Carvedilol

Carvid®

6.25 mg and 25 mg Tablet

Beta-Adrenergic Blocker / Antihypertensive

FORMULATION
Each tablet contains:

Carvedilol ..... 6.25 mg
or
25 mg

PRODUCT DESCRIPTIONS
Carvedilol (Carvid®) 6.25 mg Tablet: White, biconvex, round 1/4" diameter, plain tablet.
Carvedilol (Carvid®) 25 mg Tablet: White, square, biconvex tablet, plain on one side, quadrisect on the other side.

CLINICAL PHARMACOLOGY
• PHARMACODYNAMICS
Carvedilol is a racemic mixture in which nonselective beta-adrenoceptor blocking activity is present in the S(-) enantiomer and alpha-adrenergic blocking activity in both R(+) and S(-) enantiomers at equal potency. It has no intrinsic sympathomimetic activity and has membrane stabilizing properties.
Carvedilol is a potent antioxidant, a scavenger of reactive oxygen radicals, and an anti-proliferative agent.
Carvedilol has no adverse effect on lipid profile. The normal ratio of high-density lipoproteins to low density lipoproteins (HDL/LDL) is maintained.
Vasodilation resulting in decreased total peripheral resistance mediated through carvedilol's alpha$_1$-adrenergic blockade and decreased sympathetic tone plays a major role in the drug's hypotensive effects. Carvedilol causes reductions in cardiac output, exercise-induced tachycardia, isoproterenol-induced tachycardia, and reflex orthostatic tachycardia. Significant beta-blocking activity of carvedilol is usually observed within 1 hour of oral use. Carvedilol's alpha-adrenergic blocking effects, which contribute to the drug's hypotensive effects, are seen within 30 minutes of drug administration and include reduction in phenylephrine-induced pressor effects, vasodilation, and decreased peripheral vascular resistance. The dose-dependent hypotensive effect of carvedilol results in blood pressure (systolic and diastolic) reductions of 5 to 46% with little, if any, reflex tachycardia. This hypotensive effect occurs about 30 minutes after oral use and has a maximum effect 1.5 to 7 hours after oral administration.
Due to carvedilol's alpha$_1$-receptor blocking activity, blood pressure is reduced more in the standing than in the supine position, and symptoms of postural hypotension, including rare instances of syncope, may occur. The frequency and severity of orthostatic hypotension may be decreased by administering carvedilol with food and by strictly adhering to the usual starting dose and titration recommendations.
Therapeutic doses of carvedilol decreased renal vascular resistance with no change in glomerular filtration rate or renal plasma flow in hypertensive patients with normal renal function.
Carvedilol has little effect on plasma catecholamines, plasma aldosterone, or electrolyte levels; however, carvedilol significantly decreases plasma renin activity when given for at least 4 weeks. Carvedilol also increases atrial natriuretic peptide levels. Carvedilol has demonstrated anti-ischemic and anti-anginal properties in patients with stable angina. Acute hemodynamic studies showed that carvedilol decreases ventricular preload and afterload.
In patients with chronic heart failure and left ventricular dysfunction, carvedilol is associated with improvements in myocardial function through afterload reduction as evidenced by improved left ventricular ejection fraction, decreased left ventricular volumes, and prevention of progression of left ventricular dilatation. Reductions in systemic blood pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, and heart rate were observed in patients with heart failure.
Carvedilol significantly decreases mortality and hospitalizations and improves symptoms and left ventricular function in patients with ischemic or non-ischemic chronic heart failure. Carvedilol's effect is dose dependent.

