FINAL PACKAGE INSERT

SCHEDULING STATUS: **S3**

PROPRIETARY NAME (and dosage form):

Tenormin® 25; Tenormin® 50; Tenormin® 100 (Tablets)

COMPOSITION:

TENORMIN 25 tablets containing 25 mg atenolol.

TENORMIN 50 tablets containing 50 mg atenolol.

TENORMIN 100 tablets containing 100 mg atenolol.

PHARMACOLOGICAL CLASSIFICATION:

A. 5.2 Adrenolytics (Sympathicolytics)

PHARMACOLOGICAL ACTION:

TENORMIN (atenolol) is a beta-blocker which is beta-1-selective. Selectivity decreases with increasing dose. It is without intrinsic sympathomimetic and membrane stabilising activity. Human studies indicate that it crosses the blood-brain barrier only to a negligible extent.

The mode of action in the treatment of hypertension is unclear. It is probably the reduction in cardiac rate and contractility which makes it effective in eliminating or reducing the symptoms of patients with angina.

Pharmacokinetic properties:

Absorption of atenolol following oral dosing is consistent but incomplete (approximately 40-50%) with peak plasma concentrations occurring 2-4 hours after dosing. There is no significant hepatic metabolism of atenolol and more than 90% of that absorbed reaches the systemic circulation unaltered. The plasma half-life is about 6 hours but this may rise in severe renal impairment since the kidney is the major route of elimination. Atenolol penetrates tissues poorly due to its low lipid solubility and its concentration in brain tissue is low. Plasma protein binding is low (approximately 3%).

INDICATIONS:

Management of angina pectoris and hypertension.

CONTRA-INDICATIONS:

TENORMIN is contra-indicated:

In patients with known hypersensitivity to atenolol.

In patients with cardiogenic shock.

In the presence of second degree or third degree heart block.

In patients with hypotension.

In patients with metabolic acidoses (e.g. in diabetes).

In patients with bradycardia.

In patients with severe peripheral arterial circulatory disturbances.

In patients with untreated phaeochromocytoma.

In patients with sick sinus syndrome.

After prolonged fasting.

Special care should be taken with patients whose cardiac reserve is poor. TENORMIN should be avoided in cardiac failure, unless or until signs of failure are controlled with digitalis or diuretics.

Because of their negative inotropic effects, beta-blockers should be avoided in uncontrolled heart failure, excluding that due to hypertrophic obstructive cardiomyopathy.

Particular caution should be exercised with patients suffering from the following: asthma, bronchitis, chronic respiratory diseases. Although cardioselective (beta-1) beta-adrenoceptor blocking agents may have less effect on lung function than non-selective beta-adrenoceptor blocking agents, these should be avoided in patients with reversible obstructive airways disease, unless there are compelling clinical reasons for their use.

In the perioperative period it is generally unwise to reduce the dosage to which the patient is accustomed, as there may be danger of aggravation of angina pectoris or hypertension. A

patient's normal tachycardic response to hypovolemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard.

WARNINGS:

TENORMIN may increase the number and duration of angina attacks in patients with Prinzmetal's angina due to unopposed alpha receptor mediated coronary artery vasoconstriction. However, since TENORMIN is beta-1-selective it may be used with utmost care.

TENORMIN may aggravate less severe peripheral arterial circulatory disturbances and severe peripheral vascular disease and even peripheral gangrene may be precipitated.

Due to its negative effect on conduction time, TENORMIN should only be given with caution to patients with first degree heart block.

TENORMIN may mask the signs of thyrotoxicosis.

While taking TENORMIN, patients with a history of anaphylactic reaction to a variety of allergens may have a more severe reaction on repeated challenge. Such patients may be unresponsive to the usual dose of adrenaline used to treat allergic reactions.

Lactation:

There is significant accumulation in breast milk. Caution should be exercised when TENORMIN is administered to a nursing woman.

DOSAGE AND DIRECTIONS FOR USE:

Adults:

Angina pectoris:

Most patients with angina pectoris will respond to a dose of 100 mg daily.

This is most conveniently administered as a single 100 mg tablet once daily, which may if desired be given in the form of one 50 mg tablet twice daily. It is unlikely that additional benefit will be obtained by increasing the dose.

Hypertension:

Most patients will respond to a dose of 50-100 mg daily given orally as a single dose. It is unlikely that additional benefit will be gained by increasing the dose.

