PACKAGE LEAFLET

PROPRANOLOL

ATC code: C07AA05

PHARMACOTHERAPEUTIC GROUP

Beta-blockers, non-selective.

COMPOSITION

Propranolol hydrochloride 25 and 40 mg in one tablet.

ACTION

Propranolol is a non-selective beta-blocker. It inhibits the sympathetic excitability of the heart and has a stabilizing effect on the cellular membrane potential. The main effects of the drug on the cardiovascular system are anti-anginose - reduces oxygen consumption in the myocardium by a negative inotropic and chronotropic effect; anti-arrhythmic - decreases spontaneous excitability in the sinus node and the ectopic pacemakers, retards conductivity in the AV-node; antihypertensive - reduces cardiac discharge, inhibits the elimination of renin from the kidneys, decreases the sympathetic effect on the peripheral vascular network. Following a myocardial infarction the drug reduces significantly oxygen consumption in the myocardium, the rate of reinfarctions and post-infarction mortality.

In oral administration propranolol is absorbed up to 90% in the gastrointestinal tract.

Bioavailability varies due to the pronounced effect of the first pass through the liver. The preparation has high lipid solubility, binding 90-95% to plasma
proteins. Its biological half-life is 4 hours. Maximum therapeutic effect is attained 1-2 hours after ingestion of a single dose. Due to the marked intensive destruction during the first pass through the liver there is no linear correlation between plasma levels and therapeutic effect. The individual therapeutic dose varies considerably as a result of the different level of the sympathetic tone in particular individuals as well. Propranolol is eliminated mainly in the form of metabolites through the kidneys. It is not accumulated in renal insufficiency.

**INDICATIONS**

Arterial hypertension of various origin - alone or in combination with other antihypertensive drugs.

Angina pectoris - for prophylaxis and treatment of attacks of stable and unstable angina pectoris.

Myocardial infarction - for long-term secondary prophylaxis following myocardial infarction.

Rhythmic disorders in cardiac activity - sinus tachycardia, non-paroxysmal supraventricular tachycardia; in the complex therapy of tachycardia caused by digitalis intoxication; functional cardiovascular disorders resulting from hypersympatheticotension.

Hypertrophic cardiomyopathy - alone or in the combined therapy.

Phaeochromocytoma - for treatment of symptomatic tachycardia (only after a preceding initial treatment with alpha-adrenergic blockers due to the risk of excessive increase in arterial blood pressure).

Thyrotoxicosis - in the complex therapy for treatment of concomitant tachycardia, tremor and anxiety.
Tremor - essential tremor (as an optional agent), inherited and senile tremor, tremor in alcohol abstinence.

Propranolol is also used for prophylaxis of migrainous attacks and syndrome of prolapse of the mitral cusp.

CONTRAINDICATIONS

Absolute - severe cardiovascular insufficiency; AV-block of II-III degree; SA-block, sick-sinus syndrome; fresh myocardial infarction complicated by hypotension, bradycardia and left-ventricular cardiac insufficiency, cardiogenic shock; bradycardia (under 50 beats/min); acidosis; simultaneous venous administration of verapamil or diltiazem; bronchial asthma; history of hypersensitivity to the drug.

Relative - severe spasmodic bronchitis, pulmonary emphysema, chronic obstructive pulmonary disease; grave hepatic and renal impairment; insulin-dependent diabetes; syndromes and diseases of the peripheral vessels (Raynaud’s disease, Buerger’s disease, diabetic angiopathy etc); allergic diseases; concomitant desensitizing therapy; psoriasis.

ADVERSE REACTIONS/SIDE EFFECTS

Usually the side effects are light and short-lived, occurring at the beginning of treatment and abating with the adaptation of the patient’s system. In rare cases reduction in the dose or discontinuation of treatment may prove necessary. Aggravation of cardiac insufficiency, bradycardia, disturbances in AV-conductivity, hypotension; dryness in the mouth, gastric irritation; deterioration of pre-existing psoriasis, slight dermatic allergic reactions; short-lived muscle weakness, cramps in the calves, paresthesia, cold extremities; transitory fatigue, headache, perspiration, slight dizziness, sleep disturbances, depressions and
hallucinations; decrease in lacrimal secretion, conjunctivitis; deterioration of glucose tolerance in patients with diabetes, masking of hypoglycaemia symptoms; bronchospasm; reduced potency may occur.

In case of persistent undesirable effects such as reduced potency, dizziness, sleep disturbances, unusual exertional tiredness, nervousness and tension a readjustment of treatment and dosage is necessary.

**DRUG AND NON-DRUG INTERACTIONS**

Concomitant administration with insulin or sulphanilurea drugs may mask the symptoms of hypoglycaemia.

Combination with other antihypertensive agents, vasodilators or psychopharmaceutical preparations enhances the hypotensive effect of propranolol.

Antihypertensive medications affecting the central nervous system such as reserpin, methyldopa, clonidine, guanfacin, etc may increase the chrono- and dromotropic action of the preparation.

Simultaneous usage with antiarrhythmic drugs, verapamil, diltiazem and MAO-inhibitors potentates the cardiodepressive effect of the drug.

With anaesthetics there is a higher risk of hypoglycaemia, depression of the myocardium, bradycardia and increased central venous pressure.

Combination with amiodarone is not recommended due to the risk of impairing the automatism and conductivity of the heart.

