## Comparison of Oral Beta-Blockers

--Information in chart is from product labeling (see footnote d) unless otherwise noted.--

<table>
<thead>
<tr>
<th>Agent Pharmacokinetics</th>
<th>Dosing (Adults) (also see footnote b)</th>
<th>Comments*</th>
<th>Availability Cost of 30-day supplya</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Noncardioselective Agents (beta-1 and beta-2 antagonist activity)</strong></td>
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<tr>
<td></td>
<td>More likely to worsen peripheral vasoconstriction or bronchoconstriction, delay recovery from hypoglycemia in type 1 diabetes, and impair exercise performance.4</td>
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<tr>
<td><strong>Nadolol</strong></td>
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<tr>
<td>Corgard (US), generics</td>
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<tr>
<td>• Low lipophilicity</td>
<td>Angina/HTN: Start with 40 mg once daily (Canada: Start with 80 mg once daily. Angina patients stable on 80 mg once daily can be tried on 40 mg once daily). Usual dose 40 to 80 mg once daily. Max dose: 160 to 240 mg once daily for angina, 240 to 320 mg once daily for HTN. A-fib: Usual dose 10 to 240 mg once daily.1 Migraine prevention:5 Usual dose 80 mg once daily.3 Max 240 mg once daily.3</td>
<td>• US: Reduce dosing interval for CrCl ≤50 mL/min.</td>
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<tr>
<td>• Kidney excretion</td>
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<tr>
<td>• Long half-life</td>
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<tr>
<td><strong>Propranolol,</strong> immediate-release</td>
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<tr>
<td>• High lipophilicity</td>
<td>Angina: 80 to 320 mg/day, divided BID to QID. (Canada: Start with 10 to 20 mg TID to QID. Usual dose 160 mg/day. Max dose 320 to 400 mg/day). Arrhythmias (Canada): 10 to 30 mg TID to QID A-Fib: 10 to 40 mg TID to QID1 Essential tremor (US): Initial 40 mg BID. Usual dose 120 mg/day. Max dose 320 mg/day. HTN: Start with 40 mg BID. Usual dose 120 to 240 mg/day, divided BID or TID (Canada: 80 to 160 mg BID). Max dose 640 mg/day (US). Hypertrophic subaortic stenosis: 20 to 40 mg TID to QID Post-MI (US): 40 mg TID, titrated to target dose of 180 to 240 mg/day divided BID to QID. Migraine prevention:5 Start with 80 mg/day, divided. Usual dose 160 to 240 mg/day (Canada: 80 to 160 mg/day). Pheochromocytoma (with alpha-blocker): 60 mg/day, divided, for 3 days before surgery, or 30 mg/day, divided, for inoperable tumor, with alpha blockade.</td>
<td>• Post-MI: Reduces CV and total mortality (BHAT) • Substrate of CYP2D6 (mainly), CYP1A2, CYP2C19, and P-gp • Caution with kidney or liver impairment (Canada). Reduce starting dose in liver impairment (US). • Consider stopping one year post-MI without another indication.7 • Low concentration in breast milk.8 • Dose-related vivid dreams. • Risk of fatigue slightly higher than newer agents.5 • Wide dosing range may lead to more dosage adjustments than other agents.5</td>
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<tr>
<td>• Extensive first-pass metabolism</td>
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<tr>
<td>• Bioavailability variable; increased ~50% by high-protein food</td>
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<tr>
<td>• Liver elimination</td>
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</tbody>
</table>

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4. More likely to worsen peripheral vasoconstriction or bronchoconstriction, delay recovery from hypoglycemia in type 1 diabetes, and impair exercise performance.
5. Initial 60 mg/day, divided, with one dose 30 mg once daily.
7. Post-MI: Reduces CV and total mortality (BHAT)
8. Low concentration in breast milk.

