SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINE
GLANIL® Glibenclamide

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
GLANIL® Each tablet contains 5 mg of glibenclamide.
Excipients of known effect: Lactose monohydrate
For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM
Capsule shaped tablets

GLANIL® is a White, biplane oblong tablet with a score-line on both sides. GLI is engraved each side of the score-line and inverted. The other side is plain.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
GLANIL® is indicated as an adjunct to diet to lower the blood glucose in patients with non-insulin-dependent diabetes mellitus (type 2) whose hyperglycaemia cannot be controlled by diet alone. GLANIL® is often suitable for the management of patients who have failed to respond to other oral antidiabetics.
In initiating treatment for non-insulin-dependent diabetes, diet should be emphasised as the primary form of treatment. Caloric restriction and weight loss are essential in the obese diabetic patient. Proper dietary management alone may be effective in controlling the blood glucose and symptoms of hyperglycaemia. The importance of regular physical activity should also be stressed, and cardiovascular risk factors should be identified and corrective measures taken where possible. If this treatment programme fails to reduce symptoms and/or blood glucose the use of an oral sulphonylurea should be considered. Use of GLANIL® must be viewed by both the physician and patient as a treatment in addition to diet, and not as a substitute for diet or as a convenient mechanism for avoiding dietary restraint.

4.2 DOSE AND METHOD OF ADMINISTRATION
In principle, the dosage of glanil is governed by the desired blood sugar level. The dosage of glanil must be the lowest which is effective. Treatment with glanil must be initiated and monitored by doctor. The patient must take glanil at the times and in the doses prescribed by the doctor.

Mistakes, e.g. forgetting to take a dose, must never be corrected by subsequently taking a larger dose. Measures for dealing with such mistakes (in particular forgetting a dose or skipping a meal), or in the event a dose cannot be taken at the prescribed time, must be discussed and agreed between the Doctor and patient beforehand.

Initial Dose and dose titration
The usual initial dosage is ½ to 1caplet Glanil once daily.
It is recommended that treatment be started with the smallest possible dose. This applies in particular to patients who are prone to hypoglycaemia or who weigh less than 50kg.
It is recommended that the dose be increased gradually and not more than ½ to 1caplet at interval of one to two weeks and the increase be guided by regular blood sugar monitoring.
Secondary dosage adjustment
Glibenclamide requirements may fall as treatment proceeds. To avoid hypoglycaemia, timely dose reduction or cessation of

Glanil therapy must therefore be considered.
Correction of dosage must also be considered, whenever:
- the patients weight changes
- the patients life-style changes
- other factors arise, which cause an increased susceptibility to hypoglycaemia or hyperglycaemia(see 4.4)

Duration of treatment
Treatment with Glanil is normally a long-term treatment.

Changeover from other oral antidiabetics to Glibenclamide
Changeover from other oral antidiabetic agents to Glibenclamide should be done under the supervision of a specialist,
and due to the potential summation of effects of both medications, entails a risk of hypoglycaemia. A break from
medication may therefore be required when changing over medications. This should be decided by the attending
physician.

4.3 CONTRAINDICATIONS
Glanil should not be used in patients who have or ever had diabetic ketoacidosis or diabetic coma/precoma or
in patients who have insulin-dependent diabetes mellitus, serious impairment of renal, hepatic or adrenocortical
function, in patients who are hypersensitive to glibenclamide or any of the excipients or in circumstances of unusual
stress, e.g. surgical operations or during pregnancy, when dietary measures and insulin are essential.
Glanil should not be used in the following:
Pregnancy
Breast feeding mothers
Children and Patients with sulphonylurea or sulphonamide intolerance
Bosentan