TENORMIN is compatible with diuretics and other hypotensive agents. In refractory cases a further reduction of blood pressure may be achieved by combining TENORMIN with other antihypertensive agents.

Renal failure:

See section under "Special precautions".

Children:

There is no experience in children.

Elderly and renal dysfunction:

The normal dose should be reduced in elderly patients and may need to be reduced in patients suffering from renal dysfunction.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side-effects:

Cardiovascular:

Congestive cardiac failure and marked bradycardia may occur. Intermittent claudication may be increased if already present. Cold extremities, deterioration of heart failure, heart block and postural hypotension which may be associated with syncope. The development of Raynaud's phenomenon (due to unopposed arteriolar alpha-sympathetic activation) may occur.

CNS:

Confusion, dizziness, headaches, mood changes, nightmares, overt psychosis, hallucinations, sleep disturbances, depression and malaise.

Gastrointestinal:

Dry mouth, nausea, vomiting, diarrhoea and other gastrointestinal disturbances. Elevations of transaminase levels have been seen infrequently, infrequent cases of hepatic toxicity including intrahepatic cholestasis have been reported.

Haematological:

Purpura, thrombocytopenia.

Integumentary:

Alopecia, psoriasiform skin reactions, exacerbation of psoriasis. There have been reports of skin rashes and/or dry eyes associated with the use of beta-blocking agents. Discontinuation of the medicine should be considered if any such reaction is not otherwise explicable.

Neurological:

Paraesthesia

Respiratory:

Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints.

Special senses:

Visual disturbances.

Others:

An increase in ANA (Antinuclear Antibodies) has been observed, however the clinical relevance is not clear.

Fatigue.

Adverse reactions are more common in patients with renal decompensation.

Special precautions:

The increase in airway resistance which may occur in asthmatic patients can usually be reversed by standard doses of bronchodilators.

Patients with a phaeochromocytoma require treatment with an alpha-adrenergic blocker.

TENORMIN masks the symptoms of hypoglycaemia.

Sexual impotence has been reported following TENORMIN administration.

Abrupt discontinuation of therapy may cause exacerbation of angina pectoris in patients suffering from ischemic heart disease. Discontinuation of therapy should be gradual and patients should be advised to limit the extent of their physical activity during the period that the medicine is discontinued.

One of the pharmacological actions of TENORMIN is to reduce the heart rate. Bradycardia (usually less than 50-55 beats/minute) indicates that dosage should not be further increased.

Renal failure:

Since TENORMIN is excreted via the kidneys dosage should be adjusted in cases of severe impairment of renal function. No significant accumulation of TENORMIN occurs at a glomerular filtration rate (GFR) greater than 35 ml/min/1,73 m^2 (normal range is 100-150 ml/min/1,73 m^2). For patients with a creatinine clearance of 15-35 ml/min/1,73m^2 (equivalent to serum creatinine of 300-600 micromol/litre) the oral dose should be 50 mg daily or 100 mg once every two days.

For patients with a creatinine clearance of < 15 ml/min/1,73 m^2 (equivalent to serum creatinine of > 600 micromol/litre) the oral dose should be 25 mg daily or 50 mg on alternate days or 100 mg once every four days. Patients on haemodialysis should be given 50 mg orally after each

dialysis; this should be done under hospital supervision as marked falls in blood pressure can occur.

Pregnancy:

TENORMIN crosses the placental barrier and appears in cord blood. Administration to pregnant women has been associated with intra-uterine growth retardation.

Administration of TENORMIN to pregnant mothers shortly before giving birth, or during labour may result in the newborn infants being born hypotonic, collapsed and hypoglycaemic.

The use of TENORMIN in women who are, or may become, pregnant requires that the anticipated benefits be weighed against the possible risks, particularly in the first and second trimesters.

Interactions:

Care should be taken when using anaesthetic agents with TENORMIN. The anaesthetist should be informed and the choice of anaesthetic should be an agent with as little negative inotropic activity as possible. Use of beta-blockers with anaesthetic agents may result in attenuation of the reflex tachycardia and increase the risk of hypotension. Anaesthetic agents causing myocardial depression are best avoided.

It can be dangerous to administer this medicine concomitantly with the following medicines: hypoglycaemic agents, phenothiazines and Class I antiarrhythmic agents such as disopyramide.

