BLOCADRIL

Tablets

Composition

Blocadril 10 Tablets
Each tablet contains Propranolol hydrochloride 10 mg.

Blocadril 40 Tablets
Each tablet contains Propranolol hydrochloride 40 mg.

Action

Propranolol is a competitive antagonist at both the $beta_1$ and $beta_2$-adrenoreceptors. It has no agonist activity at the beta-adrenoreceptor but has membrane-stabilizing activity at concentrations exceeding 1 to 3 mg/liter, though such concentrations are rarely achieved during oral therapy. Competitive beta-adrenoreceptor blockade has been demonstrated in man by a parallel shift to the right in the dose-heart rate response curve to beta-agonists such as isoprenaline.

Propranolol, as with other beta-adrenoreceptor blocking medicines, has negative inotropic effects, and is therefore contraindicated in uncontrolled heart failure. Propranolol is effective and well tolerated in most ethnic populations, although the response may be less in Afro-Caribbean black patients.

Pharmacokinetics
Propranolol is completely absorbed after oral administration and peak plasma concentrations occur 1 to 2 hours after dosing in fasting patients. The liver removes up to 90% of an oral dose with an elimination half-life of 3 to 6 hours. Propranolol is widely and rapidly distributed throughout the body with highest levels occurring in the lungs, liver, kidney, brain, and heart. Propranolol is highly protein bound (80 to 95%).
Since the half-life may be increased in patients with significant hepatic or renal impairment, care should be taken when starting treatment and selecting the initial dose.

Indications

- Hypertension, angina pectoris, cardiac arrhythmias, prophylaxis of common migraine headache, hypertrophic sub aortic stenosis and pheochromocytoma.
- Blocadril is indicated to reduce cardiovascular mortality in patients who have survived the acute phase of myocardial infarction and are clinically stable.

Contraindications

- Known hypersensitivity to the drug.
- Bronchial asthma or a history of bronchial asthma, or severe chronic obstructive pulmonary disease.
- Sinus bradycardia and greater than first degree heart block, cardiogenic shock, right ventricular failure secondary to pulmonary hypertension, congestive heart failure unless secondary to a tachyarrhythmia treatable with ß-blockers.

Warnings

Cardiac Failure
Sympathetic stimulation may be a vital component supporting circulatory function in congestive heart failure, and ß-blockade always carries the potential hazard of further depressing myocardial contractility and precipitating cardiac failure.

In hypertensive and angina pectoris patients, presenting with congestive heart failure controlled by digitalis and diuretics, special caution should be exercised when administering the ß-blocker, since both digitalis and the ß-blocker depress AV conduction.

In patients without a history of cardiac failure, continued depression of the myocardium by ß-blockers over a period of time can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or given a diuretic. The response should be observed closely. If cardiac failure continues, despite adequate digitalization and diuretic therapy, ß-blocker therapy should be gradually withdrawn.

Discontinuation of Therapy

Ischemic Heart Disease

Severe exacerbation of angina and the occurrence of myocardial infarction and ventricular arrhythmia have been reported in angina patients following the abrupt discontinuation of therapy with ß-blockers. Because of the problems encountered with ß-blockers, when discontinuation of therapy is planned, patients should be carefully observed and advised to limit physical activity to a minimum.

If the angina worsens or acute coronary insufficiency develops, it is recommended that therapy be promptly reinstituted, at least temporarily.

Thyrotoxicosis

ß-Adrenergic blockade may mask certain clinical signs of hyperthyroidism (e.g. tachycardia). Abrupt withdrawal may be followed by an exacerbation of the symptoms of hyperthyroidism, including thyroid storm.

Hypotension during Anaesthesia

Some patients receiving ß-adrenergic blocking agents have been subject to protracted severe hypotension during anesthesia. Therefore, in elective surgery, ß-blockers should be withdrawn gradually. Clinical evidence suggests that the effect of ß-blockade is no longer present 48 hours after withdrawal of the drug. In emergency surgery, since ß-blockers are competitive inhibitors of ß-adrenergic receptor agonists, their effects on the heart can be reversed by the administration of such agents (e.g, dobutamine or isoproterenol) with caution. Manifestations of vagal tone (e.g. profound bradycardia or hypotension) may be corrected by the I.V. administration of atropine 1-2 mg.

If ß-blockade is continued during surgery, care should be taken when using anesthetic agents, which depress the myocardium (e.g. ether, cyclopropane, tetrachloroethylene).

