STEP THERAPY POLICY

POLICY: Beta Blocker Step Therapy Policy

Products available generically

- acebutolol capsules (generic only)
- Tenormin® (atenolol tablets – AstraZeneca, generic)
- betaxolol tablets (generic only)
- bisoprolol tablets (generic only)
- Coreg® (carvedilol tablets – Woodword, generic)
- Coreg CR™ (carvedilol extended-release capsules – Woodword, generic)
- labetalol tablets (generic only)
- Lopressor® (metoprolol tartrate tablets – Novartis, Mylan, generic)
- Toprol XL® (metoprolol succinate extended-release tablets – Aralez, generic)
- Corgard® (nadolol tablets – King, generic)
- pindolol tablets (generic only)
- propranolol tablets (generic only)
- Inderal® LA (propranolol extended-release capsules – Wyeth Ayerst, generic)
- Betapace® (sotalol tablets – Covis, generic)
- Betapace® AF (sotalol tablets – Covis, generic)
- timolol tablets (generic only)
- Tenoretic® (atenolol/chlorthalidone tablets – AstraZeneca, generic)
- Lopressor® HCT (metoprolol/hydrochlorothiazide tablets – Novartis, generic)
- propranolol/hydrochlorothiazide tablets (generic only)

Products not available generically

- bisoprolol fumarate 2.5 mg tablets (Brand) [TruPharma]
- Bystolic™ (nebivolol tablets – Allergan)
- labetalol 400 mg tablets (Brand) [Biocon Pharma]
- Inderal XL® (propranolol extended-release capsules – Mist)
- InnoPran XL® (propranolol extended-release capsules – Reliant)
- Kapspargo™ Sprinkle (metoprolol succinate capsules extended-release – Ohm/Sun)
- Metoprolol succinate/hydrochlorothiazide extended-release tablets – Solubiomix (brand product)

REVIEW DATE: 06/18/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP

SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Beta-blockers can be classified into four pharmacologic subgroups based on their effect on beta and alpha receptors: cardioselective beta-blockers, nonselective beta-blockers, combined alpha-beta blockers, and beta-blockers with intrinsic sympathomimetic activity (ISA).[1-4] Cardioselective beta-blockers are those agents that preferentially block beta-1 receptors over beta-2 receptors. Non-selective beta-blockers block both the beta-1 and beta-2 receptors. Based on the mechanism of action, cardioselective beta-blockers may be safer than nonselective beta-blockers in patients with asthma, chronic obstructive pulmonary disease, peripheral arterial disease, and diabetes mellitus who require beta-blocker therapy. However, cardioselectivity appears to be dose-dependent and at higher doses, cardioselective agents may lose their selectivity. The dose at which cardioselectivity is lost varies from patient to patient. Combined alpha-beta blockers nonselectively block beta receptors as well as alpha receptors. Beta-blockers with ISA act as partial beta-receptor agonists and therefore, resting heart rate, cardiac output, and peripheral blood flow are not as reduced. Table 1 classifies the beta-blockers by subgroup.

Table 1. Beta-Blockers by Pharmacologic Subgroup.[1-4]

Cardioselective beta-blockers	Nonselective beta-blockers	Combined alpha-beta blockers	Beta blockers with ISA
atenolol betaxolol bisoprolol metoprolol tartrate metoprolol succinate XL nebivolol[+*†]	nadolol propranolol propranolol extended-release[‡] timolol	carvedilol carvedilol extended-release[°] labetalol	acebutolol penbutolol[^] pindolol

ISA – Intrinsic sympathomimetic activity; [+] May have vasodilatory properties; [*] In extensive metabolizers and at doses less than or equal to 10 mg nebivolol is preferentially beta$_1$ selective. In poor metabolizers and at higher doses, it is nonselective; [†] Available as Bystolic; [‡] Available as a generic and as InnoPran XL; [°] Available as Coreg CR; [^] Available as Levatol.

All of the beta-blockers included in this policy are approved for the **treatment of hypertension**. Various reviews and guidelines address the role of beta-blockers in hypertension.[1-8] Betaxolol, bisoprolol, labetalol, Bystolic™ (nebivolol tablets), Levatol® (penbutalol tablets), and pindolol are only indicated for the treatment of hypertension.[1-9] The remaining beta-blockers (non-combination products) have at least one other indication. Such indications include angina pectoris, select arrhythmias, to treat and reduce cardiovascular (CV) mortality following a myocardial infarction (MI), to treat and reduce CV mortality in heart failure (HF), migraine prophylaxis, essential tremor, pheochromocytoma, and hypertrophic subaortic stenosis. All of the beta-blocker/diuretic combination products are indicated for the treatment of hypertension, although often not as initial therapy. It is notable that sotalol (Betapace, Betapace AF) is not indicated for use in hypertension but instead is used for the management of arrhythmias.[3,4,10] Specifically, Betapace/Betapace AF are indicated for the treatment of life-threatening ventricular arrhythmias as well as for the maintenance of normal sinus rhythm in patients with atrial fibrillation or flutter.[10] Sotylize™ (sotalol hydrochloride oral solution) is not included in this program as a generic is not available.[3,4,11] Also, Hemangeol™ (propranolol hydrochloride oral solution) is not included as this is indicated for the treatment of proliferating infantile hemangioma requiring systemic therapy.[12]

