BISCORDEX 5mg and 10mg
TABLETS
(BISOPROLOL)

COMPOSITION
Each tablet contains Bisoprolol 5mg or 10mg in the form fumarate.

CLINICAL PHARMACOLOGY
BISCORDEX is a beta 1-selective adrenoreceptor blocking agent without significant membrane stabilizing activity or intrinsic sympathomimetic activity in its therapeutic dosage range. Cardioselectivity is not absolute, however, and at higher doses (>/=20 mg) BISCORDEX also inhibits beta2-adrenoreceptors, chiefly located in the bronchial and vascular musculature; to retain selectivity it is therefore important to use the lowest effective dose.

PHARMACOKINETICS
The absolute bioavailability after a 10 mg oral dose of BISCORDEX is about 80%. Absorption is not affected by the presence of food. The first pass metabolism of BISCORDEX is about 20%.
Binding to serum proteins is approximately 30%. Peak plasma concentrations occur within 2-4 hours of dosing with 5 to 20 mg, & mean peak values range from 16 ng/ml at 5 mg to 70 ng/ml at 20 mg. The plasma elimination half-life is 9-12 hours and is slightly longer in elderly patients. Steady state is attained within 5 days of once daily dosing in both young and elderly populations.
BISCORDEX is eliminated equally by renal and non-renal pathways with about 50% of the dose appearing unchanged in the urine and the remainder appearing in the form of inactive metabolites.

INDICATIONS
BISCORDEX is indicated in the management of hypertension. It may be used alone or in combination with other antihypertensive agents.

CONTRAINDICATION
BISCORDEX is containdicated in patients with cardiogenic shock, overt cardiac failure, second or third degree AV block, and marked sinus bradycardia.

WARNING
Cardiac Failure
Sympathetic stimulation is a vital component supporting circulatory function in the setting of congestive heart failure, & beta-blockade may result in further depression of myocardial contractility & precipitate more severe failure. In general, beta-blocking agents should be avoided in patients with overt congestive failure.
Abrupt Cessation of Therapy
Exacerbation of angina pectoris and in some instances, myocardial infarction or ventricular arrhythmia, have been observed in patients with coronary artery disease following abrupt cessation of therapy with beta-blockers. Such patients should, therefore, be cautioned against interruption or discontinuation of therapy without the physician's advice. Even in patients without overt coronary artery disease, it may be advisable to taper therapy with BISCORDEX over approximately one week with the patient under careful observation. If withdrawal symptoms occur, BISCORDEX therapy should be reinstituted, at least temporarily.
Peripheral Vascular Disease
Beta-blockers can precipitate or aggravate symptoms of arterial insufficiency in patients with peripheral vascular disease. Caution should be exercised in such individuals.
Bronchospastic Disease
PATIENTS WITH BRONCHOSPASTIC DISEASE SHOULD, INGENERAL, NOT RECEIVE BETA-BLOCKERS. Because of its relative beta 1-selectivity. However, BISCORDEX may be used with caution in patients with bronchospastic disease who do not respond to, or who cannot tolerate other antihypertensive treatment. Since beta 1-selectivity is not absolute, the lowest possible dose of BISCORDEX should be used, with therapy starting at 2.5 mg. A beta2 agonist (bronchodilator) should be made available.
Anesthesia and Major Surgery
If BISCORDEX treatment is to be continued perioperatively particular care should be taken when anesthetic agents which depress myocardial function, such as ether, cyclopropane and trichloroethylene, are used. See OVERDOSAGE for information on treatment on bradycardia and hypotension.
Diabetes and Hypoglycemia
Beta-blockers may mask some of the manifestations of hypoglycemia , particularly tachycardia.

PRECAUTIONS
Impaired Renal or Hepatic Function
Use caution in adjusting the dose of BISCORDEX in patients with renal or hepatic impairment.