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Cost of 30-day supply:
- **US:**
  - 20, 40 mg scored tabs
  - ~$53 for 80 mg once daily
- **Canada:**
  - 40, 80, 160 mg scored tabs
  - ~$11 for 80 mg once daily

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trchealthcare.com
<table>
<thead>
<tr>
<th>Agent Pharmacokinetics**</th>
<th>Dosing (Adults)(^b)</th>
<th>Comments*</th>
<th>Availability Cost of 30-day supply(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Noncardioselective Agents, continued</strong></td>
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<tr>
<td><strong>Propranolol, extended-release</strong></td>
<td><em>Inderal LA</em> (US) &lt;br&gt; <strong>Angina:</strong> Start with 80 mg once daily. Usual dose 160 mg once daily. Max dose 320 mg once daily. <strong>HTN:</strong> Start with 80 mg once daily. Usual dose 120 to 160 mg once daily. Max dose 640 mg once daily. <strong>Hypertrophic subaortic stenosis:</strong> Usual dose 80 to 160 mg once daily. <strong>Migraine prevention:</strong> Start with 80 mg once daily. Usual dose 160 to 240 mg once daily.</td>
<td><em>Substrate of CYP2D6 (mainly), CYP1A2, CYP2C19, and P-gp&lt;br&gt;Caution with kidney or liver impairment.&lt;br&gt;Risk of fatigue slightly higher than newer agents(^3)</em></td>
<td>US: <em>Inderal LA</em>: 60, 80, 120, 160 mg extended-release caps &lt;br&gt;<em>InnoPran XL</em>: 80, 120 mg extended-release caps ~$43 for 120 mg once daily (generic for <em>Inderal LA</em>)</td>
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<td><em>InnoPran XL</em> (US) &lt;br&gt; <strong>HTN:</strong> Start with 80 mg HS. May increase up to 120 mg HS.</td>
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<td>Canada: <em>Lupin-propranolol LA</em>: 60, 80, 120, 160 mg extended-release caps ~$50 for 120 mg once daily</td>
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<td></td>
<td><em>Lupin-propranolol LA</em> (Canada) &lt;br&gt; <strong>HTN or angina:</strong> establish dose with immediate-release tablets, then switch to the equivalent daily dose of <em>Lupin-propranolol LA</em>.</td>
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<tr>
<td><strong>Sotalol</strong></td>
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<td>See our FAQ, <em>Atrial Fibrillation: Focus on Pharmacotherapy.</em></td>
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<tr>
<td><strong>Timolol</strong></td>
<td><strong>HTN:</strong> Start with 10 mg BID (Canada: 5 to 10 mg BID with other antihypertensives). Usual dose 20 to 40 mg/day. Max dose 60 mg/day, divided BID. <strong>Angina (Canada):</strong> Start with 5 mg BID to TID. Usual dose 35 to 45 mg/day, divided. <strong>Migraine prevention:</strong> Start with 10 mg BID. (US: Can give 20 mg once daily as maintenance dose). Max dose 30 mg/day, divided. Some patients may only need 10 mg once daily. <strong>Post-MI:</strong> 10 mg BID (Canada: Start with 5 mg BID)</td>
<td><em>Post-MI: Reduces cardiovascular and total mortality, including sudden death, and reduces risk of nonfatal reinfarction (NMS)(^7)&lt;br&gt;Substrate of CYP2D6&lt;br&gt;Caution with kidney or liver impairment&lt;br&gt;Consider stopping one year post-MI without another indication.&lt;br&gt;Risk of fatigue slightly higher than newer agents(^3)</em></td>
<td>US: 5, 10, 20 mg scored tabs ~$140 for 20 mg BID&lt;br&gt;Canada: 5, 10, 20 mg scored tabs ~$48 for 20 mg BID</td>
</tr>
</tbody>
</table>
### Cardioselective Agents (beta-1 antagonist activity only)

Can use in asthma or COPD.²⁰,²¹ May reduce COPD exacerbations or improve survival.²⁰

#### Atenolol

- **Tenormin, generics**
  - Low lipophilicity
  - Bioavailability about 50%
  - Kidney elimination

