Professional Information

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

GLYCOMIN 5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of GLYCOMIN contains 5 mg glibenclamide

Contains sugar: Lactose monohydrate 79,00 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

GLYCOMIN is a white, flat, oblong, bevelled edge tablet, bisected on both sides.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

GLYCOMIN is used as an adjunct in the treatment of maturity-onset (Type II) diabetes in patients for whom dietary management alone has been insufficient and insulin cannot be used.

4.2 Posology and method of administration

Posology

Dosage should be adapted to each individual patient and is determined by results of medical examinations.

The usual initial dose is 2,5 mg daily, with or immediately before breakfast, adjusted after about 7 days by amounts of 2,5 mg daily up to 15 mg daily.

Daily doses in excess of 10 mg may be given in two divided doses.

When changing over from another oral antidiabetic preparation, with a similar mode of action, the dosage of GLYCOMIN is determined by the amount of the previously administered dose and the medical examination.
In combination with a biguanide, there may be greater risk of cardiovascular mortality than with the use of GLYCOMIN alone (see section 4.5).

Special populations

Elderly population

Elderly patients may require smaller doses.

Renal impairment

GLYCOMIN is contraindicated in those with severe impairment of renal function (see section 4.3).

Hepatic impairment

GLYCOMIN is contraindicated in those with severe impairment of hepatic function (see section 4.3).

Other

GLYCOMIN is contraindicated in diabetes mellitus complicated by ketoacidosis, severe infection, stress, trauma and severe impairment of adrenal or thyroid function (see section 4.3).

Paediatric population

The safety and efficacy of GLYCOMIN in children has not yet been established. No data is available (see section 4.3 and 4.4).

Method of administration

For oral administration.

4.3 Contraindications

- Hypersensivity to sulphonylureas and any of the GLYCOMIN excipients (see section 6.1).
- Insulin-dependent diabetics.
- Diabetes in young people (see section 4.2 and 4.4).
- Diabetes mellitus complicated by ketoacidosis and in those with severe infection, stress, trauma and severe impairment of renal, hepatic or thyroid function. (see section 4.2).
- Chronic liver disease including that caused by uncompensated cardiac failure or alcoholism.(see section 4.4 and 4.5).
- Patients with seriously impaired adrenal function.
- Diabetes mellitus in patients with a history of metabolic decompensation e.g. acidosis, diabetic pre-coma and coma.
- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

A reduction in dosage may be necessary in patients with renal dysfunction.

The administration of GLYCOMIN may be associated with increased cardiovascular mortality compared to treatment with diet alone or diet plus insulin.

Adjustment of the dosage of GLYCOMIN may be required in patients suffering from recurrent infections, traumas, shock or after anaesthesia. When major surgery is to be performed, insulin therapy should be substituted for GLYCOMIN.

Intolerance to alcohol, characterised by facial flushing, may occur (see section 4.3 and 4.5).
Hypoglycaemic reactions may be experienced. The incidence of hypoglycaemia can be reduced if GLYCOMIN is taken with or immediately after a meal.

Paediatric population

GLYCOMIN is not indicated in children as safety and efficacy has not been established (see section 4.2 and 4.3).

Excipients

Lactose warning:

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Contraindicated combinations:

In combination with biguanides, there may be greater risk of cardiovascular mortality than with the use of GLYCOMIN alone. (see section 4.2).

Combinations requiring potential dose reduction:

The hypoglycaemic effects of GLYCOMIN may be enhanced by: antibiotics or anti-infectives such as chloramphenicol and sulphonamides including co-trimoxazole, coumarin anticoagulants, anti-inflammatory medicines and analgesics including azapropazone, phenylbutazone, and

salicylates, lipid regulating medicines such as clofibrate and halofenate, cimetidine and ranitidine, fenfluramine, indobufen, methyldopa, miconazole and sulphinpyrazone.

An increased hypoglycaemic effect may also be expected with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, allopurinol, azole antifungals, cyclophosphamide, dicoumarol, fluoroquinolones, heparin, octreotide, tetracycline and tricyclic antidepressants.

