Approved Professional Information for Medicines for Human Use:

AMLODIPINE 5 and 10 GDC

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

AMLODIPINE 5 GDC tablets

AMLODIPINE 10 GDC tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

AMLODIPINE 5 GDC:

Each tablet contains amlodipine besylate equivalent to 5 mg amlodipine.

AMLODIPINE 10 GDC:

Each tablet contains amlodipine besylate equivalent to 10 mg amlodipine.

Sugar free.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

AMLODIPINE 5 GDC

White to off white, flat, round, bevel edged tablet with a break line on one side. Diameter (± 8 mm).

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

AMLODIPINE 5 GDC

White to off white, flat, round, bevel edged tablet with a break line on one side. Diameter (± 11 mm).

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

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AMLODIPINE GDC is indicated for the:

- Treatment of angina pectoris
- Treatment of mild-to moderate hypertension, alone or in combination with other antihypertensives
- Treatment of chronic stable angina - first line treatment of myocardial ischaemia, whether due to fixed obstruction (stable angina) and/or vasospasm/vasoconstriction (Prinzmetal's or variant angina) of coronary vasculature. AMLODIPINE GDC may be used alone, as monotherapy, or in combination with other antianginal medicines
- Treatment of coronary artery disease - AMLODIPINE GDC is indicated to reduce the risk of coronary revascularisation and the need for hospitalisation due to angina in patients with coronary artery disease
- Risk reduction of fatal coronary heart disease and non-fatal myocardial infarction, and to reduce the risk of stroke.

4.2 Posology and method of administration

Posology

Hypertension and angina pectoris

Adults:

An initial dose of 5 mg of AMLODIPINE GDC once daily is recommended which may be increased to 10 mg once a day after 10 – 14 days of therapy if there is no improvement.
In hypertension, no dose reduction is required when adding AMLODIPINE GDC to thiazide diuretics, beta-blockers, or angiotensin-converting enzyme inhibitors.

Coronary artery disease

The recommended dosage range is 5 – 10 mg once daily. In clinical studies, the majority of patients required 10 mg.

Special populations

Elderly

AMLODIPINE GDC used at similar doses in elderly or younger patients is equally well tolerated. Normal dosage regimens are recommended in the elderly but increase of the dosage should take place with care (see sections 4.4 and 5.2).

Hepatic impairment

Dosage recommendations have not been established in patients with mild to moderate hepatic impairment; therefore, dose selection should be cautious and should start at the lower end of the dosing range (see sections 4.4 and 5.2). The pharmacokinetics of amlodipine, as in AMLODIPINE GDC, have not been studied in severe hepatic impairment. AMLODIPINE GDC should be initiated at the lowest dose and titrated slowly in patients with severe hepatic impairment.

Renal impairment

AMLODIPINE GDC may be used in such patients at normal doses. Changes in plasma concentrations are not correlated with degree of renal impairment (see section 5.2).

Paediatric population

The recommended antihypertensive oral dose in paediatric patients ages 6 – 17 years is 2,5 mg to 5 mg once daily. Doses in excess of 5 mg daily have not been studied in paediatric patients. The effect of AMLODIPINE GDC on blood pressure in patients less than 6 years of age is not known.

Method of administration

Oral use.

AMLODIPINE GDC can be administered with or without the intake of food. Do not use AMLODIPINE GDC simultaneously with grapefruit juice (see sections 4.3 and 4.5).

Missed dose

If a dose is missed, the tablet should be taken as soon as the missed dose is remembered. Two tablets should not be taken to make up for the missed dose.

Discontinuation

A gradual decrease of the amlodipine dosage under medical practitioner supervision is recommended (see section 4.5).

4.3 Contraindications

- Hypersensitivity to amlodipine besylate, dihydropyridines or to any of the excipients listed in section 6.1.
- Concomitant use with grapefruit juice (see sections 4.2 and 4.5).
- Severe hypotension.
- Shock, including cardiogenic shock.
- Haemodynamically unstable heart failure after acute myocardial infarction (during the first 28 days).
- Obstruction of the outflow tract of the left ventricle (e.g. high-grade aortic stenosis).
- Unstable angina pectoris.
- Concomitant use with grapefruit juice (see section 4.5).
- Safety in children younger than 6 years of age has not been established.
- Pregnancy and lactation.