Propranolol is not to be used in the treatment of migraine after an attack has begun.

Pregnancy

Category C

The drug should be used only if clearly needed.

Neonatal bradycardia, hypoglycemia and respiratory depression have been associated with both cardioselective and non-cardioselective ß-blocker therapy during pregnancy.

Nursing Mothers

ß-Blockers appear in breast milk. Patients using this drug should stop nursing.

Adverse Reactions

The following adverse reactions have been reported with ß-adrenergic blocking agents. Although not all of them have been specifically attributed to any individual ß-blocker, the potential exists for their occurrence. This should be borne in mind when drugs of this class are used.

Cardiovascular

Congestive heart failure, pulmonary edema, cardiac enlargement, secondary effects of decreased cardiac output which include syncope, vertigo, light-headedness and postural hypotension, severe bradycardia, lengthening of PR interval, second- and third-degree AV block, sinus arrest, palpitations, chest pains, cold extremities, Raynaud's phenomenon, claudication, hot flushes.

Respiratory

Shortness of breath, wheezing, bronchospasm, status asthmaticus.

Central Nervous System
Light-headedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, vivid dreams, acute reversible syndrome characterized by disorientation for time and place, short term memory loss, emotional liability, slightly clouded sensoriurn, decreased neuropsychometric performance.

Gastrointestinal
Diarrhea, constipation, flatulence, heartburn, anorexia, nausea and vomiting, abdominal pain, dryness of mouth, mesenteric arterial thrombosis, ischemic colitis.

Allergic
Pharyngitis, laryngospasm and respiratory distress, agranulocytosis, erythematous rash, fever combined with aching and sore throat.

Haematological
Agranulocytosis, thrornbocytopenic purpura, nonthrombocytopenic purpura.

Ophthalmological
Conjunctivitis, dry eyes, itching eyes, blurred vision. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for the ß-blocker practolol, have not been associated with this drug.

Miscellaneous
Reversible alopecia, lupus erythematosus-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely.

Precautions
In patients prone to non-allergic bronchospasm (e.g. chronic bronchitis, emphysema), this drug should be administered with caution, since it may block the bronchodilation produced by endogenous and exogenous catecholamine stimulation of ß2-receptors.

ß-Blockers may mask tachycardia occurring with hypoglycemia. However, other manifestations such as dizziness and sweating may not be significantly affected. ß-Blockers should be administered with caution to patients subject to spontaneous hypoglycemia, or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycaemic agents.

In patients with metabolic acidosis, particular caution should be observed when using this drug. ß-blockade may impair the sympathetic nervous tone required in such patients in order to maintain vital functions.

Smoking may reduce serum levels and increase the clearance of propranolol in patients receiving this drug on a chronic basis.

Drug Interactions
ß-Blockers/ Clonidine
When therapy is discontinued in patients receiving a ß-blocker and clonidine concurrently, both drugs should be withdrawn gradually, first the ß-blocker and then clonidine, in order to avoid clonidine-hypertensive crisis.

ß- Blockers/ Sympathomimetics
Concurrent use of ß-blockers with adrenaline, phenylephrine and possibly other Sympathomimetics may result in significant hypertension and excessive bradycardia with possible heart block. Concurrent use requires careful monitoring.

ß-Blockers/Hypoglycemics
ß-Adrenergic blockade may mask the premonitory signs and symptoms of acute hypoglycemia. Therefore, it is recommended to adjust the dosage of antidiabetic drugs when they are administered concurrently with ß-blockers .

ß-Blockers/ Digitalis Glycosides
Concurrent use may result in excessive bradycardia with possible heart block. Careful monitoring is necessary (see Warnings).

ß-Blockers/ Calcium Channel Blockers
Literature reports suggest that oral calcium antagonists may be used in combination with ß-adrenergic blocking agents when heart function is normal. However, they should be avoided in patients with impaired cardiac function. Hypotension, AV conduction disturbances, and left ventricular failure have been reported in some patients receiving ß-adrenergic blocking agents when an oral calcium antagonist was added to the treatment regimen.

ß-Blockers/Theophylline and its Derivatives
Concurrent administration of theophylline and ß-adrenergic blocking agents may have antagonizing effects. Theophylline inhibits phosphodiesterase and produces ß-adrenergic stimulation. ß-adrenergic blocking agents may also decrease theophylline clearance. This effect is notable in patients who have increased theophylline clearance induced by cigarette smoking.

