For the Use of a Registered Medical Practitioner Only

1. GENERIC NAME & BRAND NAME

Gliclazide Sustained Release 30 mg & Metformin Hydrochloride Sustained Release 500 mg Tablets
Zeformin™ XR 30

Gliclazide Sustained Release 60 mg & Metformin Hydrochloride Sustained Release 500 mg Tablets
Zeformin™ XR 60

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Zeformin™ XR 30
Each uncoated bilayered sustained release tablet contains:

Gliclazide I.P.	30mg
Metformin Hydrochloride I.P.	500mg
Excipients	q.s

Colour: Red oxide of Iron

Zeformin™ XR 60
Each uncoated bilayered sustained release tablet contains:

Gliclazide I.P.	60mg
Metformin Hydrochloride I.P.	500mg
Excipients	q.s

Colour: Red oxide of Iron & Yellow oxide of Iron

3. DOSAGE FORM AND STRENGTH

Kindly refer Section 1 & 2

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATION

For the management of type 2 diabetes patients when diet, exercise and monotherapy do not result in adequate glycemic control.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Treatment should be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended daily dose for either of the two drugs in ZEFORMIN XR. One tablet once a day administered with breakfast or the first main meal or as directed by the physician.
Monitoring for hypoglycaemia must be done in patients who have been switched to metformin from longer half-life sulfonylurea drugs such as chlorpropamide as they may have an overlapping of drug effects for the subsequent 1-2 weeks. Glycosylated hemoglobin should be measured at intervals of approximately three months. The therapeutic goal must be to decrease both fasting plasma glucose and glycosylated hemoglobin levels to normal or near normal.

4.3 CONTRAINDICATIONS

- The combination of and metformin is contraindicated in patients with a history of a hypersensitivity reactions/ allergic reactions to and/ or metformin
- Patients with type 1 diabetes
- Patients with renal disease (serum creatinine levels ≥ 1.5 mg/dL [males], ≥ 1.4 mg/dL [females] or abnormal creatinine clearance).
- Patients with severe hepatic disease
- Patients with cardiovascular collapse (shock), acute myocardial infarction, and septicemia
- Patients with acute or chronic metabolic acidosis such as diabetic ketoacidosis, with or without coma.
- The combination of gliclazide and metformin must be temporarily discontinued in patients undergoing radiologic studies that require intravascular administration of iodinated contrast materials, since the use of such products may result in acute renal dysfunction.
- The combination of gliclazide and metformin is not recommended for use in pregnancy
- Treatment with miconazole via systemic route or oromucosal gel

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Hypoglycemia

All sulfonylureas, including gliclazide, can cause severe hypoglycaemia. This may lead to impaired ability to concentrate and react in situations such as driving or operating machinery. Severe hypoglycemia may result in temporary or permanent impairment of brain function, unconsciousness, convulsions, or death.

Elderly patients, patients with renal or hepatic impairment, debilitated or malnourished patients, and those with adrenal, pituitary impairment and patients on other anti-diabetic medications are more prone to develop hypoglycemia. Hypoglycemia is also more likely to occur when the caloric intake is deficient, alcohol is ingested or after severe or prolonged exercise.

The early warning symptoms of hypoglycemia may be different or may be less pronounced in patients with autonomic neuropathy, the elderly, in patients who are taking beta-adrenergic blocking medications or other sympatholytic agents. These patients may therefore be unaware of hypoglycemia (hypoglycaemia unawareness) and can develop severe hypoglycemia.It is important to educate patients to recognize and manage hypoglycaemia.

With concomitant metformin hydrochloride and sulfonylurea therapy, the risk of hypoglycemia associated with sulfonylurea therapy continues and may be increased. Appropriate precautions must be taken.

Hypersensitivity Reactions

Anaphylaxis, angioedema, and Stevens - Johnson syndrome are the hypersensitivity reactions observed in patients treated with gliclazide. If a hypersensitivity reaction is suspected, promptly discontinue gliclazide, and assess for other potential causes for the reaction. An alternative treatment for diabetes must be instituted.

Hemolytic Anemia

Sulfonylureas such as gliclazide can cause haemolytic anemia in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency. But, there are also a few reports of haemolytic anemia in patients receiving who did not have known G6PD deficiency.

