Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ateni 100mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg atenolol.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet.

White film-coated, biconvex tablet, approximately 10 mm in diameter, marked 'AT100' on one side and 'G' on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Atenolol is a beta-adrenoceptor blocking drug indicated for:

- hypertension
- angina pectoris
- cardiac arrhythmias
- myocardial infarction: early intervention in the acute phase and late intervention for long term prophylaxis after recovery from myocardial infarction

4.2 Posology and method of administration

Posology

Adults
Hypertension: Initially 50 mg daily. The full effect of this dose will usually be seen within 1-2 weeks. If an optimal response is not achieved the dosage may be increased to 100 mg daily. A further reduction in blood pressure may be achieved by combining Ateni with other antihypertensive agents.

Angina pectoris: 100 mg once daily or 50 mg twice daily. It is unlikely that additional benefit will be gained by increasing the dose.

Cardiac arrhythmias: 50 mg-100 mg daily after having controlled the arrhythmias with intravenous atenolol.

Early and late intervention after myocardial infarction: Oral treatment with Ateni can be initiated in haemodynamically stable patients with 50 mg twice daily, and then 100 mg once daily. During the early phase of acute myocardial infraction, treatment with Ateni should be initiated in hospital under close monitoring.

Discontinue atenolol if bradycardia and/or hypotension requiring treatment or any other untoward effects occur.

Ateni 100 mg daily is recommended for long-term prophylaxis of myocardial infraction.

Paediatric population

There is no paediatric experience with Ateni and for this reason it is not recommended for use in children and adolescents under 18 years of age.

Older people
The elderly may require reduced dosage, particularly when renal function is impaired.

Renal impairment
Atenolol is excreted via the kidneys and dosage should be adjusted as follows:

Glomerular Filtration Rate

> 35ml/min/1.73 m²	-	Normal dosage.
15 – 35 ml/min/1.73 m²	-	Oral dose should be 50mg daily.
< 15ml/min/1.73 m²	-	Oral dose should be 25mg daily or 50mg on alternate days.

Patients on haemodialysis should be given 50mg orally after each dialysis with close monitoring as marked falls in blood pressure may occur.

Method of administration
For oral use.

4.3 Contraindications

As with other beta-blockers, Atenolol is contra-indicated in patients with the following:

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- second or third degree heart block
- cardiogenic shock
- uncontrolled heart failure
- sick sinus syndrome
- hypotension
- untreated phaeochromocytoma
- severe peripheral circulatory disturbances
- bradycardia (< 45 bpm)
- metabolic acidosis

4.4 Special warnings and precautions for use

Special care should be taken with patients whose cardiac reserve is poor. Beta-adrenoceptor blockers should be avoided in patients with uncontrolled heart failure (see section 4.3). However, they may be used in patients whose signs of failure have been controlled.

One of the pharmacological actions of atenolol is to reduce heart rate. In the rare instances when symptoms may be attributable to the slow heart rate, and the pulse rate drops to less than 50-55 bpm at rest, the dose may be reduced.

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

Atenolol may mask the symptoms of hypoglycaemia, in particular tachycardia

In patients with phaeochromocytoma, a beta-blocker should only be given with an alpha-blocker.

Ateni 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.

Although contraindicated in severe peripheral circulatory disturbances (see section 4.3), beta-blockers should be used

with great caution in patients with less severe peripheral circulatory disorders (e.g. Raynaud's disease/syndrome, intermittent claudication) as they may aggravate these disorders.

Atenolol 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 beta $_{1}$-selective beta-blocker; consequently, its use may be considered although utmost caution must be exercised.

Since atenolol is excreted via the kidneys, dosage should be adjusted in cases of severe impairment of renal function. For patients with a creatinine clearance of 35 ml/min/1.73m^2 and below, dosage should be reduced (see section 4.2).

Atenolol may cause a more serious 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.

Patients with known psoriasis should take beta-blockers only after careful consideration, as psoriasis may be aggravated.

Atenolol may cause an increase in airways resistance in asthmatic patients, therefore utmost caution must be exercised. If increase airways resistance dose occur, Ateni should be discontinued and bronchodilator therapy (e.g. salbutamol) administered if necessary.

If a beta-blocker is withdrawn before surgery therapy, it should be discontinued for 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.

Atenolol may mask the signs of thyrotoxicosis.

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 antihypertensive agents, including the vasodilator group, will have an additive effect on the hypotensive action of the drug.

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 I)
Caution must be exercised when prescribing a beta-blocker with Class I antiarrhythmic agents such as disopyramide, or with amiodarone, which may have a potentiating effect on atrial-conduction time and induce a 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.

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 (see section 4.4).

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, 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

Caution should be exercised when atenolol is administered during pregnancy or to a woman who is breast-feeing.

