For the use of only a Registered Medical Practitioner or a Hospital or a Laboratory

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Glimepiride Tablets IP 1 mg / 2 mg / 4 mg

Biocon

BLISTO® - 1/2/4 ब्लिस्टो–१/२/४

Composition :
Blisto®- 1
Each film coated tablet contains
Glimepiride IP 1 mg
Excipients q.s.
Colour: Titanium dioxide IP
Blisto®- 2
Each film coated tablet contains
Glimepiride IP 2 mg
Excipients q.s.
Colour: Ponceau 4R
Blisto®- 4
Each film coated tablet contains
Glimepiride IP 4 mg
Excipients q.s.
Colour: Quinoline Yellow

PHARMACEUTICAL FORM
Tablets

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group:
Oral blood glucose lowering drugs: Sulphonamides, urea derivatives; Biguanides

ATC code: A10BB12

Description
Glimepiride, the active ingredient of BLISTO®, is a hypoglycaemic agent belonging to sulfonylurea group.

Clinical Pharmacology
Mechanism of Action :
The Primary mechanism of action of Glimepiride appears to lower blood glucose by stimulating the release insulin through inhibition of pancreatic b-cell ATP-regulated K^+ channels. In addition, effects of Glimepiride also may involve extrapancreatic processes.

In animal studies and in clinical trials in patients with type 2 diabetes. Glimepiride has been shown to increase sensitivity of peripheral tissues to insulin. These finding are consistent with the result of a long term , randomized placebo-controlled clinical trail in which Glimepiride therapy improved postprandial insulin/C-peptide responses and overall glycemia control without producing clinical meaningful increase in fasting insulin/C-peptide levels.

Pharmacokinetics Properties:
Glimepiride is completely (100%) absorbed during fasting or with meals. Glimepiride exhibits complete bioavailability and high plasma protein binding (>99.5%). The drug is completely oxidized in the liver, partly by CYP2C9 and eliminated by formation of hydroxy-methyl and carboxy- metabolites that are excreted renally. The half-life of Glimepiride is about 3.4 ± 2.0 hours. The effects on blood sugar reaches a maximum two to three hours after each dose and duration of action is about 24 hours, which is suitable for once - daily administration. Dividing the dose may not improve the response.

Indication :
Glimepiride is indicated as an adjunct to diet and exercise to lower the blood glucose in patients with non-insulin dependent diabetes mellitus (NIDDM) now better known as type 2 Diabetes whose hyperglycaemia cannot be controlled adequately by diet and exercise alone.

Glimepiride is compatible with Metformin and can be used concomitantly when diet, exercise, or individual drug alone do not result in adequate glycemia control.

Glimepiride is also indicated for use in combination with insulin to lower blood glucose in patients whose hyperglycaemia cannot be controlled by diet and exercise alone.

Glimepiride is also indicated for use in combination with insulin to lower blood glucose in patients whose hyperglycaemia cannot be controlled by diet and exercise in conjunction with an oral hypoglycaemic agent.

Combined use of Glimepiride and insulin may increase the potential for hypoglycaemia.

Dosage and Administration :
There is no fixed dosage regimen for the management of diabetes mellitus with Glimepiride, or any other hypoglycaemic agent. The initial and the maintenance doses are set based on the results of regular checks of the patient's fasting blood glucose, glycosylated haemoglobin and glucose in urine.

The dosage of Glimepiride must be the lowest which is sufficient to achieve the desired metabolic control. The usual starting dosage is 1 to 2 mg once a day with the first meal. After reaching a dose of 2 mg, dosage increases should be made in increments of not more than 2 mg at 1-2 week intervals based upon the patient's blood glucose response. Any increase can be based on regular blood sugar monitoring and should be gradual. The usual maintenance dosage is 4 mg once daily. The maximum recommended dose is 6 mg once daily.

As the control of diabetes improves, sensitivity to insulin increases; therefore Glimepiride requirements may fall as treatment proceed. To avoid hypoglycaemia, a timely dose reduction or cessation of Glimepiride therapy must be considered.