Vitamin 12 levels – Vitamin B12 levels decrease with long term metformin therapy due to interference with B 12 absorption from the B 12 -intrinsic factor complex.But this decrease in vitamin B2 levels is rarely associated with anemia. In patients predisposed to low vitamin B12 levels, patients, routine serum vitamin B 12. Measurements at two- to three-year intervals may be useful.

Increased Risk of Cardiovascular Mortality with Sulfonylureas

A controversial warning has been issued (based on the study by University Group Diabetes Program) regarding increased cardiovascular mortality (2-½ times more) when oral hypoglycaemic drugs are given as compared to treatment with diet alone or diet plus insulin. But benefits of achieving tight glycemic control must be considered and they may overcome the risks associated with the use of Sulfonylureas.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Studies in rats at doses several thousand times the human dose for upto 30 months showed no evidence of carcinogenesis with either metformin or gliclazide and metformin were non-mutagenic in in vitro and in vivo mutagenicity studies (Ames test, somatic cell mutation, chromosomal aberration, unscheduled DNA synthesis, and mouse micronucleus test).
There was no effect of or metformin on male /female mouse fertility tests.

4.5 DRUGS INTERACTIONS

Medications that may INCREASE the glucose-lowering effect of sulfonylureas oral anti-diabetic medications, pramlintide acetate, insulin, angiotensin converting enzyme(ACE) inhibitors, H2 receptor antagonists, fibrates, propoxyphene, pentoxifylline, somatostatin analogs, anabolic steroids and androgens, cyclophosphamide, phenyramidol, guanethidine, fluconazole, sulfinpyrazone, tetracyclines, clarithromycin, disopyramide, quinolones **Medications that may DECREASE the glucose-lowering effect of sulfonylureas** Danazol, glucagon, somatropin, protease inhibitors, atypical antipsychotic medications (e.g., olanzapine and clozapine), barbiturates, diazoxide, laxatives, rifampin, thiazides and other diuretics, corticosteroids, phenothiazines, thyroid hormones,	These medications' may adversely affect the blood glucose lowering effects of Gliclazide.	These medications affect glucose metabolism and may require dose adjustment and particularly close monitoring for hypoglycemia or worsening glycemic control.

estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics (e.g., epinephrine, albuterol, terbutaline), and isoniazid.		
Furosemide	Effect of furosemide on metformin Furosemide increases the metformin plasma and blood Cmax (22% increase) and blood AUC (15% increase) without causing any significant change in metformin renal clearance. Effect of metformin on Furosemide The Cmax and AUC of furosemide are 31% and 12% lower respectively and the terminal half-life is decreased by 32%, without any significant change in furosemide renal clearance	No data on chronic co administration.
Nifedipine	Effect of nifedipine on metformin Nifedipine increases absorption of metformin, increases plasma metformin Cmax and AUC by 20% and 9%, respectively, and increased the amount excreted in the urine. Tmax and half-life are unaffected. Effect of metformin on nifedipine Metformin has minimal effects on nifedipine.	
Cationic drugs (e.g., amiloride,digoxin, morphine, procainamide, quinidine,quinine, cimetidine ranitidine, triamterene, trimethoprim, or vancomycin) that are eliminated by renal tubular secretion	Effect of cationic drugs on metformin These drugs have the potential for interaction with metformin by competing for common renal tubular transport systems A 60% increase in peak metformin plasma and whole	Careful patient monitoring and dose adjustment of Metformin hydrochloride and/or the interfering drug is recommended

	blood concentrations and a 40% increase in plasma and whole blood metformin AUC is reported	
Thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, est rogens, oral contraceptives, phenytoin,nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid	These drugs tend to produce hyperglycemia and may lead to loss of glycemic control.	When such drugs are co with of and metformin, the patient must be closely observed for loss of blood glucose contro l. When such drugs are withdrawn, the patient should be observed closely for hypoglycemia
Highly protein-bound drugs such as salicylates, sulfonamides, chloramphenicol, and probenecid	is highly protein bound drug and can have drug interactions with these drugs. Metformin is negligibly bound to plasma proteins and is, therefore, less likely to interact with highly protein-bound drugs.	When such drugs are co with the combination of and metformin, the patient must be closely observed for alterations in blood glucose levels. When these medications are withdrawn from a patient receiving monitor the patient closely for worsening glycemic control.
Miconazole	A potential interaction between oral miconazole and sulfonylureas leading to severe hypoglycemia has been reported	Patient blood glucose monitoring is recommended
Rifampicin	Effect of rifampicin on Rifampin may induce the metabolism of gliclazide, causing decreased plasma concentrations of	Worsening of glycemic control may occur Change in the combination of and metformin dose may be required depending on the change in blood glucose levels

