

PART II

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Atenogen Tablets 100mg.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100mg Atenolol.

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Orange, round, film-coated tablets marked "AT/100" on one face and the company logo on the reverse.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- 1) Management of essential hypertension.
- 2) Management of angina pectoris.
- 3) Management of cardiac dysrhythmias.
- 4) Long-term prophylaxis after recovery from acute myocardial infarction.

4.2 Posology and method of administration

Atenogen Tablets are for oral administration.

Adults:

Hypertension: 50mg daily as a single dose (higher doses rarely necessary).

The full effects of atenolol, which will be established after one to two weeks, should be achieved before determining the need to increase the dosage from 50 to 100mg daily. Atenolol may be combined with a diuretic or other antihypertensive agent to achieve further reduction in blood pressure.

Angina pectoris: The usual dose is 100mg daily, taken as a single dose or as 50mg twice daily.

Dysrhythmias: The usual maintenance dose is 50 - 100mg daily.

Myocardial infarction: The usual dose is 100mg daily for long-term prophylaxis, where beta-blockade is appropriate for patients presenting later after infarction.

Elderly:

Dosage may need to be reduced, especially in patients with impaired renal function.

Children:

As there is no paediatric experience with atenolol, it is not recommended for use in children.

4.3 Contraindications

Atenolol should not be used in the presence of second or third degree atrioventricular block, severe bradycardia, uncontrolled or digitalis/diuretic-refractory heart failure or cardiogenic shock, asthma, Prinzmetal's angina, hypotension, sick sinus syndrome, metabolic acidosis, known hypersensitivity to the active substance, or any of the excipients, severe peripheral arterial circulatory disturbances & untreated pheochromocytoma.

4.4 Special warnings and special precautions for use

Sudden withdrawal of beta-adrenoceptor blocking agents in patients with ischaemic heart disease may result in anginal attacks of increased frequency or severity or in deterioration in cardiac state. Discontinuation of therapy should, therefore, be gradual.

Beta blockers are diabetogenic, probably due to unopposed alpha₁ activity that would cause vasoconstriction and decreased blood flow to muscle, resulting in reduced glucose uptake or insulin resistance. Beta blockers can also interfere with insulin secretion from pancreatic beta cells. Furthermore, beta blockers have been associated with important increase in body weight and weight gain is closely connected with insulin sensitivity reduction. Beta blocker should therefore not be the first of choice in patient who are overweight, or diabetic.

Atenolol as with other beta-blockers may increase the number and duration of angina attacks in patients with Prinzmetal's angina due to unopposed alpha-receptor mediated coronary artery vasoconstriction. Atenolol is a beta₁-selective beta-blocker; consequently, its use may be considered although utmost caution must be exercised.

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

May mask the symptoms of hypoglycemia, in particular, tachycardia.

May mask the signs of thyrotoxicosis.

Will reduce heart rate as a result of its pharmacological action. In the rare instances when a treated patient develops symptoms which may be attributable to a slow heart rate and the pulse rate drops to less than 50–55 bpm at rest, the dose should be reduced.

May cause a more severe reaction to a variety of allergens when given to patients with a history of anaphylactic reaction to such allergens. Such patients may be unresponsive to the usual doses of adrenaline (epinephrine) used to treat the allergic reactions.

May cause a hypersensitivity reaction including angioedema and urticaria.

Should be used with caution in the elderly, starting with a lesser dose.

Although cardioselective (beta₁) beta-blockers may have less effect on lung function than non-selective beta-blockers, as with all beta-blockers, these should be avoided in patients with reversible obstructive airways disease, unless there are compelling clinical reasons for their use. Where such reasons exist, Atenolol may be used with caution. Occasionally, some increase in airways resistance may occur in asthmatic patients however, and this may usually be reversed by commonly used dosage of bronchodilators such as salbutamol or isoprenaline.

