Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Atecor 50mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Atenolol 50 mg.
Excipients with a known effect:
Each tablet contains lactose monohydrate 2.88 mg and up to 7.6 mg sodium.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
White, round, biconvex, film-coated tablet with a one-sided score notch and embossed '50' on the other side.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As a beta-adrenoceptor blocker Atecor is indicated for the treatment of:

- essential hypertension
- angina pectoris
- cardiac arrhythmias

Atecor is also indicated in early intervention in the acute phase of myocardial infarction and for the long-term prophylaxis after recovery from myocardial infarction.

4.2 Posology and method of administration

Route of Administration:
Oral.
Recommended Dosage Schedule:

Adults:
Hypertension:
The usual daily dose is 50 mg as a single dose. This can be increased to 100 mg daily if required for control but should only be done after the effects of the initial dose have been achieved (1 to 2 weeks). Atenolol may be combined with a diuretic if required or other antihypertensive agents.

Angina:
The usual daily dose is 100 mg given orally once daily or 50 mg given twice daily.

Cardiac arrhythmias:
For maintenance control the usual daily dose is 50 – 100 mg once daily.

Early and late intervention after Myocardial infarction:
Oral treatment with atenolol 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 infarction, treatment with atenolol should be initiated in hospital under close monitoring. If bradycardia and/or hypotension requiring treatment, or any other untoward effects occur, atenolol should be discontinued.

Where beta-blockade is appropriate for patients presenting later after infarction, atenolol 100 mg daily may be given for long term prophylaxis.

Paediatric population:

There is no paediatric experience with Atecor and for this reason it is not recommended for use in children.

Elderly:

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

Renal failure:

Atenolol is excreted via the kidneys and therefore 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 greater than 35 ml/min/1.73m^2 (normal range is between 100-150 ml/min/1.73m^2).

For patients with a creatinine clearance of 15-35ml/min/1.73m^2 (equivalent to serum creatinine of 300-600 micromol/litre) the oral dose should be 50 mg daily.

For patients with a creatinine clearance of less than 15 ml/min/1.73 m^2 (equivalent to serum creatinine of greater than >600 micromol/litre) the oral dose should be 25 mg daily or 50 mg on alternate 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.

4.3 Contraindications

Atecor is contra-indicated in patients with:

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

4.4 Special warnings and precautions for use

Atecor 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. Atecor 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 hypoglycaemia, 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 may 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.

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

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

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

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

Special warnings regarding excipients

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interactions

Anaesthetic agents:
In the event that a patient receiving the beta-blocker requires anaesthesia the anaesthetist should be informed of the use of the medication prior to the use of a general anaesthetic to permit his taking the necessary precautions. An anaesthetic with as little negative inotropic activity as possible should be used. 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.

Myocardial depressants:
The beta-blocker should only be used with great caution in patients who are receiving concomitant myocardial depressants such as chloroform, lignocaine, procainamide, halogenated anaesthetics, beta-adrenoceptor stimulants such as isoprenaline, noradrenalin (norepinephrine).

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.

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 the drug.

Antiarrhytmic agents:
Care should be taken in prescribing a beta-adrenoceptor blocker in conjunction with Class I antiarrhythmics such as disopyramide, quinidine and amiodarone. These agents may have potentiating effects on atrial-conduction time and induce a negative inotropic effect.

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).

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:
Alpha-adrenoceptor stimulants such as adrenalin and noradrenaline, may counteract the effect of the beta-blocker.

Concomitant administration of tricyclic antidepressants, barbiturates and phenothiazines as well asother antihypertensive agents may increase the blood pressure lowering effect.

Concomitant use of baclofen may increase the antihypertensive effect making dose adjustments necessary.

Ampicillin:
May reduce the bioavailability of atenolol. Therefore the physician should watch for evidence of altered atenolol response especially when large doses of ampicillin are administered concomitantly.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Atenolol 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.

Lactation:
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 hypoglycaemia and bradycardia.

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.

4.7 Effects on ability to drive and use machines

The use of atenolol is unlikely to result in any impairment of the ability of patients to drive or operate machinery. It should be taken into account that occasionally dizziness or fatigue may occur.