Warfarin	Effect of on warfarin causes statistically significant decrease in the pharmacodynamic response to warfarin	Change (increase) in warfarin dose may be required
Propranolol	Effect of propranolol on Concomitant administration of propranolol and significantly increases Cmax, AUC, and T ½ by 23%, 22%, and 15%, respectively, and decreases CL/f by 18%.	Monitor blood glucose levels and dose adjustment of the combination of and metformin may be required

4.6 USE IN SPECIAL POPULATIONS (SUCH AS PREGNANT WOMEN, LACTATING WOMEN, PAEDIATRIC PATIENTS, GERIATRIC PATIENTS ETC.)

Renal failure
In patients with mild and moderate renal failure (based on measured creatinine clearance) the oral and renal clearance of metformin were decreased by 33% and 50% and 16% and 53%, respectively

Hepatic Impairment
No pharmacokinetic studies of Metformin hydrochloride have been conducted in subjects with hepatic insufficiency.
It is unknown whether there is an effect of hepatic impairment on pharmacokinetics because the pharmacokinetics of Metformin has not been adequately evaluated in patients with hepatic impairment.
Geriatrics
The total plasma clearance of metformin is decreased, the half-life is prolonged and Cmax is increased in the elderly as compared to healthy young volunteers. This change in metformin pharmacokinetics in the elderly is attributed to changes in renal function. Metformin treatment must not be initiated in patients 80 years of age unless measurement of creatinine clearance indicates that that renal function is normal.
Monitoring of renal function is required to aid in the prevention of lactic acidosis, especially in the elderly population.
Metformin is significantly excreted by the kidney, and the risk of toxic reactions may be increased in elderly patients with impaired renal function. Care should be taken in dose selection, and it is important to monitor renal function.

Gender: In the pharmacokinetic studies in healthy volunteers, there were no important differences between male and female subjects for either Metformin or Gliclazide.

Pediatrics: There is no pharmacokinetic data available from studies in pediatric subjects of metformin hydrochloride. has been administered in children 8 to 17 years of age. Gliclazide is not recommended in children. Hence ZEFORMINXR is not recommended for use in children.

Surgical procedures

Metformin therapy should be temporarily stopped for any surgical procedure (except minor procedures where restricted intake of food and fluids is not required) and should not be restarted until the patient resumes oral intake and renal function normalizes.

Nursing Mothers

Studies in lactating rats show that metformin is excreted into milk and reaches levels comparable to those in plasma. Because the potential for hypoglycemia in nursing infants may exist with metformin, and because of the effects on nursing animals, the combination of and metformin should be discontinued in nursing mothers.

Pregnancy

Both the drugs in the combination of gliclazide and metformin are contraindicated in pregnancy.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients should be informed that their concentration may be affected if their diabetes is not satisfactorily controlled, especially at the beginning of treatment (see special warnings and precautions.

4.8 ADVERSE REACTIONS

Gastrointestinal disorders:

Vomiting, dyspepsia, flatulence, abdominal pain, upper abdominal distension, loose stools. In 0.7% of patients treated with Metformin hydrochloride, diarrhea was responsible for discontinuation of treatment.

In rare cases, there may be an elevation of liver enzyme levels.

Metabolic complications

Lactic acidosisis a rare but serious reaction that can occur due to metformin. It is fatal in 50% of cases.Risk factors include renal insufficiency . When metformin is implicated as the cause of lactic acidosis, metformin plasma levels > 5 pg/mL are generally found.

The onset of lactic acidosis is associated with nonspecific symptoms such as malaise, myalgias, respiratory distress, nonspecific abdominal distress, increasing somnolence, hypothermia, hypotension and resistant bradyarrhythmias.

Lactic acidosis is characterized by raised blood lactate levels (>5 mmol/L), electrolyte disturbances with an increased anion gap, decreased blood pH, and an increased lactate/pyruvate ratio.

The risk of lactic acidosis may, be significantly decreased by regular monitoring of renal function in patients taking metformin and by use of the minimum effective dose of metformin. In particular, treatment of the elderly should be accompanied by careful monitoring

Lactic acidosis should be suspected in any diabetic patient with metabolic acidosis without evidence of ketoacidosis (ketonuria and ketonemia).

