

CTD MODULE 1
ADMINISTRATIVE INFORMATION AND
PRODUCT INFORMATION

Product Name :	GLYCOREN TABLETS (Glibenclamide Tablets 5mg)
-----------------------	---

1.5 Product Information: GLYCOREN TABLETS

1.5.1 Prescribing information (Summary of products characteristics):

1. Name of the Medicinal Product: GLYCOREN TABLETS

Strength:Glibenclamide 5mg

Pharmaceutical form:Tablet

2. Qualitative and Quantitative composition:

Qualitative composition:

Sr. No.	Ingredient	Specification	Uses
1	Glibenclamide	BP	Active
2	Lactose	BP	Diluent
3	Maize starch (For Paste)	BP	Binder
4	Sodium starch Glycollate	BP	Disintegrant
5	Poly Sorbate 80	BP	Dispersing agent
6	Sodium methyl paraben	BP	Preservative
7	Sodium propyl paraben	BP	Preservative
8	Purified Talc	BP	Glidant
9	Colloidal silicon dioxide	BP/USP	Glidant
10	Sodium starch Glycollate	BP	Disintegrant
11	Magnesium Stearate	BP	Lubricant

Quantitative composition:

Sr. No.	Ingredient	Specification	Quantity mg per tablet
1	Glibenclamide	BP	5.000
2	Lactose	BP	144.190
3	Maize starch (For Paste)	BP	5.010
4	Sodium starch Glycollate	BP	7.500
5	Poly Sorbate 80	BP	2.000
6	Sodium methyl paraben	BP	0.200
7	Sodium propyl paraben	BP	0.100
8	Purified Talc	BP	2.000
9	Colloidal silicon dioxide	BP/USP	4.000
10	Sodium starch Glycollate	BP	7.500
11	Magnesium Stearate	BP	2.500

CTD MODULE 1
**ADMINISTRATIVE INFORMATION AND
PRODUCT INFORMATION**

Product Name :	GLYCOREN TABLETS (Glibenclamide Tablets 5mg)
-----------------------	---

3. Pharmaceutical form: Tablet

4. Clinical particular's:

4.1 Therapeutic indication:

Non-insulin dependent diabetes mellitus (type II): glibenclamide is used as an adjunct in patients whose hyperglycaemia cannot be controlled by diet alone.

4.2 Posology and method of administration:

Glibenclamide is usually administered as a single daily dose preferably given 30 minutes before breakfast or the first main meal. For requirements of greater than 10 mg daily, divided doses may be prescribed usually as a twice-daily regimen. The doses and scheduling should be individualized according to the patient's meal pattern and blood or urine glucose response.

Regular monitoring is required.

Initial Dosage in Previously Untreated Patients:

Adult Dose: Initially one 2.5mg tablet daily before breakfast should be given. If necessary the dose may be increased by 2.5mg increments until the diabetes is under control. As a rule, maximum effect is obtained with a daily dose of three 5mg tablets. Daily doses of up to two 5mg tablets can be taken as a single dose before breakfast, but any excess over this should be taken before the evening meal. A dose of four 5mg tablets should be divided into two tablets before breakfast, one tablet before lunch and one tablet before the evening meal.

Debilitated, malnourished or elderly patients, or those with impaired renal or hepatic function:

One 2.5mg tablet daily is recommended initially. Patients should have their blood or urine glucose monitored every 3 to 5 days and if a dosage increase is deemed necessary increments of not more than 2.5mg daily should be prescribed at weekly intervals.

Initial dosage in patients transferred from other antidiabetic agents:

Sulphonylureas: the switch to glibenclamide can be immediate. An initial dose of 10 mg should not be exceeded. Subsequent dosage adjustments are based on the patient's blood or urine glucose response. If patients were on chlorpropamide they should be closely monitored for hypoglycaemia for the first 2 weeks of the transition.

Insulin: on rare occasions, Type II diabetic patients receiving insulin may be transferred to glibenclamide. For doses less than 40 units daily, 2.5mg to 5mg is prescribed initially and insulin can be discontinued abruptly. For doses greater than 40 units daily, 5mg of glibenclamide may be prescribed whilst the insulin dose is reduced by 50%. Insulin is then withdrawn gradually and glibenclamide increased by 1.25mg to 2.5mg daily every 2 to 10 days as necessary.

Biguanides: 2.5mg glibenclamide can be substituted for the biguanide initially and adjusted as required after 3 to 5 days. On occasion, glibenclamide may be prescribed

CTD MODULE 1
ADMINISTRATIVE INFORMATION AND
PRODUCT INFORMATION

Product Name :	GLYCOREN TABLETS (Glibenclamide Tablets 5mg)
-----------------------	---

together with metformin if control is not adequate with either agent alone. Clinical benefit of the combination should be monitored from time to time.

Maintenance dose: Dosage usually ranges from 1.25 mg to 15 mg. The maximum daily dose is 20 mg.

Children:

Glibenclamide is not indicated in children, as Type II diabetes mellitus is not usual in this age group. Dosage or effectiveness has not been established.

