CARDIOSAFE®

DESCRIPTION

CARDIOSAFE is the trademark of Bisoprolol Fumarate, a β1-selective adrenergic blocking agent.
Each **CARDIOSAFE 5** and **10** coated tablet contains Bisoprolol Fumarate 5 and 10 mg, respectively.

CHEMISTRY

Bisoprolol is: 2-Propanol, 1-[4-[[2-(1-methylethoxy)ethoxy]methyl]phenoxy]-3- [(1-methylehtyl)amino]-, (±)-, (E)-2-butenedioate.

CLINICAL PHARMACOLOGY

CARDIOSAFE (Bisoprolol) is a β1-selective adrenergic blocking agent, β-adrenergic blocking agents block the agonistic effect of the sympathetic neurotransmitters by competing for receptor binding sites. The precise mechanism of antihypertensive effect of β-adrenergic blocking agents is not known. Possible mechanisms include reduced cardiac output, decreased sympathetic outflow to peripheral vasculature, and inhibition of renin release by the kidneys.

In patients with angina, the blockade of β1-receptors reduces heart action and thus reduces oxygen demand. Hence Bisoprolol is effective in eliminating or reducing the symptoms.

Bisoprolol is absorbed almost completely from the gastrointestinal tract. This results in a high bioavailability of approximately 90%.

The plasma elimination half-life (10-12 hours) provides 24 hours efficacy following a once daily dosage. About 95% of the drug substance is excreted through the kidney, there are no active metabolites in man.

INDICATIONS

CARDIOSAFE is indicated in the treatment of

- Hypertension
- Coronary heart disease (angina pectoris).

DOSAGE

Usual adult dose

Initially 5 mg once daily, if necessary, the dosage may be increased to 10 mg once daily. 20 mg once daily may be necessary only in isolated cases.

Notes:

- Usual adult prescribing limit is 20 mg once daily.
- Dosage has not been established in pediatric patients.
- Initial dose of 2.5 mg once daily may be appropriate for some patients, especially patients with bronchospastic disease.
- Dose adjustment is generally not required in patients with hepatic or renal insufficiency of mild or moderate severity. A daily dose of 10 mg should not be exceeded in patient with terminal renal insufficiency (creatinine clearance < 20 ml/min) and in patients with sever hepatic insufficiency.
- Treatment with **CARDIOSAFE** is a long-term therapy. The dosage should not be altered or discontinued without the doctor's direction.
- It is recommended to take **CARDIOSAFE** in the morning on an empty stomach or with the breakfast.

ADVERSE EFFECTS

More frequent effects:

Decreased sexual ability, drowsiness especially with higher doses, trouble in sleeping, unusual tiredness or weakness.

Less frequent effects:

Symptomatic bradycardia (Dizziness), bronchospasm, congestive heart failure, mental depression, reduced peripheral circulation, anxiety and/or nervousness, constipation, diarrhea, nasal congestion, nausea or vomiting, stomach discomfort.

USE IN PREGNANCY

β-adrenergic blocking agents cross the placenta. The safety of these agents in pregnancy is not fully established. Fetal and neonatal bradycardia, hypotension, hypoglycemia, and respiratory depression have been reported with administration of β-adrenergic blocking agents to pregnant women.

Bisoprolol should not be used during pregnancy. FDA Pregnancy Category C.

USE IN LACTATION

It is not known whether Bisoprolol is distributed into breast milk. Bisoprolol should not be used during lactation.

INTERFERENCE WITH CLINICAL AND LABORATORY TESTS

- Glaucoma screening and radionuclide ventriculography diagnostic test results may be interfered with by systemic β-blockade.
- Blood urea nitrogen (usually in patients with severe heart disease), Antinuclear antibody (ANA) titers, serum potassium concentrations, serum uric acid, Serum lipoproteins and serum triglycerides concentrations may be increased.

DRUG INTERACTIONS

- Anaesthesia: cardic output may be impaired under anaesthesis, prior to an operation the anaesthetist should be informed if the patient is being treated with Bisoprolol.
- Oral antidiabetic agents or Insulin: effect of insuline or oral antidiabetic may be potentiated.

- Other antihypertensive drug: concomitant therapy of Bisoprolol with reserpine, α-methyldopa, clonidine or guanfacine may cause a considerable decrease in heart rate. Clonidine should not be discontinued unless administration of Bisoprolol has been terminated for a few days.
- Rifampicin: rifampicin can slightly reduce the half-life of Bisoprolol.
- Calcium channel blocking agents: nifedipine may potentiate the antihpertensive effect of Bisoprolol. Concurrent use of Bisoprolol with verapamil or diltiazem or other antiarrhythmic agents can cause hypotentsion, bradycardia and other arrhythmias.
- Sympathomimetics and xanthines, especially aminophylline or theophylline: concurrent use with β-adrenergic blocking agents may result in mutual inhibition of therapeutic effects.

CONTRAINDICATIONS

Overt cardiac failure, untreated myocardial insufficiency (decompensated heart failure), recent myocardial infarction, shock, disturbances of atrioventricular conduction (AV block graded II and III), sick sinus syndrome, disturbed stimulus conduction between the sinoatrial node and atrium (Sinoatrial block), bradycardia prior to the start of treatment, hypotension, bronchial asthma and advanced stages of peripheral circulatory disturbances.

WARNINGS

- Adrenal tumor: Bisoprolol may only be administered after α-blockade.
- History of allergy: severity and duration of anaphylactic reactions to allergens and allergen immunotherapy may be increased with β-adrenergic blocking agents.
- Bronchial asthma or emphysema or nonallergenic bronchitis: β-adrenergic blocking agents may promote bronchospasm.
- Hyperthyroidism: β-adrenergic blocking agents may mask tachycardic symptoms, abrupt withdrawal may intensify symptoms.
- Mental depression or history of mental depression: use with caution in those patients.

OVERDOSE

Clinical effects of overdose includes bradycardia, severe or fainting dizziness, hypotension, irregular heartbeat, difficulty breathing, bluish-colored fingernails or palms of hands, or seizures.
Treatment with Bisoprolol should be discontinued, if necessary, the following antidotes should be administered alone or consecutively: atropine IV 0.5-2.0 mg, orciprenaline slowly IV until it takes effects, also glucagons may be given at a dose of 1-5(-10) mg.

PRECAUTIONS

- In diabetic patients with greatly fluctuating blood glucose values, during prolonged periods of fasting and in patients with acidosis, signs of low blood glucose levels (e.g. rapid heart rate) may be masked. Blood glucose levels should be monitored.
- The ability to drive or to operate machinery may be impaired especially at the start of treatment and with a change of medication and with alcohol.

HOW SUPPLIED

- Boxes of 30 blistered Tablets of **CARDIOSAFE 5**.
- Boxes of 30 blistered Tablets of **CARDIOSAFE 10**.
- Hospital packs of different presentations.

Store according to conditions specified on the package.
Do not use after the expiry date shown on the package.

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who dispensed the medicament.
- The doctor and the pharmacist are experts in medicine.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep medicaments out of the reach of children.

COUNCIL OF ARAB HEALTH MINISTERS
UNION OF ARAB PHARMACISTS

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Prescribing Information Available Upon Request

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