Glucomet®N (Tablets)

1242
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Glibenclamide and Metformin Hydrochloride

Antidiabetic

GLUCOMET®N TABLETS 5:500MG (FILM COATED)

PRESENTATION:

Glucomet®N Tablets 5:500mg: Light yellow, capsule shaped, biconvex, film coated tablet embossed 'COSMOS' on one side and a breakline on the other side. Each film coated tablet contains: Glibenclamide 5mg and Metformin Hydrochloride 500mg.

CLINICAL PHARMACOLOGY:

Glibenclamide is a sulfonylurea antidiabetic. Sulfonylureas appear to have several modes of action, apparently mediated by inhibition of ATP-sensitive potassium channels. Initially, secretion of insulin by functioning islet beta cells is increased. However, insulin secretion subsequently falls again but the hypoglycaemic effect persists and may be due to inhibition of hepatic glucose production and increased sensitivity to any available insulin.

Metformin Hydrochloride is a biguanide hypoglycaemic agent. The biguanide antidiabetics are a class of hypoglycaemic drugs used in the treatment of type 2 diabetes mellitus. They do not stimulate insulin release but require that some insulin be present in order to exert their hypoglycaemic effect. Possible mechanisms of action include delay in the absorption of glucose from the gastro-intestinal tract, an increase in insulin sensitivity and glucose uptake into cells, and inhibition of hepatic gluconeogenesis.

Pharmacokinetics:

Glibenclamide is readily absorbed from the gastro-intestinal tract, peak plasma concentrations usually occuring within 2 to 4 hours, and is extensively bound to plasma proteins. Absorption may be slower in hyperglycaemic patients and may differ according to the particle size of the preparation used. It is metabolised almost completely, in the liver, the principle metabolite being only very weakly active. Approximately 50% of a dose is excreted in the urine and 50% via the bile into the faeces.

Metformin hydrochloride is slowly and incompletely absorbed from the gastro-intestinal tract; the absolute bioavailability of a single 500mg dose is reported to be about 50 to 60%, although this is reduced somewhat if taken with food. Once absorbed plasma protein binding is negligible, and it is excreted unchanged in the urine. The plasma elimination half-life is reported to range from about 2 to 6 hours after oral doses. Metformin is distributed into breast milk in small amounts.

USES:

It is indicated as initial therapy, as an adjunct to diet and excercise , to improve glycaemic control in patients with type 2 diabetes whose hyperglycaemia cannot be satisfactorily managed with diet and exercise alone.

It is indicated as second-line therapy when diet, exercise, and initial treatment with a sulfonylurea or metformin do not result in adequate glycaemic control in patients with type 2 diabetes.

DOSAGE AND ADMINISTRATION:

Starting dose: 2.5mg / 500mg or 5mg / 500mg once or twice daily with meals. The dose should not exceed the maximum recommended daily dose of 20mg Glibenclamide/2000mg Metformin given in divided doses.

CONTRA-INDICATIONS AND WARNINGS:

Precautions:

Sulfonylureas should not be used in type 1 diabetes mellitus. Use in type 2 diabetes mellitus is contra-indicated in patients with ketoacidosis and in those with severe infection, stress, trauma, or other severe conditions where the sulfonylurea is unlikely to control the hyperglycaemia; insulin should be used in such situations.

Insulin is also preferred for therapy during pregnancy. Sulfonylureas with a long half-life such as chlorpropamide or glibenclamide are associated with an increased risk of hypoglycaemia. They should therefore be avoided in patients with impairment of renal or hepatic function, and a similar precaution would tend to apply in other groups with an increased susceptibility to this effect, such as the elderly, debilitated or malnourished patients, and those with adrenal or pituitary insufficiency.

Biguanides are inappropriate for patients with diabetic coma and ketoacidosis or for those with severe infection, stress, trauma, or other severe conditions where the biguanide is unlikely to control the hyperglycaemia; insulin should be administered in such situations. Biguanides

Glucomet®N (Tablets)

should not be given to patients with impairment of renal or hepatic function. Biguanides should also not be given to patients with heart failure, recent myocardial infarction, dehydration, alcoholism, or any other condition likely to predispose to lactic acidosis.

Adverse Effects:

Metformin

Gastro-intestinal disturbances such as anorexia, nausea, vomiting and diarrhoea may occur at the start of treatment. Patients may experience a taste disturbance and there may be weight loss. Absorption of various substances including vitamin B_{12} may be impaired. Lactic acidosis, sometimes fatal, has occurred.

Glibenclamide

Gastro-intestinal disturbances such as nausea, vomiting, heartburn, anorexia, diarrhoea, and a metallic taste may occur and are usually mild and dose-dependant; increased appetite and weight gain may occur. Mild Hypoglycaemia may occur;severe hypoglycemia is usually an indication of overdosage and is relatively uncommon. Other adverse effects include hepatitis and cholestatic jaundice, leucopenia, thrombocytopenia, aplastic anaemia, agranulocytosis, haemolytic anaemia, erythema multiforme or the Steven-Johnsons syndrome, exfoliative dermatitis and erythema nodosum.

Overdosage:

Hypoglycaemia is the most common adverse effect that occurs incase of overdosage. In cases where the hypoglycaemic is mild it is treated immediately by giving oral glucose, activated charcoal can also be given. In case of severe hypoglycemia patient should be taken to the hospital Vital signs should be monitored and appropriate supportive measures used. Observation should continue for several days in case hypoglycaemia is prolonged or recurs. Lactic acidosis occurs in case the dose of metformin is increased above 85mg. This can be treated or reduced by haemodialysis.

Interactions:

An increased hypoglycaemic effect has occurred or might be expected with ACE inhibitors, alcohol, allopurinol, some analgesics (notably azapropazone, phenylbutazone, and the salicylates), azole antifungals (fluconazole, ketoconazole and miconazole), chloramphenicol, cimetidine, clofibrate and related compounds, coumarin anticoagulants, fluoroquinolones, heparin, MAOIs, octreotide (although this may also produce hyperglycaemia), ranitidine, sulfinpyrazone, sulfonamides (including co-trimoxazole), tetracyclines, and tricyclic antidepressants. Beta blockers have been reported both to increase hypoglycaemia and to mask the typical sympathetic warning signs.

Use of biguanides concomitantly with other drugs that lower blood sugar concentrations increase the risk of hypoglycaemia, while drugs that increase blood glucose may reduce the effect of biguanide therapy.

Alcohol may increase the risk of lactic acidosis as well as of hypoglycaemia. Care should be taken if biguanides are given concomitantly with drugs that may impair renal function.

PHARMACEUTICAL PRECAUTIONS:

Store in a dry place below 30°C. Protect from light. Keep all medicines out of the reach of children.

LEGAL CATEGORY:

Prescription Only Medicine (POM)

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COSMOS

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