Monoamine oxidase inhibitors, quinidine and quinine have intrinsic hypoglycaemic activity in both diabetic and non-diabetic patients.

The risk of hypoglycaemia may be increased or prolonged if moderate or large amounts of alcohol are consumed concomitantly with GLYCOMIN (see section 4.3 and 4.4).
In all of the above, a potential dose reduction may thus be required.

Combinations requiring potential dose increases:
The hypoglycaemic effects may be diminished by aminoglutethimide, asparaginase chlorpromazine, corticosteroids, diazoxide, epinephrine (adrenaline), oral contraceptives, rifamycins, thiazide diuretics and thyroid hormones.
The effects caused by asparaginase, corticosteroids, lithium and thiazide diuretics is due to the intrinsic hyperglycaemic activity of these medicines in both diabetics and non-diabetics.
Beta-blockers may mask some of the symptoms of hypoglycaemia. Beta-adrenergic blockers may also decrease the hypoglycaemic effects of GLYCOMIN by inhibition of insulin secretion, modification of carbohydrate metabolism, and increased peripheral insulin resistance, leading to hyperglycaemia.
In all of the above an increased dose of GLYCOMIN may thus be required.*Others:*
Concomitant administration of GLYCOMIN with anticoagulants can increase the anticoagulant and hypoglycaemic effects.

Interactions due to displacement from binding sites may be less likely with GLYCOMIN than with other sulphonylureas.

The absorption of GLYCOMIN from the GIT may be reduced if it is taken together with guar gum.

4.6 Fertility, pregnancy and lactation

GLYCOMIN is contraindicated during pregnancy and breastfeeding (see section 4.3).

Pregnancy

First signs of pregnancy must be reported to the doctor without delay, because a change to insulin and/or dietary treatment is necessary.

Breastfeeding

GLYCOMIN is contraindicated in breastfeeding (see section 4.3)

Fertility

No data are available.

4.7 Effects on ability to drive and use machines

GLYCOMIN has a moderate influence on the ability to drive and use machines.

Until optimal glycaemic control is achieved, or when changing from one medicine to another, or when tablets are not taken routinely, 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.

4.8 Undesirable effects

a) *Tabulated list of adverse reactions*

System organ class	Frequent	Less frequent	Frequency unknown (cannot be estimated from the available data)
Blood and the lymphatic system disorders	Hypoglycaemia (mild, including nocturnal hypoglycaemia)	Anaemia (aplastic or haemolytic), blood dyscrasias (agranulocytosis, leukopenia, pancytopenia), eosinophilia, thrombocytopenia. Severe hypoglycaemia that leads to convulsions and coma	-
Metabolism and nutrition disorders	Weight gain	-	Hyponatraemia, lactic acidosis
Psychiatric disorders	-	-	Acute psychosis, confusion, convulsions (other than withdrawal), encephalopathy
Nervous system disorders	-	-	Cerebrovascular disorders, tremor
Eye disorders			Blindness, diplopia, temporary visual impairment (at the start of treatment)

Ear and labyrinth disorders	-	-	Deafness, tinnitus
Gastrointestinal disorders	Constipation, diarrhoea, flatulence, heartburn, loss of or increase in appetite, nausea, stomach fullness, vomiting, epigastric pain	-	Pancreatitis
Hepato-biliary disorders	-	Cholestasis, cholestatic jaundice, hepatic function impairment, hepatic porphyria, hepatitis or porphyria cutanea tarda	Acute porphyria exacerbation, increased liver enzymes (AST, ALT)
Skin and subcutaneous tissue disorders	-	Erythema multiforme or exfoliative dermatitis; photosensitivity	Allergic skin reactions that may progress to more serious disorders, alopecia/hipotrichosis, erythema nodosum, pruritis, facial oedema, angioedema, urticaria, allergic vasculitis
Musculoskeletal and connective tissue disorders	-	-	Arthralgia, arthritis
Renal and urinary disorders	Polyuria	-	Acute renal failure, mild diuresis; syndrome of inappropriate secretion of

			antidiuretic hormone (SIADH)
General disorders and administrative site conditions	Changes in sensation of taste, dizziness, drowsiness, headache, weakness, and paraesthesia	-	Intolerance to alcohol characterised by facial flushing, increased sweating

b) *Description of selected adverse reactions*

Gastrointestinal effects:

These are the most common adverse reactions, appear to be dose related and may subside following a reduction in dosage.

