case of:
- Hypersensitivity to gliclazide or metformin or to any of the excipients. Other sulfonylureas and sulfonamides.
- Type 1 diabetes
- Diabetic pre-coma and coma, diabetic keto-acidosis
- Severe renal or hepatic insufficiency: in these cases the use of insulin is recommended
- Treatment with miconazole
- Lactation
- Gliclazide should, where possible, be avoided in porphyria.
- Acute conditions with the potential to alter renal function such as: dehydration, severe infection, shock.
- Disease which may cause tissue hypoxia (especially acute disease, or worsening of chronic disease) such as: decompensated heart failure, respiratory failure, recent myocardial infarction, shock.
- Hepatic insufficiency, acute alcohol intoxication, alcoholism

DOSAGE AND ADMINISTRATION

The recommended dose is one tablet twice daily. Or as prescribed by the physician.

PRECAUTIONS

Gliclazide

Hypoglycemia: This treatment should be prescribed only if the patient is likely to have a regular food intake (including breakfast). It is important to have a regular carbohydrate intake due to the increased risk of hypoglycemia if a meal is taken late, if an inadequate amount of food is consumed or if the food is low in carbohydrate. Hypoglycemia is more likely to occur during low-calorie diets, following prolonged or strenuous exercise, alcohol intake or if a combination of hypoglycemic agents is being used.
Hypoglycemia may occur following administration of sulfonylureas. Some cases may be severe and prolonged. Hospitalization may be necessary and glucose administration may need to be continued for several days.
Careful selection of patients, of the dose used, and clear patient directions are necessary to reduce the risk of hypoglycemic episodes.
Factors which increase the risk of hypoglycemia:
- patient refuses or (particularly in elderly subjects) is unable to co-operate
- malnutrition, irregular mealtimes, skipping meals, periods of fasting or dietary change
- imbalance between physical exercise and carbohydrate intake
- renal insufficiency
- overdose of gliclazide
- severe hepatic insufficiency
- certain endocrine disorders: thyroid disorders, hypopituitarism, and adrenal insufficiency
- concomitant administration of certain other medicines

Renal and hepatic insufficiency: The pharmacokinetics and/or pharmacodynamics of gliclazide may be altered in patients with hepatic insufficiency or severe renal failure. A hypoglycaemic episode occurring in these patients may be prolonged, so appropriate management should be initiated.
Patient information: the risks of hypoglycaemia, together with its symptoms, treatment, and conditions that predispose to its development, should be explained to the patient and to family members.
The patient should be informed of the importance of following dietary advice, of taking regular exercise, and of regular monitoring of blood glucose levels.
Poor blood glucose control: blood glucose control in a patient receiving antidiabetic treatment may be affected by any of the following: fever, trauma, infection or surgical intervention. In some cases, it may be necessary to administer insulin.
The hypoglycaemic efficacy of any oral antidiabetic agent, including gliclazide, is attenuated over time in many patients: this may be due to progression in the severity of the diabetes, or to a reduced response to treatment. This phenomenon is known as secondary failure which is distinct from primary failure, when an active substance is ineffective as first-line treatment.
Adequate dose adjustment and dietary compliance should be considered before classifying the patient as secondary failure.
Dysglycaemia: Disturbances in blood glucose, including hypoglycaemia and hyperglycaemia have been reported, in diabetic patients receiving concomitant treatment with fluoroquinolones, especially in elderly patients. Indeed, careful monitoring blood glucose is recommended in all patients receiving at the same time Gliclazide and a fluoroquinolone.
Laboratory tests: Measurement of glycated haemoglobin levels (or fasting venous plasma glucose) is recommended in assessing blood glucose control. Blood glucose self-monitoring may also be useful.
Treatment of patients with G6PD-deficiency with sulfonylurea agents can lead to haemolytic anaemia. Since gliclazide belongs to the class of sulfonylurea agents, caution should be used in patients with G6PD-deficiency and a non-sulfonylurea alternative should be considered.

