SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Glibenclamide 5mg Tablets BP
Liamid 5mg Tablets,
Gliken 5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Glibenclamide 5.0mg.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet for oral use

Glibenclamide 5mg Tablets are white, dragee shaped tablets marked, ‘GL’ and ‘5’ either side of a breakline on one face and plain on the reverse.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Glibenclamide is a hypoglycaemic agent indicated in the treatment of non-insulin dependent diabetes in patients who respond inadequately to dietary measures alone.

4.2 Posology and Method of Administration

Posology

Treatement of previously untreated diabetes:

Stabilisation can be started with one 5mg tablet daily with or immediately after breakfast or the first main meal. If control is satisfactory one tablet is continued as the maintenance dose. If control is unsatisfactory, the dose can be adjusted by increments of 2.5 or 5mg at weekly intervals. The total daily dosage rarely exceeds 15mg and increasing the daily dosage above this does not generally produce any additional effect.
The total daily requirement should normally be given as a single dose at breakfast, or with the first main meal. The patient’s diet and activity should be taken into account.

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

*Changeover from other sulphonylureas:*

The changeover to glibenclamide from other drugs with similar mode of action can be carried out without any break in therapy.

Treatment is commenced with the equivalent dose of glibenclamide without exceeding an initial dose of 10mg. If response is inadequate, the dose can be raised in a stepwise fashion to 15mg daily. One 5mg tablet of glibenclamide is approximately equivalent to 1g tolbutamine or glymidine, 250mg chlorpropamide or tolazamide, 500mg acetohexamide, 25mg glibornuride or 5mg glipizide.

Changeover from biguanides: The biguanide should be withdrawn and glibenclamide treatment started with one 2.5mg tablet. The dosage should then be adjusted by increments of 2.5mg to achieve control.

Combination with biguanides: If adequate control is not possible with diet and 15mg of glibenclamide, control may be established by combined administration of glibenclamide and a biguanide derivative.

*Changeover from insulin:*

While it is appreciated that most patients who are on insulin therapy will continue to need it, there may be a few patients, particularly those on low daily doses, who will remain stabilised if transferred from insulin to glibenclamide.

**Method of administration**

Oral administration

4.3 **Contraindications**

Glibenclamide should not be used in the following groups:

i. Those patients who have or have ever had diabetic ketoacidosis or diabetic coma/precoma.
ii. Insulin dependent diabetes mellitus.
iii. Severe impairment of renal, hepatic, thyroid or adrenocortical function.
iv. Circumstances of unusual stress such as surgery, severe infection and trauma.
v. Hypersensitivity to glibenclamide or to any of the excipients listed in section 6.1
vi. 'Brittle' or juvenile diabetes.
vii. Pregnancy
ix. In patients treated with bosentan.

4.4 Special Warnings and Precautions for Use

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine. Treatment with sulphonylureas has been associated with occasional disturbances of liver function and cholestatic jaundice. If clinical jaundice occurs, glibenclamide should be discontinued.

Care is necessary in elderly the following patients:
- Elderly, debilitated or malnourished patients who are particularly susceptible to the hypoglycaemic effects of sulphonylureas.
- During excessive exercise as hypoglycaemia may be provoked.
- Patients with mild to moderate renal impairment. In long-term clinical trials with renal insufficiency have been treated satisfactorily using glibenclamide at reduced doses with careful patient monitoring.
- Patients with adrenal or pituitary insufficiency.

4.5 Interaction with other medicinal products and other forms of Interaction

Bosentan: An increased incidence of elevated liver enzymes was observed in patients receiving glibenclamide concomitantly with bosentan. Both glibenclamide and bosentan inhibit the bile salt export pump, leading to intracellular accumulation of cytotoxic bile salts. Therefore this combination should not be used.

The hypoglycaemic effect of glibenclamide may be increased by: antiinfective agents (eg: chloramphenicol, fluconazole, miconazole, sulphonamides including co-trimoxazole), anti-inflammatory/analgesic agents (e.g.: phenylbutazone, salicylates), dicoumarin anticoagulants and heparin, lipid regulating agents (e.g. clofibrate), some antidepressants (monoamine oxidase inhibitors, doxepin, nortriptyline), ACE-inhibitors captopril, enalapril, H2-blockers, cimetidine, ranitidine, fenfluramine, methylodopa and sulphinpyrazone, necessitating dosage reduction.

The hypoglycaemic effect of glibenclamide may be diminished by rifampicin, thiazide diuretics and beta-blockers, necessitating dosage increase. Betablockers may mask some of the symptoms of hypoglycaemia. Alcohol may interact with the sulphonylureas, provoking facial flushing, and has a variable effect on blood sugar levels.