Method of Administration: Oral route.

4.3 Contraindication:

- Glibenclamide should not be given as sole therapy to patients with unstable and/or Insulin dependent diabetes mellitus (Type I)
- Patients with ketoacidosis or diabetic coma
- Trauma or surgery
- Severe infection
- Obvious jaundice
- In the presence of severe hepatic or renal impairment.
- Glibenclamide is also contra-indicated in patients with known hypersensitivity or allergy to the drug.
- Pregnancy

4.4 Special warning and precaution for use:

Dietary management with or without weight reduction is the principal therapy for the management of Type II diabetes mellitus. Oral hypoglycaemic agents or insulin should only be used after these measures have failed by themselves.

Hypoglycaemia: may be severe and has occasionally been fatal thus necessitating careful monitoring and selection of both patient and dosage. Hypoglycaemia is more likely in elderly patients, those who are debilitated or who have impaired hepatic or renal function. Alcohol, severe or prolonged exercise, inadequate caloric intake, certain medicines (see drug Interactions), severe endocrine disorders, and adrenal or pituitary insufficiency may also predispose patients to hypoglycaemia. It may be necessary to institute insulin during illness, stress or surgery.

Regular monitoring of blood and/or urine glucose: It is necessary to determine the minimum effective dose; to detect primary failure (inadequate lowering of blood glucose concentration at the maximum recommended dosage); or secondary failure (loss of control of blood glucose following an initial period of effectiveness). If secondary failure occurs, glibenclamide should usually be discontinued. However, some clinicians may initially evaluate the addition of a low dose insulin regimen.

CTD MODULE 1
ADMINISTRATIVE INFORMATION AND
PRODUCT INFORMATION

Product Name :	GLYCOREN TABLETS (Glibenclamide Tablets 5mg)
-----------------------	---

4.5 Interactions with other medicinal products and other forms of interactions:

Other medicines given at the same time as sulphonylureas may cause undesirable depression or elevation of the blood sugar level.

The hypoglycaemic action of glibenclamide may be potentiated by ACE inhibitors, aminosalicic acid, anabolic steroids, β -receptor blockers, bezafibrate, biguanides, chloramphenicol, clofibrate, clonidine, co-trimoxazole, coumarin derivatives, disopyramide, fenfluramine, fluoxetine, gemfibrozil, guanethidine, heparin, MAOI's, miconazole, parenteral high dose oxpentifylline, phenylbutazone, phenyramidol, phosphamides, probenecid, quinolone antibiotics, ranitidine, reserpine, salicylates, sulphinpyrazone, tritoqualine, tetracycline compounds and certain long acting sulphonamides. Highly protein bound agents may also potentiate the hypoglycaemic action due to glibenclamide displacement from plasma proteins including oral anticoagulants, hydantoins, salicylates and other NSAIDs.

Medicines which may produce hyperglycaemia or diminish the hypoglycaemic effect of glibenclamide include alcohol, acetazolamide, calcium channel blockers, cimetidine, clonidine, diazoxide, corticosteroids, glucagon, isoniazid, high dose nicotinic acid, oestrogens, progestogens, phenothiazine derivatives, phenytoin, ranitidine, rifampicin, ritodrine, saluretics,

sympathomimetic agents, thyroid hormones and large doses of laxatives. Concomitant treatment with β -receptor blockers or clonidine may mask the warning symptoms of a hypoglycaemic attack.

Potentiation or attenuation of the blood sugar lowering effect of glibenclamide has been observed during concomitant therapy with H₂-receptor antagonists.

Intolerance to alcohol may occur. Excessive alcohol ingestion by people who drink occasionally may attenuate the hypoglycaemic effect of glibenclamide or dangerously potentiate it by delaying its metabolic inactivation. Disulfiram-like reactions have occurred very rarely following the concomitant use of alcohol and glibenclamide.

Additional information on special populations:

Elderly: In debilitated patients or aged patients who may be more liable to hypoglycaemia, treatment should be initiated with one 2.5mg tablet daily.

Paediatric population:

Glibenclamide is not recommended for use in children.

4.6 Fertility, pregnancy and lactation:

Category C.

It is important to achieve strict normoglycaemia during pregnancy. Oral hypoglycaemic agents should be replaced by insulin. The sulphonylureas may enter the foetal circulation and cause neonatal hypoglycaemia. In animal studies embryotoxicity and/or birth defects have been demonstrated. If glibenclamide is used during pregnancy it should be discontinued at least two weeks before the expected delivery date to avoid severe hypoglycaemia in the neonate following delivery.

CTD MODULE 1 ADMINISTRATIVE INFORMATION AND PRODUCT INFORMATION	
Product Name :	GLYCOREN TABLETS (Glibenclamide Tablets 5mg)

Use in Lactation

It is not known whether glibenclamide is excreted in breast milk or whether it has a harmful effect on the newborn infant. Other sulphonylureas have been found in breast milk and therefore glibenclamide is not recommended for nursing mothers unless the expected benefits outweigh any potential risks.

