Product Name: Proglicem 25 mg Capsules Applicant: MSD (Pty) Ltd	Component: Proposed Professional Information Submission date Date: 30 July 2025

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

PROGLICEM® 25 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 25 mg diazoxide, a non-diuretic thiazide.

Contains sugar: Lactose monohydrate 194.45 mg.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

PROGLICEM Capsules is useful in the management of intractable hypoglycaemia such as idiopathic hypoglycaemia of infancy or the hypoglycaemia resulting from inoperable tumours of the pancreas.

4.2 Posology and method of administration

Patients should be under close clinical observation when treatment with PROGLICEM Capsules is initiated. Clinical response and blood glucose levels should be carefully monitored until the patient's condition has stabilised satisfactorily; in most instances this may be accomplished in several days. If administration of PROGLICEM Capsules is not effective after 2 or 3 weeks, the medicine should be discontinued.

Posology

Dosage must be individualised based on the severity of the hypoglycaemic condition, the blood glucose level and the clinical response of the patient. The dosage should be adjusted until the desired clinical and laboratory effects are produced with the least amount of drug.

Adults and children: The usual dose is 3 to 8 mg/kg divided into 2 or 3 equal doses every 8 or 12 hours. In certain instances, patients with refractory hypoglycaemia may require higher doses.

The starting dosage is 3 mg/kg/day, divided into 3 equal doses every 8 hours. Thus, an average adult would receive a starting dosage of approximately 200 mg daily.

Special populations

Infants and newborns: The usual dosage is 8 to 15 mg/kg divided into 2 or 3 equal doses every 8 or 12 hours. An appropriate starting dose is 10 mg/kg/day, divided into 3 equal doses every 8 hours.

Special care should be taken to assure accuracy of dosage in infants and young children.

Method of administration

For oral use

4.3 Contraindications

The use of PROGLICEM Capsules is contraindicated in patients with functional hypoglycaemia and in patients hypersensitive to diazoxide or any of the excipients listed in section 6.1 or to other thiazides (see section 4.4 and 4.5).

4.4 Special warnings and precautions for use

PROGLICEM Capsules should be used with care in patients with impaired cardiac or cerebral circulation.

The antidiuretic property of PROGLICEM Capsules may lead to significant fluid retention, which in patients with compromised cardiac reserve, may precipitate congestive heart failure.

Patients should be under close clinical observation when treated with PROGLICEM Capsules. During prolonged therapy, blood-glucose concentrations should be monitored and the blood should be examined regularly for signs of leucopenia and thrombocytopenia. Regular monitoring of urine for sugar and ketones is also recommended (see section 4.8). In children, bone and psychological maturation and growth should be regularly assessed.

The effects of PROGLICEM Capsules on the level of serum uric acid should be kept in mind. Blood tests should be conducted periodically (see section 4.8).

Keto-acidosis and non-ketotic hyperosmolar coma have been reported in patients treated with recommended doses of PROGLICEM Capsules, usually during intercurrent illnesses. Prompt recognition and treatment are essential.

Since plasma half-life of diazoxide is prolonged in patients with impaired renal function, a reduced dosage should be considered and serum electrolyte levels should be evaluated.

Lactose

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

These potential interactions must be considered when administering PROGLICEM Capsules.

Since diazoxide is highly bound to serum protein, it may displace other substances which are also protein-bound, such as bilirubin or warfarin, resulting in higher blood levels of these substances. Accordingly, anticoagulant dosage reduction may be required when administered with PROGLICEM Capsules. The possible displacement of bilirubin should be kept in mind, particularly when treating newborns with increased bilirubinaemia.

Medicine interaction has been reported for PROGLICEM Capsules and diphenylhydantoin and their concomitant administration may result in a loss of seizure control.

Concomitant administration of thiazides or other commonly used potent diuretics may potentiate the hyperglycaemic and hyperuricaemic effects of PROGLICEM Capsules. In the presence of hypokalaemia, hyperglycaemic effects are also potentiated.

Diazoxide induced hyperglycaemia is reversed by the administration of insulin and discontinuation of PROGLICEM Capsules.

The inhibition of insulin release by PROGLICEM Capsules is antagonised by alpha-adrenergic blocking agents.

The antihypertensive effect of other medicines may be enhanced by concurrent PROGLICEM Capsules.

4.6 Fertility, pregnancy and lactation

Safety and efficacy have not been established.