**Dosing (Adults)**

- **Angina**: Start with 50 mg once daily. May increase to 100 mg once daily (Canada: or 50 mg BID). Max dose 200 mg/day.
- **A-fib**: Usual maintenance dose 25 to 100 mg once daily.¹
- **HTN**: Start with 50 mg once daily. May be increased to 100 mg once daily.
- **Migraine prevention**: Usual dose 100 mg once daily.³
- **Post-MI (US)**: 50 mg BID or 100 mg once daily (Although it is approved post-MI after IV beta-blockade, due to increased risk of cardiogenic shock in COMMIT/CCS-2 trial of IV metoprolol, IV beta-blockade is used selectively.¹⁶)

**Comments**

- Reduce dose for CrCl ≤35 mL/min/1.73 m².
- Consider stopping one year post-MI without another indication.⁷
- HTN: may not reduce CV risk.¹² Atenolol not better than placebo for CV outcomes.¹⁸ Losartan had fewer strokes and greater regression of LVH than atenolol in LIFE study.⁹ Amlodipine +/- perindopril had lower mortality and stroke than atenolol +/- bendroflumethiazide in ASCOT.¹⁰

**Availability**

- **US**: 25, 50 (scored), 100 mg tabs
  - <$5 for 50 mg BID
  - 25, 50, 100 mg <$10 for 50 mg BID

- **Canada**: 25 (unscored), 50, 100 mg <$10 for 50 mg BID

#### Betaxolol (US only)

- Moderate lipophilicity
- Low first-pass metabolism
- Bioavailability ~90%
- Mostly liver elimination

**Dosing (Adults)**

- **HTN**: Start 10 mg once daily. May increase to 20 mg once daily. Max dose 40 mg once daily.

**Comments**

- Reduce dose in severe kidney impairment. Start with 5 mg once daily. May increase to 20 mg once daily.

**Availability**

- **US**: 10 (scored), 20 mg tabs
  - ~$35 for 20 mg once daily

- **Canada**: 5 (scored), 10 mg tabs
  - <$5 for 10 mg once daily

#### Bisoprolol

- Low lipophilicity
- Low first-pass metabolism
- Bioavailability 80%
- 50% kidney elimination

**Dosing (Adults)**

- **Angina**: 5 to 20 mg once daily.³
- **A-Fib**: Usual maintenance dose 2.5 to 10 mg once daily.¹
- **HF**: Usual starting dose is 1.25 mg once daily, titrated to a target dose of 10 mg once daily.²,⁶
- **HTN**: Start 2.5 to 5 mg once daily (Canada: 5 mg once daily). Max 20 mg once daily.

**Comments**

- US: reduce starting dose to 2.5 mg once daily for CrCl <40 mL/min, liver disease, or bronchospastic disease.
- **HF**: Reduces mortality (CIBIS-II).¹³

**Availability**

- **US**: 5(scored), 10 mg tabs
  - ~$18 for 10 mg once daily

- **Canada**: 5 (scored), 10 mg tabs
  - <$5 for 10 mg once daily
<table>
<thead>
<tr>
<th>Agent Pharmacokinetics**</th>
<th>Dosing (Adults)b</th>
<th>Comments*</th>
<th>Availability Cost of 30-day supplya</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardioselective Agents, continued</strong></td>
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<tr>
<td>Metoprolol tartrate, immediate-release &lt;br&gt; Lopressor (US), generics</td>
<td>A-fib: Usual maintenance dose is 25-100 mg BID. Angina: Start with 50 mg BID. Usual dose 200 mg/day (Canada). Max dose 400 mg/day (Canada: divided BID to TID). HTN: Start with 100 mg once daily or divided (Canada: 50 mg BID. Usual dose 100 to 200 mg/day). Max dose 450 mg/day (Canada: 200 mg BID). If effect does not last 24 h with once-daily dosing, divide dose. <strong>Migraine prevention</strong>: Start with 25 mg BID. Max dose 200 mg/day, divided. <strong>Post-MI</strong>: Start with 50 mg every six hours (25 mg if not tolerated), for 48 hours. Thereafter, dose is 100 mg BID. (Approved post-MI after IV beta-blockade. Due to increased risk of cardiogenic shock in COMMIT/CCS-2 trial of IV metoprolol, IV beta-blockade is used selectively.)</td>
<td>• Substrate of CYP2D6 &lt;br&gt; • Reduce starting dose in liver impairment (US). Canada: Reduce starting dose and maintenance dose in severe liver impairment, and use caution in severe kidney impairment. &lt;br&gt; • Consider stopping one year post-MI without another indication. <strong>HF</strong>: Greater reduction in mortality with carvedilol than with immediate-release metoprolol tartrate in COMET. <strong>Post-MI</strong>: Reduces total mortality, sudden death, and reinfarction (Goteborg).</td>
<td>US: 50, 100 mg scored tabs; IV formulation &lt;$5 for 100 mg BID (generic) &lt;br&gt; Canada: 25, 50, 100 mg scored tablets; IV formulation &lt;$10 for 100 mg BID</td>
</tr>
<tr>
<td>Metoprolol succinate, extended-release (US) &lt;br&gt; Toprol-XL, generics</td>
<td>Angina: Start with 100 mg once daily. Max dose 400 mg/day. A-fib: Usual maintenance dose is 50-400 mg once daily. Angina: Start with 12.5 to 25 mg once daily. Target dose 200 mg/day. HTN: Start with 25-100 mg once daily. Max dose 400 mg/day.</td>
<td>• Substrate of CYP 2D6 &lt;br&gt; • Reduce starting dose in liver impairment &lt;br&gt; • HF: Reduces mortality and cardiovascular hospitalization (MERIT-HF).</td>
<td>US: 25, 50, 100, 200 mg scored extended-release tabs ~$22 for 200 mg once daily</td>
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</table>
### Cardioselective Agents, continued

