Carvedilol: MOA, Dosing, Indications, Interactions ...

Carvedilol is an antihypertensive belonging to a class of beta-adrenoreceptor antagonists.

Class:
Beta-adrenoreceptor antagonist (nonselective beta-blocker with selective alpha-1 blockade)

Presentation

- Tablets: 6.25 mg, 12.5 mg, 25 mg

Mechanism of Action

- Nonselectively blocks **beta-1** (myocardium) and **beta-2** (bronchial and vascular smooth muscle) adrenergic receptors
- Selective **alpha-1** adrenergic receptor blockade causing vasodilation
- Does **not** have intrinsic sympathomimetic activity (no beta-agonist effects)
- Weak membrane-stabilizing effects

Pharmacokinetics

- Well absorbed orally but extensive **first-pass hepatic metabolism** ? bioavailability ~25%
- Peak plasma concentration: 1–2 hours post-dose
- Highly lipophilic, >98% plasma protein bound
- Metabolized primarily by hepatic CYP450 enzymes **CYP2D6** and **CYP2C9**
- Excretion mainly via bile
- Elimination half-life: 6–10 hours

Indications

- Hypertension
- Angina pectoris
- Symptomatic heart failure (adjunct therapy)
- Reduce mortality post-myocardial infarction in left ventricular dysfunction

Dosage

Hypertension:

- Initial: 12.5 mg once daily (or 6.25 mg once daily)
- Titrate to 25 mg once daily after 2 days, or 12.5 mg twice daily after 1–2 weeks
- Maximum: 50 mg daily (divided doses)
- Elderly: 12.5 mg once daily usually sufficient

Angina Pectoris:

- Initial: 12.5 mg twice daily
- Increase to 25 mg twice daily after 2 days

Heart Failure:

- Initial: 3.125 mg twice daily with food (to minimize hypotension risk)
- Titrate to 6.25 mg twice daily, then gradually increase every ?2 weeks to max tolerated dose
- Max dose:
    - 25 mg twice daily (severe HF or <85 kg body weight)
    - 50 mg twice daily (mild to moderate HF and >85 kg)

Contraindications and Precautions

- Bradycardia (reduce dose if HR < 55 bpm)
- Hypotension and syncope risk — administer with food and start at low doses
- Pheochromocytoma: alpha-1 blocker must precede beta-blocker use to avoid unopposed alpha stimulation

Adverse Effects

- **Cardiovascular:** Bradycardia, hypotension, precipitate heart failure or heart block in susceptible patients
- **CNS:** Headache, confusion, hallucinations, sleep disturbances, fatigue
- **Neuromuscular:** Paresthesia, peripheral neuropathy, arthralgia, myopathies
- **Gastrointestinal:** Nausea, vomiting, diarrhea, constipation, abdominal cramps