• PHARMACOKINETICS
Carvedilol is rapidly and extensively absorbed after oral administration with absolute bioavailability of approximately 25 to 35% due to significant first-pass metabolism. After oral administration, the apparent mean terminal elimination half-life of carvedilol generally ranges from 7 to 10 hours. Plasma concentrations achieved are proportional to the oral dose administered. The rate of absorption is slowed when administered with food, as evidenced by a delay in the time to reach peak plasma levels, with no significant difference in extent of bioavailablity. Taking carvedilol with food minimizes the risk of orthostatic hypotension.
Carvedilol is extensively metabolized. After oral administration of radiolabelled carvedilol to healthy volunteers, carvedilol accounted for only about 7% of the total radioactivity in plasma as measured by area under the curve (AUC). Less than 2% of the dose is excreted unchanged in the urine. Carvedilol is metabolized primarily by aromatic ring oxidation and glucuronidation. The oxidative metabolites are further metabolized by conjugation via glucuronidation and sulfation. The metabolites of carvedilol are excreted primarily via the bile into the feces. Demethylation and hydroxylation at the phenol ring produce three active metabolites with beta receptor blocking activity. Based on preclinical studies, the 4'-hydroxyphenyl metabolite is approximately 13 times more potent than carvedilol for beta-blockade. Compared with carvedilol, the three active metabolites exhibit weak vasodilating activity. Plasma concentrations of the active metabolites are about one-tenth of those observed for carvedilol and have pharmacokinetics similar to the parent.
Carvedilol undergoes stereoselective first-pass metabolism with plasma levels of R(+) carvedilol approximately 2 to 3 times higher than S(-) carvedilol after oral administration in healthy subjects. The mean apparent terminal elimination half-lives for R(+) carvedilol range from 5 to 9 hours compared with 7 to 11 hours for the S(-) enantiomer.
Carvedilol is more than 98% bound to plasma proteins, primarily with albumin. The plasma-protein binding is independent of concentration over the therapeutic range. Carvedilol is a basic, lipophilic compound with a steady-state volume of distribution of approximately 115 L, indicating a substantial distribution into extravascular tissues. Plasma clearance ranges from 500 to 700 mL/min.
The steady-state plasma concentrations of carvedilol and its enantiomers increased proportionately over the 6.25 to 50 mg dose range in patients with congestive heart failure (CHF). Compared with healthy subjects, patients with CHF had increased mean AUC and Cmax values for carvedilol and its enantiomers, with up to 50% to 100% higher values observed in a few patients with NYHA class IV heart failure. The mean apparent terminal elimination half-life for carvedilol was similar to that observed in healthy subjects.

INDICATIONS
- Hypertension
  - For the management of essential hypertension
  - May be used alone or in combination with other antihypertensives
- Angina pectoris
  - For the prophylactic treatment of stable angina
- Symptomatic, stable, chronic heart failure
  - For the treatment of mild to severe chronic heart failure of ischemic or cardiomyopathic origin in combination with diuretics, ACE inhibitors, and digitalis, to increase survival and, also, to decrease the risk of hospitalization
- Left ventricular dysfunction following myocardial infarction
  - Decreases cardiovascular mortality in clinically stable patients who have survived the acute phase of a myocardial infarction and have a left ventricular ejection fraction of ≤40% (with or without symptomatic heart failure)

DOSAGE AND ADMINISTRATION
General Dosing Recommendations:
- Carvedilol dosage must be individualized and closely monitored by a physician.
- Fluid retention should be minimized before starting carvedilol treatment.
- Should be taken with food to slow the rate of absorption and reduce the incidence of orthostatic effects.
- Carvedilol treatment is a long-term therapy. Do not discontinue treatment abruptly but rather gradually reduce at weekly intervals. This is particularly important in patients with concomitant coronary heart disease.

RECOMMENDED ORAL CARVEDILOL DOSE

HYPERTENSION
Recommended Starting Dose: **12.5 mg once daily or 6.25 mg twice daily**
- Thereafter, the recommended dosage is **25 mg once daily** or **12.5 mg twice daily**
- Dosage may be increased at intervals of at least two weeks to the ***maximum recommended dose* of 50 mg**, given once daily or in divided doses (twice daily).
- The full antihypertensive effect of carvedilol is seen within 7 to 14 days.

Coadministration with a diuretic may produce additive effects and exaggerate the orthostatic component of carvedilol.

ANGINA PECTORIS
Adults
Recommended Starting Dose: 12.5 mg twice daily for the first two days.
- Thereafter, the recommended dosage is **25 mg twice daily**.
- Dosage may be increased at intervals of at least two weeks to the ***maximum recommended dose* of 100 mg**, given in divided doses (twice daily).

