APPROVED PACKAGE INSERT

SCHEDULING STATUS

S3

PROPRIETARY NAME (and dosage form)

NORCARD 5 (tablets)

NORCARD 10 (tablets)

COMPOSITION

Each tablet contains amlodipine besylate equivalent to 5 mg or 10 mg amlodipine base.

PHARMACOLOGICAL CLASSIFICATION

A7.1 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 anti hypertensive 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 11kg. 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

NORCARD is indicated for the:

Treatment of angina pectoris.

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

CONTRA-INDICATIONS

Hypersensitivity lo any of the ingredients.

Hypersensitivity lo 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 **NORCARD** therapy at a lower dose.

Use in Renal Failure

Although **NORCARD** 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 **NORCARD** is significantly prolonged in patients with impaired hepatic function. **NORCARD** 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. **NORCARD** may have a negative inotropic effect. AUC of **NORCARD** may increase in patients with heart failure.

Porphyria

Safely 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 **NORCARD** 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 **NORCARD** 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.

Gastrointestinal

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.

Hepatobilliary

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

Haematological

Less Frequent: Purpura, thrombocytopenia, leucopenia.

Genito-urinary

Less Frequent: Increased urinary frequency, impotence.

Body as 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 **NORCARD** overdosage. Gastric lavage may be of benefit. Gross overdosage could result in excessive peripheral vasodilatation, resulting in marked and probably prolonged systemic hypotension. Clinically significant hypotension due to **NORCARD** overdosage requires active cardiovascular support. Intravenous calcium gluconate may be of benefit in reversing the effects of calcium channel blockade. Since **NORCARD** is highly protein-bound, dialysis is not likely to be of benefit.

TREATMENT IS SYMPTOMATIC AND SUPPORTIVE.

IDENTIFICATION

NORCARD 5: Brown coloured, smooth, round, biconvex, film coated tablet plain on both the sides.

NORCARD 10: White to off-white, smooth, round, biconvex, film coated tablet plain on one side and breakline on other side.

PRESENTATION

Aluminium foil, clear PVC blister packs each containing 30 or 100 tablets in strips of 10 tablets.

STORAGE INSTRUCTIONS

Store below 25 °C. Protect from light.

Do not remove the blisters from the outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

NORCARD 5: 36/7.1/0480

NORCARD 10: 36/7.1/0481

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

Akacia Healthcare (Pty) Ltd

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Isando

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DATE OF PUBLICATION OF THE PACKAGE INSERT

25 November 2004