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
The treatment of diabetes requires regular checks. Until optimal control is achieved, or when changing from one product to another, or when caplets are not taken regularly, the patient's alertness and capacity to react may be impaired to such an extent that he or she may not be fit to drive, or to operate machinery. When situations of unusual stress arise (e.g. trauma, emergency or elective surgery, febrile infections), blood glucose regulation may deteriorate and a temporary change to insulin may become necessary to maintain good metabolic control.
It should be borne in mind that there is a possibility of cross-sensitivity to sulphonamides and their derivatives. Persons allergic to other sulphonamide derivatives may develop an allergic reaction to glibenclamide as well.
Epidemiological studies suggest that the administration of glibenclamide is associated with an increased risk of cardiovascular mortality, when compared to treatment with metformin or gliclazide. This risk was especially observed in patients with diagnosed coronary diseases.
Hypoglycaemic Reactions
Severe hypoglycaemia, which may be prolonged and is potentially lethal, can be induced by all sulphonylureas.
Debilitated, malnourished, or geriatric patients and patients with mild disease or impaired hepatic or renal function should be carefully monitored and dosage of Glanil should be carefully adjusted in

these patients, since they may be predisposed to developing hypoglycaemia. Renal or hepatic insufficiency may cause increased serum concentrations of glibenclamide and hepatic insufficiency may also diminish gluconeogenic capacity, both of which increase the risk of severe hypoglycaemic reactions.
If risk factors for hypoglycaemia are present, it may be necessary to adjust the dosage of Glanil or the entire therapy.

Elderly patients are particularly susceptible to hypoglycaemic action of glucose-lowering drugs. Hypoglycaemia may be difficult to recognise in the elderly. The initial and maintenance dosing should be conservative to avoid hypoglycaemic reactions.
Hypoglycaemia can, almost always, be promptly controlled by immediate intake of carbohydrates (glucose or sugar).

Patients receiving Glanil should be monitored with regular clinical and laboratory evaluations, including blood and urine glucose determinations, to determine the minimum effective dosage and to detect primary failure (inadequate lowering of blood glucose) concentration at the maximum recommended dosage) or secondary failure (loss of control of blood glucose concentration following an initial period of effectiveness) to the drug.

During the withdrawal period in patients in whom glibenclamide is replacing insulin, patients should be instructed to test their urine for glucose and ketones at least 3 times daily, and to report the results to their Doctor; when feasible, patient or laboratory monitoring of blood glucose concentration is preferable.
Care should be taken to avoid ketosis, acidosis and coma during the withdrawal period in patients being switched from insulin to glibenclamide. If adequate lowering of blood glucose concentration is no longer achieved during maintenance therapy with glibenclamide, the drug should be discontinued.

Patients and responsible family members should be made aware of the signs and symptoms of hyperglycaemia and hypoglycaemia and the prompt action required in the event of such occurrences.
Symptoms of hyperglycaemia include severe thirst, dry mouth, frequent micturition and dry skin. Possible symptoms of hypoglycaemia include intense hunger, nausea, vomiting, sweating, tremor, pareses, sensory disturbances, restlessness, irritability, aggressiveness, depression, confusion, speech disorders, aphasia, visual disorders, impaired concentration, impaired alertness and reactions, headaches, dizziness, disturbed sleep, helplessness, loss of self-control, delirium, transient neurological disorders such as cerebral convulsions, lassitude, sleepiness, somnolence, loss of consciousness up to and including coma, shallow respiration and bradycardia. In addition, signs of adrenergic counter-regulation may be present, such as sweating, clammy skin, anxiety, tachycardia, hypertension, palpitations, angina pectoris and cardiac arrhythmias.
The clinical picture of a severe hypoglycaemic attack may resemble that of a stroke. The symptoms of hypoglycaemia nearly always subside when hypoglycaemia is corrected.

Haemolytic anaemia
Treatment of patients with glucose-6-phospate dehydrogenase (G6PD) deficiency with sulphonylurea agents can lead to haemolytic anaemia. Since glibenclamide belongs to the class of sulphonylurea agents, caution should be used in patients with G6PD-deficiency and a non-sulphonylurea alternative should be considered.
Use in hepatic impairment
See Section 4.3 Contraindications and Section 4.4 Special warnings and precautions for use - Hypoglycaemic Reactions.

