



**INDIAN HEALTH SERVICE**  
**National Pharmacy and Therapeutics Committee**  
**Formulary Brief: Beta Blockers Class Review**  
**-April 2026-**



**Summary:**

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug class review of beta-blocker (BB) agents with a specific focus in hypertensive treatment, myocardial infarction (MI) and heart failure. The IHS National Core Formulary (NCF) currently contains [atenolol](#), [carvedilol](#), [metoprolol succinate](#), [metoprolol tartrate](#), and [propranolol](#). Following the clinical review and analysis, the NPTC made **no modifications to the NCF**.

**Background/Discussion:**

The American College of Cardiology/American Heart Association 2025 Hypertension guideline does not list BBs as first-line for hypertensive management due to comparatively less efficacy in preventing stroke.<sup>1</sup> However, European and Chinese hypertension guidelines do include BBs as an initial treatment option due to their favorable effects in various clinical conditions.<sup>2,3</sup> With regards to BB use after a MI, the European, Australian, and US guidelines all agree that BBs have a noted benefit in patients with a left ventricular ejection fraction (LVEF) <40%, but that optimal use and duration of BBs for those with a LVEF >40% remains unclear.<sup>4-6</sup>

A meta-analysis from 2023 examined the overall efficacy of BBs for use in management of hypertension. The review concluded that BBs were as effective as other therapies in reducing blood pressure (BP); risk of stroke (17-27%), cardiovascular (CV) events and mortality (11-14%, 23%), and heart failure (HF; 43-46%) when compared to placebo. Authors noted similar risk for coronary artery disease, MI, and HF and similar CV mortality benefits when comparing BBs to diuretics, calcium channel blockers (CCB), angiotensin receptor blockers (ARB), and angiotensin converting enzyme inhibitors (ACE); and similar rates of CV events between BBs, diuretics, and renin angiotensin system inhibitors (RAS).<sup>7</sup> Furthermore, the analysis reported that BBs produced an 18-32% increased risk of stroke when compared to CCB and RAS inhibitors, and an 18% increase in CV events compared to CCB.<sup>7</sup>

A 2025 study examined the efficacy of antihypertensive therapies compared to placebo in reducing BP. The average standard dose of medication reduced systolic BP as follows: 6.8 mmHg (5.9-7.7) for ACE inhibitors, 8.5 mmHg (7.8-9.3) for ARBs, 8.9 mmHg (7.8-10.0) for BBs, 9.5 mmHg (8.4-10.6) for CCBs, 10.8 mmHg (9.2-12.4) for thiazide or thiazide-like diuretics, and 8.4 mmHg (6.0-10.7) for mineralocorticoid receptor antagonists.<sup>9</sup>

The REBOOT trial evaluated the impact of beta blockers (BBs) on all-cause mortality, reinfarction, and hospitalization for heart failure in a prospective, randomized, open-label study involving 8,438 post-myocardial infarction (MI) patients with left ventricular ejection fraction (LVEF) >40%.<sup>10</sup> Authors found no significant difference in the primary composite outcome between patients receiving BB therapy and those not receiving BBs (316 vs. 307 events, respectively; p=0.63). However, subgroup analysis suggested that women may derive less benefit—and potentially harm—from BB therapy following MI (HR 1.45, 95% CI: 1.04–2.03).

In a REBOOT study sub analysis, researchers noted that women comprised 19.3% of the study population and differed significantly from men in several baseline characteristics.<sup>11</sup> On average, women were older (65 vs. 60 years, p<0.001) and had higher rates of hypertension (60.3% vs. 49.9%, p<0.001), dyslipidemia (54.7% vs. 50.6%, p=0.0027), and atrial fibrillation (3.3% vs. 2.0%, p=0.002). Women also had lower smoking rates (38.7% vs. 46.2%, p<0.001). In the female subgroup, 83 women receiving BB therapy and 57 women not receiving BB therapy experienced the primary outcome (HR 1.45, 95% CI: 1.04–2.03). Additional analyses demonstrated higher rates of all-cause mortality (HR 1.90, 95% CI: 1.16–3.12) and cardiac death (HR 2.34, 95% CI: 1.02–5.34) among women treated with BBs. These trends were not observed in the male cohort.