Glibenclamide may either potentiate or weaken the effect of coumarin derivatives.
Immunosuppressants: there is the potential for glibenclamide to raise plasma levels of ciclosporin, which would necessitate a dose reduction or ciclosporin.

4.6  Fertility, Pregnancy and Lactation

There is no specific information on the use of glibenclamide in human pregnancy, but it has been in wide, general use for many years without apparent ill consequence. It has not yet been established whether glibenclamide is transferred to human milk. However, other sulphonylureas have been found in milk and there is no evidence to suggest that glibenclamide differs from the group in this respect.

4.7  Effects on Ability to Drive and Use Machines

Alertness and reactions may be impaired by hypo- or hyperglycaemic episodes, especially when beginning or after altering treatment, or when Glibenclamide is not taken regularly. This may affect the ability to drive or operate machinery.

4.8  Undesirable Effects

Blood disorders
Potentially life-threatening changes in the blood picture may occur. They may include – rarely – mild to severe, thrombocytopenia (e.g. presenting as purpura), - isolated cases – leucopenia, agranulocytosis and (e.g. due to myelosupression) pancytopenia, haemolytic anaemia, erythrocytopenia, granulocytopenia.

Immune system disorders
Hypersensitivity including dyspnoea and swelling of the lips, face, throat or tongue

Endocrine disorders
Infrequently a syndrome of inappropriate secretion of antidiuretic hormone may be induced which may give rise to reduced serum sodium levels.

Metabolism and nutritional disorders:
Hypoglycaemia

Hypoglycaemia, sometimes prolonged and even life-threatening, may occur as a result of the blood glucose lowering action of Glibenclamide. Possible symptoms of hypoglycaemia include headache, ravenous hunger, nausea, vomiting, lassitude, sleepiness, disordered sleep, restlessness, aggressiveness, impaired concentration, alertness, and reactions, depression, confusion, speech disorders, aphasia, visual disorders, tremor, pareses, sensory disturbances, dizziness, helplessness, loss of self control, delirium, cerebral convulsions, somnolence and loss of consciousness up to and including coma, shallow respiration and bradycardia.
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.

**Eye disorders**
Temporary visual impairment

**Gastrointestinal disorders**
Gastrointestinal disturbances such as nausea, vomiting, heartburn, anorexia, metallic taste, sensations of pressure or fullness in the epigastrium, abdominal pain, diarrhoea may occur.

**Hepatobiliary disorders**
In isolated cases, there may be elevation of liver enzyme levels and even impairment of liver function (e.g. with cholestatic jaundice and hepatitis which can regress after withdrawal of Glibenclamide, although they may lead to life-threatening liver failure.)

**Skin and subcutaneous tissue disorders**
Occasionally, allergic or pseudoallergic reactions may occur, e.g. in the form of itching or rashes.

In isolated cases, photosensitivity may occur, and mild reactions in the form of urticaria may develop into serious and even life-threatening reactions.

Severe manifestations of hypersensitivity include leucopenia, thrombocytopenia, aplastic anaemia, agranulocytosis, haemolytic anaemia, erythema multiforme, Stevens-Johnson syndrome, erythema nodosum and exfoliative dermatitis, fever and cholestatic jaundice.

See also sub-section 4.4 Special warnings and precautions for use.

**Reporting of suspected adverse reactions**
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

**4.9 Overdose**

In acute poisoning activated charcoal may be considered. Hypoglycaemia should be treated urgently in the conscious patient with oral glucose.

If the patient is comatose, glucose should be administered as an intravenous infusion. Bolus glucose injections are not recommended because of the
possibility of rebound hypoglycaemia. Alternatively glucagon, may be administered in a dose of 1mg subcutaneously or intramuscularly to restore consciousness. 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

Lactose monohydrate
Maize Starch
Povidone K30
Magnesium stearate

6.2 Incompatibilities

Not applicable
6.3. Shelf Life

36 months

6.4. Special Precautions for Storage

Polyethylene/polypropylene and glass containers: Do not store above 25°C. Store in the original container. Keep the container tightly closed.


6.5 Nature and Contents of Container

Polypropylene or polyethylene container with polypropylene or polyethylene tamper evident closure containing 100, 500 or 1000 tablets

Glass container with plastic tamper evident closure containing 100, 500 or 1000 tablets.

White opaque blister (250 μm UPVC) 40gsm UPVDC sealed with 20 μm tempered aluminium foil in packs of 28 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Aurobindo Pharma Limited
Ares,
Odyssey Business Park,
West End Road,
South Ruislip HA4 6QD,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 20532/0080
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18/10/2002 / 23/02/2009

10 DATE OF REVISION OF THE TEXT

19/03/2016