Metformin

Lactic acidosis: Lactic acidosis, a very rare, but serious metabolic complication, most often occurs at acute worsening of renal function or cardiorespiratory illness or sepsis. Metformin accumulation occurs at acute worsening of renal function and increases the risk of lactic acidosis.
In case of dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), metformin should be temporarily discontinued and contact with a health care professional is recommended.
Medicinal products that can acutely impair renal function (such as antihypertensives, diuretics and NSAIDs) should be initiated with caution in metformin-treated patients. Other risk factors for lactic acidosis are excessive alcohol intake, hepatic insufficiency, inadequately controlled diabetes, ketosis, prolonged fasting and any conditions associated with hypoxia, as well as concomitant use of medicinal products that may cause lactic acidosis.
Patients and/or care-givers should be informed of the risk of lactic acidosis. Lactic acidosis is characterised by acidotic dyspnoea, abdominal pain, muscle cramps, asthenia and hypothermia followed by coma. In case of suspected symptoms, the patient should stop taking metformin and seek immediate medical attention. Diagnostic laboratory findings are decreased blood pH (< 7.35), increased plasma lactate levels (>5 mmol/L) and an increased anion gap and lactate/pyruvate ratio.
Renal function: GFR should be assessed before treatment initiation and regularly thereafter.
Metformin is contraindicated in patients with GFR<30 mL/min and should be temporarily discontinued in the presence of conditions that alter renal function.
Cardiac function: Patients with heart failure are more at risk of hypoxia and renal insufficiency. In patients with stable chronic heart failure, metformin may be used with a regular monitoring of cardiac and renal function.
For patients with acute and unstable heart failure, metformin is contraindicated.
Administration of iodinated contrast agents Intravascular administration of iodinated contrast agents may lead to contrast induced nephropathy, resulting in metformin accumulation and an increased risk of lactic acidosis.
Metformin should be discontinued prior to or at the time of the imaging procedure and not restarted until at least 48 hours after, provided that renal function has been re-evaluated and found to be stable.
Surgery: Metformin must be discontinued at the time of surgery under general, spinal or epidural anaesthesia. Therapy may be restarted no earlier than 48 hours following surgery or resumption of oral nutrition and provided that renal function has been re-evaluated and found to be stable.
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.

DRUG INTERACTIONS

Gliclazide

The following products are likely to increase the risk of hypoglycaemia

Contraindicated combination

- Miconazole (systemic route, oromucosal gel): increases the hypoglycaemic effect with possible onset of hypoglycaemic symptoms, or even coma.
- Antibacterials: Sulfonamides may enhance the hypoglycaemic effect of gliclazide

Combinations which are not recommended

- Phenylbutazone (systemic route): increases the hypoglycaemic effect of sulfonylureas (displaces their binding to plasma proteins and/or reduces their elimination).

It is preferable to use a different anti-inflammatory agent, or else to warn the patient and emphasise the importance of self-monitoring. Where necessary, adjust the dose during and after treatment with the anti-inflammatory agent.
- Alcohol: increases the hypoglycaemic reaction (by inhibiting compensatory reactions) that can lead to the onset of hypoglycaemic coma.

Avoid alcohol or medicines containing alcohol.

Combinations requiring precautions for use

Potentiation of the blood glucose lowering effect and thus, in some instances, hypoglycaemia may occur when one of the following drugs is taken: other antidiabetic agents (insulins, acarbose, metformin, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, GLP-1 receptor agonists), beta-blockers, fluconazole, angiotensin converting enzyme inhibitors (captopril, enalapril), H2-receptor antagonists, MAOIs, sulfonamides, clarithromycin and nonsteroidal anti-inflammatory agents.
- Anti-gout agents: Enhanced hypoglycaemic effect with allopurinol, sulfinpyrazone and probenecid.
- Chloramphenicol: Enhances the hypoglycaemic effect of sulfonylureas
- Beta-blockers: May reduce the hypoglycaemic effects of sulphonylureas, and mask the symptoms of hypoglycaemia.
- Fluconazole: May enhance the hypoglycaemic effect of sulphonylureas.
- ACE inhibitors: Such as captopril and enalapril, may enhance the hypoglycaemic effect of gliclazide.
- Antimalarials: Possible increase in hypoglycaemia with quinine and quinidine
- Lipid-lowering drugs: Clofibrate group drugs may improve glucose tolerance and have an additive effect.
- Sex hormones, hormone antagonists and steroids: Testosterone, and anabolic steroids may enhance the hypoglycaemic effect of gliclazide. Octreotide may cause hypoglycaemia.

The following products may cause an increase in blood glucose levels

Combination which is not recommended

- Danazol: diabetogenic effect of danazol.

If the use of this active substance cannot be avoided, warn the patient and emphasise the importance of urine and blood glucose monitoring. It may be necessary to adjust the dose of the antidiabetic agent during and after treatment with danazol.

