SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Glibenclamide 5mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains glibenclamide BP 5mg.
Excipient(s) with known effect
Lactose
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Glibenclamide should be taken with or immediately after food. There were no changes to the reference product information in the report period. The total daily dosage is preferably given as a single dose at breakfast or with the first main meal, but due consideration should be given to the patients meal habits and daily activity when apportioning dosage.

Adults:

New Diabetics:

In maturity-onset diabetes of mild to moderate severity, treatment should be started at 5mg daily, or 2.5mg in debilitated or elderly patients. If this dosage is not sufficient for proper control it should be increased by 2.5mg at intervals of one week, or as directed by the clinician. The total daily dosage rarely exceeds 15mg and increasing the daily dosage above this does not generally produce any additional effect.

Transfer from other oral sulphonylureas:
Transfer to Glibenclamide can usually 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The biguanide should be withdrawn and glibenclamide treatment started with one 2.5mg tablet.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 few patients, particularly those on low dosage, who will remain stabilised if transferred to Glibenclamide.

Patients aged 65 years and older:
Starting and maintenance doses of glibenclamide must be carefully adjusted to reduce the risk of hypoglycaemia. Treatment should be started at the lowest available dose and increased gradually if necessary (see section 4.4).

Children:

No dosage recommendations can be made for the administration of Glibenclamide to children.

Method of administration: Oral

4.3 Contraindications

Glibenclamide should not be used in the following groups:

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

4.4 Special warnings and precautions for use

Patients with rare hereditary problems of galactose intolerance, total 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 the following patients:

- Elderly patients: Age 65 years and older has been identified as a risk factor for hypoglycaemia in patients treated with sulfonylureas. Hypoglycaemia can be difficult to recognise in the elderly. Starting and maintenance doses of glibenclamide must be carefully adjusted to reduce the risk of hypoglycaemia (see section 4.2).
- 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: anti-infective
agents (e.g. chloramphenicol, fluconazole miconazole, sulphonomides including co-trimoxazole), anabolic steroids, anti-inflammatory/analgesics (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, methyldopa and sulphinpyrazone, necessitating dosage
reduction.

The hypoglycaemic effect of glibenclamide may be diminished by rifampicin, thiazide diuretics and beta-blockers, furosemide, ethacrynic acid, phenothiazines, oral
contraceptives containing oestrogens and corticosteroids, necessitating dosage increase. Beta-blockers 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.

Calcium channel blockers and lithium may occasionally impair glucose tolerance.

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 of 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 pancytopenia (e.g. due to myelosupression), 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.

Increased appetite and weight gain may occur.

Eye disorders

Temporary visual impairment.

Gastrointestinal disorders

Gastrointestinal symptoms 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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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

If 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: Sulfonylureas, 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. It is extensively metabolised by the liver and excreted as metabolites in the urine and bile.

5.3 Preclinical safety data

There are no preclinical safety data of relevance to the prescriber, which are additional to those already included in other sections.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, maize starch, gelatin, sodium carboxymethylcellulose, talc and magnesium stearate.

6.2 Incompatibilities

Not known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

(i)	Polypropylene securitainers with polyethylene closures.

(ii)	Amber glass bottles with aluminium rolls on pilfer-proof closures.

Pack sizes: 28, 30, 56, 60, 84, 90, 100, 112, 120, 250, 500 and 1,000.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 55612/0130

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

22/05/2026