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 (>1/10), common (>1/100 and <1/10), uncommon (>1/1000 and <1/100), rare (>1/10 000 and <1/1000), very rare (<1/10 000) 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 and cyanotic extremities
Rare: Postural hypotension which may be associated with syncope Raynaud's phenomenon, increase of an existing intermittent claudication

Nervous system disorders:
Rare: Headache, dizziness, paraesthesia of the extremities, peripheral neuropathy

Psychiatric Disorders:
Uncommon: Sleep disturbances of type noted with other beta blockers
Rare: Hallucinations, depression, psychoses, confusion, nightmares, anxiety, mood changes

Skin and subcutaneous tissue disorder:
Rare: Alopecia, psoriasiform skin reactions, skin rashes, exacerbation of psoriasis
Not known: Hypersensitivity reactions, including angioedema and urticaria

Musculoskeletal and connective tissue disorders:
Not known: Lupus-like syndrome

Gastrointestinal disorders:
Common: Gastrointestinal upset [nausea, vomiting, diarrhoea or constipation
Rare: Dry mouth

Hepato-biliary disorders:
Rare: Hepatic toxicity including intrahepatic cholestasis

Blood and lymphatic system disorders:
Rare: Thrombocytopenia, purpura

Eye disorders:
Rare: Visual disturbances, dry eyes

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

Endocrine disorders:
Not known: Beta blockers may mask the symptoms of thyrotoxicosis or hypo-or hyperglycemia

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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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. Website: www.hpra.ie;

4.9 Overdose

The symptoms of over-dosage may include bradycardia, hypotension, acute cardiac insufficiency and bronchospasm.

General treatment should include: close supervision, 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.

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: Beta blocking agents.
C07A B03 Beta blocking agents, selective.

Atenolol is a beta-adrenoceptor blocking drug which is cardioselective (i.e. acts preferentially on beta-adrenergic receptors in the heart). It is without intrinsic sympathomimetic and membrane stabilising activities. Human studies indicate that it crosses the blood brain - barrier only to a negligible extent.

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. As with other beta-adrenoceptor blocking drugs, its mode of action in the treatment of hypertension is unclear.

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

Additionally, atenolol is recommended in long-term prophylaxis after recovery from acute myocardial infarction.
Atenolol facilitates compliance with anti-hypertensive therapy by its acceptability to patients and simplicity of dosing. The narrow dose range and early patient response ensure that the effect of the drug in individual patients is quickly demonstrated. Atenolol is fully compatible with diuretics and other hypotensive agents (see 4.4 Special Warnings and Special Precautions for Use). Since it acts preferentially on beta-receptors in the heart, atenolol may with care be used successfully in the treatment of patients with respiratory disease who cannot tolerate non-selective beta-blockers.

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

5.2 Pharmacokinetic properties

Atenolol is well absorbed after oral dosing and excreted unchanged through the kidneys with a half-life of 6-9 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. Atenolol penetrates tissue poorly due to its low lipid solubility and its concentration in brain tissue is low. Plasma protein binding is low (approximately 3%).
Atenolol is effective for at least 24 hours after a single oral daily dose.

5.3 Preclinical safety data

There are no preclinical safety data of relevance to the prescriber, which are additional to those already included in other sections of this SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core

Maize Starch
Sodium Starch Glycollate (Type A)
Sodium Laurilsulfate
Magnesium carbonate
Magnesium stearate
Hyprolose

Film Coating

Opadry white
consisting of:
Lactose monohydrate
Hypromellose
Titanium Dioxide [E171]
Macrogol 4000

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Do no store above 25^{o}C.
Store in the original container.

6.5 Nature and contents of container

ATECOR 50 mg tablets are packaged in blisters of non-toxic polypropylene or alternatively in blisters of PVC/PE/PVDC welded on an internally film-coated aluminium semi-rigid support. Pack sizes of 30 and 100 tablets are available.

Not all pack sizes may be marketed.

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

Rowex Ltd
Newtown
Bantry
Co. Cork
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0711/003/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 November 1989

Date of last renewal: 29 November 2009

10 DATE OF REVISION OF THE TEXT

September 2020