# SUMMARY OF PRODUCT CHARACTERISTICS OF CARDINOL 50 MG FILM COATED TABLETS

## 1. Name of the medicinal product

Cardinol 50 mg film coated Tablets

## 2. Qualitative and quantitative composition

Each film coated tablet contains 50 mg Atenolol

## 3. Pharmaceutical form

Film coated tablet.

## 4. Clinical particulars

### 4.1 Therapeutic indications

Atenolol is used in the management of hypertension, angina pectoris, cardiac arrhythmias and myocardial infarction. It may also be used in the prophylactic treatment of migraine.

### 4.2 Posology and method of administration

*Posology*

The dosage should be determined on an individual basis. It is recommended to start with the lowest possible dosage so that heart failure, bradycardia and bronchial symptoms are noticed timely. This is especially important in elderly. Further adaptation should be done gradually (e.g., once a week) under controlled conditions or based on the clinical effect.

*Adults and children over 12 years*:

*Hypertension*: A starting dose of 25mg is recommended. The usual maintenance dosage in hypertension is one tablet (50-100mg) daily. The maximum effect will be reached after 1-2 weeks. If further improvement of the blood pressure is desired, atenolol may be combined with another anti-hypertensive e.g.: a diuretic.

*Angina pectoris*: 50-100mg daily, depending on the clinical effect, in order to obtain a heartbeat in rest of 55-60 beats per minute. Increasing the dose above 100mg daily does not generally lead to an increased antianginous effect. If desired the dosage of 100mg daily can be divided in two dosages.

*Dysrhythmias*: Initially controlled intravenously. A suitable oral maintenance dosage is 50-100mg daily, given as a single dose.

*Secondary prevention after myocardial infarction*: Initially controlled intravenously, followed by 50mg orally about 10 minutes after the intravenous dose provided no adverse effects occur. This should be followed by a further 50mg orally 12 hours later. Maintenance dose is 100mg daily in 1-2 dosages for 6 days or until discharge from hospital.

*The Elderly*: Dosage requirements may be reduced, especially in patients with impaired renal function. Dosage should be titrated according to clinical effect.

*Children under 12 years*: Atenolol is not recommended for use in children under 12 years of age.

**4.3 Contraindications**

Beta blockers should not be given to patients with bronchospasm or asthma or to those with a history of obstructive airways disease. Other contra-indications include metabolic acidosis, cardiogenic shock, hypotension, severe peripheral arterial disease, sinus bradycardia, second-or third-degree atrioventricular block; caution should be observed in first-degree block. Although beta blockers are used in the management of heart failure, they should not be given to patients with uncontrolled heart failure and treatment should be initiated with great care. Patients with phaeochromocytoma should not receive beta blockers without concomitant alpha-adrenoceptor blocking therapy. Beta blockers may mask the symptoms of hyperthyroidism and of hypoglycaemia. They may unmask myasthenia gravis. Psoriasis may be aggravated. Abrupt withdrawal of beta blockers has sometimes resulted in angina, myocardial infarction, ventricular arrhythmias, and death.

**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.

**Anesthesia:**

Care should be taken when using anesthetic agents with Atenolol. The anesthetist should be informed to enable the necessary precautions to be taken.

If a Beta-blocker is withdrawn prior to surgery it should be discontinued for at least 24 hours. Atenolol should only be used with caution in patients with controlled congestive cardiac failure. Evidence of development of this condition should be regarded as a signal to discontinue therapy. Beta-blockers, even those with apparent cardioselectivity, should not be used in patients with asthma or a history of obstructive airways disease, unless no alternative treatment is available. In such cases the risk of inducing bronchospasm should be appreciated and appropriate precautions taken. 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. Patients with psoriasis should take Beta-blockers only after careful consideration. Beta-blockers may increase both the sensitivity towards allergens and the seriousness of anaphylactic reactions. 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 Beta1 selective Beta adrenoceptor blocking drug; consequently, its use may be considered although utmost caution must be exercised. Although contraindicated in severe peripheral arterial circulatory disturbances, atenolol may also aggravate less severe peripheral arterial circulatory disturbances. Due to atenolol's negative effect on conduction time, caution must be exercised if it is given to patients with first degree heart block.

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

Pharmacodynamic interactions may occur with drugs whose actions enhance or antagonise the various effects of beta blockers at beta1 and beta2 receptors, including their antihypertensive effect, cardiodepressant effect, effect on carbohydrate metabolism, or effect on bronchial beta2 receptors. Drugs that enhance the antihypertensive effects of beta blockers, such as ACE inhibitors, calcium-channel blockers, and clonidine may be useful in controlling hypertension. Drugs that cause hypotension such as aldesleukin and general anaesthetics also enhance the antihypertensive effects of beta blockers while other drugs, for example NSAIDs, antagonise the antihypertensive effects. Use of beta blockers with other cardiac depressants such as antiarrhythmics and rate-limiting calcium-channel blockers can precipitate bradycardia and heart block. In diabetic patients beta blockers can reduce the response to insulin and oral hypoglycaemics through their effects on pancreatic beta receptors. Pharmacokinetic interactions occur with drugs that alter the absorption or metabolism of beta blockers. Drugs that reduce

absorption include aluminium salts and bile-acid binding resins such as colestyramine. Metabolism of some beta blockers can be increased by concomitant treatment with drugs such as barbiturates and rifampicin and decreased with drugs such as cimetidine, erythromycin , fluvoxamine and hydralazine. Drugs that alter hepatic blood flow also affect metabolism of some beta blockers. Drugs that influence hepatic metabolism affect beta blockers that are extensively metabolised, such as labetalol, propranolol, and timolol, while beta blockers that are excreted largely unchanged, for example atenolol and nadolol, are unaffected.