A dose adjustment must also be considered whenever there is a change noticed or documented in patient's weight or life-style. Other factors may also arise causing an increased susceptibility to hypo or hyperglycaemia (see under "Warnings and precautions")

Lower dosage is recommended for elderly patients and those with hepatic or renal disease, who are more likely to become hypoglycaemic.

Contraindication :
1. Hypersensitivity to drug and any of their ingredients.
2. Insulin - dependent (type 1) diabetes mellitus.
3. Diabetic ketoacidosis with or without coma.

Not much evidence has been there concerning the use of Glimepiride in patients with severe impairment of liver function and those on dialysis. In patients with severe impairment of renal or hepatic function a change-over to insulin is indicated.

Warning and Precautions :
Special Warning on risk of cardiovascular mortality
The administration of oral hypoglycaemic drugs has been associated with increased cardio-vasular mortality as compared to treatment with diet alone or diet plus insulin.

All sulphonylurea drugs are capable of producing severe hypoglycaemia. To achieve optimal control of blood sugar, a correct diet, regular and sufficient physical exercise and if necessary reduction of body weight are just as important as regular intake of Glimepride.

Clinical symptoms of inadequately normalised blood sugar (hyperglycaemia) can be, for instance increased urinary frequency, intense thirst, dryness of the mouth and dry skin.
When starting treatment the patient must be informed about the effects and risks of Glimepiride and about its role in conjunction with dietary measures and physical exercise ; the importance of adequate co-operation must also be stressed in the initial weeks of treatment. The risk of hypoglycaemia may be more and necessitates special care and blood sugar monitoring.

Factors labouring hypoglycaemia include :
- Unwillingness or (more commonly in older patients) incapacity of the patient to cooperate.
- Undernutrition, fast food, irregular mealtimes, or skipped meals.
- Imbalance between physical exertion and carbohydrate intake.
- Alterations of diet.
- Consumption of alcohol, especially in combination with skipped meals.
- Impaired renal function.
- Severe impairment of liver function.
- Overdose with Glimepiride.

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Certain uncompensated disorders of the endocrine system affecting carbohydrate metabolism or counter - regulation of hypoglycaemia (as for example in certain disorders of thyroid function and in anterior pituitary or adrenocortical insufficiency).

Concurrent administration of certain other medicines (see "Drug interactions")

If such risk factors for hypoglycaemia are present, may be necessary to adjust the dosage of Glimepiride or the entire therapy. This also applies whenever illness occurs during therapy or the patient's life style changes.

It is known from other sulfonylurea drugs that, despite initially successful countermeasures, hypoglycaemia may recur. Therefore, continued close observation is necessary. Severe hypoglycaemia requires immediate treatment and follow-up by a physician and in some circumstances, hospitalization.

In exceptional stressful situations (e.g. trauma, surgery and infections with fever) blood sugar control may deteriorate, and a temporary change to insulin may be necessary.

During treatment with Glimepiride, glucose levels in blood and urine must be checked regularly, as well as the proportion of glycosylated haemoglobin. Alertness and reactions may be impaired due to hypo-orhyperglycaemia, especially when beginning or after altering treatment, or when Glimepiride is not taken regularly, for example, affect the ability to drive or operate machinery.

Pregnancy & Lactation:
To avoid risk of harmful effects to the foetus, Glimepiride must not be taken during pregnancy; a changeover to insulin is necessary. Patients planning a pregnancy must inform their physician , and must change over to insulin.

Although it is not known whether Glimepiride is excreted in human milk, other sulfonylureas are excreted in human milk. Glimepiride must not be taken by breast -feeding women due to the chances of hypoglycaemic in nursing infant. Either a changeover to insulin or a complete discontinuation of breastfeeding is necessary.