Dermatologic reactions

These are often transient and may disappear despite continued use. If they persist, GLYCOMIN use 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 be notified immediately.

In isolated cases, allergic vasculitis may arise which in some circumstances, may be life-threatening.

Blood and the lymphatic system reactions

The mild to severe thrombopaenia (can present as purpura), haemolytic anaemia, erythrocytopaenia, granulocytopaenia, agranulocytosis and pancytopaenia can be potentially

life-threatening. In principle, these reactions are reversible once GLYCOMIN has been withdrawn.

Hepato-biliary reactions

The infrequent cases of hepatitis, elevation of liver enzymes and/or cholestasis and jaundice may progress to life-threatening liver failure but is reversed after withdrawal of the medicine.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form"**, found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

Reporting can also be done directly to Adcock Ingram Limited at:

E-mail: Adcock.aereports@adcock.com

Tel: 011 635 0134

4.9 Overdose

Symptoms

Hypoglycaemia or hypoglycaemic coma, due to low blood sugar.

If untreated, hypoglycaemia may lead to convulsions, coma and/or death. (see section 4.4 and 4.8)

Treatment

In acute poisoning the stomach should be emptied by aspiration and lavage.

Treatment is symptomatic and supportive.

Hypoglycaemic symptoms, e.g. excessive perspiration, light-headedness, etc. can be treated by giving the patient a glucose load.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 21.2 Oral hypoglycaemics

Pharmacotherapeutic group: Blood Glucose Lowering Medicines, Excluding. Insulins – Sulfonylureas

ATC code: A10BB01

Mechanism of action

Glibenclamide is a sulphonylurea which is an oral hypoglycaemic medicine. Sulphonylureas stimulate the pancreatic islet tissue to secrete insulin by causing degranulation of the β-cells.

5.2 Pharmacokinetic properties

- **Absorption**

  Glibenclamide is readily absorbed from the gastrointestinal tract.

- **Distribution**

  Glibenclamide is extensively bound to plasmaproteins and peak plasma concentrations occur within 2 to 4 hours.

- **Biotransformation**

  Glibenclamide is almost completely metabolised in the liver.

- **Elimination**

  About 50 % of the dose is excreted in the urine and 50 % via the bile.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide, lactose monohydrate, magnesium stearate, purified talc, starch maize.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months in securitainers and metallocine layflat bags.

15 months in metallised layflat bags.

6.4 Special precautions for storage

Store at or below 25 °C in a dry place and protect from light.

Keep in original packaging until required for use.

6.5 Nature and contents of container

30, 100 or 500 tablets are packed in a white polypropylene container sealed with a white low density polyethylene cap, together with a white foam or rayon insert, and a leaflet.

Patient ready packs:

28, 56 or 84 tablets are packed into metallised layflat bags (metallised polyester laminated to opaque linear low density polyethylene), with a low density polyethylene ziploc.

28, 56 or 84 tablets are packed into metallocene layflat bags (polyester laminated to aluminium foil and clear metallocene material), with a low density polyethylene ziploc.

The patient ready packs are grouped, packed and sealed into polyethylene bags together with a leaflet.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road,

Erand Gardens,

Midrand, 1685

Customer Care: 0860 ADCOCK/ 232625

8. REGISTRATION NUMBER

Q/21.2/24

9. DATE OF FIRST AUTHORISATION

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10. DATE OF REVISION OF TEXT

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