Combinations requiring precautions during use

- Chlorpromazine (neuroleptic agent): high doses (>100 mg per day of chlorpromazine) increase blood glucose levels (reduced insulin release).

Warn the patient and emphasise the importance of blood glucose monitoring. It may be necessary to adjust the dose of the antidiabetic active substance during and after treatment with the neuroleptic agent.
- Glucocorticoids (systemic and local route: intra-articular, cutaneous and rectal preparations) and tetracosactrin: increase in blood glucose levels with possible ketosis (reduced tolerance to carbohydrates due to glucocorticoids).

Warn the patient and emphasise the importance of blood glucose monitoring, particularly at the start of treatment. It may be necessary to adjust the dose of the antidiabetic active substance during and after treatment with glucocorticoids.
• Ritodrine, salbutamol, terbutaline: (I.V.)
Increased blood glucose levels due to beta-2 agonist effects.
Emphasise the importance of monitoring blood glucose levels. If necessary, switch to insulin.
• Saint John's Wort (Hypericum perforatum) preparations:
Gliclazide exposure is decreased by Saint John's Wort-Hypericum perforatum.
Emphasize the importance of blood glucose levels monitoring.
• Cytotoxic drugs: Crisantaspase may induce hyperglycaemia and the dose of gliclazide may need to be adjusted.
• Antibacterials: Isoniazid may increase blood sugar levels, so the dose of sulphonylurea may need to be adjusted. Rifamycins may reduce the hypoglycaemic effect of sulphonylureas.
• Antihypertensives: Diazoxide may reduce the hypoglycaemic effect of sulphonylureas.
• Antipsychotics: Chlorpromazine in daily doses of 100mg or more can reduce the hypoglycaemic effect of sulphonylureas.
• Diuretics: Loop and thiazide diuretics may reduce the hypoglycaemic effect of sulphonylureas.
• Lithium: May occasionally impair glucose tolerance.
• Sex hormones, hormone antagonists and steroids: Oestrogens, progesterones, oral contraceptives and corticosteroids may reduce the hypoglycaemic effect of sulphonylureas.
Octreotide may cause hyperglycaemia.
• Thyroid hormones: May reduce the effect of sulphonylureas.
Combination which must be taken into account
• Anticoagulant therapy (Warfarin):
Sulfonylureas may lead to potentiation of anticoagulation during concurrent treatment.
Adjustment of the anticoagulant may be necessary.
Metformin
Concomitant use not recommended
Alcohol
Alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in case of fasting, malnutrition or hepatic impairment.
Iodinated contrast agents
Metformin must be discontinued prior to or at the time of the imaging procedure and not restarted until at least 48 hours after, provided that renal function has been re-evaluated and found to be stable.
Combinations requiring precautions for use
Some medicinal products can adversely affect renal function which may increase the risk of lactic acidosis, e.g. NSAIDs, including selective cyclo-oxygenase (COX) II inhibitors, ACE inhibitors, angiotensin II receptor antagonists and diuretics, especially loop diuretics. When starting or using such products in combination with metformin, close monitoring of renal function is necessary.
Medicinal products with intrinsic hyperglycaemic activity (e.g. glucocorticoids (systemic and local routes) and sympathomimetics)
More frequent blood glucose monitoring may be required, especially at the beginning of treatment. If necessary, adjust the metformin dosage during therapy with the respective medicinal product and upon its discontinuation.
Organic cation transporters (OCT)
Metformin is a substrate of both transporters OCT1 and OCT2.
Co-administration of metformin with
• Inhibitors of OCT1 (such as verapamil) may reduce efficacy of metformin.
• Inducers of OCT1 (such as rifampicin) may increase gastrointestinal absorption and efficacy of metformin.
• Inhibitors of OCT2 (such as cimetidine, dolutegravir, ranolazine, trimethoprime, vandetanib, isavuconazole) may decrease the renal elimination of metformin and thus lead to an increase in metformin plasma concentration.
• Inhibitors of both OCT1 and OCT2 (such as crizotinib, olaparib) may alter efficacy and renal elimination of metformin.
Caution is therefore advised, especially in patients with renal impairment, when these drugs are co-administered with metformin, as metformin plasma concentration may increase. If needed, dose adjustment of metformin may be considered as OCT inhibitors/inducers may alter the efficacy of metformin.