<table>
<thead>
<tr>
<th>Agent</th>
<th>Pharmacokinetics**</th>
<th>Dosing (Adults)b</th>
<th>Comments*</th>
<th>Availability Cost of 30-day supplya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nebivolol</td>
<td>Bystolic, generics (US)</td>
<td>HTN: Start with 5 mg once daily. Max dose 40 mg/day (Canada: max dose 20 mg once daily). HF: Start with 1.25 mg once daily, titrated to target dose of 10 mg once daily.11 Migraine prevention: Dose is 5 mg once daily.3</td>
<td>• Substrate of CYP2D6&lt;br&gt;• Start with 2.5 mg once daily for CrCl &lt;30 mL/min or moderate hepatic impairment. Contraindicated in severe liver impairment. &lt;br&gt;• Causes peripheral vasodilation by increasing nitric oxide production4&lt;br&gt;• HF: Reduced composite endpoint of mortality and cardiovascular hospitalizations in the elderly (SENIORS)11</td>
<td>US: 2.5, 5, 10, 20 mg tabs ~$24 for 10 mg once daily Canada: 2.5, 5, 10, 20 mg tabs ~$48 for 10 mg once daily</td>
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</table>

### Agents with alpha-1 antagonist activity

These agents cause peripheral vasodilation.4 Alpha-1 antagonist activity poses risk of floppy iris syndrome.

| Carvedilol, immediate-release | Coreg (US), generics | A-Fib: Usual maintenance dose 3.125-25 mg BID.1 HF: Start with 3.125 mg BID, titrated to target dose of 25 mg BID (may use 50 mg BID for patients >85 kg [US labeling: with mild-moderate HF]).2,6 Reduce dose if HR <55. HTN (US): Start with 6.25 mg BID. Max dose 25 mg BID. LVD after MI (US): Start with 6.25 mg BID, titrated to target dose of 25 mg BID. (Can start with 3.125 mg BID if appropriate [e.g., low blood pressure, heart rate, fluid retention].) | • Substrate of CYP2D6 and CYP2C9<br>• Contraindicated in severe liver impairment. Canada: caution in milder liver impairment.<br>• Consider stopping one year post-MI without another indication.7<br>• HF: Reduces mortality in NYHA stage 2-4; has the strongest evidence for benefit in severe failure (COPERNICUS). Greater reduction in mortality than with immediate-release metoprolol tartrate in COMET.14<br>• Post-MI with LVD: Reduces mortality and reinfarction in patients taking an ACEI or ARB (CAPRICORN) | US: 3.125, 6.25,12.5, 25 mg tabs <$10 for 25 mg BID Canada: 3.125, 6.25, 25 mg tabs ~$13 for 25 mg BID |