Carvedilol, metoprolol succinate extended-release (XL) and Coreg CR™ (carvedilol extended-release capsules) are the only beta-blockers indicated in patients with HF[14-16] with published data to support their use.[17-20] Metoprolol succinate XL is indicated to reduce the risk of cardiovascular mortality and HF hospitalization in patients with HF.[14] Carvedilol and Coreg CR are indicated for the treatment of mild to severe HF of ischemic or cardiomyopathic origin.[15,16] In combination with angiotensin converting enzyme inhibitors, diuretics, and digitalis, both metoprolol succinate and carvedilol have been shown to decrease the rate of mortality and hospitalization. In addition, carvedilol and Coreg CR are indicated to reduce CV mortality in clinically stable patients who have survived the acute phase of an MI and have a left ventricular ejection fraction ≤ 40% with or without symptomatic HF. Data are available with bisoprolol in patients with HF.[21]

Guidelines

Beta blockers are mentioned in a variety of guidelines. Main guidelines are briefly summarized.

- **Heart Failure:** In 2022, the American Heart Association (AHA), American College of Cardiology (ACC), and the Heart Failure Society of America published guidelines for the management of HF.[22] The three beta-blockers proven to reduce mortality in patients with HF with reduced ejection fraction are bisoprolol, carvedilol, and sustained-release metoprolol succinate. Hospitalization can also be reduced with these agents.
- **Hypertension:** The 2017 guidelines regarding the management of high blood pressure in adults by the ACC and the AHA prominently mention the benefits with beta blockers in selected patients.[7]
- **Chronic Coronary Disease:** Guidelines for the management of patients with chronic coronary disease (CCD) from the AHA and the ACC (2023) state

that in adults with CCD and hypertension (systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥ 80 mm Hg), in addition to nonpharmacological strategies, guideline-directed medication therapy with angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), or beta blockers are recommended as first-line therapy for compelling indications (e.g., recent MI or angina), with additional antihypertensive medications (e.g., dihydropyridine calcium channel blockers [CCB], long-acting thiazide diuretics, and/or mineralocorticoid receptor antagonists) added as needed to optimize blood pressure control.[13] In patients with CCD and left ventricular ejection fraction (LVEF) ≤ 40% with or without previous MI, the use of beta-blocker therapy is recommended to reduce the risk of future major adverse CV events, including CV death. Also, in patients with CCD and LVEF < 50%, the use of sustained release metoprolol succinate, carvedilol, or bisoprolol with titration to target doses is recommended in preference to other beta blockers.

POLICY STATEMENT

The program is comprised of two rules: 1) Beta-Blocker Step Therapy rule (Step A) and 2) Sotalol Step Therapy rule (Step B). This program has been developed to encourage the use of a Step 1A product prior to a Step 2A Product and a Step 1B Product prior to the use of a Step 2B Product. If the Step Therapy rule is not met for the Step 2A or Step 2B Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Beta-Blocker Step Therapy Rule

Step 1A: generic beta-blockers (i.e., acebutolol, atenolol, betaxolol, bisoprolol, carvedilol, carvedilol extended-release, labetalol, metoprolol tartrate, nadolol, pindolol, propranolol, timolol, metoprolol succinate extended-release, propranolol extended-release), and generic beta-blocker combination products (i.e., atenolol/chlorthalidone, metoprolol/hydrochlorothiazide, propranolol/hydrochlorothiazide,)

Step 2A: brand name beta-blockers (i.e., Bystolic, Tenormin, Coreg, Coreg CR, Lopressor, Toprol XL, Corgard, Inderal LA, InnoPran XL, Inderal XL) and brand name beta-blocker combination products (i.e., Tenoretic, Lopressor HCT, Metoprolol succinate/hydrochlorothiazide extended-release), Kapspargo Sprinkle, Labetalol 400 mg tablet (brand name product), Bisoprolol fumarate 2.5 mg tablet (brand name product)

Sotalol Step Therapy Rule

Step 1B: generic sotalol

Step 2B: brand name Betapace, Betapace AF

***Beta Blocker Step Therapy Policy* product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.**

CRITERIA

Beta Blocker Step Therapy Rule

1. If the patient has tried one Step 1A Product, approve a Step 2A Product.
Note: Sotalol products do not count toward this requirement.

2. Approve bisoprolol fumarate 2.5 mg tablets if the prescribed dose cannot be obtained with whole bisoprolol 5 mg or 10 mg tablets.

3. Approve bisoprolol fumarate 2.5 mg tablets if the patient has bronchospastic disease.

Sotalol Step Therapy Rule

1. If the patient has tried one Step 1B Product, approve a Step 2B Product.

2. If the strength of the requested Step 2B Product is not available generically, approve the Step 2B Product.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/14/2023
Annual Revision	Byvalson was removed from Step 2a from the Beta Blocker Step Therapy as a beta blocker combination product as it is no longer available.	06/26/2024
Selected Revision	Labetalol 400 mg tablet (brand) was added to Step 2 of the Beta Blocker Step Therapy.	01/08/2025
Annual Revision	**Bisoprolol/hydrochlorothiazide and nadolol/Bendroflumethiazide:** Removed from Step 1A of the policy as they are no longer available. **Ziac and Dutoprol:** Removed from Step 2A of the policy as they are no longer available. **Bisoprolol fumarate 2.5 mg tablets (Brand):** Added to the policy as a Step 2A product with the following criteria: approve bisoprolol fumarate 2.5 mg tablets if the prescribed dose cannot be obtained with whole bisoprolol 5 mg or 10 mg tablets. A separate criterion was added to include approval if the patient has bronchospastic disease.	06/18/2025