

Role of Beta Blockers in Congestive Heart Failure

Beta-blocker	Strength	Titration	Target Dose ^a
Carvedilol	3.125mg (not scored), 6.25mg, 12.5mg, 25mg scored tablets	<ul style="list-style-type: none"> Initial dose 3.125 mg bid (carvedilol should be administered with food to reduce orthostatic hypotension; consider separating the ACEI, adjusting dose of diuretic, or temporary ACEI dose reduction if dizziness occurs) Dose should be doubled at a minimum of every 2 weeks to the target dose 	25 mg bid (50mg bid ≥ 85 kg; titrate with caution)
Metoprolol	50mg, 100mg scored tablets	<ul style="list-style-type: none"> Initial dose 6.25 mg qd/bid (low dosages of metoprolol are not commercially available, although various methods of titration have been used) Double dose every 2 weeks until target dose achieved <i>MDC excluded patients with SBP < 90 mmHg and HR < 45 bpm; discontinue if SBP < 90 mm Hg or HR < 40 bpm per manufacturer</i> 	50-75mg bid
Metoprolol XL	25mg, 50mg, 100mg, 200mg scored, film-coated tablets	<ul style="list-style-type: none"> Initial dose 12.5mg qd > NYHA class III HF; 25mg qd < NYHA class III HF Double dose every 2 weeks until target dose <i>MERIT-HF excluded patients with SBP < 100 mmHg</i> 	200mg qd
Atenolol ^c	25mg, 50mg (scored), 100mg tablets	<ul style="list-style-type: none"> Initial dose 12.5mg bid Increase by 12.5mg per week for the next 2 weeks, then by 25mg per week as tolerated to target dose <i>Did not proceed with titration unless SBP > 90 mm Hg and HR > 60 bpm</i> 	50-100mg divided qd-bid

Pharmacology

Carvedilol is a nonselective beta-adrenoreceptor antagonist and an α_1 -adrenoreceptor antagonist. It has no intrinsic sympathomimetic activity. Like many other classes of medications, beta blockers can be divided into three distinct groups.

- 1) The first group consists of nonselective beta blockers without ancillary properties and includes such drugs as propranolol (Inderal) and timolol maleate (Blocadren).
- 2) The second group consists of selective blockers of beta receptor subtypes without ancillary properties. This group includes metoprolol (Lopressor) and atenolol (Tenormin).
- 3) The third group consists of nonselective beta blockers that have the ancillary property of vasodilation. Included in this group are labetalol (Normodyne), carvedilol and bucindolol (currently in phase 3 trials).
- 4) Carvedilol produce relatively fewer negative chronotropic and inotropic effects when compared with beta blockers like propranolol.⁶

The beta-blocking actions of carvedilol are generally evident in humans within one hour of administration, and the alpha-mediated vasodilatory effects, manifested by decreased peripheral resistance and decreased blood pressure, are evident within about 30 minutes of administration. The clinical significance of alpha blockade in conjunction with beta blockade in the treatment of CHF is not known.

Carvedilol inhibits the generation of oxygen free radicals and prevents low-density lipoprotein (LDL) oxidation, which, in turn, reduces the uptake of LDL into the coronary vasculature. This antioxidant activity may contribute to carvedilol's cardioprotective effects.³⁶ In fact, compared with captopril, carvedilol has demonstrated similarly favorable effects on the lipid profiles of hypertensive patients with dyslipidemia.

Starting dosage

3.125 mg taken twice daily for two weeks. This dosage is the same regardless of the age or weight of the patient. Carvedilol should be taken with food. Patient should be observed in the office for one hour after initial dose is given. If previous dosage was well-tolerated, dosage should be doubled every two weeks to the maximum dosage or the highest tolerated dosage. Patient should be observed in the office for one hour after every dosage adjustment.

Monitoring

Patient should be weighed daily. Any weight gain of 0.91 to 1.36 kg (2 to 3 lb) should be reported to the physician. Blood pressure measurements should be taken with the patient standing. Parameters of glycemic and lipid control should be monitored, and medicines should be adjusted appropriately.

Sign/symptom	Titration
Dizziness, lightheadedness	Decrease diuretic, vasodilator or ACE inhibitor therapy; if symptoms persist, decrease carvedilol dosage
Edema, weight gain, dyspnea	Increase diuretic therapy; if signs and symptoms persist, decrease carvedilol dosage
Bradycardia	Adjust carvedilol dosage to maintain heart rate > 55 beats per minute

Cost and Available Forms

Carvedilol is supplied in tablet form and is available in four dosage strengths: 3.125 mg, 6.25 mg, 12.5 mg and 25 mg. The average wholesale price for all strengths is \$1.55 per tablet.

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Important Note: This document is a guideline, and not a policy statement. Always use clinical judgment when making decisions for an individual patient.