Use in renal impairment
See Section 4.3 Contraindications and Section 4.4 Special warnings and precautions for use - Hypoglycaemic Reactions.
Use in the elderly
See Section 4.4 Special warnings and precautions for use - Hypoglycaemic Reactions.
Paediatric use
The safety and efficacy of glibenclamide in children have not been established. Glibenclamide is not recommended for use in this age group.
Effects on laboratory tests
No data available.
4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS
Glanil is mainly metabolized by CYP2C9 and to a lesser extent by CYP3A4. This should be taken into account when glibenclamide is coadministered with inducers or inhibitors of CYP2C9.
Other drugs given at the same time as sulphonylureas may cause undesirable depression or elevation of the blood sugar level.

Drugs which may potentiate the hypoglycaemic action of GLANIL® include insulin, other oral antidiabetic agents, alcohol, ACE inhibitors, aminosalicylic acid, anabolic steroids and male sex hormones, azapropazone, beta-receptor blockers, bezafibrate, biguanides, chloramphenicol, clarithromycin, clofibrate, clonidine, co-trimoxazole, coumarin derivatives, cyclophosphamide monohydrate, disopyramide, fenfluramine, fenyramidol, fibrates, fluoxetine, gemfibrozil, guanethidine, heparin, ifosfamide, MAO-inhibitors, miconazole, pentoxifylline (oxpentifylline) (parenteral, in high doses), oxyphenbutazone, para-aminosalicylic acid, phenylbutazone, phenyramidol, phosphamides, probenecid, quinolone antibiotics, ranitidine, reserpine, salicylates, sulphinpyrazone, certain long-acting sulphonamides, tetracycline compounds, tritoqualine and trophosphamide. Highly protein-bound drugs which may also potentiate the hypoglycaemic action of GLANIL®due to glibenclamide displacement from plasma proteins, include oral anticoagulants, hydantoins, salicylates and other non-steroidal anti-inflammatory agents.
Drugs which may cause an attenuation of the hypoglycaemic action of GLANIL® include adrenaline (epinephrine) and other sympathomimetic agents, alcohol, acetazolamide, barbiturates, calcium channel blockers, cimetidine, clonidine, corticosteroids, diazoxide, diuretics, glucagon, isoniazid, large doses of laxatives, nicotinic acid (high dosage), oestrogens, progestogens, phenothiazine derivatives, phenytoin, ranitidine, rifampicin, ritodrine and thyroid hormones.
Concomitant treatment with beta-receptor blockers, clonidine, reserpine, guanethidine or other sympatholytic drugs may mask the warning symptoms of a hypoglycaemic attack. The symptoms of hypoglycaemia may also be milder or absent where hypoglycaemia develops gradually or where there is autonomic neuropathy. In rare instances, potentiation or attenuation of the blood-sugar-lowering effect of GLANIL® have been observed during concomitant treatment with H2 receptor antagonists, clonidine or reserpine.
In very rare cases, an intolerance to alcohol may occur. Both acute and chronic alcohol intake, or 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.
Glibenclamide may either potentiate or weaken the effect of coumarin derivatives.
Glibenclamide may increase ciclosporin plasma concentration and potentially lead to its increased toxicity. Monitoring and dosage adjustment of ciclosporin are therefore recommended when both drugs are co-administered.
Colesevelam binds to glibenclamide and reduces glibenclamide absorption from the gastro-intestinal tract. No interaction was observed when glibenclamide was taken at least 4 hours before colesevelam. Therefore, glibenclamide should be administered at least 4 hours prior to colesevelam.

An increased incidence of elevated liver enzymes was observed in patients receiving glibenclamide concomitantly with bosentan. Both bosentan and glibenclamide inhibit the bile salt export pump, leading to intracellular accumulation of cytotoxic bile salts. Therefore, this combination should not be used (see Section 4.3 Contraindications).
Food does not alter the bioavailability or other pharmacokinetic parameters of glibenclamide.

4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy

Glanil must not be taken during pregnancy. The patient must change over to insulin during pregnancy.
Animal studies showed some teratogenic effects.

