SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

AMLOTEL 40 / 5 (Tablets)

AMLOTEL 40 / 10 (Tablets)

AMLOTEL 80 / 5 (Tablets)

AMLOTEL 80 / 10 (Tablets)

COMPOSITION

AMLOTEL 40 / 5 mg tablets: Each tablet contains 40 mg Telmisartan and 5 mg Amlodipine base (as besylate salt). Contains sugar (mannitol) 169,94 mg per tablet

AMLOTEL 40 / 10 mg tablets: Each tablet contains 40 mg Telmisartan and 10 mg Amlodipine base (as besylate salt). Contains sugar (mannitol) 169,94 mg per tablet

AMLOTEL 80 / 5 tablets: Each tablet contains 80 mg Telmisartan and 5 mg Amlodipine base (as besylate salt). Contains sugar (mannitol) 339,88 mg per tablet

AMLOTEL 80 / 10 tablets: Each tablet contains 80 mg Telmisartan and 10 mg Amlodipine base (as besylate salt). Contains sugar (mannitol) 339,88 mg per tablet

Inactive ingredients: Mannitol, meglumine, povidone-k, sodium stearyl fumarate, magnesium stearate, microcrystalline cellulose, corn starch, iron oxide black, blue colourant, crospovidone,

PHARMACOLOGICAL CLASSIFICATION

A 7.1.3 Vascular medicine – other hypotensives.

PHARMACOLOGICAL ACTION:

Pharmacodynamic Properties:

AMLOTEL combines two antihypertensive medicines with different mechanisms of action: an angiotensin II receptor antagonist, telmisartan, and a dihydropyridinic calcium channel blocker, amlodipine.

The combination of these medicines has an additive antihypertensive effect.

Telmisartan

Telmisartan is a specific angiotensin II receptor (type AT_1) antagonist. Telmisartan displaces angiotensin II from its binding site at the AT_1 receptor subtype, which is responsible for the known actions of angiotensin II. Telmisartan does not exhibit any partial agonist activity at the AT_1 receptor. The binding is long lasting.

Telmisartan does not show affinity for other receptors, including AT_2 and other less characterised AT receptors. The functional role of these receptors is not known, nor is the effect of their possible overstimulation by angiotensin II, whose levels are increased by telmisartan. Plasma aldosterone levels are decreased by telmisartan monotherapy. Telmisartan monotherapy does not inhibit human plasma renin or block ion channels.

In man, an 80 mg dose of telmisartan monotherapy almost completely inhibits the angiotensin II evoked blood pressure increase. The inhibitory effect is maintained over 24 hours and is still measurable up to 48 hours.

After administration of the first dose of telmisartan monotherapy, onset of antihypertensive activity occurs within 3 hours. The maximum reduction in blood pressure is generally attained 4 weeks after the start of treatment and is sustained during long-term therapy.

There is an apparent trend to a dose relationship with regard to a time to recovery of baseline systolic blood pressure. In this respect data concerning diastolic blood pressure are inconsistent. In patients with hypertension telmisartan monotherapy reduces both systolic and diastolic blood pressure without affecting pulse rate.

Amlodipine:

Amlodipine is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle.

The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle, leading to reductions in peripheral vascular resistance and in blood pressure. Experimental data indicate that amlodipine binds to both dihydropyridine and non-dihydropyridine binding sites. Amlodipine is relatively vessel-selective, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells.

In patients with hypertension, once daily dosing provides clinically significant reductions of blood pressure in both the supine and standing positions throughout the 24-hour interval. Due to the slow onset of action, acute hypotension is not a feature of amlodipine administration.

In hypertensive patients with normal renal function, therapeutic doses of amlodipine results in a decrease in renal vascular resistance and an increase in glomerular filtration rate and effective renal plasma flow, without a change in filtration fraction or proteinuria.

AMLOTEL

Treatment with each combination dose of **AMLOTEL** results in significantly greater diastolic and systolic blood pressure reductions and higher control rates compared to the respective monotherapy components.

The majority of the antihypertensive effect is attained within 2 weeks after initiation of therapy.

The antihypertensive effect of **AMLOTEL** is similar irrespective of age and gender*, and is similar in patients with and without diabetes.*

Pharmacokinetic Properties:

Pharmacokinetics of the fixed dose combination (Telmisartan and Amlodipine):

The rate and extent of absorption of **AMLOTEL** are similar to the bioavailability of Telmisartan and Amlodipine when administered as individual tablets.