ß-Blockers/ Nondepolarizing Neuromuscular Blocking Agents
ß-Blockers may potentiate and prolong the action of nondepolarizing neuromuscular blocking agents such as gallamine, pancuronium and tubocurarine.

ß-Blockers/ Reserpine
Reserpine and other catecholamine-depleting drugs may have an additive and possibly excessive effect when given with ß-blocking agents. Therefore, patients should be closely observed for evidence of excessive reduction of sympathetic tone (hypotension and/or excessive bradycardia), which may produce vertigo, syncope or postural hypotension.

ß-Blockers⁄Non-steroidal Anti-inflammatory Drugs
Blunting of the antihypertensive effect of ß-adrenergic receptor blocking agents by non-steroidal anti-inflammatory drugs has been reported. When using these agents concomitantly, patients should be observed carefully to confirm that the desired therapeutic effect has been obtained.

Propranolol⁄Chlorpromazine
An increase in ß-adrenergic blockade may occur.

Propranolol⁄Cimetidine
Cimetidine appears to inhibit the hepatic enzymes responsible for propranolol first-pass metabolism, leading to increased propranolol bioavailability.

Diagnostic Interference
ß-Blockers may produce hypoglycemia and interfere with glucose insulin tolerance tests. Propranolol may interfere with the glaucoma-screening test due to a reduction in intraocular pressure.

Dosage and Administration
The dosage range for Blocadril varies according to indication.

Hypertension
Dosage must be individualized. The usual initial dosage is 40 mg Blocadril twice daily, whether used alone or added to a diuretic. Dosage may be increased gradually until adequate blood pressure is

achieved. The usual dosage is 160-480 mg/day. In some instances, a dosage of 640 mg/day may be required.

Angina Pectoris
Dosage must be individualized. Starting with 10-20 mg 3-4 times daily before meals and at bedtime, dosage should be gradually increased at 3-7 day intervals until optimum response is obtained. If treatment is to be discontinued, the dosage should be reduced gradually over a period of several weeks.

Arrhythmias
10-30 mg 3-4 times daily, before meals and at bedtime.

Migraine
Dosage must be individualized. The initial oral dose is 80 mg Blocadril daily, in divided doses. The usual effective dose range is 160-240 mg/day. The dosage may be increased gradually to achieve optimum migraine prophylaxis.

Hypertrophic Subaortic Stenosis
20-40 mg 3-4 times daily, before meals and at bedtime.

Pheochromocytoma
Preoperatively
60 mg daily in divided doses for 3 days prior to surgery, concomitantly with an alpha-adrenergic blocking agent.

Management of Inoperable Tumor
30 mg daily, in divided doses.

Myocardial Infarction
The recommended dosage is 180-240 mg/day, in divided doses. The effectiveness and safety of daily dosages greater than 240 mg for the prevention of cardiac mortality has not been established.

Over Dosage

Manifestations
The most common signs and symptoms to be expected with overdosage with a ß-adrenergic receptor blocking agent are symptomatic bradycardia, hypotension, hypoglycemia, bronchospasm, and acute cardiac failure.

Treatment
Therapy with the ß-blocker should be discontinued and the patient observed closely.
In addition to gastric lavage, the following measures should be employed, as appropriate.

Bradycardia
If hemodynamically stable, no specific therapy is indicated. If hypotensive, give atropine 0.6 mg I.V. or adrenaline. If there is no response to vagal blockade, repeat every 3 minutes to a total of 2-3 mg. Isoproterenol I.V. may be administered cautiously. Large doses of glucagon (5-10 mg I.V. rapidly over 30 seconds, followed by continuous I.V. infusion of 5 mg/hour) may increase heart rate, even if atropine and isoproterenol have failed. In refractory cases, transvenous cardiac pacing may be needed.

Bronchospasm
Administer a ß2-Stimulating agent and/or a theophylline derivative.

Acute Cardiac Failure

Administer a digitalis glycoside, a diuretic, and oxygen immediately. In refractory cases, the use of I.V. aminophylline is suggested. This may be followed by glucagon if necessary. In shock resulting from inadequate cardiac contractility, dobutamine may be considered.

Hypotension
Administer vasopressors (e.g. dopamine, dobutamine, noradrenaline) with serial monitoring of blood pressure. Evidence exists indicating that adrenaline is the drug of choice. In refractory cases, glucagon has been reported to be useful.

Heart Block (second or third degree)
Use isoproterenol or a transvenous cardiac pacemaker.

Presentation

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Box of 20 tablets.

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