Elderly
***Recommended maximum dose:* 50 mg** given in divided doses (twice daily)

SYMPTOMATIC, STABLE, CHRONIC HEART FAILURE
In patients receiving diuretics and/or digoxin and/or ACE inhibitors, dosing of these other drugs should be stabilized before starting carvedilol.
Recommended Starting Dose: **3.125 mg twice daily** for two weeks.
- If this dose is tolerated, dosage should be increased subsequently to **6.25 mg twice daily**, followed by **12.5 mg twice daily** and thereafter **25 mg twice daily**, at intervals of not less than two weeks. Maintain patients on lower doses if higher doses are not tolerated.
- At initiation of each new dose, observe patients for signs of dizziness or light headedness for one hour.
- ***Maximum Recommended Dose:*** **25 mg twice daily** for patients with severe heart failure and for patients with mild to moderate heart failure weighing less than 85 kg (187 lbs) and **50 mg twice daily** in patients with mild to moderate heart failure weighing more than 85 kg.
- Treat fluid retention (with or without transient worsening heart failure symptoms) with increased doses of diuretics. Occasionally, it may be necessary to lower carvedilol dose and, rarely, temporarily discontinue carvedilol.
- If carvedilol treatment is discontinued for more than one week, resume therapy at half the dose the patient is previously taking and up-titrate in line with the above dosing recommendation. If carvedilol treatment is discontinued for more than two weeks, resume therapy at 3.125 mg twice daily and up-titrate in line with the above dosing recommendation.
- Deterioration of renal and/or cardiac functions may occur during up-titration of the dose in patients with systolic blood pressure <100 mmHg. Therefore, before each dose increase, these patients should be evaluated by a physician for renal function and symptoms of worsening heart failure or vasodilation. Transient worsening of heart failure, vasodilation or fluid retention may be treated by adjusting doses of diuretics or ACE inhibitors or by modifying or temporarily discontinuing carvedilol treatment. Under these circumstances, do not increase carvedilol until symptoms of worsening heart failure or vasodilation have been stabilized.

LEFT VENTRICULAR DYSFUNCTION FOLLOWING MYOCARDIAL INFARCTION
Before Starting Carvedilol Treatment: Hemodynamically stable patients should have received an ACE inhibitor for at least 48 hours, given at a stable dose during at least the preceding 24 hours. Carvedilol can then be started between day 3 and day 21 after the myocardial infarction.
First Carvedilol Dose:
Recommended Starting Dose: 6.25 mg.
- Patients should be under close medical supervision for at least 3 hours after the first dose.

Subsequent Carvedilol Doses:
- Increase dose to **6.25 mg twice daily** and maintain for 3 to 10 days based on patient's tolerability (i.e.,heart rate >50 beats/min, systolic blood pressure >80 mmHg, absence of clinical signs of intolerance).
- Decrease dose to **3.125 mg twice daily** if patient develops signs of intolerance (i.e., bradycardia <50 beats/min, systolic blood pressure <80 mmHg or fluid retention). Discontinue carvedilol if this dose is not tolerated.
- If it is well tolerated, increase dose again to **6.25 mg twice daily** after 3 to 10 days.

Subsequent Up-titration:
- If **6.25 mg twice daily** is well tolerated, increase dose at intervals of 3 to 10 days to **12.5 mg twice daily** and then to **25 mg twice daily**.
- The maintenance dose is the maximum dose tolerated by the patient.

Maximum Recommended Dose: 25 mg twice daily (irrespective of the patient's weight)
Or, as prescribed by a physician.

CONTRAINDICATIONS
- Hypersensitivity to any component of the formulation
- Unstable/decompensated heart failure
- Clinically manifest hepatic impairment
- Marked fluid retention or overload requiring intravenous inotropic support
- Second or third degree AV block (unless a permanent pacemaker is in place)
- Severe bradycardia (<50 beats/min)
- Sick sinus syndrome (including sino-atrial block)
- Severe hypotension (systolic blood pressure <85 mmHg)
- Cardiogenic shock
- Metabolic acidosis
- History of bronchospasm or asthma, or other obstructive lung disorders