- Low lipophilicity4
- Bioavailability not determined
- Not cardioselective4
- Moderate lipophilicity4
- Bioavailability 25% to 35% due to first-pass metabolism
- Liver elimination
- Take with food to slow absorption, thereby reducing risk of orthostatic hypotension.
### Carvedilol phosphate, extended-release (US)
*Coreg CR, generics*

<table>
<thead>
<tr>
<th>Pharmacokinetics**</th>
<th>Dosing (Adults)b</th>
<th>Comments*</th>
<th>Availability Cost of 30-day supplya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained-release formulation that maintains therapeutic plasma concentrations for 24 hours</td>
<td>HF: Start with 10 mg once daily, titrated to a target dose of 80 mg once daily (equal to 25 mg BID immediate-release product). Reduce dose if HR &lt;55. HTN: Start 20 mg once daily. Max dose 80 mg once daily. LVD after MI: Start with 20 mg once daily, titrated to target dose of 80 mg once daily. (Can start with 10 mg once daily if appropriate [e.g., low blood pressure, heart rate, fluid retention].)</td>
<td>Contraindicated in severe hepatic impairment When switching from carvedilol immediate-release 12.5 mg BID or 25 mg BID, consider a starting dose of Coreg CR 20 mg or 40 mg once daily, respectively, especially in patients at increased risk of hypotension, dizziness, or syncope (e.g., the elderly) Consider stopping one year post-MI without another indication.7</td>
<td>US: 10, 20, 40, 80 mg extended-release caps ~$240 for 40 mg QD</td>
</tr>
<tr>
<td>Not cardioselective4 Moderate lipophilicity4</td>
<td>Bioavailability 25% to 35% due to first-pass metabolism Liver elimination</td>
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<tr>
<td></td>
<td>Take with food.</td>
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### Labetalol
*Trandate* (Canada), generics

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<tr>
<th>Pharmacokinetics**</th>
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<th>Comments*</th>
<th>Availability Cost of 30-day supplya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not cardioselective4 Low lipophilicity4</td>
<td>HTN: Start with 100 mg BID. Usual dose 200-400 mg BID. Max dose 2,400 mg/day (Canada: max dose 600 mg BID). If nausea and/or dizziness occur, consider TID dosing.</td>
<td>Wide dosing range may lead to more dosage adjustments than other agents Caution with liver impairment Rare liver injury A preferred antihypertensive in pregnancy.19 Low concentrations in breast milk.8</td>
<td>US: 100, 200, 300 mg scored tabs; IV formulation ~$25 for 200 mg BID</td>
</tr>
<tr>
<td>Bioavailability 20% to 40% due to first-pass metabolism4 Bioavailability may be increased by food4 Liver elimination4</td>
<td>Preferably taken after food (Canada).</td>
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<td>Canada: 100, 200 mg scored tabs; IV formulation ~$23 for 200 mg BID</td>
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</table>
### Agent Pharmacokinetics**

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<th>Availability Cost of 30-day supplya</th>
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<tbody>
<tr>
<td><strong>Agents with intrinsic sympathomimetic activity (ISA)</strong> Decrease in resting heart rate and negative inotropic activity may be less than with other beta-blockers.4</td>
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<tr>
<td>Acebutolol</td>
<td>HTN: Start with 400 mg/day once daily or divided BID (Canada: Start with 100 mg BID). Usual dose 400-800 mg/day. Some patients may only need 200 mg/day. Max dose 600 mg BID (Canada: max dose 400 mg BID). <strong>Angina (Canada):</strong> Start with 200 mg BID. Usual dose 200 to 600 mg/day, divided BID. Max dose 300 mg BID. Patients stable on 400 mg/day can be tried on 100 mg BID. <strong>Ventricular arrhythmias (US):</strong> Start with 200 mg BID. Max dose 300-600 mg BID.</td>
<td>• Agents without ISA are preferred for HTN in patients with angina.16 • Reduce dose for CrCl &lt;50 mL/min</td>
<td>US: 200, 400 mg caps ~$36 for 200 mg BID Canada: 100, 200, 400 mg caps &lt;$10 for 200 mg BID</td>
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<tr>
<td>Pindolol <strong>Visken</strong> (Canada), generics</td>
<td>HTN: Start with 5 mg BID. Max dose 60 mg/day (Canada: max dose 45 mg/day. Doses &gt;30 mg should be divided TID.) <strong>Angina (Canada):</strong> Start with 5 mg TID. Usual dose 15 to 40 mg/day • Take with food (Canada).</td>
<td>• Agents without ISA are preferred for HTN in patients with angina16 • Caution with liver or kidney impairment. Dose reduction is not usually needed in mild to moderate impairment.</td>
<td>US: 5, 10 mg scored tabs ~$74 for 10 mg BID Canada: 5, 10, 15 mg scored tabs ~$41 for 10 mg BID</td>
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</table>