Pharmacokinetics of the single components*:*

Absorption of telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for telmisartan is about 50 %. When the fixed dose combination is taken with food, the reduction in the area under the plasma concentration-time curve (AUC) of telmisartan was approximately 25 % at a dose of 80/10 mg. By 3 hours after administration plasma concentrations are similar whether telmisartan is taken fasting or with food. The reduction in AUC is not expected to cause a reduction in the therapeutic efficacy.

After oral administration of therapeutic doses of amlodipine alone, peak plasma concentrations of amlodipine are reached in 6 – 12 hours. Absolute bioavailability has been calculated as between 64 % and 80 %. Amlodipine bioavailability is unaffected by food ingestion.

Telmisartan is largely bound to plasma protein (> 99.5 %), mainly albumin and alpha-1 acid glycoprotein. The mean steady state apparent volume of distribution (V_{ss}) is approximately 500 L. The volume of distribution of amlodipine is approximately 21 L /kg. *In vitro* studies with amlodipine have shown that approximately 97.5 % of circulating drug is bound to plasma proteins in hypertensive patients.

Telmisartan is metabolised by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown for the conjugate. Amlodipine is extensively (approximately 90 %) metabolised by the liver to inactive metabolites.

Telmisartan is characterised by bi-exponential decay pharmacokinetics with a terminal elimination half-life of > 20 hour. The maximum plasma concentration (C_{max}) and, to a smaller extent, area under the plasma concentration-time curve (AUC) increase disproportionately with dose. There is no evidence of clinically relevant accumulation of telmisartan.

After oral (and intravenous) administration telmisartan is nearly exclusively excreted with the faeces, mainly as unchanged compound. Cumulative urinary excretion is < 2 % of dose. Total plasma clearance (CL_{tot}) is high (approximately 900 mL/min) compared with hepatic blood flow (about 1 500 mL/min).

Amlodipine elimination from plasma is biphasic, with a terminal elimination half-life of approximately 30 to 50 hours. Steady state plasma levels are reached after continuous administration for 7 – 8 days. Ten percent of original amlodipine and 60 % of amlodipine metabolites are excreted in urine.

Paediatric patients (age below 18 years):

No pharmacokinetic data are available in the paediatric population.

Gender effects:

Gender differences in plasma concentration of telmisartan were observed, C_{max} and AUC being approximately 3 and 2-fold higher, respectively, in females compared to males without relevant influence on efficacy.

Elderly patients:

The pharmacokinetics of telmisartan do not differ between younger and elderly patients. Time to peak plasma amlodipine concentrations is similar in young and elderly patients. In elderly patients, amlodipine clearance tends to decline, causing increases in the area under the curve (AUC) and elimination half-life.

Patients with renal impairment:

Lower plasma concentrations of telmisartan were observed in patients with renal insufficiency undergoing dialysis. Telmisartan is highly bound to plasma protein in renal-insufficient subjects and cannot be removed by dialysis. The elimination half-life is not changed in patients with renal impairment.

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

Patients with hepatic impairment:

Pharmacokinetics properties in patients with hepatic impairment shows an increase in absolute bioavailability of telmisartan up to nearly 100 %. The elimination half-life is not changed in patients with hepatic impairment.

Patients with hepatic insufficiency have decreased clearance of amlodipine with resulting increase of approximately 40 – 60 % in AUC.

INDICATIONS

Replacement therapy:

Treatment of essential hypertension in patients who have been stabilised on the two component medicines used at the same dose.

Add on therapy:

AMLOTEL is indicated in patients whose blood pressure is not adequately controlled on Amlodipine monotherapy.

