Australian Product Information - TENORMIN® (atenolol)

1. NAME OF THE MEDICINE

Atenolol

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TENORMIN tablets contain 50 mg of the active ingredient atenolol.

Excipient with known effect: sulfites.

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Tenormin 50 mg tablets are white, round, biconvex, film-coated, tablets intagliated with 50 on one side and bisected on the other.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

TENORMIN is indicated in the management of:

- All grades of hypertension, including hypertension of renal origin.
- Frequent disabling angina without evidence of cardiac failure.
- Cardiac arrhythmias (acute treatment of supraventricular and ventricular arrhythmias including those associated with acute myocardial infarction).
- Myocardial infarction - Late intervention (beta-blocker class effect greater than 12 hours after onset of chest pain)

4.2 DOSE AND METHOD OF ADMINISTRATION

Oral dosage in adults

Hypertension

Therapy should be initiated with 50 mg of TENORMIN daily. This may be increased each week in daily doses of 50 mg up to a maximum of 200mg. Where patients are controlled on daily doses of 50 to 100 mg this may be given once daily. Doses above 100 mg daily should be given on a divided basis. Where necessary, a further reduction in blood pressure may be achieved by combining TENORMIN with other antihypertensive agents.

Patients can be transferred to TENORMIN from other antihypertensive treatments with the exception of clonidine. (See Section 4.4 Special Warnings and Precautions for Use)

Angina pectoris

Therapy should be initiated with 50 mg of TENORMIN daily. This may be increased, if required, to 100 mg daily given as a single or divided dose. It is unlikely that additional benefit will be gained by increasing dose.

Cardiac Dysrhythmias

Having controlled the dysrhythmias with other intravenous agents, TENORMIN given orally at a dosage of 50 to 100 mg daily will help maintain control.

Acute Myocardial Infarction – Late Intervention (>12 hours from onset of chest pain)

TENORMIN has been shown to reduce infarct size, reduce the incidence of ventricular dysrhythmias, reduce the need for opiate analgesics and reduce mortality in the first 7 post-infarction days, most of the benefit

being in the first 48 hours. Data from other beta-blocker trials suggest that there is a significant reduction in mortality and a reduced incidence of non-fatal reinfarction if the beta-blocker is continued for 1 to 3 years.

Hence, maintenance oral therapy of 50mg daily of TENORMIN is recommended for 1 to 3 years following myocardial infarction, beginning after early intervention with other agents, or immediately in those patients who present more than 12 hours after suffering an acute myocardial infarction.

Special patient populations

Renal impairment

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 creatinine clearance greater than 35 mL/min/1.73m2 (normal range is 100 to 150 mL/min/1.73m2). For patients with a creatinine clearance of 15 to 35 mL/min/1.73m2 (equivalent to serum creatinine of 300 to 600 micromol/L) the oral dose should be 50 mg daily, or 100 mg on alternate days. For patients with a creatinine clearance of less than 15 mL/min/1.73m2 (equivalent to serum creatinine of greater than 600 micromol/L) the oral dose should be 50 mg on alternate days or 100 mg every fourth day.

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.>

Use in the elderly

Dosage requirements may be reduced especially in patients with impaired renal function.

Use in children

There is no experience with TENORMIN in children.

4.3 CONTRAINDICATIONS

- Bronchospasm

  Beta-adrenergic blockade of the smooth muscle of bronchi and bronchioles may result in an increased airways resistance. These drugs also reduce the effectiveness of asthma treatment. This may be dangerous in susceptible patients.

  Therefore, beta-blockers are contraindicated in any patient with a history of airways obstruction or tendency to bronchospasm. Use of cardioselective beta blockers can also result in severe bronchospasm. If such therapy must be used, great caution should be exercised. Alternative therapy should be considered.

- Congestive heart failure.
- Allergic disorders (including allergic rhinitis) which may suggest a predisposition to bronchospasm.
- Right ventricular failure secondary to pulmonary hypertension.
- Significant right ventricular hypertrophy.
- Sick sinus syndrome.
- Sinus bradycardia (less than 45 to 50 beats/minute).
- Second and third degree A-V block.
- Shock (including cardiogenic and hypovolaemic shock).
- Anaesthesia with agents that produce myocardial depression (eg ether, chloroform, cyclopropane).
- Hypersensitivity to the drug.
- Hypotension.
- Metabolic acidosis.
- Severe peripheral arterial circulatory disturbances.
- Untreated phaeochromocytoma.
- Pregnancy and Lactation. (See Section 4.5 Fertility, Pregnancy and Lactation)