4.4 Special warnings and precautions for use

Cardiovascular conditions

The safety and efficacy of AMLODIPINE GDC in hypertensive crisis has not been established.

AMLODIPINE GDC should not be used to treat angina attack in chronic stable angina, nor should it be used for the acute reduction of blood pressure in adults.

In patients with severe aortic stenosis, AMLODIPINE GDC may increase the risk of developing heart failure.

Sudden withdrawal of AMLODIPINE GDC might be associated with an exacerbation of angina. A gradual decrease of dosage with medical practitioner supervision is recommended.

AMLODIPINE GDC should be stopped in patients who have ischaemic pain after use.

Concomitant use with potent cytochrome CYP3A4 inhibitors

The blood pressure lowering effect may be enhanced when potent CYP3A4 inhibitors such as ketoconazole, itraconazole or ritonavir are co-administered (see section 4.5).

Diabetes mellitus

AMLODIPINE GDC effect on insulin and glucose responses may require antidiabetic therapy to be adjusted.

Interference with diagnostic tests

Calcium channel blockers, such as AMLODIPINE GDC, reduce the plasma aldosterone: renin ratio by increasing renin production and reducing plasma aldosterone concentrations, consequently, primary hyperaldosteronism has been misdiagnosed as essential hypertension (see sections 4.5 and 4.8).

Use in the elderly

Amlodipine clearance is decreased (40 - 60 %) in the elderly, which results in increases of amlodipine concentration in the area under the concentration-time curve (AUC) and elimination half-life. AUC and elimination half-life in patients with congestive heart failure (CHF) were increased with age. Therefore, elderly patients should start AMLODIPINE GDC therapy at a lower dose (see sections 4.2 and 5.2).

Use in renal failure

Although AMLODIPINE GDC is excreted primarily via the kidney, mild renal impairment does not appear to have an effect on the plasma concentrations. Severe renal impairment may however require a dosage reduction. Amlodipine is not dialysable (see sections 4.2 and 5.2).

Use in impaired hepatic function

The half-life of AMLODIPINE GDC is significantly prolonged in patients with impaired hepatic function. AMLODIPINE GDC should therefore be administered at lower (5 mg) initial doses in these patients. Caution should be used, both on initial treatment and when increasing the dose. Slow dose titration and careful monitoring may be required in patients with severe hepatic impairment (see sections 4.2 and 5.2).

Use in cardiac failure

In a reported long-term, placebo-controlled study (PRAISE-2) of amlodipine in patients with New York Heart Association (NYHA) class III and IV heart failure of non-ischaemic aetiology, amlodipine was associated with increased reports of pulmonary oedema despite no significant difference in the incidence of worsening heart failure as compared to placebo.

AMLODIPINE GDC may have a negative inotropic effect. The AUC of AMLODIPINE GDC may increase in patients with heart failure. Calcium channel blockers, including AMLODIPINE GDC, should be used with caution in patients with hypotension, patients whose cardiac reserve is poor and those with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality.

AMLODIPINE GDC is contraindicated in cardiogenic shock or in patients who have suffered myocardial infarction in the previous 2 to 4 weeks, or in acute unstable angina (see section 4.3).

Porphyria

Safety has not been established.

Anaesthesia

Patients who are taking AMLODIPINE GDC should inform the anaesthetist accordingly, before receiving anaesthesia.

Sodium

AMLODIPINE GDC contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

Paediatric population

Safety and efficacy have been established in paediatric patients ages 6 - 17 years with recommended doses of 2,5 mg – 5 mg once daily.

Safety and efficacy have not been established for doses exceeding 5 mg daily and in patients younger than 6 years of age as the effect of AMLODIPINE GDC on blood pressure is not known.