CONTRAINDICATIONS:

- Hypersensitivity to telmisartan, amlodipine or any of the other components of **AMLOTEL**
- Hypersensitivity to dihydropyridine derivatives
- A history of angioedema related to previous therapy with ACE inhibitors or angiotensin receptor blockers (ARBs): These patients must never again be given these medicines
- Hereditary or idiopathic angioedema
- Hypertrophic obstructive cardiomyopathy (HOCM)
- Severe renal function impairment (creatine clearance less than 30 mL / min)
- Bilateral renal artery stenosis
- Renal artery stenosis in patients with a single kidney
- Aortic stenosis

- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride (see INTERACTIONS).
- Porphyria
- The concomitant use of **AMLOTEL** with aliskiren-containing products is contraindicated (see WARNINGS AND SPECIAL PRECAUTIONS and INTERACTIONS
- Lithium therapy: concomitant administration with **AMLOTEL** may lead to toxic blood concentrations of lithium (see INTERACTIONS).
- Pregnancy and lactation (see PREGNANCY AND LACTATION)
- Biliary obstructive disorders
- Severe hepatic impairment,
- Cardiogenic shock

WARNINGS AND SPECIAL PRECAUTIONS:

Pregnancy:

Should a woman become pregnant while receiving **AMLOTEL**, the treatment should be stopped promptly and switched to a different class of antihypertensive medicine. (See CONTRAINDICATIONS and PREGNANCY AND LACTATION).

AMLOTEL should not be initiated during pregnancy (see **CONTRAINDICATIONS**). Patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy.

When pregnancy is diagnosed, treatment with **AMLOTEL** should be stopped immediately, and if appropriate, alternative therapy should be started (see **PREGNANCY AND LACTATION**).

Hepatic impairment:

Telmisartan (ingredient of **AMLOTEL**) is mostly eliminated in the bile. Patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. Amlodipine's half-life is prolonged in patients with impaired liver functions and dosage recommendations have not been established.

AMLOTEL should therefore be used with caution in patients with mild to moderate impairment of liver function, and should not be used in patients with severe liver impairment (see **CONTRAINDICATIONS)**.

Renal impairment and kidney transplant:

When **AMLOTEL** is used in patients with impaired renal function, a periodic monitoring of potassium and creatinine serum levels is recommended. There is no experience regarding the administration of **AMLOTEL** in patients with a recent kidney transplant. Telmisartan and amlodipine are not dialysable.

Renovascular hypertension:

There is an increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicines that affect the renin-angiotensin-aldosterone system (RAAS) (see CONTRAINDICATONS).

Intravascular hypovolaemia

Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by e.g. vigorous diuretic therapy, dietary salt restrictions, diarrhoea or vomiting. Such conditions should be corrected before the administration of **AMLOTEL**.

Dual blockade of the renin-angiotensin-aldosterone system (RAAS)

There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren may increase the risk of hypotension, hyperkalaemia and decreases renal function (including acute renal failure). Dual blockade of RAAS through the combined use of **AMLOTEL** and aliskiren is therefore contraindicated (see CONTRAINDICATIONS).

AMLOTEL should not be used concomitantly with aliskiren (see CONTRAINDICATIONS)

Other conditions with stimulation of the renin-angiotensin- aldosterone systems:

In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin -aldosterone system (e.g patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis) treatment with **AMLOTEL**, that affects this system, has been associated with acute hypotension, hyperuremia, oliguria or rarely acute renal failure.

Primary aldosteronism:

Patients with primary aldosteronism generally will not respond to antihypertensive medicines acting through inhibition of the renin-angiotensin system. Therefore, the use of **AMLOTEL** is not recommended.

Aortic and mitral valve stenosis, hypertrophic obstructive cardiomyopathy:

AMLOTEL is contraindicated in patients suffering from aortic or mitral stenosis, or hypertrophic obstructive cardiomyopathy.

Unstable angina pectoris, acute myocardial infarction:

There are no data to support the use of **AMLOTEL** in unstable angina pectoris and during or within one month of a myocardial infarction.

Heart failure:

The use of amlodipine in patients with NYHA III and IIII heart failure of non-ischaemic aetiology is associated with pulmonary oedema.

Hyperkalaemia:

During treatment with **AMLOTEL,** hyperkalaemia may occur, especially in the presence of renal impairment and/or heart failure. Monitoring of serum potassium in patients at risk is recommended.

Based on experience with the use of medicines that affect the renin-angiotensin-system, concomitant use with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicines that may increase the

potassium level (heparin, etc.) may lead to an increase in serum potassium and should therefore be co-administered cautiously with **AMLOTEL**.

Other:

Excessive reduction of blood pressure in patients with ischaemic cardiopathy or ischaemic cardiovascular disease may result in a myocardial infarction or stroke.