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Cardiac Failure

Beta-blockade depresses myocardial contractility and may precipitate cardiac failure in some patients with a history of cardiac failure, chronic myocardial insufficiency or unsuspected cardiomyopathy as may occur in

chronic alcoholism. In patients without a history of cardiac failure, continuing depression of the myocardium may lead to cardiac failure. If signs of cardiac failure present, the patients should be fully digitalised and/or given an ACE inhibitor or vasodilators with or without a diuretic and carefully monitored. If cardiac failure persists, the beta-blocker should be withdrawn. (See Section 4.4 Special Warnings and Precautions for Use - Abrupt withdrawal of therapy)

(NOTE: Although congestive heart failure has been considered to be a contraindication to the use of beta-blockers, there is a growing literature on the experimental use of beta-adrenergic blocking drugs in heart failure. As further trials are needed to identify which patients are most likely to respond to which drugs, beta-blockers should not normally be prescribed for heart failure outside of specialist centres).

Abrupt Withdrawal of Therapy

Care should be taken if beta-blockers have to be discontinued abruptly in patients with coronary artery disease. Severe exacerbation of angina and precipitation of myocardial infarction and ventricular arrhythmias have occurred following abrupt discontinuation of beta-blockade in patients with ischaemic heart disease. Therefore, it is recommended that the dosage be reduced gradually over a period of about 8 to 14 days during which time the patient's progress should be reassessed. The drug may be reinstituted temporarily if the angina worsens. If the drug must be withdrawn abruptly, close observation is required. In the peri operative period, beta-blockers should not be withdrawn, unless indicated.

History of Anaphylactic Reaction

While taking beta-adrenoreceptor blocking drugs, 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 doses of adrenaline used to treat the allergic reactions.

First Degree Heart Block

Due to its negative effect on conduction time, caution must be exercised if TENORMIN is given to patients with first degree heart block.

Peripheral Circulation

Beta-blockade may impair the peripheral circulation and exacerbate the symptoms of peripheral vascular disease.

Prinzmetal Angina

There is a risk of exacerbating coronary artery spasm if patients with Prinzmetal or variant angina are treated with a beta-blocker. If this treatment is essential, it should only be undertaken in a Coronary or Intensive Care Unit.

Euthyroid Hyperthyroxinaemia

The effects of beta-blockers on thyroid hormone metabolism may result in elevations of serum free thyroxine (T4) levels. In the absence of any signs or symptoms of hyperthyroidism, additional investigation is necessary before a diagnosis of thyrotoxicosis can be made.

Use in Acute Myocardial Infarction

In addition to the contraindications listed (see Section 4.3 Contraindications), patients with the following conditions are not suitable for treatment with TENORMIN:

Systolic blood pressure less than 120 mmHg (systolic blood pressure less than 120 mmHg in combination with a heart rate greater than 90 beats/min has a particularly poor prognosis).

First degree A-V block. There is an increased incidence of cardiogenic shock (and need for inotropes), complete heart block and cardiovascular death in these patients, following TENORMIN.

Patients with atrial fibrillation following myocardial infarction, who were treated with TENORMIN, also had increased cardiovascular mortality compared with those not treated with TENORMIN. It is suggested that such patients be digitalised before TENORMIN therapy is commenced.

Bradycardia

If a treated patient develops symptoms which may be attributable to a slow heart rate, the dose may be reduced.

Anaesthesia and the Peri-operative Period

Beta-blockade may have beneficial effects in decreasing the incidence of arrhythmias and myocardial ischaemia during anaesthesia and the post-operative period. It is currently recommended that maintenance of beta-blockade be continued peri-operatively. The anaesthetist must be made aware of beta-blockade because of the potential for interactions with other drugs, resulting in severe bradyarrhythmias and hypotension, the decreased reflex ability to compensate for blood loss, hypovolaemia and regional sympathetic blockade, and the increased propensity for vagal-induced bradycardia. Incidents of protracted severe hypotension or difficulty restoring normal cardiac rhythm during anaesthesia have been reported. Modern inhalational anaesthetic agents are generally well tolerated, although older agents (ether, cyclopropane, methoxyflurane, trichlorethylene) were sometimes associated with severe circulatory depression in the presence of beta-blockade.

Diabetes

Beta-blockers affect glucose metabolism and may mask some important premonitory signs of acute hypoglycaemia, such as tachycardia.