Atenogen should only be used with caution in patients with controlled congestive cardiac failure or with a family history of asthma and evidence of recrudescence of either condition should be regarded as a signal to discontinue therapy.

Atenogen may be used with caution in patients with obstructive respiratory disorders provided that adequate supervision is maintained. If increased airways resistance develops consideration must be given to discontinuation of the β -blocker, depending on the degree of airways resistance and the benefit derived from β -blockade.

The initial treatment of severe malignant hypertension should be so designed as to avoid sudden reduction in diastolic blood pressure with impairment of autoregulatory mechanisms. Where Atenogen is administered to patients in renal failure, the interval between doses may need to be increased or the dosage reduced in order to avoid accumulation of the drug.

Some cases of ocular changes (conjunctivitis and 'dry eye') and/or skin rashes (including a psoriasiform type) have been reported in association with the use of beta-adrenoceptor blocking drugs. Until their significance is known, it is recommended that consideration be given to discontinuing such therapy if these effects appear.

If a patient is receiving atenolol, the anaesthetist should be informed of this prior to the use of a general anaesthetic so that the necessary precautions may be taken.

Atenolol must be used with caution in patients with first degree of AV block, postural hypertension, renal impairment, and myasthenia gravis. Reduce dose in renal impairment.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interactions with other medicaments and other forms of interaction

Atenolol should only be used with great caution in patients who are receiving concomitant myocardial depressants such as chloroform, lidocaine, procainamide or verapamil, or beta-adrenoceptor stimulants such as isoprenaline, or alpha-adrenoceptor stimulants such as nor-adrenaline. Adrenergic-neurone blocking agents such as guanethidine, reserpine, diuretics and other antihypertensive agents, including the vasodilator group, will have an additive effect on the hypotensive action of atenolol. If a beta-adrenoceptor blocking agent and clonidine are administered concurrently, the clonidine should not be discontinued until several days after withdrawal of the betablocker.

Care should be taken in prescribing a beta-adrenoceptor blocking drug in conjunction with Class I antidysrhythmics such as disopyramide. As with other beta-blockers, in patients with a phaeochromocytoma, an alpha-blocker should be given concomitantly.

Digitalis glycosides, in association with beta-blockers, may increase atrioventricular conduction time.

Concomitant use with insulin and oral antidiabetic drugs may lead to the intensification of the blood sugar lowering effects of these drugs. Symptoms of hypoglycaemia, particularly tachycardia, may be masked.

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

Caution must be exercised when using anaesthetic agents with atenolol. 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 drugs may result in attenuation of the reflex tachycardia and increase the risk of hypotension. Anaesthetic agents causing myocardial depression are best avoided.

4.6 Pregnancy and lactation

Atenolol has been given in pregnancy-associated hypertension after 20 weeks gestation. Although the drug crosses the placental barrier and is present in cord blood, there is no evidence up to the present time of foetal abnormalities. Nonetheless, the possibility cannot be excluded and the drug should only be used if considered essential and with the patient under close supervision. Atenolol is excreted in breast milk. This should be kept in mind if it is intended for use in nursing mothers. Neonates born to mothers who are receiving Atenolol at parturition or breast-feeding may be at risk of hypoglycaemia and bradycardia.

4.7 Effects on ability to drive and use machines

Although use of atenolol is unlikely to result in any impairment of the ability to drive or operate machinery, symptoms such as dizziness or tiredness may occasionally occur and patients should be advised not to drive or to operate machinery if affected.

4.8 Undesirable effects

Adverse reactions are listed by frequency:

Common >1/100, <1/10; Uncommon >1/1,000, <1/100; Rare >1/10,000, <1/1,000; Very rare <1/10,000.

Blood and lymphatic system disorders:

Rare: Purpura, thrombocytopenia.

