NABILOC Tablets نیبیلوک گولیاں

(N e b i v o l o l) (نیبیو یلول)

COMPOSITION: Each tablet contains:
Nebivolol HCl equivalent to Nebivolol ... 2.5mg, 5mg and 10mg. [NQ Specs.]

DESCRIPTION: Nebivolol is chemically described as (1RS, 1'RS)-1, 1'-[(2RS,2'SR)-bis(6-fluoro-3,4-dihydro-2H-1-benzopyran-2-yl)]-2,2'-iminodiethanol hydrochloride. Its molecular formula is $C_{22}H_{25}F_2NO_4$.

CLINICAL PHARMACOLOGY: Mechanism of Action: Nebivolol, a racemic mixture of SRRR and RSSS, is a competitive β_1-selective adrenoceptor antagonist whose hemodynamic effects differ from those of classical β-adrenoceptor antagonist as a result of a vasodilating action. It has mild vasodilating properties attributed to its interaction with the L-arginine/nitric oxide pathway, a property not shared by other β-blockers. Nebivolol lacks intrinsic sympathomimetic and membrane stabilizing activity at therapeutically relevant concentrations. At clinically relevant doses, Nebivolol does not demonstrate α_1-adrenergic receptor blockade activity.

Pharmacokinetics: Nebivolol is rapidly absorbed following oral administration. The absorption of Nebivolol is not affected by food. It is extensively metabolised in the liver by alicyclic and aromatic hydroxylation, N-dealkylation, and glucuronidation; the hydroxy metabolites are reported to be active. The rate of aromatic hydroxylation by cytochrome P450 isoenzyme CYP2D6 is subject to genetic polymorphism and bioavailability and half-life vary widely. In fast metabolisers, the elimination half-life of Nebivolol is about 10 hours and of the hydroxy metabolites is about 24 hours. Peak plasma concentration of unchanged drug plus active metabolites are 1.3 to 1.4 times higher in slow metabolisers and the half-lives of Nebivolol and its hydroxy metabolites are prolonged. Nebivolol is about 98% bound to plasma proteins. It is excreted in the urine and feces, almost entirely as metabolites. The pharmacokinetics of Nebivolol are not affected by age. One week after administration, 38% of the dose is excreted in the urine and 48% in the feces. Urinary excretion of unchanged Nebivolol is less than 0.5% of the dose.

INDICATIONS: Nabiloc (Nebivolol) tablets is indicated for the treatment of the following:
Hypertension: Treatment of essential hypertension.
Chronic heart failure (CHF): Treatment of stable mild and moderate chronic heart failure in addition to standard therapies in elderly patients > 70 years. **Nabiloc** (Nebivolol) tablets may be used alone or in combination with other anti-hypertensive agents.

DOSAGE AND ADMINISTRATION: Hypertension: Adults: The dose is one tablet 5mg daily, preferably at the same time of the day. Tablets may be taken with or without meals. The initial up titration should be done at 1-2 weekly intervals based on patient tolerability. The maximum recommended dose is 10mg Nebivolol once daily. The blood pressure lowering effect becomes evident after 1-2 weeks of treatment. Occasionally, the optimal effect is reached only after 4 weeks.
Patients with renal insufficiency: In patients with renal insufficiency, the recommended starting dose is 2.5mg daily. If needed, the daily dose may be increased to 5mg. The upward titration should be performed cautiously.
Patients with hepatic insufficiency: In patients with moderate hepatic insufficiency, the recommended initial dose is 2.5mg once daily. Upward titration should be performed cautiously if needed.
Elderly: In patients over 65 years, the recommended starting dose is 2.5mg daily. If needed, the daily dose may be increased to 5mg.
Chronic heart failure: The treatment of stable chronic heart failure has to be initiated with a gradual uptitration of dosage until the optimal individual maintenance dose is reached. Patients should have stable chronic heart failure without acute failure during the past six weeks. It is recommended that the treating physician should be experienced in the management of chronic heart failure. For those patients receiving cardiovascular drug therapy including diuretics and/or digoxin and/or ACE inhibitors and/or angiotensin II antagonists, dosing of these drugs should be stabilized during the past two weeks prior to initiation of Nebivolol treatment. The initial uptitration should be done according to the following steps at 1-2 weekly intervals based on patient tolerability: 1.25mg Nebivolol, to be increased to 2.5mg Nebivolol once daily, then to 5mg once daily and then to 10mg once daily. The maximum recommended dose is 10mg Nebivolol once daily.