4.5 Interaction with other medicines and other forms of interaction

Effects of other medicines on amlodipine

CYP3A4 inhibitors

Concomitant use of amlodipine with strong or moderate CYP3A4 inhibitors (protease inhibitors like saquinavir, ritonavir, indinavir, nelfinavir, amprenavir, lopinavir and atazanavir; azole antifungals like fluconazole, itraconazole, ketoconazole; macrolides like erythromycin or clarithromycin; verapamil or diltiazem) may give rise to significant increase in amlodipine exposure resulting in an increased risk of hypotension. The clinical translation of these pharmacokinetic variations may be more pronounced in the elderly. Clinical monitoring and dose adjustment may thus be required (see sections 4.2 and 4.4).

CYP3A4 inducers

Upon co-administration of known inducers of the CYP3A4, the plasma concentration of amlodipine may vary. Therefore, blood pressure should be monitored and dose regulation considered both during and after concomitant medication particularly with strong CYP3A4 inducers (e.g. rifampicin, St John's Wort (*Hypericum perforatum)*). AMLODIPINE GDC should be used with caution together with CYP3A4 inducers.

Grapefruit or grapefruit juice

Administration of amlodipine with grapefruit or grapefruit juice is contraindicated as bioavailability may be increased in some patients resulting in increased blood pressure lowering effects (see sections 4.2 and 4.3).

Dantrolene (infusion)

In animals, lethal ventricular fibrillation and cardiovascular collapse are observed in association with hyperkalaemia after administration of verapamil and intravenous dantrolene. Due to risk of hyperkalaemia, it is recommended that the co-administration of calcium channel blockers such as amlodipine be avoided in patients susceptible to malignant hyperthermia and in the management of malignant hyperthermia.

Antianginal and antihypertensive medicines

Concurrent administration of sublingual nitro-glycerine, long acting nitrates, beta-blockers or other antianginal medicines with AMLODIPINE GDC may produce additive antihypertensive and antianginal effects. Sublingual nitro-glycerine may be used as needed to abort acute angina attacks during amlodipine therapy. Nitrate medication may be used during amlodipine therapy for angina prophylaxis.

AMLODIPINE GDC may enhance the antihypertensive effects of other antihypertensive medicines such as beta blockers. AMLODIPINE GDC will not protect against the consequences of abrupt beta-blocker withdrawal; gradual beta-blocker dose reduction is recommended. Although no "rebound effect" has been reported upon discontinuation of AMLODIPINE GDC, a gradual decrease of dosage with medical practitioner supervision is recommended (see section 4.2).

Aldesleukin and antipsychotics

Enhanced antihypertensive effects may be seen in concomitant use with medicines such as aldesleukin and antipsychotics that cause hypotension.

Anti-epileptics

The plasma concentrations of amlodipine may be decreased and therefore the effects of AMLODIPINE GDC may be reduced in combination with enzyme-inducing anti-epileptics such as carbamazepine, phenobarbitone and phenytoin. In contrast, sodium valproate has been reported to increase plasma concentrations.

Cimetidine

Co-administration with cimetidine did not alter the pharmacokinetics of amlodipine.

Aluminium/magnesium (antacid)

Co-administration of an aluminium/magnesium antacid with a single dose of amlodipine had no significant effect on the pharmacokinetics of amlodipine.

Sildenafil

A single 100 mg dose of sildenafil in subjects with essential hypertension had no effect on the pharmacokinetic parameters of amlodipine. When amlodipine and sildenafil were used in combination, each medicine independently exerted its own blood pressure lowering effect.

Effects of amlodipine on other medicines

Antihypertensive medicines

The blood pressure lowering effects of amlodipine adds to the blood pressure-lowering effects of other medicinal products with antihypertensive properties.

Antidiabetic medicines

AMLODIPINE GDC may modify insulin and glucose responses and therefore diabetic patients may need to adjust their antidiabetic treatment when receiving AMLODIPINE GDC (see section 4.4).

Lithium

The use of lithium with AMLODIPINE GDC may cause lithium induced neurotoxicity in the form of nausea, vomiting, diarrhoea, ataxia, tremors and/or tinnitus, caution is therefore recommended.