Pregnancy
Atenolol crosses the placental barrier and appears in 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.

Breast-feeding
Atenolol is excreted in breast milk with accumulation occurring at concentrations significantly greater than corresponding plasma levels. Nursing infants must be closely monitored for bradycardia and hypoglycaemia and other signs and symptoms of beta-blockade if the mother is receiving atenolol, although breast feeding is not recommended.

4.7 Effects on ability to drive and use machines

Although symptoms such as dizziness and fatigue have occasionally been reported in association with the use of beta-blockers, the ability to drive and use machines is usually unaffected by atenolol therapy.

4.8 Undesirable effects

Atenolol tablets are well tolerated. In clinical studies, the undesired effects 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 (≥ 1/10), common (≥1/100 < 1/10), uncommon (≥1/1,000,< 1/100), rare (≥1/10,000, < 1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Blood and lymphatic system disorders:
Rare: Purpura, thrombocytopenia

Psychiatric disorders:
Uncommon: Sleep disturbances of the type noted with other beta-blockers.
Rare: Mood changes, nightmares, confusion, psychoses and hallucinations

Nervous system disorders:
Rare: Dizziness, headache, paraesthesia.

Eye disorders:
Rare: Dry eyes, visual disturbances.

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.

Respiratory, thoracic and mediastinal disorders:
Rare: Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints.

Gastrointestinal disorders:
Common: Gastrointestinal disturbances.
Rare: Dry mouth.

Hepatobiliary disorders:
Rare: Hepatic toxicity including intrahepatic cholestasis.

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

Reproductive system and breast disorders:
Rare: Impotence.

General disorders and administration site conditions:
Common: Fatigue.

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.

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

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

Treatment
Close supervision is required. Gastric emptying, activated charcoal and a laxative to prevent absorption of any drug still present in the gastrointestinal tract. The use of plasma and plasma substitutes to treat hypotension and shock, and the possible uses of haemoialysis or haemoperfusion may be considered.

Excessive bradycardia can be countered with atropine 1–2 mg intravenously and/or a cardiac pacemaker. 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 response. If no response to glucagon occurs or if glucagon is unavailable, a beta-adrenoceptor stimulant such as dobutamine 2.5 to 10 micrograms/kg/minute by intravenous infusion may be given. Dobutamine, because of its positive inotropic effect could also be used to treat hypotension and acute cardiac insufficiency. It is likely that these doses would be inadequate to reverse the cardiac effects of beta-blockade if a large overdose has been taken. The dose of dobutamine should therefore be increased if necessary to achieve the required response according to the clinical condition of the patient.

Bronchospasm can usually be reversed by bronchodilators.

Symptomatic therapy
Haemodialysis could be used with severe poisoning, especially in patients with impaired renal function.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: beta-blocking agents, plain, selective; ATC Code: C07AB03.

Mechanism of action
Atenolol is a beta-blocker which has preferential effect on the $beta_1$-receptors chiefly located in the heart (cardioselective). This selectivity diminishes with increased dosage. Atenolol does not possess intrinsic sympathomimetic activity or membrane stabilising activity. It 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.

Clinical efficacy and safety
Atenolol is effective and well tolerated in most ethnic populations although the response may be less in black patients.

Atenolol is effective for at least 24 hours after a single oral dose. The drug facilitates compliance by its acceptability to patients and simplicity of dosing

Atenolol is compatible with diuretics, other hypertensive agents and antianginal agents (see section 4.5).

5.2 Pharmacokinetic properties

Absorption
Atenolol is incompletely absorbed (40-50%) after oral administration with peak plasma concentrations occurring within 2-4 hours. 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

Distribution
Atenolol penetrates tissues poorly due to its low lipid solubility. It exhibits low (approximately 3 %) plasma protein binding.

Elimination
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.

5.3 Preclinical safety data

Atenolol is a drug on which extensive clinical experience has been obtained. Relevant information for the prescriber is provided elsewhere in the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core
Calcium hydrogen phosphate (anhydrous)
Magnesium carbonate, heavy
Sodium starch glycolate (type A)
Maize starch
Colloidal anhydrous silica
Magnesium stearate

Film Coat

Opadry White Y-1-7000, consisting of the following:
Hypromellose
Titanium dioxide (E171)
Macrogol 400

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 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

Polypropylene pots with polyethylene child resistant cap with tamper evident seal - Pack sizes 28, 100, 250, 500 and 1000
PVdC/Aluminium foil blister packs - Pack sizes 7, 10, 14, 15 and 28

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Generics [UK] Limited
Station Close
Potters Bar
Hertfordshire
EN6 1TL
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0405/019/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th April 1987

Date of last renewal: 9th April 2007

10 DATE OF REVISION OF THE TEXT

June 2016