ADVERSE REACTIONS: Adverse events are listed separately for hypertension and CHF because of differences in the background diseases.
Hypertension: Common: Headache, dizziness, paresthesia, dyspnea, constipation, nausea, diarrhea, tiredness, edema.
Uncommon: Nightmares, depression, impaired vision, bradycardia, heart failure, slowed AV conduction/AV-block, hypotension, (increase of) intermittent claudication, bronchospasm, dyspepsia, flatulence, vomiting, pruritus, rash, erythematous, impotence.

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Rare: Syncope, psoriasis aggravated.
Chronic heart failure (CHF): The most commonly reported adverse reactions are bradycardia and dizziness. The other adverse reactions that occurred are aggravation of cardiac failure, postural hypotension, drug intolerance, first degree AV-block, edema of the lower limb.

CONTRA-INDICATIONS: Nebivolol is contra-indicated in patients with; hypersensitivity to the active substance or to any of the components, severe hepatic insufficiency, acute heart failure, cardiogenic shock or episodes of heart failure decompensation requiring I.V. inotropic therapy, sick sinus syndrome, including sino-atrial block, second and third degree heart block (without a pacemaker), history of bronchospasm and bronchial asthma, untreated phaeochromocytoma, metabolic acidosis, bradycardia (heart rate < 60bpm prior to start of therapy), hypotension (systolic blood pressure < 90mmHg), severe peripheral circulatory disturbances.

PRECAUTIONS: Anesthesia: Caution should be observed with certain anesthetics that cause myocardial depression. The patient can be protected against vagal reactions by intravenous administration of atropine.
Cardiac Failure: In patients who have compensated congestive heart failure, Nebivolol should be administered cautiously. **If heart failure worsens, discontinuation of Nebivolol should be considered.**
Metabolic/Endocrinological: Care should be taken in diabetic patients however, as Nebivolol may mask certain symptoms of hypoglycemia (tachycardia, palpitations). b-adrenergic blocking agents may mask tachycardic symptoms in hyperthyroidism. Abrupt withdrawal may intensify symptoms.
Abrupt Cessation of Therapy: The treatment with Nebivolol is not recommended to be stopped abruptly since this might lead to a transitory worsening of heart failure.
Peripheral Vascular Diseases: β-blockers can precipitate or aggravate symptoms of arterial insufficiency in patients with peripheral vascular diseases. Caution should be exercised in these patients.
Renal Insufficiency: Nebivolol should be used with caution in patients on dialysis.
Geriatric Patients: In patients above 75 years, caution must be exercised and these patients should be monitored closely.
Others: Patients with a history of psoriasis should take β-adrenergic antagonists only after careful consideration. Patients with rare hereditary problems of galactose intolerance, the Lapp-lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.
Pregnancy: Nebivolol should be used during pregnancy (category C) only if the potential benefit justifies the potential risk to the fetus.
Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for β-blockers to produce serious adverse reactions in nursing infants, especially bradycardia, Nebivolol is not recommended during nursing.

DRUG INTERACTIONS: Nebivolol 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. Both digitalis glycosides and β-blockers slow atrioventricular conduction and decrease heart rate. Concomitant use can increase the risk of bradycardia. Patients receiving catecholamine-depleting drugs such as reserpine or guanethidine should be closely monitored. In patients who are receiving Nebivolol and clonidine, Nebivolol should be discontinued for several days before the gradual tapering of clonidine. Caution should be used when Nebivolol is co-administered with CYP2D6 inhibitors (quinidine, propafenone, fluoxetine, paroxetine etc.) Cimetidine causes a 23% increase in the plasma levels of Nebivolol. The co-administration of Nebivolol and sildenafil decreased AUC and C_{max} of sildenafil by 21 and 23% respectively.

OVERDOSE: The most common signs and symptoms associated with Nebivolol overdosage are bradycardia and hypotension. Other adverse events associated with β-blocker overdose include bronchospasm and heart block. If overdose occurs, Nebivolol should be stopped and general supportive and specific symptomatic treatment should be provided.

INSTRUCTIONS:
Store below 30°C. Protect from heat, light and moisture. Keep out of reach of children.

PRESENTATION:
Nabiloc (Nebivolol) tablets 2.5mg, 5mg and 10mg are available in packs of 14's.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

PHARMA
Manufactured by:
NABIQASIM INDUSTRIES (PVT) LTD.
17/24, Korangi Industrial Area,
Karachi-Pakistan.

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