SCHEDULING STATUS: S3

PROPRIETARY NAME AND DOSAGE FORM:

GULF AMLODIPINE 5 (Tablets)

GULF AMLODIPINE 10 (Tablets)

COMPOSITION:

GULF AMLODIPINE 5**:** Each tablet contains amlodipine besylate equivalent to 5 mg amlodipine

GULF AMLODIPINE 10: Each tablet contains amlodipine besylate equivalent to 10 mg amlodipine

PHARMACOLOGICAL CLASSIFICATION:

A 7.1 Vasodilators, hypotensive medicines

PHARMACOLOGICAL 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). 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.

Pharmacokinetics:

Complete absorption of amlodipine is slow following oral administration with peak plasma levels being attained after 6 to 12 hours. Amlodipine has a bioavailability of about 64 % and 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. The volume of distribution is about 20 l/kg. Metabolism is via the liver and is extensive with less than 10 % of amlodipine appearing unchanged in the urine. Metabolites are inactive and primarily (up to 60 %) excreted via the kidney.

INDICATIONS:

Gulf Amlodipine is indicated for the:

- Treatment of angina pectoris
- Treatment of mild-to moderate hypertension, alone or in combination with other antihypertensives.

CONTRA INDICATIONS:

- Hypersensitivity to any of the ingredients
- Hypersensitivity to dihydropyridines

WARNINGS:

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. Therefore, elderly patients should start Gulf Amlodipine therapy at a lower dose.

Use in renal failure:

Although Gulf Amlodipine 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.

Use in impaired hepatic function:

The half life of Gulf Amlodipine is significantly prolonged in patients with impaired hepatic function. Gulf Amlodipine should therefore be administered at lower doses in these patients.

Use in children:

Safety and efficacy has not been established.

Use in heart failure:

An increased incidence of pulmonary oedema has been reported. Gulf Amlodipine may have a negative inotropic effect. AUC of Gulf Amlodipine may increase in patients with heart failure.

Porphyria:

Safety has not been established.

INTERACTIONS:

Concurrent administration of sublingual nitroglycerin, long acting nitrates, beta-blockers or other antianginal agents with amlodipine may produce additive antihypertensive and antianginal effects. Sublingual nitroglycerin 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 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, a gradual decrease of dosage with medical practitioner supervision is recommended.

PREGNANCY AND LACTATION:

Safety in pregnancy and lactation has not been established (See **Contraindications**).

DOSAGE AND DIRECTIONS FOR USE:

Hypertension and Angina pectoris:

Adults:

An initial dose of 5 mg of Gulf Amlodipine 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.

No dose reduction is required when adding Gulf Amlodipine to thiazide diuretics, beta-blockers, or angiotensin-converting enzyme inhibitors.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side-Effects:

Very common (>1/10); common (>1/100, <1/10); uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000)

Cardiovascular:

Very common: Peripheral oedema, palpitations

Common: arrhythmia (including ventricular tachycardia and atrial fibrillation)

Uncommon: Syncope, vasculitis, myocardial infarction, chest pain, hypotension (including orthostatic hypotension)

Neurological

Very common: Dizziness, headaches, somnolence.

Uncommon: Hypertonia, hypoesthesia/paresthesia, peripheral neuropathy, tremor, insomnia

Rare: Mood changes.

Gastro-intestinal:

Common: Nausea, abdominal pain.

Uncommon: Altered bowel habits, vomiting, dyspepsia, gingival hyperplasia, pancreatitis

Musculoskeletal:

Common: Fatigue

Uncommon: Arthralgia, asthenia, back pain, muscle cramps, myalgia

Autonomic nervous system:

Very common: Flushing

Uncommon: Dry mouth, increased sweating.

Hepatobilliary:

Rare: Hepatitis, jaundice, raised liver enzymes (mostly consistent with cholestasis).

Haematological:

Very rare: Purpura, thrombocytopenia, leucopenia.

Genitourinary;

Uncommon: Increased urinary frequency, impotence.

Body as whole:

Uncommon: Pain, weight increase/decrease

Endocrine:

Uncommon: Gynaecomastia

Metabolic:

Very rare: Hyperglycemia

Skin and appendages:

Uncommon: Alopecia

Respiratory:

Uncommon: Coughing, dyspnoea

Vision:

Uncommon: Visual disturbances.

Special senses:

Rare: Taste perversion, tinnitus.

Hypersensitivity reactions:

Uncommon: Allergic reactions with pruritus, rash, angioedema and erythma multiforme.

KNOWN SYMPTOMS OF OVER-DOSAGE AND PARTICULARS OF ITS TREATMENT:

There is no documented experience with Gulf Amlodipine over-dosage. Gastric lavage may be of benefit. Gross over-dosage could result in excessive peripheral vasodilation, resulting in marked and probably prolonged systemic hypotension. Clinically significant hypotension due to Gulf Amlodipine over-dosage requires active cardiovascular support. 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.

IDENTIFICATION:

Gulf Amlodipine 5 – White to off white, flat, round, bevel edged tablet with a breakline on one side.

Diameter (± 8mm)

Gulf Amlodipine 10 – White to off white, flat, round, bevel edged tablet with a breakline on one side.

Diameter (±11 mm)

PRESENTATION:

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

STORAGE INSTRUCTIONS:

Store below 25 °C in a cool, dry place. Protect from light and moisture. Keep tightly closed.

Do not remove tablets from blisters until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER(S):

Gulf Amlodipine 5 – 41/8.1/0812

Gulf Amlodipine 10 – 41/8.1/0813

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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