WARNINGS AND PRECAUTIONS
Cessation of Carvedilol Therapy: Advise patients with coronary artery disease against abrupt discontinuation of therapy. Severe exacerbation of angina and occurrence of myocardial infarction and ventricular arrhythmias have been reported in angina patients after the abrupt discontinuation of beta-blocker therapy. When discontinuation of carvedilol is planned, carefully observe patient and advise to limit physical activity to a minimum. Carvedilol should be discontinued over 1 to 2 weeks whenever possible. If angina worsens or acute coronary insufficiency develops, carvedilol should be promptly reinstituted, at least temporarily. It may be prudent not to discontinue carvedilol abruptly even in patients treated only for hypertension or heart failure since coronary artery disease is common and may be unrecognized.
Bradycardia: Carvedilol may cause bradycardia. Reduce carvedilol dose if pulse rate drops below 55 beats per minute.
Hypotension: Starting with a low dose, administration with food, and gradual up-titration should decrease the possibility of syncope or excessive hypotension. During initiation of carvedilol treatment, advise the patient to avoid situations such as driving or hazardous tasks, where injury could result should syncope occur.
Heart Failure / Fluid Retention: Worsening heart failure or fluid retention may occur during up-titration of carvedilol patients with heart failure. If such symptoms occur, diuretics should be increased and carvedilol dose should not be advanced until clinical stabilization occurs. Occasionally, decreasing carvedilol dose may be necessary or, in rare cases, temporarily discontinue carvedilol. Such episodes do not preclude subsequent successful carvedilol titration. Carvedilol should be used with caution in combination with digitalis glycosides, as both medicines slow AV conduction.
Non-allergic Bronchospasm: In general, patients with bronchospastic disease (e.g., chronic bronchitis and emphysema) should not receive beta-blockers. However, carvedilol should be used with caution in patients who do not respond to, or cannot tolerate, other antihypertensives. If carvedilol is used, it is prudent to use the lowest effective dose, so that inhibition of endogenous or exogenous beta-agonists is minimized.
Diabetes and Hypoglycemia: Beta-blockers may mask some of the manifestations of hypoglycemia, particularly tachycardia. Nonselective beta-blockers may potentiate insulin-induced hypoglycemia and delay recovery of serum glucose levels. Patients subject to spontaneous hypoglycemia, or diabetic patients receiving insulin or oral hypoglycemic agents, should be cautioned about these possibilities and carvedilol should be used with caution. In congestive heart failure patients, there is a risk of worsening hyperglycemia which responds to intensification of hypoglycemic therapy. Blood glucose should be monitored when carvedilol dosing is started, adjusted, or discontinued.
Peripheral Vascular Disease: Beta-blockers can precipitate or aggravate symptoms of arterial insufficiency in patients with peripheral vascular disease. Exercise caution in such individuals.
Renal Function Deterioration: Rarely, reversible deterioration of renal function has been observed with carvedilol in patients with heart failure. Patients at risk are those with low blood pressure (systolic blood pressure <100 mmHg), ischemic heart disease and diffuse vascular disease, and/or underlying renal insufficiency. Monitor renal function during up-titration of carvedilol and discontinue the drug or decrease dosage if worsening of renal function occurs.
Hepatic Injury: Reversible hepatic injury has occurred after short- and long-term therapy with minimal clinical symptomatology. No deaths due to liver function abnormalities have been reported. At the first symptom/sign of liver dysfunction, perform laboratory testing. If the patient has laboratory evidence of liver injury or jaundice, carvedilol should be stopped and not restarted.
Anesthesia and Major Surgery: If carvedilol 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.
Thyrotoxicosis: Beta-adrenergic blockade may mask clinical signs of hyperthyroidism, such as tachycardia. Abrupt withdrawal of beta-blockade may be followed by an exacerbation of the symptoms of hyperthyroidism or may precipitate thyroid storm.
Pheochromocytoma: An alpha-blocker should be initiated prior to the use of any beta-blockers in patients with pheochromocytoma. There has been no experience with the use of carvedilol in this condition even if carvedilol has both alpha- and beta-blocking pharmacologic effects. Carvedilol should be used with caution in patients suspected of having pheochromocytoma.
Prinzmetal's Variant Angina: Agents with non-selective beta-blocking activity may provoke chest pain in patients with Prinzmetal's variant angina. In these patients, there is no clinical experience with carvedilol although the alpha-blocking activity of carvedilol may prevent such symptoms. Carvedilol should be used with caution in patients suspected of having Prinzmetal's variant angina.
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 treat allergic reaction.
Raynaud's Phenomenon: Use with caution in patients suffering from peripheral circulatory disorders (e.g., Raynaud's phenomenon) as there may be exacerbation of symptoms.
Psoriasis: Patients with a history of psoriasis associated with beta-blocker therapy should take carvedilol only after consideration of the risk-benefit ratio.
Contact lenses: Wearers of contact lenses should bear in mind the possibility of decreased lacrimation.