Effects on the ability to drive and use machines:

Patients may experience undesirable effects such as syncope (fainting), somnolence, dizziness, or vertigo during treatment. Therefore, caution should be recommended when driving a vehicle or operating machinery. If patients experience these adverse effects, they should avoid potentially hazardous tasks such as driving or operating machinery.

Mannitol:

AMLOTEL tablets contain mannitol and may have a laxative effect.

INTERACTIONS:

There are no interactions between the two components (telmisartan and amlodipine) of the fixed dose combination.

Interactions common to the combination:

No interaction studies have been performed with **AMLOTEL** and other medicines.

Interactions to be taken into account with concomitant use:

Other antihypertensive medicines:

The blood pressure lowering effect of **AMLOTEL** can be increased by concomitant use of other antihypertensive medicines.

Medicines with blood pressure lowering potential:

Based on their pharmacological properties it can be expected that the following medicines may potentiate the hypotensive effects of **AMLOTEL** e.g. baclofen, amifostine. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics, or antidepressants.

Corticosteroids (systemic route):

Concomitant use with corticosteroids causes a reduction of the antihypertensive effect.

Interactions linked to the telmisartan component of AMLOTEL:

Telmisartan may increase the hypotensive effect of other antihypertensive medicines. Other interactions of clinical significance have not been identified.

Co-administration of telmisartan does not result in a clinically significant interaction with digoxin, warfarin, hydrochlorothiazide, glibenclamide, ibuprofen, paracetamol, simvastatin and amlodipine. For digoxin in a 20 % increase in median plasma digoxin trough concentration has been observed (39 % in a single case); monitoring of plasma digoxin levels should be considered.

The co-administration of telmisartan and ramipril led to an increase of up to 2,5-fold in the AUC_{0-24} and C_{max} of Ramipril and ramiprilat. The clinical relevance of this observation is not known.

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Increased serum levels have also been reported with telmisartan.

Treatment with NSAIDs (i.e. aspirin at anti-inflammatory dosage regimens, COX-2 inhibitors and non-selective NSAIDs) is associated with the potential for acute renal insufficiency in patients who are dehydrated. Compounds acting on the renin-angiotensin-system like telmisartan may have synergistic effects. Patients receiving NSAIDs and telmisartan should be adequately hydrated and be monitored for renal function at the beginning of combined treatment.

A reduced effect of antihypertensive medicines like telmisartan by inhibition of vasodilating prostaglandins occurs during combined treatment with NSAIDs.

Dual blockade of the RAAS with ARB's ACE inhibitors or aliskiren:

Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (see CONTRAINDICATIONS, WARNINGS AND SPECIAL PRECAUTIONS).

Interactions linked to the amlodipine component of AMLOTEL:

Concomitant use requiring caution:

CYP3A4 inhibitors:

Diltiazem inhibits the metabolism of amlodipine, probably via CYP3A4 (plasma concentration increases by approximately 50 % and the effect of amlodipine is increased).

The possibility that more potent inhibitors of CYP3A4 (i.e. ketoconazole, itraconazole, ritonavir) may increase the plasma concentration of amlodipine to a greater extent than diltiazem cannot be excluded.

CYP3A4 inducers (anticonvulsant medicines [e.g. carbamazepine, phenobarbitone, phenytoin, fosphenytoin, primidone], rifampicin, Hypericum perforatum):

Co-administration may lead to reduced plasma concentrations of amlodipine. Clinical monitoring is indicated, with possible dosage adjustment of amlodipine during the treatment with the inducer and after its withdrawal.

Concomitant use to be taken into account:

Others:

In monotherapy, amlodipine is safely administered with thiazide diuretics, beta blockers, ACE inhibitors, long-acting nitrates, sublingual nitroglycerin, non-steroidal anti-inflammatory medicines, antibiotics and oral hypoglycaemic combination. When amlodipine and sildenafil were used in combination, each medicine independently exerts its own blood pressure lowering effect.

Additional information:

Concomitant administration of 240 mL of grapefruit juice with a single oral dose of 10 mg amlodipine does not show a significant effect on the pharmacokinetic properties of amlodipine.

Co-administration of amlodipine with cimetidine has no significant effect on the pharmacokinetics of amlodipine.

