BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**1/21/2016**
LAST REVIEW DATE:	**8/19/2021**
LAST CRITERIA REVISION DATE:	**8/19/2021**
ARCHIVE DATE:	

CORLANOR® (ivabradine) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

CORLANOR® (ivabradine) oral

Criteria:

- **Criteria for initial therapy:** Corlanor (ivabradine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist

2. A confirmed diagnosis is **ONE** of the following:
   a. Adult 18 years of age or older with stable symptomatic heart failure (NYHA class II-IV, see Definition section)
   b. Pediatric individual age of 6 months or older with stable symptomatic heart failure due to dilated cardiomyopathy (NYHA class II-IV or Ross Heart Failure class II-IV, see Definition section)

3. Left ventricular ejection fraction is **ONE** of the following:
   a. ≤ 35% in an individual 18 years or older
   b. ≤ 45% in an individual 6 months to 17 years

4. Individual is in sinus rhythm with a resting heart rate of **ONE** of the following:
   a. ≥ 70 beats per minute in an individual 18 years or older
   b. In the normal range for age in an individual 6 months to 17 years (See Definition section)

5. Will be added to a maximally tolerated dose of **ONE** of the following beta-blockers:
   a. Bisoprolol, carvedilol, or sustained release metoprolol

6. Documented failure, contraindication per FDA label, intolerance, or not a candidate to maximally tolerated doses, where clinically appropriate for age and condition, of one or more of the following:
   a. Angiotensin converting enzyme inhibitors or angiotensin II receptor blockers
   b. Aldosterone antagonist or other diuretic agent
   c. Hydralazine plus isosorbide dinitrate
   d. Digitalis

7. There are **NO** FDA-label contraindications, such as:
   a. Acute decompensated heart failure
   b. Blood pressure < 90/50 mmHg or clinically significant hypotension
   c. Sick sinus syndrome, unless has a functioning demand pacemaker
   d. Sinoatrial block, unless has a functioning demand pacemaker
   e. Third degree AV block, unless has a functioning demand pacemaker
   f. Resting heart rate < 60 bpm prior to treatment or clinically significant bradycardia
   g. Severe hepatic impairment (Child-Pugh Class C)
   h. Heart rate that is maintained exclusively by the pacemaker
   i. Simultaneous use of strong CYP450 3A4 inhibitors – see Definitions section

8. Will not be used in individual with second degree AV block, unless has a functioning demand pacemaker

9. Will not be used in individual with a demand pacemaker set to rates ≥ 60 beats per minute

10. There are no significant interacting drugs

Initial approval duration:
- If the individual has **NOT** been seen by a cardiologist within 6 months **AND** the request is for initial **OR** continuation of therapy: 60-day transition of care period to permit ample time to be seen by a cardiologist
- If seen by a cardiologist: 12 months

- **Criteria for continuation of coverage (renewal request):** Corlanor (ivabradine) is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist at least yearly

2. Individual's condition responded while on therapy is **ONE** of the following:
    a. Response in an individual 6 months of age or older is defined as:
        i. Achieved and maintains a heart rate (HR) reduction of at least 20%, based on tolerability, without bradycardia or symptoms of bradycardia

    b. Response in an individual 18 years of age or older is defined as:
        i. There are no hospitalizations for heart failure in the last 12 months while on therapy
        ii. Achieved and maintains a resting heart rate between 50 and 60 beats per minute (bpm)

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use, such as:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Atrial fibrillation
        ii. Bradycardia
        iii. Sinus arrest
        iv. Heart block

5. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of a Non-Cancer Medications**

2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

CORLANOR® (ivabradine) oral

Description:

Corlanor (ivabradine) is indicated **to reduce the risk of hospitalization for worsening heart failure in** adult patients with **stable, symptomatic chronic heart failure** 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** and is indicated for the treatment of stable symptomatic heart failure due to dilated cardiomyopathy (DCM) in pediatric patients aged 6 months and older, who are in sinus rhythm with an elevated heart rate.

Heart failure (HF) is a complex chronic progressive clinical syndrome in which the heart muscle is unable to pump enough blood to meet the body's needs. Diagnosis is made based on a careful history and physical examination. Mortality rate is high, approximately 50% of patients die within five years of diagnosis despite the availability of medications with proven mortality benefit.

NYHA categorizes HF into four classes depending on a patient's functional status, ranging from no limitation in physical activity (Class I), to an inability to carry out any physical activity without discomfort (Class IV). Treatment options for NYHA class II to IV heart failure with reduced ejection fraction include ACE inhibitors or ARB, angiotensin receptor neprilysin inhibitors (ARNIs), beta-blockers (bisoprolol, carvedilol, or sustained release metoprolol), and aldosterone antagonists (eplerenone or spironolactone). Loop diuretics and vasodilators (hydralazine with isosorbide dinitrate) are added depending on symptoms and ethnicity. Digoxin may also be used in certain circumstances.

According to current guidelines, beta-blockers and ACE inhibitors, ARBs, or ARNIs are the cornerstone of the management of HF, and have been shown in randomized controlled studies to reduce HF associated morbidity and mortality. Corlanor (ivabradine) has not been evaluated as monotherapy in the treatment of heart failure with reduced ejection fraction or in the treatment of HF with preserved ejection fraction.

