APPROVED PACKAGE INSERT FOR AMLODAC 5 / 10 TABLETS

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

AMLODAC 5 tablets

AMLODAC 10 tablets

COMPOSITION

Active ingredients:

Each tablet contains amlodipine besilate equivalent to 5 mg or 10 mg amlodipine.

Inactive ingredients:

Colloidal silicon dioxide, dibasic calcium phosphate, iron oxide, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, starch and talc.

AMLODAC 5 also contains wincoat wt aq-1255 brown (colourant).

AMLODAC 10 also contains hydroxypropyl methyl cellulose and titanium dioxide.

Sugar free.

PHARMACOLOGICAL CLASSIFICATION

A 7.1 Vasodilators, hypotensive medicines.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties:

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.

Pharmacokinetic properties:

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 a 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

AMLODAC is indicated for the:

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

CONTRAINDICATIONS

- Hypersensitivity to amlodipine or to any of the inactive ingredients of **AMLODAC** (see **COMPOSITION**).
- Hypersensitivity to dihydropyridines.

WARNINGS AND SPECIAL PRECAUTIONS

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 **AMLODAC** therapy at a lower dose.

Use in renal failure:

Although **AMLODAC** 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 **AMLODAC** is significantly prolonged in patients with impaired hepatic function. **AMLODAC** 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.

AMLODAC may have a negative inotropic effect. AUC of **AMLODAC** 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 **AMLODAC** may cause severe hypotension.

PREGNANCY AND LACTATION

Safety in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE

Hypertension and angina pectoris:

Adults:

An initial dose of 5 mg **AMLODAC** 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 **AMLODAC** to thiazide diuretics, beta-blockers, or angiotensin-converting enzyme inhibitors.

SIDE EFFECTS

Blood and the lymphatic system disorders:

Less frequent: Purpura, thrombocytopenia, leucopenia.

Immune system disorders:

Less frequent: Allergic reactions with pruritus, rash, angioedema and erythema multiforme.

Endocrine disorders:

Less frequent: Gynaecomastia.

Metabolism and nutrition disorders:

Less frequent: Hyperglycaemia.

Nervous system disorders:

Frequent: Dizziness, headache, somnolence.

Less frequent: Hypertonia, hypoesthesia/paraesthesia, peripheral neuropathy, tremor, insomnia, mood changes.

Eye disorders:

Less frequent: Visual disturbances.

Ear and labyrinth disorders:

Less frequent: Tinnitus.

Cardiac disorders:

Frequent: Peripheral oedema, palpitations.

Less frequent: Syncope, vasculitis, myocardial infraction, arrhythmia (including ventricular tachycardia and atrial fibrillation), chest pain.

Vascular disorders:

Frequent: Flushing.

Less frequent: Increased sweating, hypotension (including orthostatic hypotension).

Respiratory, thoracic and mediastinal disorders:

Less frequent: Coughing, dyspnoea.

Gastrointestinal disorders:

Frequent: Nausea, abdominal pain.

Less frequent: Altered bowel habits, vomiting, dyspepsia, gingival hyperplasia, pancreatitis, dry mouth, taste perversion.

Hepato-biliary disorders:

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

Skin and subcutaneous tissue disorders:

Less frequent: Alopecia.

Musculoskeletal, connective tissue and bone disorders:

Frequent: Fatigue.

Less frequent: Arthralgia, asthenia, back pain, muscle cramps, myalgia.

Renal and urinary disorders:

Less frequent: Increased urinary frequency.

Reproductive system and breast disorders:

Less frequent: Impotence.

General disorders:

Less frequent: Pain, weight increase/decrease.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

There is no documented experience with **AMLODAC** overdosage. Gastric lavage may be of benefit. Gross over-dosage could result in excessive peripheral vasodilatation, resulting in marked and probably prolonged systemic hypotension. Clinically significant hypotension due to **AMLODAC** overdosage requires active cardiovascular support. Intravenous calcium gluconate may be of benefit in reversing the effects of calcium channel blockade. Since **AMLODAC** is highly protein-bound, dialysis is not likely to be of benefit.

TREATMENT IS SYMPTOMATIC AND SUPPORTIVE.

IDENTIFICATION

AMLODAC 5: A brown, round, biconvex, film coated tablets, with a breakline on one side, and plain on other side.

AMLODAC 10: A white, round, biconvex, film coated tablets, with a breakline on one side, and plain on other side.

PRESENTATION

AMLODAC 5: PVC / Aluminium foil blister strips containing 10 tablets. 3 or 10 blister strips are packed in an outer carton.

AMLODAC 10: PVC / Aluminium foil blister strips containing 10 tablets. 3 or 10 blister strips are packed in an outer carton.

STORAGE INSTRUCTIONS

Store at or below 25 °C, in a cool dry place. Protect from light. Do not remove blister strips from outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

AMLODAC 5: A39/7.1/0532

AMLODAC 10: A39/7.1/0533

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

Zydus Healthcare SA (Pty) Ltd.

Southdowns Office Park

Building B, Ground Floor

22 Karee Street

Centurion

0157

DATE OF PUBLICATION OF THE PACKAGE INSERT

Date of registration:

07 July 2006