



Drug Coverage Policy

Effective Date.....10/15/2024

Coverage Policy Number.....IP0286

Policy Title..... Ivabradine

Cardiology – Ivabradine

- Corlanor® (ivabradine tablets and oral solution - Amgen, generic [tablets only])

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 and have discretion in making individual coverage determinations. 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 Healthcare Coverage Policy

OVERVIEW

Ivabradine, a hyperpolarization-activated cyclic nucleotide-gated channel blocker, is indicated for the following uses:¹

- **Heart failure, in adults**, to reduce the risk of hospitalization for worsening of the disease in those with stable, symptomatic chronic heart failure with left ventricular ejection fraction (LVEF) \leq 35%, who are in sinus rhythm with a resting heart rate \geq 70 beats per minute (bpm) and either are receiving maximally tolerated doses of beta blockers or have a contraindication to beta blocker use.
- **Heart failure, in pediatric patients \geq 6 months and older**, for treatment of stable symptomatic disease due to dilated cardiomyopathy, among those who are in sinus rhythm with an elevated heart rate.

Data are available with ivabradine that note improvement in symptoms and increased exercise performance in patients with inappropriate sinus tachycardia, defined as a sinus heart rate > 100 bpm at rest (with a mean 24-hour heart rate > 90 bpm not due to primary causes) which is generally associated with distressing symptoms such as palpitations, weakness, dizziness and syncope.²⁻⁹ Beta blockers have also been used for this condition. Limited data are available for other treatments that have been used and/or effectiveness have not been established (e.g., beta blockers, fludrocortisone, volume expansion, clonidine, and erythropoietin).

Guidelines

A few guidelines have recommendations that involve ivabradine.

- **Heart Failure:** The American Heart Association/American College of Cardiology/Heart Failure Society of America published guidelines in 2022 for the management of heart failure.¹⁰ For patients with symptomatic (New York Heart Association Class II to III) stable chronic heart failure with reduced ejection fraction (LVEF \leq 35%) who are receiving guideline-directed medical therapy, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of \geq 70 beats per minute at rest, ivabradine can be beneficial to reduce heart failure hospitalizations and cardiovascular death.
- **Inappropriate Sinus Tachycardia:** The 2015 Heart Rhythm Society Expert Consensus Statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope state that ivabradine can be useful for treating patients with inappropriate sinus tachycardia.² Additionally, the 2015 American College of Cardiology, American Heart Association Task Force on Clinical Practice Guidelines, and the Heart Rhythm Society also state that ivabradine is reasonable for ongoing management in patients with symptomatic inappropriate sinus tachycardia (class IIa recommendation).³ Beta blockers may be considered for ongoing management in patients with symptomatic inappropriate sinus tachycardia (class IIb recommendation). Also, the guidelines state that the combination of beta blockers and ivabradine may be considered for the ongoing management of patients with inappropriate sinus tachycardia (class IIb recommendation).

Medical Necessity Criteria

Ivabradine is considered medically necessary when the following criteria are met:

FDA-Approved Indications

1. **Heart Failure.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
 - A) Patient is \geq 18 years of age; AND
 - B) Patient has a left ventricular ejection fraction (LVEF) \leq 35% currently or prior to initiation of Ivabradine therapy; AND
 - C) Patient is in normal sinus rhythm or sinus tachycardia with a resting heart rate of \geq 70 beats per minute; AND
 - D) Patient meets ONE of the following (i or ii):
 - i. Patient has tried or is currently receiving one beta blocker for heart failure treatment; OR Note: Examples of beta blockers are metoprolol succinate sustained-release, carvedilol, bisoprolol, and Coreg CR (carvedilol extended-release capsules).
 - ii. Patient has a contraindication to use of beta blocker therapy; AND Note: Examples that are contraindications to use of beta blockers are bronchospastic disease such as chronic obstructive pulmonary disease and asthma, severe hypotension or bradycardia.
 - E) The medication is prescribed by or in consultation with a cardiologist.

- 2. Heart Failure due to Dilated Cardiomyopathy in Pediatric Patients.** Approve for 1 year if the patient meets BOTH of the following (A and B):
- A)** Patient is < 18 years of age; AND
 - B)** Medication is prescribed by or in consultation with a cardiologist.