In patients with insulin or non-insulin dependent diabetes, especially labile diabetes, or with a history of spontaneous hypoglycaemia, beta-blockade may result in the loss of diabetic control and delayed recovery from hypoglycaemia. The dose of insulin or oral hypoglycaemic agent may need adjustment.

Other Metabolic Effects

Beta-adrenoreceptors are involved in the regulation of lipid as well as carbohydrate metabolism. Some drugs affect the lipid profile adversely although the long-term clinical significance of this change is unknown and the effect appears to be less for drugs with intrinsic sympathomimetic activity.

Phaeochromocytoma

In patients with this condition, an alpha-blocking drug (eg phentolamine / phenoxybenzamine) should be administered before the beta-blocker to avoid exacerbation of hypertension.

Eye and Skin Reactions

Various skin rashes and conjunctival xerosis have been reported with beta blockers. Cross-reactions may occur between beta-blockers, therefore, substitutions within the group may not necessarily preclude occurrence of symptoms.

During the long-term treatment with the beta-blocking drug, practolol, a specific rash bearing a superficial resemblance to psoriasis was occasionally described. In a number of patients affected, this rash was accompanied by adverse effects on the eye (xerophthalmia and/or keratoconjunctivitis) of varying severity. This condition is called the oculomucocutaneous syndrome or practolol syndrome. In a few patients, these eye changes occurred independently of a skin rash. On rare occasions, serous otitis media, sclerosing peritonitis, pericarditis and pleurisy have been reported. Although the practolol syndrome has not been observed in patients taking other beta-blockers, the possibility of such side effects occurring should be borne in mind.

More recently an association between Peyronie's disease (a fibrosing induration of the penis) and various beta-blockers has been suggested but is not proven.

Allergic Conditions

These may be exaggerated by beta-blockade (eg allergic rhinitis during the pollen season and allergic reactions to bee and wasp stings). Beta-blockers should be avoided if there is a risk of bronchospasm.

Hyperthyroidism

Because beta-blockers may mask the clinical signs of developing or continuing hyperthyroidism, resulting in symptomatic improvement without any change in thyroid hormone status, special care should be exercised in those patients who are hyperthyroid and are also receiving beta-blockers.

Significant Cardiomegaly

Use in renal impairment

In patients with severe renal disease, haemodynamic changes following beta blockade may impair renal function further. Beta-blockers which are excreted mainly by the kidney may require dose adjustment in patients with renal failure.

Use in the elderly

See Section 4.2 Dose and Method of Administration.

Paediatric use

No data available.

Effects on laboratory tests

No data available. See Section 4.8 Adverse Effects (Undesirable Effects) for Biochemical Abnormalities.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Concomitant Therapy with Calcium Antagonists

The concomitant use of beta-blockers and calcium antagonists with myocardial depressant and sinus node activity (eg verapamil and, to a lesser extent, diltiazem) may cause hypotension, bradycardia and asystole, particularly in patients with impaired ventricular function and/or SA or AV conduction abnormalities. Extreme caution is required if these drugs have to be used together.

The dihydropyridine calcium antagonists (eg nifedipine) have a weaker myocardial depressant effect and can be administered cautiously with beta-blockers. If excessive hypotension develops, the calcium antagonist should be stopped or the dosage reduced.

Antiarrhythmic Drugs

Class 1 anti-arrhythmic drugs (eg disopyramide) and the Class III agent, amiodarone may have potentiating effect on atrial conduction time and induce negative inotropic effect, this is seen less frequently with quinidine; Class IB agents, tocainide, mexiletine and lidocaine (lignocaine); Class IC agents, flecainide and propaferone (not available in Australia); and the Class IV antiarrhythmic agents.

Use of Catecholamine-Depleting Agents

Concomitant use of drugs such as reserpine and guanethidine requires careful monitoring since the added effect of beta-blockade may produce an excessive reduction of the resting sympathetic nervous tone.

Clonidine

Concurrent use of beta-blockers and clonidine should be avoided because of the risk of adverse interaction and severe withdrawal symptoms. If administered concomitantly, the clonidine should not be discontinued until several days after the withdrawal of the beta-blocker.

Insulin and oral hypoglycaemics

(see Section 4.4 Special Warnings and Precautions for Use – Diabetes)

Anaesthetics

Anaesthetics, such as methoxyflurane, are contraindicated with TENORMIN (see Section 4.4 Special Warnings and Precautions for Use - Anaesthesia and the Peri-operative Period).

