**Medication Policy Manual** | **Policy No:** dru413

**Topic:** Corlanor®, ivabradine | **Date of Origin:** August 14, 2015

**Committee Approval Date:** August 11, 2017 | **Next Review Date:** April 2018

**Effective Date:** September 1, 2017

## IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

### Description

Ivabradine (Corlanor) is a self-administered hyperpolarization-activated cyclic nucleotide-gated channel blocker indicated to reduce the risk of hospitalization for worsening heart failure (HF) in patients with stable, symptomatic HF with reduced ejection fraction (HFrEF).

**Policy/Criteria**

**I.** Most contracts require prior authorization approval of ivabradine (Corlanor) prior to coverage. Ivabradine (Corlanor) may be considered medically necessary when criteria A, B, C, D, and E below are met:

**A.** A diagnosis of New York Heart Association (NYHA) class II to IV heart failure with an ejection fraction of ≤ 35%.

**AND**

**B.** Documentation that the patient has had a previous admission to a hospital for worsening heart failure within the past 12 months while on at least two medications from two different medication classes used in the treatment of heart failure with reduced ejection fraction. (*See Appendix 1*)

**AND**

**C.** Documentation that the patient is in sinus rhythm with a resting heart rate of ≥ 70 beats per minute.

**AND**

**D.** Ivabradine (Corlanor) is administered with a beta-blocker shown to reduce heart failure associated morbidity or mortality, unless all are not tolerated or beta-blocker use is contraindicated. (*See Appendix 1*)

**AND**

**E.** Ivabradine (Corlanor) is administered with an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB), unless both are not tolerated or contraindicated. (*See Appendix1*)

**II.** Administration, Quantity Limitations, and Authorization Period

**A.** OmedaRx considers ivabradine (Corlanor) to be a self-administered medication.

**B.** When prior authorization is approved, ivabradine (Corlanor) may be authorized in quantities of up to 60 tablets per month.

**C.** Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

**III.** Ivabradine (Corlanor) is considered not medically necessary when used for coronory artery disease with or without stable heart failure.

**IV.** Ivabradine (Corlanor) is considered investigational when used for all other conditions, including but not limited to:

**A.** Heart failure with preserved ejection fraction (≥ 40%).

**Position Statement**

- Ivabradine (Corlanor) is indicated to reduce the risk of hospitalization for worsening heart failure (HF) in patients with stable, symptomatic chronic HF with left ventricular ejection fraction ≤ 35%, who are in sinus rhythm with resting heart rate ≥ 70 beats per minute and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use.[1]
- In the pivotal clinical study, the majority of patients were on concurrent beta-blocker and ACE inhibitor/ARB therapy. [2]
- According to current guidelines, beta-blockers and ACE inhibitors, ARBs, or angiotensin receptor neprilysin inhibitors (ARNIs) are the cornerstone of the management of HF amongst other HF medication classes, and have been shown in randomized controlled studies to reduce HF associated morbidity and mortality. [3]
- Certain beta-blockers, particularly bisoprolol, carvedilol, and metoprolol have been shown in randomized controlled trials to improve overall and event-free survival in patients with HFrEF. Atenolol has also been shown to be of benefit in patients with HFrEF in retrospective studies. [3]
- Beta-blockers should be initiated and titrated to target doses, as tolerated, before assessing the resting heart rate for consideration of ivabradine initiation.[3]
- Ivabradine (Corlanor) has not been evaluated as monotherapy in the treatment of HFrEF or in the treatment of HF with preserved ejection fraction.
- Two large randomized-controlled studies have demonstrated that ivabradine (Corlanor) has no benefit in patients with stable coronary artery disease with or without HF. [4,5]

*Clinical Efficacy*

- Ivabradine (Corlanor) was approved based on results from the SHIFT trial, in which ivabradine (Corlanor) reduced the composite endpoint of cardiovascular death or HF hospitalization. [2]
    * The trial enrolled patients with stable NYHA class II to IV heart failure, left ventricular ejection fraction ≤ 35%, and resting heart rate ≥ 70 bpm.
    * Patients had to have been clinically stable for at least 4 weeks on an optimized and stable clinical regimen, which included maximally tolerated doses of beta-blockers and, in most cases, ACE inhibitors or ARBs, spironolactone, and diuretics.
    * The benefit of ivabradine (Corlanor) was driven by a reduction in HF hospitalization.
- Guidelines state that ivabradine (Corlanor) can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤35%) who on maximized therapy, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest. [3]
    * The guidelines also state that beta-blockers have well-proven mortality benefits and should be initiated and up-titrated to target doses prior to assessing heart rate for consideration of ivabradine (Corlanor).

*Not Medically Necessary Uses*

- Two large outcomes studies (BEATIFUL and SIGNIFY) have demonstrated that ivabradine (Corlanor) has no benefit in patients with stable coronory artery disease with or without stable heart failure. [1]
    * In BEATIFUL the primary endpoint was the composite of time to first cardiovascular death, hospitalization for acute myocardial infarction, or hospitalization for new-onset or worsening heart failure. Through a median follow-up of 19 months, Corlanor did not significantly affect the primary composite endpoint (HR 1.00, 95% CI = 0.91, 1.10). [4]
    * In SIGNIFY the primary endpoint was a composite of the first occurrence of either cardiovascular death or myocardial infarction. Through a median follow-up of 24.1 months, Corlanor did not significantly affect the primary composite endpoint (HR 1.08, 95% CI = 0.96, 1.20). [5]

*Investigational Uses*

- Ivabradine (Corlanor) has not been evaluated as monotherapy in the treatment of HFrEF or in the treatment of HF with preserved ejection fraction.

**Appendix 1: Classes of medications used for the treatment of HFrEF**

| ACE inhibitors | ARBs | ARNI | Aldosterone antagonists | Beta-blockers | Vasodilators |
|---|---|---|---|---|---|
| benazepril | azilsartan | valsartan-sacubitril | eplerenone | atenolol | hydralazine |
| captopril | candesartan | | spironolactone | bisoprolol | isosorbide dinitrate |
| enalapril | eprosartan | | | carvedilol | isosorbide mononitrate |
| fosinopril | irbesartan | | | metoprolol | |
| lisinopril | losartan | | | | |
| moexipril | olmesartan | | | | |
| perindopril | telmisartan | | | | |
| quinapril | valsartan | | | | |
| ramipril | | | | | |
| trandolapril | | | | | |

HFrEF = heart failure with reduced ejection fraction

| Cross References |
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| Entresto®, sacubitril/valsartan, dru414 |

| Codes | Number | Description |
|---|---|---|
| N/A | | |

## References


1. Corlanor® [Prescribing Information]. Thousand Oaks, CA: Amgen; January 2017.
2. Swedberg, K, Komajda, M, Bohm, M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. *Lancet*. 2010;376:875-85. PMID: 20801500
3. Yancy, CW, Jessup, M, Bozkurt, B, et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Journal of the American College of Cardiology*. 2016 May 17. PMID: 27216111
4. Fox, K, Ford, I, Steg, PG, Tendera, M, Ferrari, R. Ivabradine for patients with stable coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2008;372:807-16. PMID: 18757088
5. Fox, K, Ford, I, Steg, PG, Tardif, JC, Tendera, M, Ferrari, R. Ivabradine in stable coronary artery disease without clinical heart failure. *The New England journal of medicine*. 2014 Sep 18;371(12):1091-9. PMID: 25176136


*Revision History*

| Revision Date | Revision Summary |
|---|---|
| 8/11/2017 | No changes with this annual update. |
| 8/12/2016 | Moved use for the treatment of CAD from investigational to not medically necessary. |