Carnovas®

Nebivolol
Tablet

Description

Nebivolol is a β adrenergic receptor blocking agent. Nebivolol inhibits both β1 and β2-adrenergic receptors. Nebivolol lacks intrinsic sympathomimetic and membrane stabilizing activity at therapeutically relevant concentrations. At clinically relevant doses, Nebivolol does not demonstrate β1-adrenergic receptor blockade activity. Nebivolol is metabolized by a number of routes, including glucuronidation and hydroxylation by CYP2D6. The active isomer (d-Nebivolol) has an effective half-life of about 12 hours in extensive metabolizers. Mean peak plasma Nebivolol concentrations occur approximately 1.5 to 4 hours. Plasma protein binding of Nebivolol is approximately 98%, mostly to albumin.

Indications

Hypertension: Nebivolol is a β-adrenergic blocking agent indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions.

Chronic Heart Failure (CHF): Treatment of stable mild and moderate chronic heart failure in addition to standard therapies in elderly patients 70 years old or above.

Dosage & Administration

Hypertension: 5 mg daily; elderly initially 2.5 mg daily, increased if necessary to 5 mg daily.

Adjunct in Heart Failure: Initially 1.25 mg once daily, then if tolerated increased at intervals of 1-2 weeks to 2.5 mg once daily, then to max. 10 mg once daily.

Contraindications

Carnovas® is contraindicated in the following conditions:

- Severe bradycardia
- Heart block greater than first degree
- Patients with cardiogenic shock
- Decompensated cardiac failure
- Sick sinus syndrome (unless a permanent pacemaker is in place)
- Patients with severe hepatic impairment (Child-Pugh >B)
- Hypersensitive to any component of this product

Adverse Reactions

Most common adverse reactions are as follows:

- Body as a Whole: asthenia
- Gastrointestinal System Disorders: abdominal pain, diarrhea
- Metabolic and Nutritional Disorders: hypercholesterolemia
- Nervous System Disorders: paraesthesia, headache, dizziness
- General Disorders: peripheral edema, fatigue

Use in Specific Populations

Pregnancy & Lactation

β-blockers may cause intra-uterine growth restriction, neonatal hypoglycemia, and bradycardia; the risk is greater in severe hypertension. If β-blockers are used close to delivery, infants should be monitored for signs of β-blockade.

Nebivolol is advised to avoid during breast-feeding as there is risk of toxicity due to β-blockade.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established. Pediatric studies in ages newborn to 18 years old have not been conducted because of incomplete characterization of developmental toxicity and possible adverse effects on long-term fertility.

Geriatric Use

No overall differences in efficacy or in the incidence of adverse events were observed between older and younger patients.

Overdosage

If overdose occurs, provide general supportive and specific symptomatic treatment.

Bradycardia: Administer IV atropine.

Hypotension: Administer IV fluids and vasopressors. Intravenous glucagon may be useful.

Heart Block (second or third degree): Monitor and treat with isoproterenol infusion.

Congestive Heart Failure: Initiate therapy with digitalis glycoside and diuretics.

Bronchospasm: Administer bronchodilator therapy such as a short acting inhaled β2 agonist and/or aminophylline.

Hypoglycemia: Administer IV glucose.

Drug Interactions

- CYP2D6 enzyme inhibitors may increase nebivolol levels.
- Reserpine or clonidine may produce excessive reduction of sympathetic activity.
- Both digitalis glycosides and β-blockers slow atrioventricular conduction and decrease heart rate.
- Concomitant use can increase the risk of bradycardia.
- Verapamil or diltiazem-type calcium channel blockers may cause excessive reductions in heart rate, blood pressure and cardiac contractility.