Tacrolimus

There is a risk of increased tacrolimus blood levels when co-administered with AMLODIPINE GDC. In order to avoid toxicity of tacrolimus, administration of AMLODIPINE GDC in a patient treated with tacrolimus requires monitoring of tacrolimus blood levels and dose adjustment of tacrolimus when appropriate.

Mechanistic target of rapamycin (mTOR) inhibitors

mTOR inhibitors such as sirolimus, temsirolimus and everolimus are CYP3A substrates. AMLODIPINE GDC is a weak CYP3A inhibitor. With concomitant use of mTOR inhibitors, AMLODIPINE GDC may increase exposure of mTOR inhibitors.

Ciclosporin

No medicine interaction studies have been conducted with ciclosporin and amlodipine in healthy volunteers or other populations, with the exception of renal transplant patients. Various studies in renal transplant patients report that co-administration of amlodipine with ciclosporin increased the trough concentrations of ciclosporin and increased ciclosporin toxicity, from no change up to an average increase of 40 %.

Consideration should be given for monitoring ciclosporin levels in renal transplant patients on AMLODIPINE GDC, and ciclosporin dose reductions should be made as necessary.

Simvastatin

Co-administration of multiple doses of 10 mg of amlodipine, as in AMLODIPINE GDC with 80 mg simvastatin resulted in a 77 % increase in exposure to simvastatin compared to simvastatin alone. Limit the dose of simvastatin in patients on AMLODIPINE GDC to 20 mg daily.

Digoxin

Co-administration of amlodipine with digoxin did not change serum digoxin levels or digoxin renal clearance in healthy volunteers.

Ethanol (alcohol)

Single and multiple 10 mg doses of amlodipine, as in AMLODIPINE GDC had no significant effect

on the pharmacokinetics of ethanol.

Warfarin

Co-administration of amlodipine with warfarin did not change the warfarin prothrombin response time.

Antidysrhythmic medicines

AMLODIPINE GDC is extensively metabolised in the liver by the cytochrome P450 isoenzyme CYP3A4 and interactions may occur with other medicines, such as quinidine or procainamide, sharing the same metabolic pathway, since both groups possess negative inotropic properties.

Medicine/laboratory test interactions

AMLODIPINE GDC may lead to the misdiagnosis of primary hyperaldosteronism as essential hypertension due to the reduction in the plasma aldosterone: renin ratio
(see sections 4.4 and 4.8).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females

Women of childbearing potential and their partners should be advised to ensure adequate contraceptive cover.

Pregnancy

AMLODIPINE GDC in pregnancy and lactation is contraindicated (see section 4.3). Since teratogenic effects were noted in animals, amlodipine should not be administered to pregnant women.

Breastfeeding

AMLODIPINE GDC is excreted in human milk and therefore should not be administered in lactating women (see section 4.3).

Fertility

Reversible biochemical changes in the head of spermatozoa have been reported in some patients treated by calcium channel blockers. Clinical data are insufficient regarding the potential effect of amlodipine on fertility. In one rat study, adverse effects were found on male fertility.

4.7 Effects on ability to drive and use machines

Amlodipine can have minor or moderate influence on the ability to drive
and use machines. AMLODIPINE GDC can cause side effects such as dizziness, visual disturbances, headache, fatigue or nausea therefore the ability to react may be impaired (see section 4.8). Patients should be warned against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of coordination may lead to accidents.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequently reported adverse reactions during treatment are somnolence, dizziness, headache, palpitations, flushing, abdominal pain, nausea, ankle swelling, oedema and fatigue.

b. Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during reported clinical trials and postmarket spontaneous reports with amlodipine.