INFORMATION FOR PATIENTS
Patients, especially those with coronary artery disease, should be warned about discontinuing use of BISCORDEX without a physician's supervision. Patients Should also be advised to consult a physician if any difficulty in breathing occurs, or if they develop signs or symptoms of congestive heart failure or excessive bradycardia.
Patients subject to spontaneous hypoglycemia, or diabetic patients receiving insulin or oral hypoglycemic agents, should be cautioned that beta-blockers may masks some of the manifestations of hypoglycemia, particularly tachycardia , and bisoprolol fumarate should be used with caution.
Patients should know how they react to this medicine before they operate automobiles and machinery or engage in other tasks requiring alertness.

DRUG INTERACTION

BISCORDEX should not be combined with other beta-blocking agents. Patients receiving catecholamine-depleting drugs, such as reserpine or guanethidine, should be closely monitored, because the added beta-adrenergic blocking action of BISCORDEX may produce excessive reduction of sympathetic activity. In patients receiving concurrent therapy with clonidine. If therapy is to be discontinued, it is suggested that BISCORDEX be discontinued for several days before the withdrawal of clonidine.

BISCORDEX should be used with care when myocardial depressants or inhibitors of AV conduction, such as certain calcium antagonists (particularly of the phenylalkylamine (verapamil) and benzothiazepine (diltiazem) classes), or antiarrhythmic agents, such as disopyramide, are used concurrently.

Concurrent use of rifampin increases the metabolic clearance of BISCORDEX. resulting in a shortened elimination half-life of BISCORDEX. However, initial dose modification is generally not necessary. Pharmacokinetic studies document no clinically relevant interactions with other agents given concomitantly, including thiazide diuretics, digoxin and cimetidine.

Risk of Anaphylactic Reaction: While taking beta-blockers, patients with a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge, either accidental, diagnostic, or therapeutic. Such patients may be unresponsive to the usual doses of epinephrine used to teat allergic reactions.

ADVERSE REACTIONS

Dizziness, vertigo, headache, paresthesia, hypoesthesia, somnolence, anxiety/restlessness, decreased, concentration/memory, dry mouth. Bradycardia; palpitations and other rhythm disturbances, cold extremities, claudication, hypotension. Orthostatic hypotension, chest pain, congestive heart failure, dyspnea on exertion, vivid dreams, Insomnia, depression, gastric/epigastric/abdominal pain, gastritis, dyspepsia, nausea, vomiting. diarrhea, constipation, muscle/joint pain back/neck pain, muscle cramps, twitching/tremor. Skin: rash. acne, eczema, skin irritation, pruritus, flushing, sweating, alopecia. angioedema, exfoliative dermatitis are observed.

Also visual disturbances, ocular pain/pressure, abnormal lacrimation, tinnitus, earache, taste abnormalities, asthma/bronchospasm. bronchitis, coughing, dyspnea, pharyngitis, rhinitis, sinusitis. URI, decreased libido/impotence, peyronie's disease, cystitis. renal colic, purpura, fatigue, asthenia, chest pain, malaise, edema, weight gain have been reported.

OVERDOSAGE

The most common signs expected with overdosage of a beta-blocker are bradycardia. hypotension, congestive heart failure, bronchospasm. & hypoglycemia. In general. if overdose occurs. BISCORDEX therapy should be stopped & supportive and symptomatic treatment should be provided.

DOSAGE AND ADMINISTRATION

The dose of BISCORDEX must be individualized to the needs of the patient. The usual starting dose is 5 mg once daily. In some patients, 2.5 mg may be an appropriate starting dose. If the antihypertensive effect of 5 mg is inadequate, the dose may be increased to 10 mg and then, if necessary, to 20 mg once daily.

Patients with Renal or Hepatic impairment

In patients with hepatic impairment (hepatitis or cirrhosis) or renal dysfunction (creatinine clearance less than 40 ml/min). the initial daily dose should be 2.5 mg and caution should be used in dose-titration.

It is not necessary to adjust the dose in the elderly, unless there is also significant renal or hepatic dysfunction.

STORAGE

Store at Controlled room temperature 15-30°(59-86oF)

PRESENTATION

Box of 30 tablets

Orbucell Pharma

20 KONRAD CRESCENT, MARKHAM, ONTARIO, L3R 8T4. CANADA