Drug Interactions :
The hypoglycaemic action of sulphonylurea drugs may be potentiated by Certain drugs, including nonsteroidal antiinflammatory drugs and other drugs that are highly protein bound, such as insulin and other oral antidiabetics, ACE inhibitors, allopurinol, anabolic steroids and male sex hormones, chloramphenicol, coumarin derivatives cyclophosphamide, disopyramide, fenfluramine, fenyramidol, fibrates, fluoxetine, guanethidine, ifosfamide, MAO inhibitors, miconazole, para-aminosalicylic acid, pentoxifylline (high dose parenteral), phenylbutazone, azapropazone, oxyphenbutazone, probenecid, quinolones, salicylates, sulfinpyrazone, sulphonamides, tetracyclines, tritoqualine, trofosfamide

Weakening of the blood-sugar-lowering effect and, thus, raised blood sugar levels may occur when one of the following medicines is taken, for example acetazolamide, barbiturates, corticosteroids, diazoxide, diuretics, epinephrine (adrenaline) and other sympathomimetic agents, glucagon, laxatives (after protracted use), nicotinic acid (in high doses), oestrogen and progesterone, phenothiazines, phenytoin, rifampicin, thyroid hormones.

H2 receptor antagonists, clonidine and reserpine may lead to either potentiation or weakening of the blood-sugar-lowering effects.

Beta-blockers decrease glucose tolerance in patients with diabetes mellitus, this may lead to deterioration of metabolic control. In addition beta blockers may increase the tendency to hypoglycaemia (due to impaired counter-regulation)

Under the influence of sympatholytic drugs such as beta-blockers, clonidine, guanethidine and reserpine the sings of adrenergic counter-regulation to hypoglycaemia may be reduced or absent. Both acute and chronic alcohol intake may potentiate or weaken the blood-sugar-lowering action of Glimepiride unpredictably.

Driving a vehicle or operating machinery:
Alertness and reactions may be impaired due to hypoglycemia or hyperglycemia, especially when beginning or after altering treatment or when glimepiride is not taken regularly. This may, for example, affect the ability to drive or to operate machinery.

Side effects :
The most common adverse effects of Glimepiride is Hypoglycaemia, asthenia, dizziness, headache and nausea have also been reported.

Occasionally, allergic or pseudoallergic reactions may occur, e.g. in the form of itching , urticartia or rashes. Such reactions are mild, but may become more serious and are accompanied by dyspnoea and a fall in blood pressure sometimes progressing to shock. If urticaria occur, physician must be notified immediately.

Vomiting, gastrointestinal pain and diarrhoea have been reported, but the incidence is less than 1% in isolated cases, liver transaminase elevations have been reported. Impairment of liver function (e.g. cholestasis and jaundice) and hepatitis may develop possibly resulting in liver failure. Leucopenia, agranulocytosis, thrombocytosis, thrombocytopenia, haemolytic anaemia, aplastic-anaemia and pancytopenia have been reported with Glimepiride, and most often in patients who are on other medications or have medical conditions known to cause hyponatraemia or increase release of antidiuretic hormone. Changes in accommodation and/or blurred vision may occur with the use of Glimepiride. This is thought to be due to changes in blood glucose and may be more prominent treatment should be initiated. This conditions is also seen in untreated diabetic patient, and may actually be reduced after the treatment.

Overdosage:
Overdosage of Glimepiride can induce hypoglycaemic symptoms with loss of consciousness or neurologic finding should be treated aggressively with oral glucose and adjustment with drug dosage and/or meal patterns. Once hypoglycaemia has been corrected, all of the above-mentioned symptoms almost always subside.

PHARMACEUTICAL PARTICULARS
Presentation:
Blisto tablets are available in the strengths of 1 mg,
2 mg and 4 mg in Alu- Alu Foil Strips of 10 tablets each.

Shelf life: Refer carton / blister.

Storage:
Store at a temperature not exceeding 30°C. Protect from light & moisture.
Keep out of reach of children.

Special Precautions for Disposal and Other Handling
Any unused medicinal product or waste material should be disposed off in accordance with local requirements

Marketed by:
Biocon Biologics India Limited
Biocon House, Semicon Park,
Electronics City, Phase - II,
Bengaluru - 560 100, India.

BFALL0808101

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