BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 1/21/16**
SECTION: DRUGS	**LAST REVIEW DATE: 9/20/18**
	LAST CRITERIA REVISION DATE: 9/20/18
	ARCHIVE DATE:

CORLANOR® (ivabradine) oral tablet

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.**

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Criteria:

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

1. Request is from a Cardiologist or a provider in consultation with a Cardiologist
2. Individual is 18 years of age or older
3. A confirmed diagnosis of stable, chronic heart failure, New York Heart Association (NYHA) class II-IV
4. Left ventricular ejection fraction is ≤ 35%
5. Individual is in sinus rhythm with a resting heart rate of ≥ 70 beats per minute
6. Individual has had hospital admissions for worsening heart failure within the last 12 months despite use of medications shown to reduce heart failure morbidity and mortality
7. Failure, contraindication or intolerance to a beta-blocker at maximally tolerated dose:
   - Bisoprolol, carvedilol, or sustained release metoprolol
8. Failure, contraindication or intolerance to at maximally tolerated dose of:
   - Angiotensin converting enzyme inhibitors or angiotensin II receptor blockers
   - Aldosterone antagonist
   - Hydralazine plus isosorbide dinitrate
9. There are **NO** contraindications
   - Contraindications include:
     - Acute decompensated heart failure
     - Blood pressure < 90/50 mmHg
     - Sick sinus syndrome, unless has a functioning demand pacemaker
     - Sinoatrial block, unless has a functioning demand pacemaker
     - Third degree AV block, unless has a functioning demand pacemaker
     - Resting heart rate < 60 bpm prior to treatment
     - Severe hepatic impairment (Child-Pugh Class C)
     - Pacemaker dependence – heart rate maintained exclusively by the pacemaker
     - Simultaneous use of strong CYP450 3A4 inhibitors – see definitions section

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

CORLANOR® (ivabradine) oral tablet (cont.)

- **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. Continues to be seen by Cardiologist at least yearly
  2. There are no hospitalizations for heart failure in the last 12 months while on therapy
  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:
     - Contraindications as listed in the criteria for initial therapy section
     - Significant adverse effect such as:
       - Atrial fibrillation
       - Bradycardia
  5. There are no significant interacting drugs

  Renewal duration: 12 months

Description:

Corlanor (ivabradine) is indicated **to reduce the risk of hospitalization for worsening heart failure in** 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**.

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.

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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.

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

Resources:

Corlanor (ivabradine). Package Insert. Revised by manufacturer 04-2015. Accessed 10-23-2015.

Corlanor (ivabradine). Package Insert. Revised by manufacturer 01-2017. Accessed 08-23-2017, 07-19-2018.

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UpToDate: Use of ivabradine in heart failure with reduced ejection fraction. Current through Jul 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/use-of-ivabradine-in-heart-failure-with-reduced-ejection-fraction?source=see_link&sectionName=SELECTION%20OF%20CANDIDATES%20FOR%20IVABRADINE%20THERAPY&anchor=H3224395818#H3224395818

UpToDate: Pharmacologic therapy of heart failure with reduced ejection fraction. Current through Jul 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/pharmacologic-therapy-of-heart-failure-with-reduced-ejection-fraction?source=search_result&search=heart%20failure%20treatment&selectedTitle=2~150#H17678370

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.