Hypoglycemia

The incidence of hypoglycemia with in clinical trials, as documented by blood glucose values <60 mg/dL, ranged from 11.1% to 11.6% .

Hepatic porphyria reactions and disulfiram-like reactions have been reported with sulfonylureas, including Gliclazide. Hyponatremia has reported with / all other sulfonylureas, in patients who are on other medications or have medical conditions known to cause hyponatremia or increase release of antidiuretic hormone. The syndrome of inappropriate antidiuretic hormone (SIADH) secretion may occur with sulfonylureas, including Gliclazide. Some sulfonylureas may augment the antidiuretic action of ADH and/or increase release of ADH.

Dermatologic Reactions
Porphyria cutanea tarda, photosensitivity reactions, and allergic vasculitis have been reported with sulfonylureas, including Gliclazide. Allergic skin reactions, e.g., pruritus, erythema, urticaria, and morbilliform or maculopapular eruptions, occur in less than 1% of treated patients. These may be transient and may disappear despite continued use of Gliclazide. If these hypersensitivity reactions persist or worsen (e.g., dyspnea, fall in blood pressure, shock), should be discontinued.

Hematologic Reactions
Leukopenia, agranulocytosis, thrombocytopenia, hemolyticanemia, aplastic anemia, and pancytopenia have been reported with sulfonylureas, including Gliclazide.
Vision disturbances: Changes in accommodation and/or blurred vision may occur with. This may be due to changes in blood glucose and may be more pronounced when treatment is initiated. These changes are also seen in untreated diabetic patients and may actually be reduced by treatment.

4.9 OVERDOSAGE

More intense adverse reactions including epigastric discomfort, nausea, and vomiting followed by diarrhea, drowsiness, weakness, dizziness, malaise and headache may be seen due to metformin. Should those symptoms persist, lactic acidosis should be excluded. The combination of and metformin must be discontinued and proper supportive therapy must be instituted Hemodialysis may be useful for removal of accumulated drug from patients in whom metformin overdosage is suspected. Metformin clearance of up to 170 mL/min can occur under good hemodynamic conditions.

Overdosage can produce severe hypoglycemia. Mild episodes of hypoglycemia can be treated with oral glucose. Severe hypoglycemic reactions will require immediate emergency medical treatment. Severe hypoglycemia can be associated with coma, seizure, or neurological impairment and can be treated with glucagon or intravenous glucose. Monitoring and additional carbohydrate intake may be necessary because hypoglycemia may recur after apparent clinical recovery.

5. PHARMACOLOGIC PROPERTIES

5.1 MECHANISM OF ACTION

Gliclazide

Gliclazide reduces blood glucose levels by stimulating insulin secretion from the □-cells of the islets of Langerhans. Gliclazide shows high affinity, strong selectivity and reversible binding to the β-cell KATP channels with a low affinity for cardiac and vascular KATP channels. Increased postprandial insulin and C-peptide secretion persists after two years of treatment.

In type II diabetes, gliclazide restores the first- peak of insulin secretion in response to glucose and increases the second phase of insulin secretion. A significant increase in insulin release is seen in response stimulation induced by a meal or glucose.
Gliclazide also has extra-pancreatic effects and haemovascular properties.
It has been shown to increase peripheral insulin sensitivity:
- In muscle, euglycaemic hyperinsulinaemic clamp studies with gliclazide have demonstrated significantly increased (35%) insulin mediated glucose uptake which may improve diabetes control. Gliclazide potentiates insulin action on muscle glycogen synthase. These effects are consistent with a posttranscriptional action of gliclazide on GLUT4 glucose transporters.
- Studies on glucose turnover have further shown that gliclazide decreases hepatic glucose production, leading to an improvement in fasting blood glucose levels.
Gliclazide has been shown in some studies to have actions independent of that on glucose levels. These haemovascular effects of gliclazide include:
- Partial inhibition of platelet aggregation and adhesion with a decrease in markers of platelet activation (beta thromboglobulin, thromboxane B2).
- Increased vascular endothelial fibrinolytic activity (increased tPA activity).
- Anti-oxidant properties, notably a reduction in plasma lipid peroxides and increased erythrocyte superoxide dismutase activity.
- Inhibition of the increased adhesiveness of type II diabetic patient's monocytes to endothelial cells in vitro.
The anti-oxidant, platelet inhibiting and fibrinolytic actions of gliclazide involve processes which
have been implicated in the pathogenesis of vascular complications of type II diabetes. There is no clinical evidence that the haemovascular effects of gliclazide are of therapeutic benefit in type II diabetes patients.