4.7 Effects on ability to drive and use machines:

Until optimal control has been achieved, when changing the antidiabetic preparation, or when the tablets have not been taken regularly, alertness and reaction time may be altered to such an extent that the patient cannot safely cope with road traffic or operate machinery.

4.8 Undesirable effects:

Adverse effects serious enough to require discontinuation of therapy are uncommon however if adverse effects persist glibenclamide should be discontinued.

Hypoglycaemia:

May be not only severe but also prolonged and fatal (see Warnings and Precautions).

Gastrointestinal:

Gastrointestinal effects e.g. nausea, vomiting, epigastric fullness or sensation of pressure, heartburn, anorexia, dyspepsia and diarrhoea are the most common adverse reactions and occur in 1-2% of patients. Effects tend to be dose related and may disappear when dosage is reduced. Pancreatitis has been reported rarely.

Dermatological:

Allergic skin reactions to sulphonylureas such as pruritus, erythema, urticaria, and erythematous, maculopapular and bullous skin eruptions or psoriasiform drug eruption occur in 1.5% of treated patients. These may be transient and may disappear despite continued use of glibenclamide. If they persist glibenclamide should be discontinued. Porphyria cutanea tarda, pellagra-like changes and photosensitivity reactions have been reported with sulphonylureas.

Haematological:

Anaemia, leucopenia, thrombocytopenia, thrombocytopenic purpura, agranulocytosis, pancytopenia, eosinophilia, haemolytic anaemia, aplastic anaemia, bone marrow aplasia and coagulation disorders have been reported with sulphonylureas.

Hepatic:

Increased hepatic enzymes (AST, ALT), abnormal hepatic function, cholestasis, cholestatic hepatitis, granulomatous hepatitis and bilirubinaemia have been reported with sulphonylureas.

Miscellaneous:

Although a causal relationship has not been established, the following adverse effects have been reported in patients receiving glibenclamide: paraesthesia, blindness, deafness, diplopia, visual disturbances, tremor, convulsions, encephalopathy, confusion, acute psychosis, abnormal renal function, acute renal failure, ocular disturbances, lactic

CTD MODULE 1 ADMINISTRATIVE INFORMATION AND PRODUCT INFORMATION	
Product Name :	GLYCOREN TABLETS (Glibenclamide Tablets 5mg)

acidosis, alopecia/hypotrichosis, hyponatraemia, syndrome of inappropriate secretion of antidiuretic hormone, arthralgia, arthritis, cerebrovascular disorders, headache, facial oedema, angioedema, hypersensitivity vasculitis and increased sweating.

4.9 Overdose and Treatment:

Over dosage of sulphonylureas including glibenclamide can produce hypoglycaemia. In acute poisoning, the stomach should be emptied by aspiration and lavage. Hypoglycaemia may be treated with glucose tablets or powder or 3 to 4 teaspoons of sugar mixed with a little water. This should be followed by a snack of complex carbohydrate e.g. a sandwich. Alternatively, 1 mg glucagon may be administered subcutaneously or intramuscularly in the absence of oral glucose. If the patient is comatose or the hypoglycaemia is severe, glucose should be given as an intravenous infusion. The patient should be observed over several days in case hypoglycaemia recurs.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties:

Pharmacotherapeutic Group: Sulfonamides, Urea derivatives- ATC code: A10BB01.
Glibenclamide is an orally active hypoglycaemic agent which acts by stimulating insulin secretion.

5.2 Pharmacokinetic properties:

Glibenclamide is rapidly absorbed and is extensively bound to plasma proteins, but is not readily displaced by acidic drugs. The drug is metabolised extensively in the liver and excreted as metabolites in the urine and bile.

5.3 Preclinical safety data:

There are no pre-clinical data of any relevance to the prescriber, which are additional to those already included in other sections.

6. Pharmaceutical Particulars:

6.1 List of excipients

Glycoren tablets contains the following excipients:

Maize starch, Lactose monohydrate, Sodium starch glycollate, Poly sorbate 80, Sodium methyl paraben, Sodium propyl paraben, Colloidal silicon dioxide, Purified talc and magnesium stearate.

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precaution for storage

Store in cool & dry place. Below 30°C.

CTD MODULE 1
**ADMINISTRATIVE INFORMATION AND
PRODUCT INFORMATION**

Product Name :	GLYCOREN TABLETS (Glibenclamide Tablets 5mg)
-----------------------	---

6.5 Nature and contents of container

10 tablets are packed in Aluminium/PVC blister; such tenblisters are packed in a unit carton along with literature insert.
1000 Tablets packed in polythene bag and contained in HDPE Container with leaflet.

6.6 Special precautions for disposal

No special precaution.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES:

Marketing Authorization Holder:

Rene Industries Ltd

Address : PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

Manufactured by:

Rene Industries Ltd

Address : PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

8. MARKETING AUTHORISATION NUMBER:

Not Applicable

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION:

Not Applicable

10. DATE OF REVISION OF THE TEXT:

Not Applicable

11. DOSIMETRY (IF APPLICABLE):

Not Applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE):

Not Applicable