Warnings and Precautions

Abrupt Cessation of Therapy

Do not abruptly discontinue Carnovas® therapy in patients with coronary artery disease. Severe exacerbation of angina, myocardial infarction and ventricular arrhythmias have been reported in patients with coronary artery disease following the abrupt discontinuation of therapy with β-blockers. Myocardial infarction and ventricular arrhythmias may occur with or without preceding exacerbation of the angina pectoris. Caution patients without overt coronary artery disease against interruption or abrupt discontinuation of therapy. As with other β-blockers, when discontinuation of Carnovas® is planned, carefully observe and advise patients to minimize physical activity. Taper Carnovas® over 1 to 2 weeks when possible. If the angina worsens or acute coronary insufficiency develops, re-start Carnovas® promptly, at least temporarily.

Angina and Acute Myocardial Infarction

Carnovas® was not studied in patients with angina pectoris or who had a recent MI.

Bronchospastic Diseases

In general, patients with bronchospastic diseases should not receive β-blockers.

Anesthesia and Major Surgery

Because β-blocker withdrawal has been associated with an increased risk of MI and chest pain, patients already on β-blockers should generally continue treatment throughout the perioperative period. If Carnovas® is to be continued perioperatively, monitor patients closely when anesthetic agents which depress myocardial function, such as ether, cyclopropane, and trichloroethylene, are used. If β-blocking therapy is withdrawn prior to major surgery, the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

The β-blocking effects of Carnovas® can be reversed by β-agonists, e.g., dobutamine or isoproterenol.

However, such patients may be subject to protracted severe hypotension. Additionally, difficulty in restarting and maintaining the heartbeat has been reported with β-blockers.

Diabetes and Hypoglycemia

β-blockers may mask some of the manifestations of hypoglycemia, particularly tachycardia. Nonselective β-blockers may potentiate insulin-induced hypoglycemia and delay recovery of serum glucose levels. It is not known whether nebivolol has these effects. Advise patients subject to spontaneous hypoglycemia and diabetic patients receiving insulin or oral hypoglycemic agents about these possibilities.

Tyrotoxicosis

β-blockers may mask clinical signs of hyperthyroidism, such as tachycardia. Abrupt withdrawal of β-blockers may be followed by an exacerbation of the symptoms of hyperthyroidism or may precipitate a thyroid storm.

Peripheral Vascular Disease

β-blockers can precipitate or aggravate symptoms of arterial insufficiency in patients with peripheral vascular disease.

Non-dihydropyridine Calcium Channel Blockers

Because of significant negative inotropic and chronotropic effects in patients treated with β-blockers and calcium channel blockers of the verapamil and diltiazem type, monitor the ECG and blood pressure in patients treated concomitantly with these agents.

Use with CYP2D6 Inhibitors

Nebivolol exposure increases with inhibition of CYP2D6. The dose of Carnovas® may need to be reduced.

Impaired Renal Function

Renal clearance of nebivolol is decreased in patients with severe renal impairment. Carnovas® has not been studied in patients receiving dialysis.

Impaired Hepatic Function

Metabolism of nebivolol is decreased in patients with moderate hepatic impairment. Carnovas® has not been studied in patients with severe hepatic impairment.

Risk of Anaphylactic Reactions

While taking β-blockers, patients with a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge. Such patients may be unresponsive to the usual doses of epinephrine used to treat allergic reactions.

Pheochromocytoma

In patients with known or suspected pheochromocytoma, initiate an α-blocker prior to the use of any β-blocker.

Pharmaceutical Precautions

Keep in a dry place, below 30° C. Protect from light. Keep out of the reach of children.

Commercial Pack

Carnovas® 2.5 Tablet: Box containing 30 tablets in 3x10's Alu-Alu form packs. Each film coated tablet contains Nebivolol Hydrochloride INN equivalent to Nebivolol 2.5 mg.

Carnovas® 5 Tablet: Box containing 30 tablets in 3x10's Alu-Alu form packs. Each film coated tablet contains Nebivolol Hydrochloride INN equivalent to Nebivolol 5 mg.

Carnovas® 10 Tablet: Box containing 30 tablets in 3x10's Alu-Alu form packs. Each film coated tablet contains Nebivolol Hydrochloride INN equivalent to Nebivolol 10 mg.

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