Metformin

Metformin is a biguanide with antihyperglycaemic effects, lowering both basal and postprandialplasma glucose. It increases insulin sensitivity but does not stimulate insulin secretion. Metformin reduces blood glucose levels probably via:
• reducing hepatic glucose production by inhibiting gluconeogenesis
• increasing the transport capacity of membrane glucose transporters (GLUT) and thus improving peripheral glucose uptake and utilisation in skeletal muscles, and
• delaying intestinal glucose absorption.
Metformin also increases glycogen synthase activity and stimulates intracellular glycogen synthesis.
In humans, independently of its action on glycaemia, metformin has favourable effects on lipid metabolism. This has been shown at therapeutic doses in controlled, medium-term and long-term clinical studies: metformin reduces total cholesterol, LDL-cholesterol and triglyceride levels.

5.2 PHARMACODYNAMIC PROPERTIES

Gliclazide and metformin are oral blood-glucose-lowering drugs used for the management of type 2 diabetes. (Sulfonylurea class) is an insulin secretagogue used in the management of type 2 diabetes . selectively closes ATP K+ channels in the functioning beta cells of the pancreas and increases insulin secretion. It does not close the ATP K+ channels in the heart. Metformin hydrochloride (Biguanide class) is an insulin sensitizer. It inhibits the hepatic output of glucose and increases peripheral utilization of glucose. Both metformin and are used to improve glycemic control in adults with type 2 diabetes mellitus.

5.3 PHARMACOKINETIC PROPERTIES

Co-administration of a single dose of 500 mg Metformin hydrochloride and did not result in any changes in metformin pharmacokinetics as AUC; Cmax as well as Tmax were unchanged

	Metformin	**Gliclazide**
Absorption	The mean Cmax values were 473 ± 145, 868 ± 223, 1171 ± 297, and 1630 ± 399 ng/mL for single doses of 500, 1000, 1500, and 2500 mg For AUC, the mean values were 3501 ± 796, 6705 ± 1918, 9299 ± 2833, and 14161 ± 4432 ng·hr/mL for single doses of 500, 1000, 1500, and 2500 mg, respectively. Low-fat and high-fat meals increased the systemic exposure (as measured by AUC) from Metformin hydrochloride tablets by about 38% and 73%, respectively, relative to fasting.	The peak drug concentrations (Cmax) 2 to 3 hours post-dose. When gliclazide was given with meals, the mean Cmax and AUC (area under the curve) were decreased by 8% and 9%, respectively. The mean AUC at steady state for the older patients is about 13% lower than that for the younger patients.
Distribution	The apparent volume of distribution (V/F) of metformin following single oral doses of 850 mg immediate release metformin hydrochloride averaged 654 ± 358 L. Metformin partitions into erythrocytes, most likely as a function of time.	The volume of distribution (Vd) was 8.8 L (113 mL/kg).
Metabolism	Metformin does not undergo hepatic metabolism	Gliclazide is completely metabolized by oxidative biotransformation. Cytochrome P450 2C9 causes the biotransformation of gliclazide to cyclohexylhydroxy methyl derivative (M1 derivative). M1 is further metabolized to the carboxyl derivative M2 by one or several cytosolic enzymes. M2 is inactive

Excretion	Metformin is excreted unchanged in the urine by tubular secretion. Approximately 90% of the absorbed drug is eliminated via the renal route within the first 24 hours Renal clearance is approximately 3.5 times greater than creatinine clearance.	80-90% of M1 and M2 are recovered in the urine. No parent drug is recovered from urine or feces. The mean weight-adjusted clearance for the older patients is about 11% higher than that for the younger patients No biliary excretion has been observed.
Half life	In blood, the elimination half-life is approximately 17.6 hours, suggesting that the erythrocyte mass may be a compartment of distribution.	
Plasma protein binding	Negligible	Protein binding is greater than 99.5%.