PREGNANCY AND LACTATION
Pregnancy
Gliclazide
There is no or limited amount of data (less than 300 pregnancy outcomes) from the use of gliclazide in pregnant women, even though there are few data with other sulfonylureas.
Studies in animals have shown reproductive toxicity.
As a precautionary measure, it is preferable to avoid the use of Gliclazide during pregnancy.
Control of diabetes should be obtained before the time of conception to reduce the risk of congenital abnormalities linked to uncontrolled diabetes.
Oral hypoglycaemic agents are not suitable, insulin is the drug of first choice for treatment of diabetes during pregnancy. It is recommended that oral hypoglycaemic therapy is changed to insulin before a pregnancy is attempted, or as soon as pregnancy is discovered.
Metformin
Uncontrolled diabetes during pregnancy (gestational or permanent) is associated with increased risk of congenital abnormalities and perinatal mortality.
A limited amount of data from the use of metformin in pregnant women does not indicate an increased risk of congenital abnormalities. Animal studies do not indicate harmful effects with respect to pregnancy, embryonic or foetal development, parturition or postnatal development.
When the patient plans to become pregnant and during pregnancy, it is recommended that diabetes is not treated with metformin but insulin be used to maintain blood glucose levels as close to normal as possible, to reduce the risk of malformations of the foetus.
Breast-feeding
Gliclazide
It is unknown whether gliclazide or its metabolites are excreted in human milk. Given the risk of neonatal hypoglycaemia, the product is therefore contraindicated in breast-feeding mothers.
A risk to the newborns/infants cannot be excluded.
Metformin
Metformin is excreted into human breast milk. No adverse effects were observed in breastfed newborns/infants. However, as only limited data are available, breast-feeding is not recommended during metformin treatment. A decision on whether to discontinue breastfeeding should be made, taking into account the benefit of breast-feeding and the potential risk to adverse effects on the child.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINE
Gliclazide have no or negligible influence on the ability to drive and use machines. However, patients should be informed that their concentration might be affected if their diabetes is not satisfactorily controlled, especially at the beginning of treatment.
Metformin monotherapy does not cause hypoglycemia and therefore has no effect on the ability to drive or to use machines. However, patients should be alerted to the risk of hypoglycemia when metformin is used in combination with other antidiabetic agents (e.g. sulfonylureas, insulin or meglitinides).