Fertility

Patients planning a pregnancy must inform their doctor. It is recommended that such patients change over to insulin.

Breast-feeding

Glanil must not be taken by breast-feeding women. If necessary, the patient must change over to insulin, or must stop breast-feeding

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Alertness and reactions may be impaired by hypoglycaemic or hyperglycaemic episodes, especially when treatment is changed, or when Glanil is not taken as prescribed by the doctor. This may affect the ability to drive or operate machinery.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical experience in the use of GLANIL® has shown that side effects serious enough to compel discontinuation of therapy are uncommon, even during long-term therapy. However, if adverse effects persist, the drug should be discontinued.

Hypoglycaemia

Hypoglycaemia may not only be severe, but also prolonged and fatal (see Section 4.4 Special warnings and precautions for use - Hypoglycaemic Reactions and Section 4.9 Overdose).

Eye disorders

Especially at the start of treatment, there may be temporary visual impairment due to the change in blood glucose levels. The cause is a temporary alteration in the turgidity and hence the refractive index of the lens, this being dependent on blood glucose level.

Gastrointestinal Reactions

Adverse gastrointestinal effects such as nausea, vomiting, epigastric fullness or sensation of pressure, abdominal pain, anorexia, heartburn, dyspepsia and diarrhoea are the most common adverse reactions to glibenclamide, occurring in about 1-2% of patients. Glibenclamide-induced adverse gastrointestinal effects appear to be dose related and may subside following a reduction in dosage. Pancreatitis has been reported rarely.

Dermatologic Reactions

Hypersensitivity reactions, allergic or pseudoallergic reactions may occur. Allergic skin reactions e.g. pruritus, erythema, urticaria, erythematous and maculo-papular and bullous skin eruptions or psoriasiform drug eruptions occur in 1.5% of treated patients. transient and may disappear despite continued use of glibenclamide; if skin reactions persist, the drug should be discontinued. In isolated cases, mild reactions in the form of urticaria may develop into serious and even life-threatening reactions with dyspnoea and fall in blood pressure, sometimes progressing to shock. In the event of urticaria, a physician must therefore be notified immediately.
A hypersensitivity reaction may be directed against glibenclamide itself, but may alternatively be triggered by excipients. Allergy to sulphonamide derivatives may also be responsible for an allergic reaction to glibenclamide.

In isolated cases, allergic vasculitis may arise and, in some circumstances, may be life-threatening. In isolated cases, hypersensitivity of the skin to light may occur, and sodium concentration in the serum may decrease. Porphyria cutanea tarda and pellagra-like changes have been reported with sulphonylureas.

Haematologic Reactions

Anaemia, leukopaenia, thrombocytopaenia, thrombocytopaenic purpura, agranulocytosis, pancytopaenia, eosinophilia, haemolytic anaemia, aplastic anaemia, bone marrow aplasia, eosinophilia and coagulation disorders have been reported with sulphonylureas. Potentially life-threatening changes in the blood picture may occur. They may include, rarely, mild to severe thrombopaenia (e.g. presenting as purpura) and, in isolated cases, haemolytic anaemia, erythrocytopaenia, granulocytopaenia, agranulocytosis and (for example, due to myelosuppression) pancytopaenia. In principle, these reactions are reversible once glibenclamide has been withdrawn.

Hepatic Reactions

Increased liver enzymes (AST, ALT), abnormal liver function, cholestasis, cholestatic hepatitis, granulomatous hepatitis and bilirubinaemia have been reported with sulphonylureas. In isolated cases there may be hepatitis, elevation of liver enzyme levels and/or cholestasis and jaundice which may progress to life-threatening liver failure but can regress after withdrawal of glibenclamide.

Miscellaneous

Although a causal relationship has not been established, the following adverse effects have been reported in patients receiving glibenclamide: paresthesia, blindness, deafness, diplopia, visual disturbances, tremor, convulsions (other than withdrawal), encephalopathy, confusion, acute psychosis, abnormal renal function, acute renal failure, ocular disturbances (accommodation changes, crystalline lens changes), lactic acidosis, alopecia/hipotrichosis, hyponatraemia, syndrome of inappropriate secretion of antidiuretic hormone (SIADH), arthralgia, arthritis, cerebrovascular disorders, headache, facial oedema, angioedema, weight gain, hypersensitivity vasculitis and increased sweating.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via **ADR e-Reporting Form** online.