INTERACTIONS WITH OTHER MEDICAMENTS
Inhibitors of CYP2D6; Poor Metabolizers of Debrisoquin: Interactions of carvedilol with strong inhibitors of CYP2D6 (such as quinidine, fluoxetine, paroxetine, and propafenone) have not been studied, but these drugs would be expected to increase blood levels of the R(+) enantiomer of carvedilol. In clinical studies, poor 2D6 metabolizers had a higher rate of dizziness during up-titration resulting from the vasodilating effects of the higher concentrations of the alpha blocking R(+) enantiomer.
Catecholamine Depleting Agents: Patients taking both agents with beta-blocking properties and a drug that can deplete catecholamines (e.g., reserpine and monoamine oxidase inhibitors) should be observed closely for signs of hypotension and/or severe bradycardia.
Clonidine: Concomitant administration of clonidine with agents with beta-blocking properties may potentiate blood pressure- and heart-rate-lowering effects. When concomitant treatment with agents with beta-blocking properties and clonidine is to be terminated, the beta-blocking agent should be discontinued first. Clonidine therapy can then be discontinued several days later by gradually decreasing the dosage.
Ciclosporin: Due to wide interindividual variability in the dose adjustment required, it is recommended that ciclosporin concentrations be monitored closely after initiation of carvedilol and that the dose of ciclosporin be adjusted as appropriate.
Digoxin: Both carvedilol and digoxin slow atrioventricular conduction and decrease heart rate. Concomitant use may increase the risk of bradycardia. Digoxin concentrations are increased by about 15% when digoxin and carvedilol are administered concomitantly. Thus, increased monitoring of digoxin is recommended when initiating, adjusting, or discontinuing carvedilol.
Inducers and Inhibitors of Hepatic Metabolism: Rifampicin reduced plasma concentrations of carvedilol by about 70%. Cimetidine increased AUC by about 30% but caused no change in C_{max}. Exercise caution in patients taking inducers of mixed function oxidases (e.g., rifampicin) as serum carvedilol levels may be decreased, or inhibitors of mixed function oxidases (e.g., cimetidine) as serum carvedilol levels may be increased.
Calcium Channel Blockers: Coadministration with diltiazem has been associated with conduction disturbance (rarely with hemodynamic compromise). If carvedilol is to be administered with calcium channel blockers of the verapamil or diltiazem type, it is recommended that ECG and blood pressure be monitored.
Insulin or Oral Hypoglycemics: Agents with beta-blocking properties may enhance the blood-sugar-reducing effect of insulin and oral hypoglycemics. Therefore, in patients receiving insulin or oral hypoglycemic agents, regular monitoring of blood sugar is recommended.
Amiodarone: Amiodarone, and its metabolite desethyl amiodarone, inhibitors of CYP2C9 and P-glycoprotein, increased concentrations of the S(-) enantiomer of carvedilol by at least 2-fold. Coadministration of carvedilol with amiodarone or other CYP2C9 inhibitors (e.g., fluconazole) may increase the beta-blocking properties of carvedilol resulting in further slowing of heart rate or cardiac conduction. Observe patients for signs of bradycardia or heart block, particularly when one agent is added to pre-existing treatment with the other.
Anesthesia: During general anesthesia, be aware of the synergistic negative inotropic and hypotensive effects of carvedilol and anesthetic drugs.
Others: Carvedilol, as with other agents with beta-blocking activity, may potentiate the effect of other coadministered medicines that are antihypertensive in action (e.g., alpha$_1$-receptor antagonists) or have hypotension as part of their adverse effect profile.

STATEMENT ON USAGE FOR HIGH RISK GROUPS
Pregnancy: Pregnancy Category C. Beta-blockers decrease placental perfusion, which may result in intrauterine fetal death, and immature and premature deliveries. Also, adverse effects (particularly hypoglycemia and bradycardia) may occur in the fetus and neonate. An increased risk of cardiac and pulmonary complications in the neonate in the postnatal period may be observed. There are no adequate and controlled studies to date using carvedilol in pregnant women. Carvedilol should be used in pregnancy only when the potential benefits justify the potential risks to the fetus.

Lactation: In animal studies, carvedilol and its metabolites are excreted in breast milk. It is not known whether carvedilol is excreted in human milk. Thus, breastfeeding is not recommended during carvedilol administration.

Use in Children: The safety and efficacy of carvedilol in patients below 18 years old have not been established.

Use in the Elderly: There were no notable differences in efficacy or the incidence of adverse events between older and younger patients.