Digitalis / digitalis glycosides

Digitalis/digitalis glycosides and beta-blockers are commonly used together, although there have been reports of excessive bradycardia when beta-blockers are used to treat digitalis intoxication.

Sympathomimetic agents

Concomitant use of sympathomimetic agents, e.g. adrenaline (epinephrine), may counteract the effects of beta-blockers.

Prostaglandin synthetase inhibitors

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy – Category C

Beta-adrenergic blocking agents may cause bradycardia in the foetus and newborn infant. During the final part of pregnancy and parturition, these drugs should therefore only be given after weighing the needs of the mother against the risk to the foetus.

TENORMIN crosses the placental barrier in pregnant women, and under steady state conditions, maternal and foetal blood levels of TENORMIN are approximately equal.

No studies have been performed on the use of TENORMIN in the first trimester and the possibility of foetal injury cannot be excluded. TENORMIN has been used under close supervision for the treatment of hypertension in the third trimester. Administration of TENORMIN for longer periods to pregnant women in the management of mild to moderate hypertension has been associated with intra uterine growth retardation. The use of TENORMIN in women who are, or may become pregnant, requires that the anticipated benefit be weighed against the possible risks, particularly in the first and second trimesters. In general, beta-blockers reduce placental perfusion, which has been associated with growth retardation, intrauterine death, abortion and early labour.

TENORMIN has been shown to produce a dose-related increase in embryo/foetal resorptions in rats at doses equal to or greater than 50 mg/kg. Although similar effects were not seen in rabbits, the compound was not evaluated in rabbits at doses above 25 mg/kg.

Use in lactation

There is significant accumulation of TENORMIN in breast milk. Caution should be exercised when TENORMIN is administered to nursing women and the infant should be regularly assessed for signs of beta-blockade.

4.7 EFFECTS 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

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Adverse reactions reported in clinical trials of TENORMIN are mainly attributable to pharmacological actions. The adverse reactions listed below have been observed in patients in clinical trials who have received dosages of about 100 mg per day. It is not possible to give percentage incidences for each reaction, but if all mild and transient reactions are included as well as more serious ones, up to 10% of patients may experience some form of adverse reaction.

Table 1 Adverse reactions observed in patients in clinical trials who have received dosages of about 100 mg per day

More Common Reactions	
Gastrointestinal:	Dry mouth, gastrointestinal disturbance including indigestion, constipation.
Nervous System:	Fatigue, dizziness.
Respiratory:	Wheezing, bronchospasm. (See Section 4.3 Contraindications).

More Common Reactions	
Less Common Reactions	
Biochemical Abnormalities	Increases in SGOT, blood urea and serum creatinine have been reported
Cardiovascular:	Bradycardia, left ventricular insufficiency, postural hypotension which may be associated with syncope, intermittent claudication may occur if already present, Raynaud's phenomenon, cold extremities, deterioration in heart failure, heart block.
Dermatological:	Rash, alopecia, psoriasiform skin reactions, exacerbation of psoriasis.
Gastrointestinal:	Diarrhoea, Elevations of transaminase levels have been seen infrequently, rare cases of hepatic toxicity including intrahepatic cholestasis have been reported.
Genito-Urinary:	Impotence
Musculo-Skeletal:	Ataxia
Nervous System:	Vivid dreams, nightmares, paraesthesia, tinnitus, vertigo, malaise, headache, insomnia, mood changes, confusion.
Ocular:	Dry eyes, visual disturbances.
Psychiatric:	Hallucinations, depression, psychoses.
Respiratory:	Asthma, dyspnoea, nasal congestion.
Haemopoietic:	Thrombocytopenia, purpura. An increase in ANA (Antinuclear Antibodies) has been observed, however the clinical relevance of this is not clear.

Serious or Life-Threatening Reactions

Myocardial insufficiency may require treatment with digitalis and diuretics. Bradycardia may respond to atropine. Bronchospasm may be reversed with a beta2-stimulant. Hypotension, if severe, may require use of a vasopressor.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

Overdosage has not been reported with TENORMIN, but in overdosage with other beta-blocking agents, severe bradycardia and hypotension are commonly found. Acute heart failure and bronchospasm may also occur.

MANAGEMENT

Severe bradycardia

Atropine, 1 to 2 mg intravenously, may be used to induce vagal blockade. If bradycardia persists an inotrope, such as intravenous isoprenaline (25 micrograms initially) may be given. In refractory cases, the use of a cardiac pacemaker may be considered.

Hypotension

Severe hypotension should respond to a sympathomimetic amine such as noradrenaline. In refractory cases, the use of glucagon hydrochloride should be considered.