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	Less frequent	Leukocytopenia, thrombocytopenia, haemorrhagic complications in surgical patients, blood dyscrasias
Immune system disorders	Less frequent	Hypersensitivity reactions including pruritus, rash, angioedema and erythema multiforme
Metabolism and nutrition disorders	Less frequent	Hyperglycaemia
Psychiatric disorders	Less frequent	Insomnia, mood changes (including anxiety), depression
Nervous system disorders	Frequent	Headache, somnolence, dizziness
	Less frequent	Tremor, dysgeusia, syncope, hypoaesthesia, paraesthesia, hypertonia, peripheral neuropathy, extrapyramidal disorder
Eye disorders	Less frequent	Visual disturbances (including diplopia)
Ear and labyrinth disorders	Less frequent	Tinnitus

Cardiac disorders	Frequent	Palpitations
	Less frequent	Myocardial infarction, chest pain, dysrhythmia (including ventricular tachycardia, atrial fibrillation, bradycardia)
Vascular disorders	Frequent	Flushing, peripheral oedema
	Less frequent	Hypotension (including orthostatic hypotension), vasculitis
Respiratory, thoracic and mediastinal disorders	Less frequent	Coughing, dyspnoea, rhinitis
Gastrointestinal disorders	Frequent	Abdominal pain, nausea, dyspepsia, altered bowel habits (including diarrhoea and constipation)
	Less frequent	Vomiting, dry mouth, pancreatitis, gastritis, gingival hyperplasia
Hepatobiliary disorder	Less frequent	Hepatitis, jaundice, raised liver enzymes (mostly consistent with cholestasis)

Skin and subcutaneous tissue disorders	Less frequent	Alopecia, purpura, skin discolouration, hyperhidrosis, pruritus, rash, exanthema, urticaria, angioedema, erythema multiforme, exfoliative dermatitis, Stevens Johnson syndrome, Quincke oedema, photosensitivity
	Frequency unknown	Toxic Epidermal Necrolysis
Musculoskeletal, connective tissue and bone disorders	Frequent	Ankle swelling
	Less frequent	Arthralgia, back pain, muscle cramps, myalgia
Renal and urinary disorders	Less frequent	Increased urinary frequency, micturition disorder, nocturia
Reproductive system and breast disorders	Less frequent	Impotence, qynaecomastia

General disorders and administration site conditions	Frequent	Oedema, fatigue, asthenia
	Less frequent	Pain, malaise
Investigations	Less frequent	Weight increase, weight decrease
	Frequency unknown	AMLODIPINE GDC may lead to the misdiagnosis of primary hyperaldosteronism as essential hypertension (see sections 4.4 and 4.5)

Paediatric population

Paediatric patients (ages 6 – 17 years)

Adverse events were similar to those seen in adults. The most frequently reported adverse events were:

System Organ Class	**Frequency**	**Side effects**
Nervous system disorders	Frequent	Headache, dizziness
Vascular disorders	Frequent	Vasodilation
Respiratory, thoracic and mediastinal disorders	Less frequent	Epistaxis
Gastrointestinal disorders	Frequent	Abdominal pain
General disorders and administrative site conditions	Frequent	Asthenia

Severe adverse events (predominantly headache) were experienced by 7,2 % with amlodipine 2,5 mg, 4,5 % with amlodipine 5 mg, and 4,6 % with placebo. The most common cause of discontinuation from the study was uncontrolled hypertension. There were no discontinuations due to laboratory abnormalities. There was no significant change in heart rate.

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 reactions to SAHPRA via the
Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Alternately you can contact Gulf Drug Company (Pty) Ltd at +27 31 538 8700 or per info@gulfdrug.co.za.

4.9 Overdose

In humans experience with intentional overdose is limited.

Signs and symptoms

Overdosage could result in excessive peripheral vasodilatation, resulting in marked and probably prolonged systemic hypotension.

Available data for amlodipine suggest that gross overdosage could result in excessive peripheral vasodilation, and possibly reflex tachycardia. Marked and probably prolonged systemic hypotension up to and including shock with fatal outcome have been reported.

Non-cardiogenic pulmonary oedema has rarely been reported as a consequence of amlodipine overdose that may manifest with a delayed onset (24 – 48 hours post-ingestion) and require ventilatory support. Early resuscitation measures (including fluid overload) to maintain perfusion and cardiac output may be precipitating factors.