N.B. Such drug-drug interactions can have life-threatening consequences.

Special note:

Digitalisation of patients receiving long term TENORMIN therapy may be necessary if congestive cardiac failure is likely to develop. This combination can be considered despite the potentiation of negative chronotropic effect of the two medicines. Careful control of dosages and of the individual patient's response (and notably pulse rate) is essential in this situation.

Combined use of TENORMIN and calcium channel blockers with negative inotropic effects, e.g. verapamil and diltiazem, can lead to an exaggeration of these effects, particularly in patients with impaired ventricular function and/or SA or AV conduction abnormalities. Neither medicine should be administered intravenously within 48 hours of discontinuing the other. Concomitant therapy with dihydropyridines, e.g. nifedipine, may increase the risk of hypotension and cardiac failure may occur in patients with latent cardiac insufficiency.

TENORMIN may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two medicines are co-administered, the TENORMIN should be withdrawn several days before discontinuing clonidine. If replacing clonidine by TENORMIN therapy, the introduction of the latter should be delayed for several days after clonidine administration has stopped.

Concomitant use of sympathomimetic agents, e.g. adrenaline, may counteract the effect of beta-blockers.

Concomitant use of prostaglandin synthetase inhibiting drugs, e.g. ibuprofen and indomethacin, may decrease the hypotensive effect of beta-blockers.

Effect on ability to drive and use machines:

Use is unlikely to result in any impairment of the ability of patients to drive or operate machinery. However, it should be taken into account that occasionally dizziness or fatigue may occur.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Overdosage may produce bradycardia and severe hypotension. Bronchospasm and heart failure may be produced in certain individuals.

Cases of mild overdose should be observed for at least 4 hours, as apnoea and cardiovascular collapse may appear suddenly.

Gastric lavage should be performed if within 4 hours of suspected overdose. Repeated activated charcoal is necessary in severe overdoses.

Excessive bradycardia can be countered with atropine 1-2 mg intravenously. If necessary, this may be followed by a bolus dose of glucagon 10 mg intravenously. If required, this may be repeated or followed by an intravenous infusion of glucagon 1-10 mg/hour, depending on the response. If no response to glucagon occurs or if glucagon is unavailable, a beta-adrenoceptor such as dobutamine 2,5 to 10 micrograms/kg/minute by intravenous infusion or isoprenaline 10 to 25 micrograms given as an infusion at a rate not exceeding 5 micrograms/minute may be given, although larger doses may be required.

Bronchospasm should be treated with IV aminophylline or inhaled or IV beta-agonist, e.g. salbutamol.

IDENTIFICATION:

TENORMIN 25 Tablets:

White, round, biconvex, film-coated tablets impressed TENORMIN 25 on one face and a trademark on the reverse face.

TENORMIN 50 Tablets:

White, round, biconvex, film-coated tablets imprinted on one face with TENORMIN 50.

TENORMIN 100 Tablets:

Orange, round, biconvex, film-coated tablets imprinted on the one face with TENORMIN and scored on the reverse face.

PRESENTATION:

TENORMIN 25:	Blister packs of 30 tablets.
TENORMIN 50:	Blister packs of 30 tablets.
TENORMIN 100:	Blister packs of 30 tablets.

STORAGE INSTRUCTIONS:

Store protected from light and moisture. Store at or below 25 °C. Keep out of reach of children.

REGISTRATION NUMBERS:

TENORMIN 25:	27/5.2/0251
TENORMIN 50:	P/5.2/174
TENORMIN 100:	J/5.2/120

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

AstraZeneca Pharmaceuticals (Pty) Limited

Building 2, Northdowns Office Park

17 Georgian Crescent West,

Bryanston, Johannesburg

2191, South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

January 1994

Ref.: Tenormin tablets – EPI (21-01-2003)

Inclusion of Namibia + Botswana registration details (15-11-2010)

TENORMIN 25	TENORMIN 50	TENORMIN 100
NAMIBIA: NS2	NAMIBIA: NS2	NAMIBIA: NS2
Reg. Nr.:	Reg. Nr.:	Reg. Nr.:
04/5.2/1762	90/5.2/00287	90/6.2/00286

TENORMIN 50	TENORMIN 100
BOTSWANA: S2	BOTSWANA: S2
Reg. Nr.: B9311780	Reg. Nr.: B9311785