Corlanor (ivabradine) is a hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker. The HCN channel is responsible for the cardiac pacemaker inward funny (I_f) current, which regulates heart rate. The current is activated during the resting potential stage and accelerates diastolic depolarization of the sinus node. In clinical electrophysiology studies, the cardiac effects were most pronounced in the sinoatrial (SA) node, but prolongation of the AH interval has occurred on the surface ECG, as has PR interval prolongation. Ivabradine reduces the spontaneous pacemaker activity of the cardiac sinus node by selectively inhibiting I_f current, resulting in a reduction in heart rate with no effect on ventricular repolarization and no effects on myocardial contractility.

Corlanor (ivabradine) causes a dose-dependent reduction in heart rate. The size of the effect is dependent on the baseline heart rate (i.e., greater heart rate reduction occurs in subjects with higher baseline heart rate). It does not have negative inotropic effects. Ivabradine increases the uncorrected QT interval with heart rate slowing but does not cause rate-corrected prolongation of QT.

Ivabradine can also inhibit the retinal current I_h. I_h is involved in limiting retinal responses to bright light stimuli. Under triggering circumstances (e.g., rapid changes in luminosity), partial inhibition of I_h by ivabradine may cause luminous phenomena experienced by patients. Luminous phenomena (phosphenes) are described as a transient enhanced brightness in a limited area of the visual field.

CORLANOR® (ivabradine) oral

Definitions:

Strong inhibitors of Cytochrome P450 3A4: (list is not all inclusive)

Azole antifungals: itraconazole, ketoconazole
Macrolide antibiotics: clarithromycin, telithromycin
HIV protease inhibitors: nelfinavir
Nefazodone

Moderate inhibitors of Cytochrome P450 3A4: (list is not all inclusive)

Calcium channel blockers: diltiazem, verapamil
Grapefruit juice

Inducers of Cytochrome P450 3A4: (list is not all inclusive)

St. John's wort
Rifampin
Barbiturates
Phenytoin

New York Heart Association (NYHA)/Ross Heart Failure Classification:

	Adult – NYHA Heart Failure	Infant and Children – Ross Heart Failure
Class I	No symptoms and no limitation in ordinary physical activity, e.g. shortness of breath when walking, climbing stairs etc	No limitations or symptoms
Class II	Mild symptoms mild dyspnea and/or angina, fatigue, palpitations, and slight limitation during ordinary activity or moderate exercising but not during rest	Infant: mild tachypnea or diaphoresis with feeding; older child: mild to moderate dyspnea on exertion; no growth failure
Class III	Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20-100 m) or minimal exertion that interfere with normal daily activity, comfortable only at rest	Infant: marked tachycardia or diaphoresis with feeding, prolonged feeding times; older child: marked dyspnea on exertion; growth failure from CHF
Class IV	Severe limitations, unable to carry out any physical activity because experiences symptoms even while at rest that worsen with any exertion, mostly bedbound patients	Symptomatic at rest with tachypnea, retractions, grunting, or diaphoresis

American College of Cardiology (ACC)/American Heart Association (AHA) Stages of HF:

- Stage A: At high risk for HF but without structural heart disease or symptoms of HF
- Stage B: Structural heart disease but without signs or symptoms of HF
- Stage C: Structural heart disease with prior or current symptoms of HF
- Stage D: Refractory HF requiring specialized interventions

Normal Resting Heart Rate and Bradycardia for age:

Age	Normal
0-1 months	70-190 beats per minute
1-11 months	80-160 beats per minute
1-2 years	80-130 beats per minute
3-4 years	80-120 beats per minute
5-6 years	75-115 beats per minute
7-9 years old	70-110 beats per minute
10 years and older	60-100 beats per minute
Well trained athletes	40-60 beats per minute

CORLANOR® (ivabradine) oral

Resources:

Corlanor (ivabradine) product information, revised by Amgen, Inc. 04-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on June 11, 2020, June 18, 2021.

Colucci WS. Overview of the management of heart failure with reduced ejection fraction in adults. In: UpToDate, Gottlieb SS, Dardas TF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 18, 2021.

Givetz MM, Colucci WS. Pharmacologic therapy of heart failure with reduced ejection fraction: Mechanisms of action. In: UpToDate, Pfeffer MA, Dardas TF (Ed), UpToDate, Gottlieb SS, Dardas TF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 18, 2021.

Meyer TE. Initial pharmacologic therapy of heart failure with reduced ejection fraction in adults. In: UpToDate, Gottlieb SS, Dardas TF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 18, 2021.

Colucci WS. Secondary pharmacologic therapy in heart failure with reduced ejection fraction (HfrEF) in adults. In: UpToDate, Gottlieb SS, Dardas TF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 18, 2021.

Singh RK, Singh TP. Heart failure in children: Management. In: UpToDate, Triedman JK, Armsby C (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 18, 2021.

Bonnet D, Berger F, Jokinen E, et al.: Ivabradine in children with dilated cardiomyopathy and sysptomatic chronic heart failure. JACC 2017; 70 (10): 1262-1272. Accessed on June 18, 2021.