**Abbreviations:** ACEI = angiotensin converting-enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin receptor blocker; A-fib = atrial fibrillation; BID = twice daily; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P450; HF = heart failure; HR = heart rate; HS = at bedtime; HTN = hypertension; ISA = intrinsic sympathomimetic activity; LVD = left ventricular dysfunction; LVH = left ventricular hypertrophy; MI = myocardial infarction; NYHA = New York Heart Association; P-gp = P-glycoprotein; QID = four times daily; TID = three times daily.

b. Consider reducing starting doses in elderly patients.11
c. For more information on beta-blockers for migraine prophylaxis, see our chart, *Migraine Prophylaxis.*
d. **US product information used for the above chart (unless otherwise noted):** Corgard (August 2021), propranolol immediate-release (Mylan,
March 2022), Inderal LA (August 2023), InnoPran XL (May 2023), timolol (Athem, May 2021), Tenormin (June 2021), betaxolol (KVK Tech, April 2020), bisoprolol (Solco, June 2023), Lopressor (July 2023), Toprol-XL (April 2023), Bystolic (June 2023), Coreg (May 2022), Coreg CR (November 2020), labetalol (Cadila, September 2022), acebutolol (ANI, August 2022), pindolol (ANI, August 2022).

**Canadian product monographs used for the above chart (unless otherwise noted):** nadolol (Apotex, August 2020), propranolol immediate-release (Teva, September 2011), propranolol LA (Lupin, January 2022), timolol (AA Pharma, February 2018), Tenormin (May 2023), bisoprolol (Sivem, October 2022), metoprolol tartrate (Pro Doc Ltée, August 2023), Bystolic (November 2022), carvedilol (Sivem, August 2022), acebutolol (Apotex, October 2018), Visken (May 2021).

*Clinical Trial Acronyms:* ASCOT = Anglo-Scandinavian Cardiac Outcomes Trial, BHAT = Beta-Blocker Heart Attack Trial, CAPRICORN = Carvedilol Post Infarction Survival Control in Left Ventricular Dysfunction, CIBIS-II = Cardiac Insufficiency Bisoprolol Study II, COMET = Carvedilol or Metoprolol European Trial, COMMIT/CCS-2 = Clopidogrel and Metoprolol in Myocardial Infarction Trial – Second Chinese Cardiac Study, COPERNICUS = Carvedilol Prospective Randomized Cumulative Survival, LIFE = Losartan Intervention For End point Reduction in Hypertension, MERIT-HF = Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure, NMS = Norwegian Multicenter Study, SENIORS = Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalisation in Seniors with Heart Failure.
Levels of Evidence
In accordance with our goal of providing Evidence-Based information, we are citing the LEVEL OF EVIDENCE for the clinical recommendations we publish.

<table>
<thead>
<tr>
<th>Level</th>
<th>Definition</th>
<th>Study Quality</th>
</tr>
</thead>
</table>
| A     | Good-quality patient-oriented evidence.* | 1. High-quality randomized controlled trial (RCT)  
2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings  
3. All-or-none study |
| B     | Inconsistent or limited-quality patient-oriented evidence.* | 1. Lower-quality RCT  
2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings  
3. Cohort study  
4. Case control study |
| C     | Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate end points); case series for studies of diagnosis, treatment, prevention, or screening. |


References


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