Other Uses with Supportive Evidence

- 3. Inappropriate Sinus Tachycardia.** Approve for 1 year if the patient meets BOTH of the following (A and B):
- A)** Patient meets one of the following (i or ii):
 - i.** Patient has tried or is currently receiving one beta blocker for inappropriate sinus tachycardia; OR
Note: Examples of beta blockers are metoprolol and bisoprolol.
 - ii.** Patient has a contraindication to use of beta blocker therapy; AND
Note: Examples that are contraindications to use of beta blockers are bronchospastic disease such as chronic obstructive pulmonary disease and asthma, severe hypotension or bradycardia.
 - B)** The medication is prescribed by or in consultation with a cardiologist.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

- 1. Stable Angina Pectoris, in Patients Without Chronic Heart Failure.** Ivabradine has been studied as a treatment for stable angina pectoris but further data are needed.¹¹⁻¹³ The 2023 American Heart Association/American College of Cardiology guidelines for chronic coronary disease (CCD) state that in patients with CCD and normal left ventricular function, the addition of ivabradine to standard anti-anginal therapy is potentially harmful.¹⁴

References

1. Corlanor® tablets and oral solution [prescribing information]. Thousand Oaks: CA; Amgen; August 2021.
2. Sheldon RS, Grubb BP, Olshansky B, et al. 2015 Heart Rhythm Society Expert Consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. *Heart Rhythm*. 2015;12(6):e41-e63.
3. Page RL, Caldwell MA, Calkins H, et al. 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia. A report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines, and the Heart Rhythm Society. *Circulation*. 2016;133:e506-e574.
4. Abed HS, Fulcher J, Kilborn NJ, Keech AC. Inappropriate sinus tachycardia: focus on ivabradine. *Intern Med J*. 2016;46(8):875-883.
5. Oliphant CS, Owens RE, Bolorunduro OB, Jha SK. Ivabradine: a review of labeled and off-label uses. *Am J Cardiovasc Drugs*. 2016;16:337-347.

6. Ruzieh M, Moustafa A, Sabbagh E, et al. Challenges in treatment of inappropriate sinus tachycardia. *Curr Cardiol Rev.* 2018;14:42-44.
7. Mathew ST, Po SS, Thadani U. Inappropriate sinus tachycardia – symptoms and heart rate reduction with ivabradine: a pooled analysis of prospective studies. *Heart Rhythm.* 2018;15:240-247.
8. Koruth JS, Lala A, Pinne S, et al. The clinical use of ivabradine. *J Am Coll Cardiol.* 2017;70(14):1777-1784.
9. Bonnet D, Berger F, Jokinen E, et al. Ivabradine in children with dilated cardiomyopathy and symptomatic chronic heart failure. *J Am Coll Cardiol.* 2017;70:1262-1272.
10. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation.* 2022;145(18):e895-e1032.
11. Werdan K, Ebelt H, Nuding S, et al. Ivabradine in combination with beta-blocker improves symptoms and quality of life in patients with stable angina pectoris: results from the ADDITIONS study. *Clin Res Cardiol.* 2012;101(5):365-373.
12. Perings S, Stockl G, Kelm M, et al, on behalf of the RESPONSIVE study investigators. Effectiveness and tolerability of ivabradine with or without concomitant beta-blocker therapy in patients with chronic stable angina in routine clinical practice. *Adv Ther.* 2016;33:1550-1564.
13. Glezer M, Vasyuk Y, Karpov Y. Efficacy of ivabradine in combination with beta-blockers versus uptitration of beta-blockers in patients with stable angina (CONTROL-2 Study). *Adv Ther.* 2018;35:341-352.
14. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2023;82(9):833-955.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	<p>Policy Name: Updated title from “Ivabradine” to “Cardiology – Ivabradine.”</p> <p>Added ivabradine generic tablets to the policy.</p> <p>Heart Failure: For the criterion that the patient has a left ventricular ejection fraction $\leq 35\%$ prior to initiation of Corlanor therapy, “Corlanor” was changed to “ivabradine”.</p> <p>Added “Note: Examples of beta blockers are metoprolol succinate sustained-release, carvedilol, bisoprolol, and Coreg CR (carvedilol extended-release capsules).” Added “Note: Examples that are contraindications to use of beta blockers are bronchospastic disease such as chronic obstructive pulmonary disease and asthma, severe hypotension or bradycardia.” Added criterion, “Medication is prescribed by or in consultation with a cardiologist.”</p> <p>Heart Failure due to Dilated Cardiomyopathy in Pediatric Individuals: Removed criterion, “Individual has a left ventricular ejection fraction (LVEF) less than or equal to 45% prior to initiation of ivabradine (Corlanor) therapy.” Removed criterion, “Individual is on stable treatment for heart failure.” Removed criterion,</p>	10/15/2024

	"Individual is in sinus rhythm with specific resting heart rate for different age groups (≥ 105 bpm for ages 6-12 months, ≥ 95 bpm for 1-3 years, ≥ 75 bpm for ages 3-5 years; and ≥ 70 bpm for ages 5-18 years)." Added criterion, "Medication is prescribed by or in consultation with a cardiologist."	
--	--	--

The policy effective date is in force until updated or retired.

"Cigna Companies" refers to operating subsidiaries of The Cigna Group. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of The Cigna Group. © 2024 The Cigna Group.