A combined analysis of the BETAMI and DANBLOCK trials examined the effects of BBs following MI on death from any cause or major adverse CV events, with further subgroup analysis of females vs. males and by LVEF.<sup>12</sup> The authors reported that the primary outcome occurred in 14.2% of patients treated with BBs and 16.3% of those not (HR 0.85, 95% CI: 0.75-0.98), 14.8% vs. 19.1% of females (HR 0.77, 95% CI: 0.62-0.96), 14% vs. 15.6% of men (HR 0.91, 95% CI: 0.81-1.03), 18.4% vs. 23.4% of those with LVEF 40-49% (HR 0.82, 95% CI: 0.65-1.02), and 13.4% vs. 15.1% in those with LVEF ≥50% (HR 0.93, 95% CI: 0.85-1.01).

A 2025 meta-analysis of 24 studies examined the effects of BBs on all-cause mortality in patients post-MI with no HF (LVEF >40%). Secondary outcomes included major adverse cardiac and cerebrovascular events (MACCE) and CV

mortality. Overall, patients receiving BBs demonstrated an 11% reduction in all-cause mortality (HR 0.89; 95% CI: 0.81-0.97,  $I^2 = 40\%$ ). Interestingly, an ad hoc analysis revealed that continued use of BBs in patients without an event (e.g., death, MI, revascularization, or HF) within one year post-MI demonstrated no difference (i.e., benefit) in primary or secondary outcomes, however those who had an event within one year post-MI derived benefit from receiving a BB in all of the aforementioned primary and secondary outcomes.<sup>13</sup> A nonsignificant trend favoring avoidance of BB use in patients having a qualifying event within one year post-MI and a LVEF  $\geq 50\%$  was however noted.

To explore the effect of BBs on the composite of all-cause death, new MI, or HF in patients with LVEF 40-49%, data was pooled from 4 RCT studies of  $\geq 1$  year in duration.<sup>14</sup> The primary outcome occurred in 11% of patients receiving a BB and 14% of those that were not (HR 0.75, 95% CI: 0.58-0.97;  $p=0.031$ ). Authors concluded that BB therapy was associated with reductions in the composite outcomes in patients with acute MI and mildly reduced LVEF.

A 2024 parallel-group, open-label trial was performed to determine the effect of a BB in patients with an acute MI and LVEF  $\geq 50\%$  on death from any cause or new MI.<sup>15</sup> After a median follow-up of 3.5 years, the authors did not find a significant difference between the treatment arms with 7.9% receiving a BB and 8.3% not receiving a BB achieving the primary endpoint (HR 0.96, 95% CI: 0.79-1.16;  $p=0.64$ ).<sup>15</sup>

Finally, a 2026 meta-analysis of 5 open-label trials examined the effect of a BB on death from any cause, MI, or HF in patients with an acute MI and LVEF  $\geq 50\%$ .<sup>16</sup> They reported similar findings with 8.1% of patients receiving a BB and 8.3% of patients not receiving a BB achieving the primary endpoint (HR 0.97, 95% CI: 0.87-1.07;  $p=0.54$ ). Subgroup analysis of effects on females was also not significant (HR 1.01, 95% CI: 0.82-1.24).

### Findings:

Based on the current body of evidence and guideline recommendations, the NPTC recommended no changes to the NCF at this time. Beta-blockers are effective in reducing BP but may not provide the same protection against stroke and CV events as other antihypertensive classes. Current data on BB therapy following MI appear to trend towards limited benefit in patients with LVEF  $\geq 50\%$ . However, for higher-risk patients (e.g., earlier events post-MI, LVEF 40-49%), benefits for continued BB use remain.

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*If you have any questions regarding this document, please contact the NPTC at [IHSNPTC1@ihs.gov](mailto:IHSNPTC1@ihs.gov). For more information about the NPTC, please visit the [NPTC website](#).*

### References:

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