Treatment

Clinically significant hypotension due to AMLODIPINE GDC overdosage requires active cardiovascular support including frequent monitoring of cardiac and respiratory function, elevating of extremities and attention to circulating fluid volume and urine output. A vasoconstrictor may be helpful in restoring vascular tone and blood pressure, provided there in no contraindication to its use. Intravenous calcium gluconate may be of benefit in reversing the effects of calcium channel blockade. Since amlodipine is highly protein-bound, dialysis is not likely to be of benefit.
Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 7.1 Vasodilators, hypotensive medicines
Pharmacotherapeutic group: Calcium channel blockers, selective calcium channel blockers with mainly vascular effects.
ATC code: C08CA01.

Mechanism of action

Amlodipine is a dihydropyridine calcium channel blocker. It inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle without affecting serum calcium concentrations. Direct relaxation of vascular smooth muscle forms the basis of the antihypertensive action.

In angina pectoris, amlodipine acts as a peripheral arteriolar vasodilator resulting in a reduction in total peripheral resistance (afterload).
Dilatation of the main coronary arteries and the coronary arterioles also probably plays a role in its action.

Myocardial energy and oxygen requirements are reduced. Amlodipine exerts its activity by binding to the dihydropyridine binding sites. It exerts minimal action on cardiac conduction, contraction and heart rate.

5.2 Pharmacokinetic properties

Absorption

Complete absorption of amlodipine is slow following oral administration with peak plasma levels being attained after 6 to 12 hours. Amlodipine has an absolute bioavailability of the unchanged compound of about 64 – 80 % The absorption of amlodipine is unaffected by the concomitant intake of food.

Distribution

The volume of distribution is about 21 L/kg. Plasma protein binding *in vitro* is approximately 97,5 %.

Biotransformation

Amlodipine is extensively metabolised by the liver to inactive metabolites.

Elimination

Less than 10 % of amlodipine appears unchanged in the urine. Metabolites are inactive and primarily (up to 60 %) excreted via the kidney.

The terminal plasma elimination half-life of 35 to 50 hours, allowing for once daily oral dosing. Steady state plasma concentrations are achieved after 7 to 8 days of consecutive dosing.

Special patient populations

Hepatic impairment

Patients with hepatic insufficiency have decreased clearance of amlodipine resulting in a longer half-life and an increased AUC, and a lower initial dose may be required.

Renal impairment

The pharmacokinetics of amlodipine are not significantly influenced by renal impairment.

Elderly

The time to reach peak plasma concentrations of amlodipine is similar in elderly and younger subjects. Amlodipine clearance tends to be decreased with resulting increases in AUC and elimination half-life in elderly patients, and a lower initial dose may be required. A similar increase in AUC may be observed in patients with moderate to severe heart failure.

Paediatric population

A population pharmacokinetic study has been conducted in 74 hypertensive children aged from 1 to 17 years (with 34 patients aged 6 to 12 years and 28 patients aged 13 to 17 years) receiving amlodipine between 1,25 and 20 mg given either once or twice daily. In children 6 to 12 years and in adolescents 13 – 17 years of age the typical oral clearance (CL/F) was 22,5 and 27,4 L/hr respectively in males and 16,4 and 21,3 L/hr respectively in females. Large variability in exposure between individuals was observed. Data reported in children below 6 years is limited.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous dicalcium phosphate

Colloidal silicon dioxide

Magnesium stearate

Microcrystalline cellulose

Sodium starch glycollate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 ºC in a cool, dry place.

Protect from light and moisture.

Keep container tightly closed.

Do not remove tablets from container/blister until required for use.

6.5 Nature and contents of container

Push- through PVC/Al blister strips of 10 tablets in packs of 30 tablets in a unit carton. White HDPE containers of 30, 100, 500 and 1000 tablets.

Not all pack sizes may be marketed.

6.6 Special precaution for disposal and or handling

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Gulf Drug Company (Pty) Ltd

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8. REGISTRATION NUMBER(S)

AMLODIPINE 5 GDC -41/7.1/0812

AMLODIPINE 10 GDC - 41/7.1/0813

9. DATE OF FIRST AUTHORISATION

15 August 2008

10. DATE OF REVISION OF THE TEXT

19 August 2025.