NEW ZEALAND DATA SHEET

ATENOLOL VIATRIS

1. Product Name

Atenolol Viatris, 50 mg and 100 mg, film coated tablets.

2. Qualitative and Quantitative Composition

Each Atenolol Viatris tablet contains 50 mg or 100 mg of atenolol.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Atenolol Viatris 50 mg tablets: White to off-white, circular, biconvex film coated tablets with '50' embossed on one side and breakline on the other side.

Atenolol Viatris 100 mg tablets: White to off-white, circular, biconvex film coated tablets with '100' embossed on one side and breakline on the other side.

The 50 mg or 100 mg tablets can be divided into equal doses.

4. Clinical Particulars

4.1 Therapeutic indications

- Control of hypertension.
- Management of angina pectoris.
- Control of cardiac dysrhythmias.
- Myocardial infarction: early intervention in the acute phase and long term prophylaxis after recovery.

4.2 Dose and method of administration

Dose

Hypertension

Most patients respond to 50 to 100 mg daily given orally in a single dose. The effect will be fully established after one to two weeks. A further reduction in blood pressure may be achieved by combining atenolol tablets with other antihypertensive agents.

Angina

Most patients with angina pectoris will respond to 100 mg daily given orally as a single or divided dose. It is unlikely that additional benefit will be gained by increasing the dose.

Dysrhythmias

Having controlled the dysrhythmias with intravenous atenolol, a suitable oral maintenance dosage is 50 to 100 mg daily, given as a single dose.

Myocardial infarction

Early intervention with atenolol in acute myocardial infarction reduces infarct size and decreases morbidity and mortality. Fewer patients with a threatened infarction progress to a frank infarction; the incidence of ventricular arrhythmias is decreased and marked pain relief may result in reduced need of opiate analgesics. Early mortality is decreased. Atenolol is an additional treatment to standard coronary care.

For patients suitable for treatment with intravenous beta-blockade and presenting within 12 hours of the onset of chest pain, atenolol (5 to 10 mg) should be given immediately by slow intravenous injection (1 mg/minute) followed by atenolol (50 mg) orally about 15 minutes later, provided no untoward effects occur from the intravenous dose. This should be followed by 50 mg orally 12 hours after the intravenous dose and then 12 hours later by 100 mg orally to be given once daily. If bradycardia and/or hypotension, or any other untoward effects requiring treatment occur, atenolol should be discontinued.

For patients who present some days after suffering an acute myocardial infarction, an oral dose of 100 mg daily is recommended for long term prophylaxis.

Special populations

Elderly

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

Renal impairment

Since atenolol is excreted via the kidneys, dosage should be adjusted in cases of severe impairment of renal function.

No significant accumulation of atenolol occurs in patients who have a creatinine clearance >35 mL /min/1.73m^2 (normal range is 100 to 150 mL/min/1.73m^2).

For patients with a creatinine clearance of 15 to 35 mL/min/1.73m^2 (equivalent to serum creatinine of 300 to 600 micromol/litre) the oral dose should be 50 mg daily and the intravenous dose should be 10 mg once every two days.

For patients with a creatinine clearance of <15 mL/min/173m^2 (equivalent to serum creatinine of 600 micromol/litre) the oral dose should be 25 mg daily or 50 mg on alternate days and the intravenous dose should be 10 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.

Paediatric

Safety and efficacy in children have not been established. Therefore, there is no recommendation for administration of atenolol in children.

Method of administration

For administration daily by the oral route.

4.3 Contraindications

- Hypersensitivity to the active substance atenolol, or to any of the excipients listed in section 6.1.
- Bronchospasm. Beta-adrenergic blockade of the smooth muscle of bronchi and bronchioles may result in an increased airway resistance. These medicines 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 (e.g. ether, chloroform, cyclopropane).
- Hypotension.
- Metabolic acidosis.
- Severe peripheral arterial circulatory disturbances.
- Untreated phaeochromocytoma.
- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

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 medicine may be reinstituted temporarily if the angina worsens. If the medicine must be withdrawn abruptly, close observation is required. In the peri-operative period, beta-blockers should not be withdrawn, unless indicated.

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).

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 medicines in heart failure. As further trials are needed to identify which patients are most likely to respond to which medicines, beta-blockers should not normally be prescribed for heart failure outside of specialist centres.

Prinzmetal angina

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

Peripheral circulation

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

First degree heart block

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

History of anaphylactic reaction

While taking beta-blockers, 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.

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), patients with the following conditions are not suitable for treatment with atenolol:

1. 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).

2. 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 atenolol administration.

Patients with atrial fibrillation following myocardial infarction, who were treated with atenolol, also had increased cardiovascular mortality compared with those not treated with atenolol. It is suggested such patients be digitalised before atenolol 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 medication, 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 and trichloroethylene) 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-blockers are involved in the regulation of lipid as well as carbohydrate metabolism. Some medicines affect the lipid profile adversely although the long-term clinical significance of this change is unknown and the effect appears to be less for medicines with intrinsic sympathomimetic activity.

Phaeochromocytoma

In patients with this condition, an alpha-blocking agent (e.g. 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 have been suggested but is not proven.