**4.6 Fertility, pregnancy and lactation**

Atenolol should not be given during pregnancy and lactation unless it is considered essential by the physician. Beta-blockers reduce placental perfusion, which may result in intrauterine foetal death, immature and premature deliveries. In addition, adverse effects (especially hypoglycaemia and bradycardia) may occur in the foetus and the neonate in the postnatal period. As most Beta-blockers will pass into breast milk to a variable extent, breast feeding is not recommended during treatment with atenolol. Atenolol has been used effectively under close supervision for the treatment of hypertension associated with pregnancy. Animal studies do not suggest a teratogenic effect with the drug. There is an accumulation of Atenolol in breast milk. However, detrimental effects in the baby during breast feeding have not been reported.

**4.7 Effects on ability to drive and use machines**

Atenolol may occasionally produce drowsiness, dizziness, light-headedness and blurred vision. Patients should observe caution while driving or performing other tasks requiring alertness.

**4.8 Undesirable effects**

Atenolol is generally well-tolerated and side effects associated with it are infrequent and generally mild. These can include: coldness of the extremities and muscular fatigue may occur and, in isolated cases, bradycardia. Sleep disturbances which are associated with some other Beta-blocking preparations are rare. There have been reports of skin rashes and/or dry eyes associated with the use of Beta-adrenergic blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment is withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy

with a Beta-blocker should be gradual. Beta-adrenergic blocking drugs can cause dry mouth and gastrointestinal disturbances including nausea and vomiting, diarrhoea, constipation and abdominal cramping. The signs of thyrotoxicosis may be masked by atenolol treatment. Bronchospasm may occur in patients with bronchial asthma or a history of asthmatic complaints.

### 4.9 Overdose

After investigation of an overdose or in the case of hypersensitivity the patient should be kept under close supervision and be treated in an intensive care ward. Absorption of any drug material still present in the gastrointestinal tract can be prevented by gastric lavage, administration of activated charcoal and a laxative. Administration of calcium ions, or the use of a cardiac pacemaker may also be considered. In patients intoxicated with hydrophilic Beta-antagonists haemodialysis or haemoperfusion may be considered. From first principles, excessive bradycardia may be countered by atropine 1 - 2 mg intravenously, and if necessary, this may be followed by a Beta-agonist, such as isoprenaline 25 μg initially, or orciprenaline 0.5 mg given by slow intravenous injection. Care must be taken to ensure that the blood pressure does not fall too low if the dose of the Beta-adrenoceptor agonist has to be increased. Glucagon has also been reported to be useful as a cardiac stimulant in a dose of 10 mg intravenously.

## 5. Pharmacological properties

### 5.1 Pharmacodynamic properties

Atenolol is a cardioselective beta blocker. It is reported to lack intrinsic sympathomimetic activity and membrane-stabilising properties. Beta blockers (beta-adrenoceptor blocking drugs or antagonists) are competitive antagonists of catecholamines at beta-adrenergic receptors in a wide range of tissues. Although they have broadly similar properties they differ in their affinity for beta1 or beta2 receptor subtypes, intrinsic sympathomimetic activity, membrane-stabilising activity, blockade of alpha-adrenergic receptors, and pharmacokinetic properties including differences in lipid solubility. Beta blockers have different affinities for beta1 or beta2 receptors. Beta1 receptors are found mainly in the heart while beta2 receptors are found in noncardiac tissue including bronchial tissue, peripheral blood vessels, uterus, and pancreas.

### 5.2 Pharmacokinetic properties

About 50% of a dose is absorbed following oral administration. Peak plasma concentrations are reached in 2 to 4 hours. Atenolol has low lipid solubility. It crosses the placenta and is distributed into breast milk where concentrations higher than those in maternal plasma have been achieved. Only small amounts are reported to cross the blood-brain barrier, and plasma-protein binding is minimal. The plasma half-life is about 6 to 7 hours. Atenolol undergoes little or no hepatic metabolism and is excreted mainly in the urine.

## 6. Pharmaceutical particulars

### 6.1 List of excipients

Maize Starch BP

Calcium Hydrogen Phosphate BP

Povidone BP

Sodium lauryl Sulphate BP

Purified Water BP

Magnesium Stearate BP

Purified Talc BP

Sodium Starch Glycollate BP

Colloidal Anhydrous Silica BP

Microcrystalline Cellulose BP

<u>Coating Materials</u>

Hypromellose BP

Macrogol 300 BP

Purified Talc BP

Purified Water BP

Titanium Dioxide BP

Lake of Sunset Yellow

Lake of Ponceau 4R

Macrogol 6000

Isopropyl alcohol

Hard paraffin BP/Chloroform BP

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

3years

### 6.4 Special precautions for storage

Store in a dry place below 30ºC.  Protect from light.

### 6.5 Nature and contents of container

Blister Packing using PVDC coated PVC blister film and aluminium foil.

### 6.6 Special precautions for disposal and other handling

No special requirements for disposal.

## 7. Registrant

Cosmos Limited

## 8. Marketing authorization holder

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