Gastrointestinal disorders:

Rare: Gastrointestinal signs and symptoms NEC

Cardiac disorders:

Common: Bradycardia, Heart failures NEC, Cardiac conduction disorders

Rare: Precipitation of heart block

Nervous System disorder:

Very common: headache, syncope, dizziness

Rare: Paraesthesias and dysaesthesias

Vascular disorders:

Very Common: Hypotension

Very rare: Raynaud's phenomenon

Psychiatric disorders:

Very common: Hallucination, depression, sleep disorder

Common: sexual desire disorders

Rare: Mood changes, nightmares, confusion, and psychoses.

Eye disorders:

Common: Ocular disorders NEC

Rare: Dry eyes

Skin and subcutaneous tissue disorder

Very common: psoriasis

Rare: Skin disorder(alopecia, psoriariform skin reactions, exacerbation of psoriasis).

Respiratory, Thoracic and Mediastinal disorder:

Very common: Bronchospasm

Hepato-biliary disorders:

Uncommon: Elevations of transaminase levels.

Rare: Hepatic toxicity including intrahepatic cholestasis.

Reproductive system and breast disorders:

Rare: Impotence.

Investigations:

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

4.9 Overdose

The symptoms of overdosage may include bradycardia, hypotension, acute cardiac insufficiency and bronchospasm.

Bronchospasm can usually be reversed by bronchodilators

Following recent overdosage, the stomach should be emptied by gastric lavage.

Excessive bradycardia can be countered with atropine 1 - 2mg intravenously. If necessary, this may be followed by a bolus dose of glucagon 5 to 10mg intravenously, followed if necessary by an intravenous infusion of glucagon 1 - 5mg per hour or more according to response. If the response to glucagon is unsatisfactory or if glucagon is unavailable, a beta-adrenoceptor stimulant such as prenalterol or dobutamine may be used.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: C07AB03

Pharmacotherapeutic Group: Beta blocking agents, selective.

Atenolol is a beta-blocker which is beta1-selective (i.e. acts preferentially on beta1-adrenergic receptors in the heart). Selectivity decreases with increasing dose.

Atenolol is without intrinsic sympathomimetic and membrane-stabilising activities and as with other beta-blockers, has negative inotropic effects (and is therefore contraindicated in uncontrolled heart failure).

As with other beta-blockers, the mode of action of atenolol in the treatment of hypertension is unclear.

It is probably the action of atenolol in reducing cardiac rate and contractility which makes it effective in eliminating or reducing the symptoms of patients with angina.

It is unlikely that any additional ancillary properties possessed by S (-) atenolol, in comparison with the racemic mixture, will give rise to different therapeutic effects.

5.2 Pharmacokinetic properties

Atenolol is well absorbed after oral administration and is excreted unchanged through the kidney with a half-life of 6 to 9 hours.

Atenolol is well absorbed after oral administration and is excreted unchanged through the kidney with a half-life of 6 to 9 hours.

Absorption of atenolol following oral dosing is consistent but incomplete (approximately 40–50%) with peak plasma concentrations occurring 2–4 hours after dosing. The atenolol blood levels are consistent and subject to little variability. 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%).

5.3 Preclinical safety data

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Lactose Monohydrate

Microcrystalline Cellulose

Sodium Laurilsulfate

Sodium Starch Glycollate (Type A)

Maize Starch

Magnesium Stearate

Gelatin

Film-coat

Hypromellose (E464)

Titanium Dioxide (E171)

Ethylcellulose 10 cps

Sunset Yellow (E110)

Erythrosine (E127)

Propylene Glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25° C.

Store in the original package.

6.5 Nature and contents of container

Blister packs which consist of 2 strips made from hard PVC with a foil lid and packed in cardboard cartons to contain 2 x 14 tablets.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7. MARKETING AUTHORIZATION HOLDER

Antigen Pharmaceuticals Ltd.

Roscrea

Co. Tipperary

8. MARKETING AUTHORIZATION NUMBER

PA 73/117/2

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

22nd March 1990/22nd March 2005

10. DATE OF (PARTIAL) REVISION OF THE TEXT

March 2009