6. NONCLINICAL PROPERTIES

6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY

Preclinical data reveal no special hazards for humans based on conventional studies of repeated dose toxicity and genotoxicity. Long term carcinogenicity studies have not been done. No teratogenic changes have been shown in animal studies, but lower foetal body weight was observed in animals receiving doses 9.4-fold higher than the maximum recommended dose in humans. Fertility and reproductive performance were unaffected after gliclazide administration in animal studies

7. DESCRIPTION

ZEFORMIN XR 30:

ZEFORMIN XR 30 is supplied for oral administration, as an uncoated bilayered sustained release tablet of Gliclazide & Metformin Hydrochloride. Each uncoated bilayered sustained release tablet of ZEFORMIN XR 30 contains Gliclazide 30 mg & Metformin Hydrochloride 500 mg.

ZEFORMIN XR 60:

ZEFORMIN XR 60 is supplied for oral administration, as an uncoated bilayered sustained release tablet of Gliclazide & Metformin Hydrochloride. Each uncoated bilayered sustained release tablet of ZEFORMIN XR 60 contains Gliclazide 60 mg & Metformin Hydrochloride 500 mg.

8. PHARMACEUTICAL PARTICULARS

8.1 INCOMPATIBILITIES

Not Applicable

8.2 SHELF-LIFE

Refer Pack

8.3 PACKAGING INFORMATION
Refer Pack

8.4 STORAGE CONDITION AND HANDING INSTRUCTIONS
Refer Pack

9. PATIENT COUNSELLING INFORMATION

1. Follow all directions given to you by your doctor carefully.
   They may differ to the information contained in this leaflet.
2. If you do not understand the instructions on the box, ask your doctor or pharmacist for help.
3. **How much to take-** Your doctor will tell you how much of this medicine you should take. This will depend on your condition and whether you are taking any other medicines. The starting dose is usually 40 mg (half a tablet) per day. This will be adjusted slowly over several weeks,depending on how well your body responds to the dose.
4. **How to take it -** Swallow the tablets whole with a glass of water. Tablets can be broken in half, however they should not be crushed or chewed.Crushing or chewing the tablets may change the effectiveness of the tablet. Taking these tablets with food can help to minimise the risk of hypoglycaemia.
5. Do not skip meals while taking these tablets.
6. **When to take it -** Take your medicine at about the same time each day, usually with breakfast. Taking it at the same time each day will have the best effect. It will also help you remember when to take them.
7. **How long to take it for -** Continue taking your medicine for as long as your doctor tells you.Gliclazide can help control your diabetes but cannot cure it. Therefore you may have to take it for a long time.Make sure you have enough of this medicine to last over weekends and holiday
8. **If you forget to take it -** If it is almost time for your next dose, skip the dose you missed and take your next dose when you are meant to.Otherwise, take it as soon as you remember (with food), then go back to taking your tablets as you would normally.Missed doses can cause hyperglycaemia (high blood glucose). Do not take a double dose to makeup for the dose that you missed.
   If you double a dose, this may cause hypoglycaemia (low blood glucose).If you are not sure what to do, ask your doctor or pharmacist. If you have trouble remembering to take your medicine, ask your pharmacist for some hints to help you remember.
9. **If you take too much - (overdose)** Immediately telephone your doctor or the Poisons Information Centrr(telephone 13 11 26) for advice, or go to Accident and Emergency at your nearest hospital, if you think that you or anyone else may have taken too much of this medicine.Do this even if there are no signs of discomfort or poisoning. You may need urgent medical attention. If you take too much gliclazide you may experience symptoms of hypoglycaemia (low blood glucose). If not treated quickly, these symptoms may progress to loss of co-ordination, slurred speech, confusion, loss of consciousness and fitting. At the first signs of hypoglycaemia (low blood glucose), raise your blood glucose quickly by following the instructions at the end of this leaflet. If you experience any of these symptoms, immediately get medical help.
10. **While you are taking this medicine**

Things you must do -If you are about to be started on any new medicine, remind your doctor and pharmacist that you are taking gliclazide.Tell any other doctors, dentists and pharmacists who are treating you that you take this medicine.If you become pregnant while taking this medicine, tell your doctor immediately.Tell your doctor if you are about to have any blood tests. Tell your doctor if you are going to have surgery or are going into hospital.Take your tablets exactly as your doctor has prescribed. Otherwise you may not get the full benefits from treatment. Make sure you check your blood glucose levels regularly.This is the best way to tell if your diabetes is being controlled properly. Your doctor or diabetes educator will show you how and when to do this.Make sure that you, your friends, family and work colleagues can recognise the symptoms of hypoglycaemia (low blood glucose) and hyperglycaemia (high blood glucose) and know how to treat them. Instructions at the end of this leaflet can help you with this.Visit your doctor for regular blood tests and checks of your eyes, feet, kidneys, heart, circulation, blood, and blood pressure.