ADVERSE EFFECTS
Gliclazide
Based on the experience with gliclazide, the following undesirable effects have been reported.
The most frequent adverse reaction with gliclazide is hypoglycemia.
As for other sulfonylureas, treatment with Gliclazide can cause hypoglycemia, if mealtimes are irregular and, in particular, if meals are skipped. Possible symptoms of hypoglycemia are:
headache, intense hunger, nausea, vomiting, lassitude, sleep disorders, agitation, aggression, poor concentration, reduced awareness and slowed reactions, depression, confusion, visual and speech disorders, aphasia, tremor, paresis, sensory disorders, dizziness, feeling of powerlessness, loss of self-control, delirium, convulsions, shallow respiration, bradycardia, drowsiness and loss of consciousness, possibly resulting in coma and lethal outcome.
In addition, signs of adrenergic counter-regulation may be observed: sweating, clammy skin, anxiety, tachycardia, hypertension, palpitations, angina pectoris and cardiac arrhythmia.
Usually, symptoms disappear after intake of carbohydrates (sugar). However, artificial sweeteners have no effect.
Experience with other sulfonylureas shows that hypoglycemia can recur even when measures prove effective initially.
If a hypoglycemic episode is severe or prolonged, and even if it is temporarily controlled by intake of sugar, immediate medical treatment or even hospitalization are required.
Gastrointestinal disturbances, including abdominal pain, nausea, vomiting dyspepsia, diarrhoea, and constipation have been reported: if these should occur they can be avoided or minimised if gliclazide is taken with breakfast.
The following undesirable effects have been more rarely reported:
• Skin and subcutaneous tissue disorders: rash, pruritus, urticaria, angioedema, erythema, maculopapular rashes, bullous reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis), and exceptionally, drug rash with eosinophilia and systemic symptoms (DRESS).
• Blood and lymphatic system disorders: changes in haematology are rare. They may include anaemia, leucopenia, thrombocytopenia, granulocytopenia. These are in general reversible upon discontinuation of medication.
• Hepato-biliary disorders: raised hepatic enzyme levels (AST, ALT, alkaline phosphatase), hepatitis (isolated reports).
Discontinue treatment if cholestatic jaundice appears. These symptoms usually disappear after discontinuation of treatment.
• Eye disorders: Transient visual disturbances may occur especially on initiation of treatment, due to changes in blood glucose levels.
• Class attribution effects: As for other sulfonylureas, the following adverse events have been observed: cases of erythrocytopenia, agranulocytosis, haemolytic anaemia, pancytopenia, allergic vasculitis, hyponatremia, elevated liver enzyme levels and even impairment of liver function (e.g. with cholestasis and jaundice) and hepatitis which regressed after withdrawal of the sulfonylurea or led to life-threatening liver failure in isolated cases.
Metformin
During treatment initiation, the most common adverse reactions are nausea, vomiting, diarrhoea, abdominal pain and loss of appetite which resolve spontaneously in most cases.
To prevent them, it is recommended to take metformin in 2 or 3 daily doses and to increase slowly the doses.
The following adverse reactions may occur under treatment with metformin. Frequencies are defined as follows: very common: >1/10; common >1/100, <1/10; uncommon >1/1,000, <1/100; rare >1/10,000, <1/1,000; very rare <1/10,000.
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.
Metabolism and nutrition disorders
Very rare
• Lactic acidosis
• Decrease of vitamin B12 absorption with decrease of serum levels during long-term use of metformin. Consideration of such aetiology is recommended if a patient presents with megaloblastic anaemia.
Nervous system disorders
Common
• Taste disturbance
Gastrointestinal disorders
Very common
• Gastrointestinal disorders such as nausea, vomiting, diarrhoea, abdominal pain and loss of appetite. These undesirable effects occur most frequently during initiation of therapy and resolve spontaneously in most cases. To prevent them, it is recommended that metformin be taken in 2 or 3 daily doses during or after meals. A slow increase of the dose may also improve gastrointestinal tolerability.
Hepatobiliary disorders
Very rare
• Isolated reports of liver function tests abnormalities or hepatitis resolving upon metformin discontinuation.
Skin and subcutaneous tissue disorders
Very rare
• Skin reactions such as erythema, pruritus, urticaria

OVERDOSE AND TREATMENT
Gliclazide
An overdose of sulfonylureas may cause hypoglycemia.
Moderate symptoms of hypoglycemia, without any loss of consciousness or neurological signs, must be corrected by carbohydrate intake, dose adjustment and/or change of diet. Strict monitoring should be continued until the doctor is sure that the patient is out of danger.
Severe hypoglycemic reactions, with coma, convulsions or other neurological disorders are possible and must be treated as a medical emergency, requiring immediate hospitalization.
If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid I.V. injection of 50 mL of concentrated glucose solution (20 to 30 %). This should be followed by continuous infusion of a more dilute glucose solution (10 %) at a rate that will maintain blood glucose levels above 1 g/L. Patients should be monitored closely and, depending on the patient's condition after this time, the doctor will decide if further monitoring is necessary.
Dialysis is of no benefit to patients due to the strong binding of gliclazide to proteins.
Metformin
Hypoglycaemia has not been seen with metformin hydrochloride doses of up to 85 g, although lactic acidosis has occurred in such circumstances. High overdose of metformin or concomitant risks may lead to lactic acidosis. Lactic acidosis is a medical emergency and must be treated in hospital. The most effective method to remove lactate and metformin is haemodialysis.

STORE AT TEMPERATURES NOT EXCEEDING 30°C.
PROTECT FROM LIGHT.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA : www.fda.gov.ph
Seek medical attention immediately at the first sign of any adverse drug reaction.

AVAILABILITY
Metformin HCl + Gliclazide 500mg / 80mg Film-Coated Tablet (**Glyzeric**®) Alu / Alu blister pack x 10's, (box of 30's)
Metformin HCl + Gliclazide 850mg / 80mg Film-Coated Tablet (**Glyzeric**®) Alu / Alu blister pack x 10's, (box of 30's)

Glyzeric® is a registered trademark of Ajanta Pharma Philippines, Inc.

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Plot No. B-4/5/6, MIDC, Paithan, Aurangabad 431 148
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Unit 1702 Phil. Axa Life Center,
#1286 Sen. Gil Puyat Ave. Cor. Tindalo St.,
Brgy. San Antonio, Makati City