Approved Professional Information for Medicines for Human Use:

Austell-Amlodipine 5 mg

Austell-Amlodipine 10 mg

SCHEDULING STATUS:

S3

PROPRIETARY NAME (and dosage form):

Austell-Amlodipine 5 mg Tablets

Austell-Amlodipine 10 mg Tablets

COMPOSITION:

Austell-Amlodipine 5 mg:

Each tablet contains amlodipine besilate equivalent to 5 mg amlodipine.

Austell-Amlodipine 10 mg:

Each tablet contains amlodipine besilate 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 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

AUSTELL-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 **AUSTELL-AMLODIPINE** therapy at a lower dose.

Use in Renal Failure:

Although **AUSTELL-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 **AUSTELL-AMLODIPINE** is significantly prolonged in patients with impaired hepatic function. **AUSTELL-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.

AUSTELL-AMLODIPINE may have a negative inotropic effect. AUC of **AUSTELL-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 **CONTRA-INDICATIONS**).

DOSAGE AND DIRECTIONS FOR USE

Hypertension and Angina Pectoris:

Adults:

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

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side-effects:

Cardiovascular

- *Frequent:* Peripheral oedema, palpitations.
- *Less Frequent:* Hypotension (including orthostatic hypotension), syncope, vasculitis, myocardial infarction, arrhythmia (including ventricular tachycardia and atrial fibrillation), chest pain.

Neurological

- *Frequent:* Dizziness, headache, somnolence.
- *Less Frequent:* Hypertonia, hypoesthesia/paresthesia, peripheral neuropathy, tremor, insomnia, mood changes.

Gastro-intestinal

- *Frequent:* Nausea, abdominal pain.
- *Less Frequent:* Altered bowel habits, vomiting, dyspepsia, gingival hyperplasia, pancreatitis.

Musculoskeletal

- *Frequent:* Fatigue.
- *Less Frequent:* Arthralgia, asthenia, back pain, muscle cramps, myalgia.

Autonomic Nervous system

- *Frequent:* Flushing.
- *Less Frequent:* Dry mouth, increased sweating.

Hepatobiliary

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

Hematological

Less Frequent: Purpura, thrombocytopenia, leucopenia.

Genito-urinary

Less Frequent: Increased urinary frequency, impotence.

Body as a whole

Less Frequent: Pain, weight increase/decrease.

Endocrine

Less Frequent: Gynaecomastia.

Metabolic

Less Frequent: Hyperglycemia.

Skin and appendages

Less Frequent: Alopecia.

Respiratory

Less Frequent: Coughing, dyspnoea.

Vision

Less Frequent: Visual disturbances.

Special Senses

Less Frequent: Taste perversion, tinnitus

.

Hypersensitivity reactions

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

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

There is no documented experience with **AUSTELL-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 **AUSTELL-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

Austell-Amlodipine 5 mg Tablets:

White to off-white, round, biconvex, uncoated tablets, with '5' debossing on one side.

Austell-Amlodipine 10 mg Tablets:

White to off-white, round, biconvex, uncoated tablets, with '10' debossing on one side.

PRESENTATION:

Austell-Amlodipine 5 mg Tablets:

Blister pack (Opaque PVDC coated PVC film and Aluminium foil) of 2, 4 or 6 blister strips each containing 14 tablets and 3 blister strips each containing 10 tablets.

Austell-Amlodipine 10 mg Tablets:

Blister pack (Opaque PVDC coated PVC film and Aluminium foil) of 2, 4 or 6 blister strips each containing 14 tablets and 3 blister strips each containing 10 tablets.

STORAGE INSTRUCTIONS

Store in a cool dry place at or below 25 ºC. Protect from light.

Keep blisters in the carton until required for use.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER:

Austell-Amlodipine 5 mg: A39/7.1/0545

Austell-Amlodipine 10 mg: A39/7.1/0546

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE

CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd.

1 Sherborne Road,

Parktown,

Johannesburg, 2193

South Africa.

DATE OF PUBLICATION OF THE PACKAGE INSERT

Date of registration: 02 March 2007