Cimetidin decreases the hepatic clearance of the preparation and raises its plasma levels and therapeutic effect.
Nonsteroidal anti-inflammatory agents and particularly indometacin reduce the antihypertensive action of the drug.

Cocaine inhibits the therapeutic effect of propranolol. The administration of the medication in cocaine abuse increases the risk of hypotension, severe bradycardia and cardiac block due to the alpha-blocking adrenergic action of cocaine.

Contrasting iodine-containing agents can raise the risk of moderate to severe anaphylactic reaction which is resistant to therapy.

Estrogens reduce the antihypertensive action of the drug by inducing liquid retention.

Neuromuscular blockers may potentate and prolong the effect of the non-depolarizing myorelaxants.

Discontinuation of smoking may increase the therapeutic effect of propranolol as a result of reduced metabolism and elevating of its plasma levels.

Combined administration with phenotiazines induces an incomplete rise in the plasma levels of both drugs.

In employment of allergens for immunotherapy or dermatic tests beta-blockers can increase the risk of grave allergic reactions to these agents.

Simultaneous usage with aminophylline, theophylline or caffeine may neutralize the therapeutic effect of both medications, and the plasma levels of theophylline can raise.

**PRECAUTIONS AND WARNINGS**

Treatment should start with small doses which are gradually raised according to the individual sensitivity of the patient.
Discontinuation of treatment should be effected stepwise over a period of 8-10 days, especially in patients with angina pectoris since the abrupt interruption of the medication may lead to anginous attack or rhythmic disorders. In patients with an impaired hepatic function the dose should be reduced. The drug should be administered with caution in elderly patients due to the possibility of hyper- or hyposensitivity to the usual doses of the medication. In diabetics beta-blockers may mask the symptoms of hypoglycaemia.

Prior to surgical intervention (including dental or urgent ones) one should be informed whether the patient is taking a beta-blocker. Treatment should be discontinued 48 hours before general anaesthesia.

Physical activity should be very cautiously increased in patients with angina pectoris in whom the pain symptoms have been reduced as a result of propranolol treatment.

Beta-blockers may induce changes in some laboratory and other functional studies - elevated levels of serum lipoproteins and triglycerides; increased serum potassium; false rise in the level of catecholamines and their disintegration products in the urine and blood; raised level of antinuclear antibodies; negative screening tests for glaucoma.

Beta-blockers may cause aggravation of allergy to foodstuffs, medications or insects. Consequently, these drugs should be employed with caution in patients with a history of grave allergy to such agents since they may aggravate it.

It is advisable that propranolol is taken regularly, particularly in case of a single daily dose. In the event of an intake omission the dose should be taken at once except when the next ingestion is due soon.
PREGNANCY AND BREAST-FEEDING

Since the drug is excreted in the breast milk it should not be used in pregnancy or during the lactation period except for compelling reasons and under strict medical control of the foetus or the baby.

EFFECTS ON ACTIVE ATTENTION, DRIVING ABILITY AND OPERATION OF MACHINERY

Adverse effects on the active attention, reflexes and motor activity have not been reported.

MODE OF ADMINISTRATION AND DOSAGE

The drug is taken orally with some liquid during or immediately after meals.

Angina pectoris - initial dose 12.5-25 mg 2-4 times daily; therapeutic dose 80-320 mg daily, divided into 2-4 intakes. The dose is gradually increased until therapeutic effect or beta-block has been attained.

Arterial hypertension - initial dose 25-50 mg 2 times daily. The dose is gradually increased depending on the therapeutic needs and individual tolerance to the drug.

In single patients with arterial hypertension or angina pectoris a good therapeutic effect is achieved with single or 2 single intakes of the daily dose.

Myocardial infarction - treatment can be initiated within 5-21 days following infarction, the initial dose being 25 mg 2-3 times daily, increased to 180-240 mg depending on the therapeutic needs and individual tolerance of the patient.

Phaeochromocytoma - in the combined therapy 25 mg 3 times daily up to 50 mg 3-4 times daily (until a lasting beta-block is attained, not later than 3 days prior to surgery with a concomitant alpha-adrenoblocking therapy). The drug should not
be administered until at least a partial alpha-blockage has been attained. In inoperable tumour the daily dose is 25-160 mg divided into several intakes.

Migrainous attacks - for prophylaxis 25 mg 4 times daily; if necessary the dose can be gradually increased to 240 mg (depending on the individual tolerance).

Thyrotoxicosis - in the combined therapy 12.5 up to 50 mg 3-4 times daily, gradually raising the dose until optimum beta-blockage is achieved.

In children the initial daily dose is 0.5-1 mg/kg, divided into 2-4 intakes. Maintenance dose 2-4 mg/kg, divided into 2 daily intakes.

**OVERDOSAGE**

In case of overdosage symptoms such as bradycardia, dizziness; hypotension, irregular pulse, bronchospasm; cyanosis of the fingers and toes may occur.

Treatment: atropine in extreme bradycardia; dobutamine or dopamine in severe hypotension; glucagone may affect favourably bradycardia and hypotension in treatment of beta-adrenergic block; depending upon the severity of the symptoms temporary pacemaker, furosemide, digitalis preparations, beta₂-agonists (isoproterenol and/or aminophylline) in bronchospasm may be also indicated. Propranolol is not eliminated in haemodialysis.

**DOSAGE FORM AND PACKAGES**

Tablets of 25 and 40 mg in packs of 50.

**STORAGE**

In a dry place protected from light at 15-25°C.