Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Atenogen 50 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 50 mg Atenolol.

Excipients - Contains Lactose Monohydrate 28.0mg

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated Tablet.
White, round, film-coated tablets marked “AT/50” 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 film coated 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 or two weeks, should be achieved before determining the need to increase the dosage from 50 to 100 mg 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 precautions for use

Atenolol as with other beta-blockers:

- Should not be withdrawn abruptly. The dosage should be withdrawn gradually over a period of 7–14 days, to facilitate a reduction in beta-blocker dosage. Patients should be followed during withdrawal, especially those with ischaemic heart disease.

- When a patient is scheduled for surgery, and a decision is made to discontinue beta blocker therapy, this should be done at least 24 hours prior to the procedure. The risk benefit assessment of stopping beta-blockade should be made for each patient. If treatment is continued, an anaesthetic with little negative inotropic activity should be selected to minimise the risk of myocardial depression. The patient may be protected against vagal reactions by intravenous administration of atropine.

- Although contraindicated in uncontrolled heart failure (see section 4.3), may be used in patients whose signs of heart failure have been controlled. Caution must be exercised in patients whose cardiac reserve is poor

- 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.

- Although contraindicated in severe peripheral arterial circulatory disturbances (see section 4.3), may also aggravate less severe peripheral arterial circulatory disturbances.

- 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.

- May cause an increase in airways resistance in asthmatic patients. Atenolol is a beta1-selective beta-blocker; consequently its use may be considered although utmost caution must be exercised. If increased airways resistance does occur, Atenolol should be discontinued and bronchodilator therapy (e.g. salbutamol) administered if necessary.

- Atenogen should only be used with caution in patients with a family history of asthma and evidence of recrudescence of the 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 ß-blocker, depending on the degree of airways resistance and the benefit derived from ßblockade.

- The initial treatment of severe malignant hypertension should be so designed as to avoid sudden reduction in diastolic blood pressure with impairment of auto regulatory 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.

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

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

- Should only be given to patients with psoriasis after careful consideration, as psoriasis may be aggravated.

- Since Atenolol is excreted via the kidneys, dosage should be reduced in patients with a creatinine clearance of below 35 ml/min/1.73 m2.

- As with other beta-blockers, in patients with a phaeochromocytoma, an alphablocker should be given concomitantly.

4.5 Interaction with other medicinal products and other forms of interaction

Adrenergic neurone-blocking agents

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.

Anaesthetic agents

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.

Antiarrhythmic agents (Class 1)

Class I anti-arrhythmic drugs (e.g. disopyramide) and amiodarone may have a potentiating effect on atrial-conduction time and induce negative inotropic effect.

Calcium channel blockers

Combined use of beta-blockers and calcium channel blockers with negative inotropic effects, e.g. verapamil or diltiazem, can lead to an exaggeration of these effects particularly in patients with impaired ventricular function and/or sinoatrial or atrioventricular conduction abnormalities. This may result in severe hypotension, bradycardia and cardiac failure. Neither the beta-blocker nor the calcium channel blocker should be administered intravenously within 48 hours of discontinuing the other.

Clonidine

Beta-blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two drugs are co-administered, the beta-blocker should be withdrawn several days before discontinuing clonidine. If replacing clonidine by beta-blocker therapy, the introduction of beta-blockers should be delayed for several days after clonidine administration has stopped. (See also prescribing information for clonidine).

Digitalis glycosides

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

Dihydropyridines
Concomitant therapy with dihydropyridines, e.g. nifedipine, may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency.

Insulin and oral antidiabetic drugs

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.

Myocardial depressants

The beta-blocker should only be used with caution in patients who are receiving concomitant myocardial depressants such as halogenated anaesthetics, lidocaine, procainamide and beta-adrenoceptor stimulants such as noradrenaline (norepinephrine).

Prostaglandin synthetase-inhibiting drugs

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

Sympathomimetic agents

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

4.6 Fertility, pregnancy and lactation

Atenogen crosses the placental barrier and appears in the cord blood. 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 to pregnant women in the management of mild to moderate hypertension has been associated with intra-uterine 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.

There is significant accumulation of Atenolol in breast milk.
Neonates born to mothers who are receiving Atenolol at parturition or breast-feeding may be at risk for hypoglycemia and bradycardia. Caution should be exercised when Atenolol is administered during pregnancy or to a woman who is breast-feeding.

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

Atenolol is well tolerated. In clinical studies, the undesired events reported are usually attributable to the pharmacological actions of atenolol.

The following undesired events, listed by body system, have been reported with the following frequencies: very common (≥10%), common (1–9.9%), uncommon (0.1– 0.9%), rare (0.01–0.09%), very rare (<0.01%) including isolated reports, not known (cannot be estimated from the available data).

Cardiac disorders:

Common: Bradycardia.

Rare: Heart failure deterioration, precipitation of heart block.

Vascular disorders:

Common: Cold extremities.

Rare: Postural hypotension which may be associated with syncope, intermittent claudication may be increased if already present, in susceptible patients Raynaud's phenomenon.

Nervous system disorders:

Rare: Dizziness, headache, paraesthesia.

Psychiatric disorders:

Uncommon: Sleep disturbances of the type noted with other beta-blockers.

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

Gastrointestinal disorders:

Common: Gastrointestinal disturbances.

Rare: Dry mouth.

Investigations:

Uncommon: Elevations of transaminase levels.

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

Hepato-biliary disorders:

Rare: Hepatic toxicity including intrahepatic cholestasis.

Blood and lymphatic system disorders:

Rare: Purpura, thrombocytopenia.

Skin and subcutaneous tissue disorders:

Rare: Alopecia, psoriasiform skin reactions, exacerbation of psoriasis, skin rashes.

Not known: Hypersensitivity reactions, including angioedema and urticaria.

Musculoskeletal and connective tissue disorders:

Not known: Lupus-like syndrome

Eye disorders:

Rare: Dry eyes, visual disturbances.

Reproductive system and breast disorders:

Rare: Impotence.

Respiratory, thoracic and mediastinal disorders:

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

General disorders and administration site conditions:
Common: Fatigue.

Discontinuance of the drug 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 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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517;Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

The symptoms of overdosage may include bradycardia, hypotension, acute cardiac insufficiency, cardiovascular collapse 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 l0mg 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 $beta_1$-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 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.

Absorption of atenolol following oral dosing is consistent but incomplete (approximately 40-50%) with peak plasma concentrations occuring 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.

6 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)
Macrogol 400

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 in order to protect from light.

6.5 Nature and contents of container

Blister packs which consist of 2 strips made from hard PVC with 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 AUTHORISATION HOLDER

Mercury Pharmaceuticals (Ireland) Ltd
4045 Kingswood Road
Citywest Business Park
Co Dublin
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0073/117/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 March 1990

Date of last renewal: 22 March 2010

10 DATE OF REVISION OF THE TEXT

November 2015