11. **Follow carefully your doctor's advice** on diet, drinking alcohol and exercise. Tell your doctor immediately if you notice the return of any symptoms of hyperglycaemia that you had before starting gliclazide. These may include lethargy or tiredness, headache, thirst, passing large amounts of urine and blurred vision.These may be signs that gliclazide is no longer working, even though you may have been taking it successfully for some time.
12. **Things you must not do -** Do not give this medicine to anyone else, even if they have the same condition as you. Do not take your medicine to treat any other complaints unless your doctor or pharmacist tells you to. Do not stop taking your medicine or change the dosage without first checking with your doctor.Do not skip meals while taking gliclazide.
13. **Things to be careful of -** Be careful when driving or operating machinery until you know how this medicine affects you. Also, be careful not to let your blood glucose levels fall too low.Gliclazide may cause dizziness and drowsiness in some people. Hypoglycaemia may slow your reaction time and affect your ability to drive or operate machinery. A section at the end of this leaflet contains advice about recognizing and treating hypoglycaemia.Drinking alcohol can make this worse. If either of these occurs, do not drive, operate machinery or do anything else that could be dangerous. If you drink alcohol while taking gliclazide, you may get flushing, headache, breathing difficulties, rapid heartbeat, stomach pains or feel sick and vomit.
14. Protect your skin when you are in the sun, especially between 10am and 3pm.Gliclazide may cause your skin to be more sensitive to sunlight than it is normally. Exposure to sunlight may cause a skin rash, itching, redness, or severe sunburn. If outdoors, wear protective clothing and use a 30+ sunscreen.If your skin does appear to be burning, tell your doctor immediately.
15. If you are travelling, it is a good idea to: • wear some form of identification showing you have diabetes carry some form of sugar to treat hypoglycaemia if it occurs, for example, sugar sachets or jellybeans • carry emergency food rations in case of a delay, for example, dried fruit, biscuits or muesli bars • keep gliclazide readily available
16. If you become sick with a cold, fever or flu, it is very important to continue taking gliclazide, even if you feel unable to eat your normal meal. If you have trouble eating solid food, use sugar-sweetened drinks as a carbohydrate substitute or eat

small amounts of bland food. Your diabetes educator or dietician can give you a list of foods to use for sick days.

17. **How to take** - Metformin XR Follow all directions given to you by your doctor and pharmacist carefully. They may differ from the information contained in this
18. The dose varies from person to person. Your doctor will decide the right dose for you The usual starting dose is 1 tablet (500 mg) once daily with the evening meal. Your doctor may increase the dose slowly, depending on your blood glucose levels. The maximum recommended dose is 2 grams once per day. The elderly and people with kidney problems may need smaller doses.
19. **How long to take** - Metformin XR for Keep taking for as long as your doctor recommends.
20. If you forget to take Metformin XR If it is almost time for your next dose, skip the dose you missed and take your next dose when you are meant to. Otherwise, take it as soon as you remember, and then go back to taking your medicine as you would normally. Do not take a double dose to make up for the dose you missed. If you are not sure what to do, ask your doctor or
21. **Things to be careful of** If you have to be alert, for example when driving, be especially careful not to let your blood glucose levels fall too low. Low blood glucose levels may slow your reaction time and affect your ability to drive or operate machinery. Drinking alcohol can make this worse. However, Metformin XR by itself is unlikely to affect how you drive or operate machinery.

10. DETAILS OF MANUFACTURER

Refer Pack for manufacturer details.

Marketed By
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. D-4, Gala No. 1 to 6 &
11 to 16 Ground Floor, 101 to 106 &
111 to 116 First Floor, 201 to 206 & 211 to 216
2nd Floor, Pimplas, Dist. Thane, Bhiwandi - 421 302, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER

Refer Pack for Permission/License details.

12. DATE OF REVISION

Version 4.0, dated 06/09/2023

For Product Complaints/Adverse events or Queries please write to
webmasterindia@abbott.com