Allergic conditions

These may be exaggerated by beta-blockade (e.g. 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.

Renal disease

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.

Effects on laboratory tests

No data available. See section 4.8 for Biochemical Abnormalities.

4.5 Interaction with other medicines and other forms of interaction

Concomitant therapy with calcium antagonists

The concomitant use of beta-blockers and calcium antagonists with myocardial depressant and sinus node activity (e.g. 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 medicines are to be used together.

The dihydropyridine calcium antagonists (e.g. 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 agents

Class I anti-arrhythmic agents (e.g. 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; and the Class IV antiarrhythmic agents.

Use of catecholamine-depleting agents

Concomitant use of medicines 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.

Anaesthetics

Anaesthetics, such as methoxyflurane, are contraindicated with atenolol (see section 4.4).

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) may counteract the effect of beta-blockers.

Prostaglandin synthetase inhibitors

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

4.6 Fertility, pregnancy and lactation

Use in pregnancy – Category C

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

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

No studies have been performed on the use of atenolol in the first trimester, and the possibility of foetal injury cannot be excluded. Atenolol has been used under close supervision for the treatment of hypertension in the third trimester.

Administration of atenolol for longer periods to pregnant women in the management of mild to moderate hypertension has been associated with intrauterine growth retardation. The use of atenolol 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.

Breast-feeding

There is significant accumulation of atenolol in breast milk. Caution should be exercised when atenolol is administered to a breast-feeding woman and the infant should be regularly assessed for signs of beta-blockade.

Fertility

No data available. For pre-clinical fertility data refer to section 5.3.

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 Undesirable effects

Adverse reactions reported in clinical trials of atenolol are mainly attributable to the 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 transient reactions are included as well as more serious ones, up to 10% of patients may experience some form of adverse reaction.

The following adverse reactions observed in patients in clinical trials who have received dosages of about 100 mg per day.

More Common

Gastrointestinal: Dry mouth, gastrointestinal disturbance including indigestion, constipation.

Nervous System: Fatigue, dizziness.

Respiratory: Wheezing, bronchospasm (see section 4.3).

Less Common

Biochemical Abnormalities: Increases in SGOT, blood urea and serum creatinine.

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.

Genito-Urinary: Impotence.

Musculo-Skeletal: Ataxia.

Nervous System: Vivid dreams, confusion, headache, mood changes, nightmares, paraesthesia, tinnitus, vertigo, malaise, insomnia.

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 beta$_2$-stimulant. Hypotension, if severe, may require use of a vasopressor.

Discontinuance of the medicine should be considered if, according to clinical judgement, the well-being of the patient is adversely affected by any of the above reactions.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

The symptoms of overdosage may include severe bradycardia, hypotension, acute heart failure and bronchospasm.

General treatment should include close supervised treatment in an intensive care ward, the use of gastric lavage activated charcoal and a laxative to prevent absorption of any drug still present in the gastrointestinal tract, the use of plasma or plasma substitutes to treat hypotension and shock. The possible uses of haemodialysis or haemoperfusion may be considered.

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.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta-blocking agents, plain, selective, ATC code: CO7A B03

Mechanism of action

Atenolol is a beta-adrenoreceptor blocking drug which acts preferentially on $beta_1$-adrenergic 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 non-selective beta-blockers. The inhibition of exercise induced tachycardia is correlated with blood levels but there is no correlation between plasma concentrations and antihypertensive effect. Atenolol 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 atenolol 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 atenolol 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, atenolol 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-blocking agents should be avoided in uncontrolled heart failure.

Clinical efficacy and safety

No data available.

Paediatric population

Safety and efficacy in children have not been established.

5.2 Pharmacokinetic properties

Absorption

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 2 to 4 hours after a single 100 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.

Distribution & Biotransformation

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.

Elimination

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

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

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. Pharmaceutical Particulars

6.1 List of excipients

Atenolol Viatris film coated tablet also contains:

Tablet core:

- Magnesium carbonate
- Maize starch
- Sodium starch glycollate
- Silicon dioxide
- Magnesium stearate
- Sodium laurilsulfate.

Tablet film coat:

- Hypromellose
- Macrogol
- Purified talc
- Titanium dioxide (E171).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container

Blister pack, PVC/PVDC/Aluminium. Pack sizes of 28, 56 and 84 tablets.

HDPE bottle with HDPE closure. Pack sizes of 100, 250 and 500 tablets.

Not all pack types or sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

Viatris Ltd
PO Box 11-183
Ellerslie
AUCKLAND
www.viatris.co.nz
Telephone 0800 168 169

9. Date of First Approval

06 December 2007

10. Date of Revision of the Text

27 July 2021

Section	
Header	Changed to Viatris logo.
All	Change of trade name to Atenolol Viatris.
4.2	Removed reference to 2.5mg tablet as this strength is now approval lapsed.
4.4	Added Effects on Laboratory Tests
4.6	Additional safety statement added for pregnancy. Minor editorial change.
4.8	Editorial changes.
5.1	Minor editorial changes.
5.2	Minor editorial change.
5.3	Added subheadings for genotoxicity and carcinogenicity.
8	Change of sponsor to Viatris Ltd, website added and updated contact number.