GLUCOMET

Tablets

Composition
Each coated tablet contains Metformin hydrochloride 850 mg.

Action
Metformin is an oral biguanide hypoglycemic agent. It causes an increased peripheral uptake of glucose by increasing the biological efficiency of available exogenous or endogenous insulin.

The mode of action of metformin may be linked to an increase of insulin sensitivity. It does not stimulate insulin release but does require the presence of insulin to exert its hypoglycemic effect. Possible mechanisms of action include inhibition of gluconeogenesis in the liver, delay in glucose absorption from the gastrointestinal tract and an increase in peripheral uptake of glucose.

Metformin has an antiketogenic activity that is comparable, though inferior, to insulin itself. Metformin lowers both basal and post-prandial blood glucose in diabetic patients but does not cause hypoglycemia in either diabetics or normal individuals.

Pharmacokinetics
Absorption: After oral administration, metformin hydrochloride is absorbed along the entire gastrointestinal mucosa.
After oral administration, Metformin absorption is saturable and incomplete. It is assumed that the pharmacokinetics of metformin absorption is nonlinear.

At usual clinical doses and dosing schedules of Metformin tablets, steady-state plasma concentrations are reached in 24 to 48 hours and are generally less than 1 µg/ml. During controlled clinical trials, maximum Metformin plasma levels did not generally exceed 5 µg/ml, even at maximum doses.

Distribution: Metformin is not bound to plasma proteins.

Metabolism: Metformin is excreted unchanged in the urine and does not undergo hepatic metabolism.

Excretion: In patients with decreased renal function (based on measured creatinine clearance), the plasma half-life of metformin is prolonged and renal clearance is decreased in proportion to the decrease in creatinine clearance, e.g. if creatinine clearance is 10 to 30 ml/min, renal clearance is reduced to 20% of normal.

Indications
- Glucomet is indicated in diet-failed, noninsulin dependent diabetic patients, especially if overweight, either alone as initial therapy or in combination with a sulfonylurea.
- Occasionally, as adjuvant therapy in insulin-dependent diabetic patients who are usually obese and not well controlled with insulin.

Contraindications
- Juvenile diabetes mellitus that is uncomplicated and well regulated on insulin
- Diabetes mellitus regulated by diet alone
- During or immediately following surgery where insulin is essential
- Hypersensitivity to metformin hydrochloride and other biguanides, or to any of the excipients
- Diabetic ketoacidosis, diabetic precoma
- Renal failure or renal dysfunction (creatinine clearance < 60 mL/minute)
- Acute conditions with the potential to alter renal function such as dehydration, severe infection, shock, intravascular administration of iodinated contrast agents.

- Acute or chronic disease which may cause tissue hypoxia such as cardiac failure, recent myocardial infarction, respiratory failure, pulmonary embolism, shock, acute significant blood loss, sepsis, gangrene, pancreatitis
- Severe hepatic insufficiency, acute alcohol intoxication, alcoholism
- History of lactic acidosis
- Lactation

Warnings

Metformin is not recommended for use in children.
Metformin is indicated in the elderly, but not when renal function is impaired.

Adverse Reactions

Metformin is well tolerated. However, gastrointestinal upsets, which are usually minor and transient, may occur**.** They may often be avoided by taking the drug with meals (which is always recommended). Occasionally, a temporary lowering of the dose may be needed. Only 3% of patients have had to discontinue Metformin therapy because of this complication. Therefore, it is important that treatment is not abandoned at the first sign of intolerance, since this has been found to resolve spontaneously, and it is usual for gastrointestinal upsets to disappear within the period during which diabetic control is achieved. It is unusual for these upsets to return and if symptoms occur, an alternative reason should be sought.

Lactic acidosis is a serious and often fatal metabolic complication that has been reported in a number of diseases, including diabetes. It is characterized by acidosis (decreased blood pH); electrolyte disturbances with an increased anion gap and an increased lactate level with altered lactate/pyruvate ratio. Azotemia may also be present. Lactic acidosis often has an insidious onset and non-specific symptomatology. Marked anorexia or unexplained weight loss may indicate the onset and precede the full clinical manifestations of lactic acidosis presenting with nausea, vomiting, hyperventilation, malaise and/or abdominal pain. In the majority of fatal cases, patients with these early symptoms have not been investigated for lactic acidosis. In patients with metabolic acidosis lacking evidence of ketoacidosis (ketonuria and ketonemia), lactic acidosis should be suspected. Lactic acidosis is a medical emergency that must be treated in hospital immediately.

The few cases of lactic acidosis reported with Metformin therapy have occurred in patients with complications. This problem of lactic acidosis with Metformin is unusual, if patients are correctly selected and attention paid to correct diet and dosage.

Precautions

The use of this drug does not dispense with the need for low caloric and low carbohydrate diet.
The usual biological tests must be performed routinely. Serum creatinine should be determined and urine should be checked for ketones before initiating treatment.

Metformin treatment should be stopped 2-3 days before surgery and clinical investigations such as intravenous urography and intravenous angiography. It should be reinstated only after control of renal function has been regained.

The use of Metformin is not recommended in conditions that may cause dehydration, or in patients suffering from serious infections or trauma.

Certain hyperglycaemic drugs (e.g. corticosteroids, thiazide diuretics, oral contraceptives) are liable to modify the trend of the diabetic condition and require either increased dosage, concurrent administration of sulfonylureas, or changing over to insulin.

Metformin used as sole therapy does not induce hypoglycemia. Care should be taken when administering in combination with insulin or sulfonylureas. Monitor blood sugar readings regularly. If it is decided to stabilize diabetic patients with Metformin and insulin therapy, it is recommended that

this is carried out in hospital until the correct ratio of the two drugs is determined, because of the possibility of hypoglycemia.

Patients receiving continuous Metformin therapy should have an annual estimation of vitamin B_{12}, in view of reports of decreased absorption of this substance.

Drug Interactions

Metformin / Anticoagulants
Patients receiving the two drugs may need adjustment of the anticoagulant therapy.

Metformin / Cimetidine
Reduced renal clearance of Metformin has been reported during cimetidine therapy. Therefore, dose reduction should be considered.

Dosage and Administration

It is important that Glucomet be taken in divided doses with meals. The dose should be increased gradually. One tablet twice a day is often enough to provide good diabetic control. This may be achieved within a few days, but it is not unusual for the full effect to be delayed for up to 2 weeks. If control is incomplete, a cautious increase in dosage to 3-4 times daily is justified. Once control has been obtained, it may be possible to reduce the dosage.

Over Dosage

Manifestations
Hypoglycemia is not normally a problem encountered with Metformin when used alone (50 tablets have been ingested with no untoward effects). In combination therapy with a sulfonylurea or insulin or with alcohol, hypoglycemia can occur.

In excessive dosage, particularly if there is a possibility of accumulation, lactic acidosis should be suspected. Some of the signs and symptoms suggestive of this condition are nausea, diarrhea, abdominal pain and dyspnea.

Treatment
Intensive supportive therapy is recommended. It should be particularly directed at correcting fluid loss and metabolic disturbance.

Presentation

Box of 30 coated tablets.