**IRISH MEDICINES BOARD ACT 1995, as amended**

**Medicinal Products (Control of Placing on the Market) Regulations, 2007, as amended**

**PPA1151/055/002**
Case No: 2083791

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

**Imbat Limited**

**Unit L2**, **North Ring Business Park**, **Santry**, **Dublin 9**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

**Atecor 50mg Film-Coated Tablets**

the particulars of which are set out in the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **31/08/2010**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

# Part II

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Atecor 50mg Film-Coated Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50mg Atenolol
Excipients: lactose
For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Film-coated tablet
*Product imported from Germany:*
White, round, biconvex, film-coated tablet with a score line on one face and marked '50' on the other side.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

As a beta-adrenoceptor blocker ATECOR is indicated for the treatment of essential hypertension, angina pectoris and cardiac dysrhythmias. 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.

**Dysrhythmias**:
For maintenance control the usual daily dose is 50 – 100 mg twice daily.

**Myocardial Infarction**:
Where beta-blockade is appropriate for patients presenting later after infarction, Atenolol 100 mg daily may be givenfor long term prophylaxis.

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

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

**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 35ml/min/1.73m (normal range is between 100-150ml./min/1.73m ). For patients with a creatinine of 15-35ml/min/1.73m (equivalent to serum creatinine of 300-600 micromol/litre) the intravenous dose should be 10mg once every two days and the oral dose should be 50mg daily. For patients with a creatinine clearance of < 15ml/min/1.73m (equivalent to a serum creatinine of > 600micromol/litre) the intravenous dose should be 25mg daily or 50mg on alternate days. Patients on haemodialysis should be given 50mg 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. ATECOR should not be used if there is severe bradycardia.

ATECOR should not be used in uncontrolled or digitalis/diuretic refractory heart failure or in cardiogenic shock or with metabolic acidosis.

ATECOR should not be used in patients with a known hypersensitivity to the active substance or any excipients.

## 4.4 Special warnings and precautions for use

Sudden withdrawal of beta-adrenoceptor blocking agents in patients with ischaemic heart disease may result in the appearance of anginal attacks of increased frequency or severity or deterioration in cardiac state. Discontinuation of therapy should be gradual. The beta-blocker should only be used with caution in patients with controlled congestive cardiac failure or with a family history of asthma. Evidence of recrudescence of either condition should be regarded as a signal to discontinue therapy.

The beta-blocker can be administered to patients with obstructive respiratory disorders provided that adequate supervision is maintained to permit any necessary adjustment of dosage of the bronchodilator employed. If increased airways resistance develops consideration must be given to discontinuation of the beta-blocker, depending on the degree of airways resistance and the benefit derived from beta-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.

When this agent is administered to patients in renal failure the interval between doses may need to be increased or the dosage reduced 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 blockers. Until their significance is known it is recommended that consideration be given to discontinuing such therapy if these effects appear.

Use with caution in diabetes mellitus as symptoms of hypoglycaemia could be masked.

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

Atenolol should not be given to patients with pheochromocytoma without concomitant alpha-adrenoreceptor blocking therapy.

## 4.5 Interaction with other medicinal products and other forms of interaction

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.

The beta-blocker should only be used with great caution in patients who are receiving concomitant myocardial depressants such as chloroform, lignocaine, procainamide, beta-adrenoceptor stimulants such as isoprenaline, or calcium antagonists such as verapamil, nifedipine and diltiazem. The simultaneous use of calcium channel blockers may result in hypotension, bradycardia and cardiac failure. Alpha-adrenoceptor stimulants such as noradrenaline, may counteract the effect of the beta-blocker.

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.

The beta-blocker may mask some of the symptoms of thyrotoxicosis and of hypoglycaemia by inhibition of sympathetic nerve functions. The effects of hypoglycaemic agents may be increased, particularly by the noncardioselective beta blockers. The tachycardia of hypoglycaemia may be modified.

If the beta-blocker and clonidine are given concurrently the clonidine should not be discontinued until several days after withdrawal of the beta-blocker.

Care should be taken in prescribing a beta-adrenoceptor blocker in conjunction with Class I antidysrhythmics such as disopyramide.

## 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.

The drug is excreted in breast milk. This should be kept in mind if it is intended for use in nursing mothers.

The possibility of foetal injury cannot be excluded and the use of the drug in women who are, or may become pregnant or who are nursing the newborn infant, requires that anticipated benefits be weighed against possible risks.

Neonates born to mothers who are receiving atenolol at parturition or breastfeeding may be at risk of hypoglycaemia.

## 4.7 Effects on ability to drive and use machines

The use of Atecor is unlikely to result in any impairment of the ability of patients to drive or operate machinery, but see section 4.8. Also patients should be stabilised on treatment before driving or operating machinery.

## 4.8 Undesirable effects

The following undesired effects, listed by body system, have been reported for atenolol.

**Cardiovascular**: bradycardia, syncope, hypotension, Raynauds phenomena and cold extremities.

**CNS**: headache, hallucinations, depression, sleep disorders, dizziness.

**Dermatology**: psoriasiform skin reactions, skin rashes.

**Gastrointestinal**: gastrointestinal upset [nausea, diarrhoea or constipation] rare cases of hepatic toxicity including intrahepatic cholestasis have been reported.

**Haematological**: thrombocytopenia, purpura.

**Neurological**: paraesthesia, peripheral neuropathy.

**Ocular**: visual disturbances, dry eyes.

**Respiratory**: bronchospasm.

**Others**: alopecia, fatigue, hypo-or-hyperglycemia.

## 4.9 Overdose

The symptoms of overdosage 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 use 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.
CO7A B03: Beta blocking agents, selective.

Atecor (Atenolol) is a beta-adrenoceptor blocking drug, which is cardioselective (i.e. acts preferentially on betaadrenergic 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 Atecor 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 Atecor 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. Atecor is an additional treatment to standard coronary care.

Additionally, Atecor is recommended in long-term prophylaxis after recovery from acute myocardial infarction.

Atecor 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. Atecor 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, Atecor may with care be used successfully in the treatment of patients with respiratory disease who cannot tolerate non-selective beta-blockers.

## 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 the 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 laurilsulfate
Magnesium stearate
Heavy magnesium carbonate
Gelatin

**Film coating:**
Lactose
Hypromellose
Titanium dioxide (E171)
Macrogol 4000

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf Life

The shelf life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

## 6.4 Special precautions for storage

Do not store above 25ºC.
Store in the original container.

## 6.5 Nature and contents of container

Cardboard outer containing blister strips. Pack size 30.

## 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 PARALLEL PRODUCT AUTHORISATION HOLDER

Imbat Limited
Unit L2
North Ring Business Park
Santry
Dublin 9

## 8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1151/55/2

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 7th March 2008

## 10 DATE OF REVISION OF THE TEXT

August 2010