4.7 Effects on ability to drive and use machines

Certain side effects that have been reported with PROGLICEM Capsules may affect some patients' ability to drive or operate machinery. Individual responses to PROGLICEM Capsules may vary (see section 4.8).

4.8 Undesirable effects

Tabulated summary of adverse reactions

The table below lists the adverse reactions by system organ class and frequency using the following convention: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000) and not known (cannot be estimated from the available data).

System organ class	Frequency	Side effect
Cardiac disorders	Common	Sodium and fluid retention, tachycardia, palpitations, increased levels of serum uric acid, hypotension
	Rare	Chest pain
	Frequency not known	Transient hypertension, pulmonary hypertension, pericardial effusion
Metabolism and nutrition disorders	Common	Hyperglycaemia or glycosuria
	Frequency not known	Diabetic ketoacidosis, hyperosmolar non-ketotic coma, gout
Gastrointestinal disorders	Common	Anorexia, nausea, vomiting,

		abdominal pain, transient loss of taste
	Uncommon	Diarrhoea
	Rare	Ileus, acute pancreatitis
	Frequency not known	Pancreatic necrosis
Blood and lymphatic system disorders	Common	Thrombocytopenia, with or without purpura, neutropenia
	Frequency not known	Eosinophilia, decreased haemoglobin/haematocrit, excessive bleeding, decreased IgG, lymphadenopathy
Investigations	Frequency not known	Increased serum AST, alkaline phosphatase, decreased creatinine clearance, decreased urinary output.
Renal and urinary disorders	Frequency not known	Uraemia, nephrotic syndrome, haematuria, albuminuria, azotemia
Psychiatric disorders	Frequency not known	Anxiety, insomnia
Nervous system disorders	Common	Dizziness, headache, extrapyramidal signs, polyneuropathy, paraesthesia
Skin and subcutaneous	Common	Hirsutism

tissue disorders	Frequency not known	Pruritus, skin rash, loss of scalp hair
Eye disorders	Common	Blurred vision
	Frequency not known	Cataracts, subconjunctival haemorrhage, ring scotoma, diplopia, lacrimation
Musculoskeletal and connective tissue disorders	Frequency not known	Osteoporosis
General disorders and administration site conditions	Frequency not known	Fever, malaise
Infections and infestations	Frequency not known	Herpes simplex
Reproductive system and breast disorders	Frequency not known	Galactorrhoea

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. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

An overdosage of PROGLICEM Capsules causes marked hyperglycaemia which may be associated with keto-acidosis.

It will respond to prompt insulin administration and restoration of fluid and electrolyte balance. Because of the long half-life of this product, symptoms of overdosage require prolonged surveillance for periods up to 7 days, until the blood sugar level stabilises within the normal range. Successful lowering of diazoxide blood levels by peritoneal dialysis and by haemodialysis has been reported.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.21.11 Hyperglycaemic agents

Orally administered diazoxide produces an increase in blood glucose level, due primarily to an inhibition of pancreatic release of insulin, and also to an extra-pancreatic effect possibly stemming from catecholamine enhancement.

Diazoxide decreases sodium and water excretion, resulting in fluid retention, which may be clinically significant.

Other pharmacologic actions of diazoxide include increased pulse rate and blood pressure, increased serum uric acid levels due to decreased excretion, decreased chloride excretion,

increased serum free fatty acid levels and decreased para-aminohippuric acid (PAH) clearance with no appreciable effect on glomerular filtration rate.

5.2 Pharmacokinetic properties

Diazoxide is extensively bound (more than 90 %) to serum protein and is excreted by the kidneys. The plasma half-life following intravenous administration is 28 ± 8,3 hours. Limited data on oral administration revealed a plasma half-life of 24 and 36 hours in adults, and in children, aged 4 months to 6 years, the half-life varied from 9,5 to 24 hours on long-term oral administration. The half-life may be prolonged in patients with impaired renal function (see section 4.4).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Inactive ingredients: lactose monohydrate, magnesium stearate, gelatin.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

Cartons of 100 capsules, packed as 4 PVC/aluminium blisters of 25 capsules.

6.6 Special precautions for dispisal and other handling

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

MSD (Pty) Ltd

117 16th Road

Halfway House

1685

South Africa

8 REGISTRATION NUMBER

G3217 (Act 101/1965)

9 DATE OF FIRST AUTHORISATION

01 October 1974

10 DATE OF REVISION OF THE TEXT

28 October 2025