Co-administration of amlodipine with atorvastatin, digoxin, warfarin or ciclosporin has no significant effect on the pharmacokinetics or pharmacodynamics of these medicines.

PREGNANCY AND LACTATION:

Pregnancy:

Safety in pregnancy has not been established (see **Contraindications**).

When pregnancy is planned or confirmed, **AMLOTEL** should be discontinued (see WARNINGS and SPECIAL PRECAUTIONS).

Medicines affecting the renin-angiotensin system, such as **AMLOTEL**, can cause embryonal toxicity, foetal and neonatal morbidity and mortality when administered to pregnant women

Patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. Should exposure to **AMLOTEL** have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended.

Infants whose mothers have taken **AMLOTEL** should be closely observed for hypotension

Women of Childbearing potential:

Women of childbearing age should ensure adequate contraception.

Lactation:

Safety in lactation has not been established (see **CONTRAINDICATIONS***).*

It is not known whether telmisartan and/or amlodipine (as in **AMLOTEL**) are excreted in human milk. Excretion of telmisartan in breast milk is shown in animal studies. Because of the potential adverse reactions in breastfed infants, **AMLOTEL** should not be used by breast feeding mothers.

DOSAGE AND DIRECTIONS FOR USE

AMLOTEL should be taken once daily.

Replacement Therapy:

Patients taking telmisartan and amlodipine as separate tablets can instead take **AMLOTEL** containing the same component doses in one tablet once daily.

Add on therapy:

AMLOTEL may be administered in patients whose blood pressure is not adequately controlled with amlodipine alone.

The usual starting dose of **AMLOTEL** is 40/5 mg once daily.

If additional blood pressure lowering is needed after at least 2 weeks of therapy, the dose may be titrated up to a maximum of 80/10 mg once daily.

AMLOTEL may be taken with or without food.

Renal impairment:

No dosage adjustment is required for patients with mild to moderate renal impairment (see **WARNINGS AND SPECIAL PRECAUTIONS**).

Amlodipine and telmisartan are not dialysable.

Hepatic impairment:

In patients with mild to moderate hepatic impairment **AMLOTEL** should be administered with caution. For telmisartan the dose should not exceed 40/5 mg or 40/10 mg once daily.

Elderly:

No dose adjustment is necessary for elderly patients.

Children and adolescents:

AMLOTEL is not recommended for use in patients aged below 18 years.

SIDE EFFECTS

Fixed dose combination:

Infections and infestations:

Less frequent: Cystitis

Psychiatric disorders:

Less frequent: depression, anxiety, insomnia

Nervous system disorders:

Frequent: Dizziness

Less frequent: Somnolence, migraine, headache, paraesthesia, syncope (fainting), peripheral neuropathy, hypoaesthesia, dysgeusia, tremor

Ear and labyrinth disorders:

Less frequent: Vertigo

Cardiac disorders:

Less frequent: Bradycardia, palpitation

Vascular disorders:

Less frequent: Hypotension, orthostatic hypotension, flushing

Respiratory, thoracic and mediastinal disorders:

Less frequent: Cough

Gastro-intestinal disorders:

Less frequent: Abdominal pain, diarrhoea, nausea, vomiting, gingival, hypertrophy, dyspepsia, dry mouth

Skin and subcutaneous tissue disorders:

Less frequent: Pruritus, eczema, erythema, rash

Musculoskeletal, connective tissue and bone disorders:

Less frequent: Arthralgia, muscle spasms,

myalgia, back pain, pain in extremity

Renal and urinary disorders:

Less frequent: Nocturia

Reproductive system and breast disorders:

Less frequent: Erectile dysfunction

General disorders:

Frequent: Oedema, peripheral

Less frequent: Asthenia, chest pain, fatigue, oedema, malaise

Investigations:

Less frequent: Hepatic enzymes increased, blood uric acid increased

The following side effects are expected based on experience with telmisartan monotherapy, but the frequencies are not determined:

Infections and infestations:

Frequency not known: Sepsis including fatal outcome, urinary tract infections, upper respiratory tract infections

Blood and the lymphatic system disorders:

Frequency not known: Anaemia, eosinophilia, thrombocytopenia

Immune system disorders:

Frequency not known: Angioedema, anaphylactic reaction, hypersensitivity

Metabolism and nutritional disorders:

Frequency not known: Hyperkalaemia

Eye disorders:

Frequency not known: Visual disturbance

Cardiac disorders:

Frequency not known: Tachycardia

Respiratory, thoracic, mediastinal disorders:

Frequency not known: Dyspnoea

Gastrointestinal disorders:

Frequency not known: Flatulence, stomach discomfort

Hepato-biliary disorders:

Frequency not known: Hepatic function abnormal, liver disorder

Skin and subcutaneous tissue disorders:

Frequency not known: Hyperhidrosis, urticaria, medicine eruption, toxic skin eruption

Musculoskeletal, connective tissue and bone disorders:

Frequency not known: Tendon pain

Renal and urinary disorders:

Frequency not known: Renal impairment

General disorders:

Frequency not known: Influenza-like illness

Investigations:

Frequency not known: haemoglobin decreased, blood creatinine increased, blood creatinine phosphokinase (CPK) increased.

The following side effects are expected based on experience with amlodipine monotherapy, but the frequencies are not determined:

Blood and the lymphatic system disorders:

Frequency not known: Thrombocytopenia

Immune system disorders:

Frequency not known: Angioedema, hypersensitivity

Metabolism and nutritional disorders:

Frequency not known: Hyperglycaemia

Psychiatric disorders:

Frequency not known: Mood change

Eye disorders:

Frequency not known: Visual impairment

Ear and labyrinth disorders:

Frequency not known: Tinnitus

Cardiac disorders:

Frequency not known: Myocardial infarction, dysrhythmia, ventricular tachycardia, atrial fibrillation

Vascular disorders:

Frequency not known: Vasculitis

Respiratory, thoracic and mediastinal disorders:

Frequency not known: Dyspnoea, rhinitis

Gastrointestinal disorders:

Frequency not known: Change of bowel habit, pancreatitis, gastritis

Hepato-biliary disorders:

Frequency not known: Hepatitis, jaundice, hepatic enzyme elevations (mostly consistent with cholestasis)

Skin and subcutaneous tissue disorders:

Frequency not known: Hyperhidrosis, urticaria, alopecia, purpura, skin discolouration, erythema multiforme

Renal and urinary disorders:

Frequency not known: Micturition disorder, pollakiuria

Reproductive and breast-feeding disorders:

Frequency not known: Gynaecomastia

General disorders:

Frequency not known: Pain, weight increased, weight decreased

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Signs and symptoms of overdosage are expected to be in line with exaggerated pharmacological effects.

Available data for amlodipine suggest that gross overdosage could result in excessive peripheral vasodilatation 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 resuscitative measures (including fluid overload) to maintain perfusion and cardiac output may be precipitating factors.

Therapy:

Supportive treatment should be instituted. Intravenous calcium gluconate may be beneficial in reversing the effects of calcium channel blockade. Telmisartan and amlodipine are not removed by haemodialysis.

IDENTIFICATION

AMLOTEL 80/5: Oval shaped biconvex, bilayer, uncoated tablets with one white to off-white colour layer and one blue colour mottled layer debossed with “L391”

AMLOTEL 80/10: Oval shaped biconvex, bilayer, uncoated tablets with one white to off- white colour layer and one blue colour mottled layer debossed with “L388”

AMLOTEL 40/5: Oval shaped biconvex, bilayer, uncoated tablets with one white to off- white colour layer and one blue colour mottled layer debossed with “L389”

AMLOTEL 40/10: Oval shaped biconvex, bilayer, uncoated tablets with one white to off- white colour layer and one blue colour mottled layer debossed with *“L390”*

PRESENTATION

30 Tablets in aluminium blister strips of 10 tablets per strip with 3 strips packed in a unit carton.

STORAGE INSTRUCTIONS

Store at or below 30 °C. Store in the original package.

Keep out of reach of children.

Protect from light and moisture.

REGISTRATION NUMBER:

AMLOTEL 40/5: 50/7.1.3/0344

AMLOTEL 40/10: 50/7.1.3/0345

AMLOTEL 80/5: 50/7.1.3/0346

AMLOTEL 80/10: 50/7.1.3/0347

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

Innovata Pharmaceuticals (Pty) Ltd

100 Northern Parkway

Crownwood Office Park, Block D

Ormonde

Johannesburg

2091

South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

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