UNDESIRABLE EFFECTS
Body as a Whole: Asthenia, allergy, fatigue, fever, hypovolemia, malaise, edema (generalized, peripheral, dependent, genital, leg, hypervolemia, fluid overload), flu syndrome, pain in extremities
Cardiovascular: Bradycardia, hypotension/postural hypotension, fluid overload, syncope (including presyncope), AV block, palpitation, angina pectoris (including chest pain), cardiac failure, hypertension, peripheral ischemia, tachycardia, bundle branch block, myocardial ischemia, peripheral circulation disturbances (e.g., cold extremities, peripheral vascular disorder, exacerbation of intermittent claudication, Reynaud's phenomenon)
Gastrointestinal: Diarrhea, nausea, vomiting, melena, periodontitis, gastrointestinal pain, abdominal pain, bilirubinemia, dry mouth, gastrointestinal hemorrhage, constipation
Hematologic: Prolongation of prothrombin time, purpura, thrombocytopenia, anemia, leukopenia, pancytopenia, atypical lymphocytes, aplastic anemia (rare)
Metabolic and Nutritional: Hyperglycemia, hypoglycemia, hyperuricemia, hyponatremia, hypercholesterolemia, hyperkalemia, hypokalemia, hypertriglyceridemia, glycosuria, weight increase, weight loss, diabetes mellitus, gout; *Elevations of the following:* alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gammaglutamyl transferase (GGT), blood urea nitrogen (BUN), non-protein nitrogen (NPN), creatinine; decreased high-density lipoprotein
Musculoskeletal: Arthralgia, arthritis, hypotonia, muscle cramps
Nervous: Dizziness, headache, hypesthesia, vertigo, somnolence, paresthesia, cerebrovascular accident, depression, hypokinesia, nervousness, sleep disorder, impaired concentration, abnormal thinking, paroniria, emotional lability, cerebrovascular disorder, convulsions, migraine, neuralgia, paresis, amnesia
Reproductive, male: Impotence, decreased libido
Respiratory: Increased cough, rales, dyspnea, lung edema, asthma, bronchospasm, bronchitis, pneumonia, upper respiratory tract infection, pulmonary edema, wheezing, stuffy nose, respiratory alkalosis, interstitial pneumonitis (rare)
Skin and Appendages: Pruritus, rash (erythematous, maculopapular, psoriaform), allergic exanthema, photosensitivity reaction, increased sweating, anaphylactoid reaction, angioedema, urticaria, exfoliative dermatitis, dermatitis, severe skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme (rare)
Special Senses: Abnormal or blurred vision, eye irritation, decreased lacrimation, tinnitus, decreased hearing
Urogenital: Abnormal renal function, renal failure, albuminuria, hematuria, increased micturition frequency, urinary tract infection, urinary incontinence in women (rare)
Class Effect: Due to beta-blocking properties, it is possible for latent diabetes mellitus to become manifest, manifest diabetes to be aggravated, and blood glucose counter-regulation to be inhibited.

OVERDOSE AND TREATMENT
Quantities ingested in carvedilol overdose cases exceeded 1000 mg. Symptoms of overdosage include severe hypotension, bradycardia, cardiac insufficiency, cardiogenic shock, and cardiac arrest. Respiratory problems, bronchospasms, vomiting, lapses of consciousness, and generalized seizures may also occur.

Place the patient in a supine position and, where necessary, keep under observation and treat under intensive-care conditions. Gastric lavage or pharmacologically induced emesis may be used shortly after ingestion.

The following agents may be administered:
For excessive bradycardia: Atropine, 2 mg IV.
To support cardiovascular function: Glucagon, 5 to 10 mg IV rapidly over 30 seconds, followed by a continuous infusion of 5 mg/hour.
Sympathomimetics (e.g., dobutamine, isoprenaline, epinephrine) at doses according to body weight and effect.
If positive inotropic effect is required, phosphodiesterase (PDE) inhibitors (e.g., milrinone) must be considered.
If peripheral vasodilation dominates, it may be necessary to administer epinephrine or norepinephrine with continuous monitoring of circulatory conditions.
For therapy-resistant bradycardia, pacemaker therapy should be performed.
For bronchospasm, beta-sympathomimetics (as aerosol or IV) or aminophylline IV should be given.
In the event of seizures, slow IV injection of diazepam or clonazepam is recommended.

STORAGE CONDITION
Store at temperatures not exceeding 30°C
Keep the product out of sight and reach of children

CAUTION
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY
Carvedilol (Carvid®) 6.25mg Tablet Foil Strip x 10's (Box of 30's)
Carvedilol (Carvid®) 25mg Tablet Foil Strip x 10's (Box of 30's)

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Manufactured by AMHERST LABORATORIES, INC.
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