4.9 OVERDOSE

Signs and Symptoms

Acute overdose as well as long-term treatment with too high a dose of Glanil may lead to severe, protracted,
life-threatening hypoglycaemia.

Treatment

In case of overdosage with glibenclamide, a doctor has to be called immediately. At the first signs of hypoglycaemia, the patient must immediately take sugar, preferably glucose, unless a doctor has already started care.

Since hypoglycaemia and its clinical symptoms may recur after apparent clinical recovery (even after several days), close and continued medical supervision and possibly referral to a hospital are indicated. In particular, significant overdosage and severe reactions, e.g. with unconsciousness or other neurological dysfunctions, are emergency cases and require immediate care and hospitalisation.

If hypoglycaemic coma is diagnosed or suspected, administration of glucagon (adults: 0.5 - 1 mg) i.v., s.c. or i.m., or i.v. infusion of a 20% glucose solution (adults: 40-100 mL) is indicated, until the patient recovers consciousness.

In infants and young children, glucose must be dosed very carefully, accompanied by close monitoring of blood glucose, taking into account the risk of potentially severe hyperglycaemia. Other symptomatic therapy (e.g. anticonvulsants) should be administered as necessary.

In cases of acute intake of large amounts of Glanil, detoxification e.g. by medicinal charcoal as an absorbent, is indicated.
After acute glucose replacement has been completed, it is usually necessary to give an intravenous glucose infusion in lower concentration to ensure that the hypoglycaemia does not recur. The patient's blood glucose level should be carefully monitored for at least 24 hours. In severe cases with a protracted course, hypoglycaemia, or the danger of slipping back into hypoglycaemia, may persist for several days.

5 PHARMACOLOGICAL PROPERTIES

Oral hypoglycaemia.

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Drugs used in diabetes, Sulfonylureas,
ATC code: A10BB01.

Mechanism of action

Glibenclamide, appears to lower the blood glucose acutely in patients with type 2 diabetes by stimulating the release of insulin from the pancreas, an effect dependent upon functioning beta cells. It acts in concert with glucose (improved sensitivity of beta cells to physiological glucose stimulus) and leads to an insulin secretion in the rhythm of meals. Other mechanisms of the hypoglycaemic action associated with short term therapy appear to include reduction of basal hepatic glucose production and enhancement of peripheral insulin action at post-receptor (probably intracellular) sites.
Glibenclamide also exerts a direct inhibitory effect on glucagon-producing alpha cells of the pancreas and increases the release of somatostatin.
In addition to its blood glucose lowering effect, glibenclamide has a mild diuretic action and increases free water clearance.

5.2 PHARMACOKINETIC PROPERTIES

Glanil is rapidly absorbed and inducing its effect within 3 hours with a duration of up to 15 hours although the half-life(T½) of the drug is 5 to 10 hours. The drug is metabolised extensively in the liver and excreted via bile and urine. It is strongly protein-bound.

5.3 PRECLINICAL SAFETY DATA

Non of clinical relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Monohydrated Lactose,
Maize starch,
Talcum,
Colloidal silicon Dioxide,
Magnesium stearate

6.2 INCOMPATIBILITIES

Not applicable

6.3 SHELF LIFE

3 YEARS

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

Blister packs of 10 X 10 caplets in outer carton.
Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
No special requirements

7 Marketing authorisation holder
SYGEN PHARMACEUTICAL LTD
KM38 LAGOS ABEOKUTA EXPRESSWAY
SANGO OTA
OGUN STATE
NIGERIA

8. Marketing authorisation number

NAFDAC NO:04-2450

9 DATE OF FIRST APPROVAL

Not reported

10 DATE OF REVISION
06 -06- 2024