Bronchospasm

Therapy with a beta$_2$-stimulant such as salbutamol or terbutaline or therapy with aminophylline may be considered.

Acute Cardiac Failure

Conventional therapy with digitalis, diuretics and oxygen should be instituted immediately. In refractory cases, the use of intravenous isoprenaline followed, if necessary, by glucagon hydrochloride or intravenous aminophylline should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

TENORMIN is a beta-adrenoreceptor blocking drug which acts preferentially on beta-receptors in the heart. Selectivity decreases with increasing dose. It has little intrinsic sympathomimetic activity and no membrane stabilising activity. Atenolol is a racemic mixture and its activity resides in the S(-) enantiomer. It reduces raised blood pressure by an unknown mechanism and also inhibits exercise induced tachycardia and decreases plasma renin concentration. It causes slight airways obstruction but less than that seen with nonselective beta blockers. The inhibition of exercise induced tachycardia is correlated with blood levels but there is no correlation between plasma concentrations and antihypertensive effect. TENORMIN is effective and well tolerated in most ethnic populations although the response may be less in Afro-Caribbean black patients.

The possible mechanism of the anti-anginal activity of TENORMIN appears to be due to a reduction in left ventricular work and oxygen utilisation resulting (mainly) from the decrease in heart rate and contractility.

The anti-arrhythmic effect of TENORMIN is apparently due to its anti-sympathetic effect. There is no evidence that membrane stabilising activity or intrinsic sympathomimetic activity are necessary for anti-arrhythmic efficacy. By its anti sympathetic effect, TENORMIN depresses sinus node function, atrioventricular node function and prolongs atrial refractory periods. It has no direct effect on electrophysiological properties of the HIS-purkinje system.

Because of their negative inotropic effects, beta-adrenoreceptor blocking agents should be avoided in uncontrolled heart failure.

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

Although absorption of atenolol is variable and incomplete (40 to 60%) the virtual lack of liver metabolism results in a relatively consistent systemic bioavailability compared to other beta-blockers. Blood levels in humans peak two to four hours after a single l00 mg oral dose and are of the order of 0.4 to 0.9 microgram/mL. Blood levels are consistent and the levels after chronic oral administration are in good agreement with those predicted from single dose results. The drug is distributed throughout the body tissues and less than 10% of the dose is metabolised, the minor urinary metabolite identified being a hydroxylated

derivative. The main route of elimination is renal excretion. The plasma half-life, measured by blood level decay or urinary build up, is approximately 7 to 9 hours. In patients with impaired renal function there is a progressive prolongation of the half-life. In patients with normal renal function, the therapeutic effect (that is, control of raised blood pressure) lasts for at least 24 hours following a 50 mg oral dose.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The tablets contain magnesium carbonate hydrate, maize starch, sodium lauryl sulfate, gelatin, magnesium stearate, hypromellose, glycerol, and titanium dioxide

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

See Section 4.5 Interactions with Other Medicines and Other Forms of Interactions.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Protect from light and moisture. Store below 25°C

6.5 NATURE AND CONTENTS OF CONTAINER

The tablets are packed into PVC/aluminium blister strips in packs of 30 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

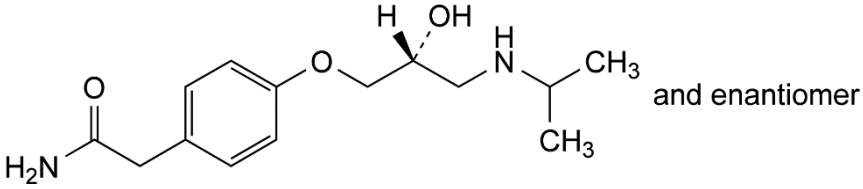
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Atenolol is a beta-adrenoreceptor blocking agent structurally related to propranolol and differing from it by substitution on the aromatic ring.

Chemical structure

Figure 1 The Chemical structure of atenolol is



and enantiomer

Molecular Formula: $C_{14}H_{22}N_2O_3$

Molecular weight: 266.34

CAS number

29122-68-7

7. MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription only medicine

8. SPONSOR

Atnahs Pharma Australia Pty Ltd

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Sydney, NSW, 2000, Australia

Ph: 1800 899 005

9. DATE OF FIRST APPROVAL

11 July 1991

10.DATE OF REVISION

15 May 2025

Summary table of changes

Section changed	Summary of new information
6.5	Removal of ‘calendar’