Hyperpolarization-Activated Cyclic Nucleotide-Gated (HCN) Channel Blocker (Corlanor) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
9/1/2023	10/1/2016

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Corlanor® (ivabradine) Tablet, Solution	To reduce the risk of hospitalization for worsening heart failure in adult patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction less than or equal to 35%, who are in sinus rhythm with resting heart rate greater than or equal to 70 beats per minute and either are on maximally tolerated doses of beta blockers or have a contraindication to beta-blocker use. 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.		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Heart Failure

The ACCF/AHA/HFSA (American College of Cardiology/Heart Failure Society of America) 2022 Guideline for the Management of Heart Failure states that ivabradine can be beneficial to reduce HF hospitalizations and cardiovascular death for patients with symptomatic (NYHA class II-III) stable chronic heart failure with reduced ejection fraction (HFrEF) (LVEF less than or equal to 35%) who are receiving guideline directed medical therapy (GDMT), 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 ACCF/AHA guideline classifies heart failure by the following in relation to New York Heart Association (NYHA) Functional Classification:(2)

ACCF/AHA Stages of HF	ACCF/AHA Stage Description	NYHA Functional Classification	NYHA Functional Classification Description
A	At high risk for HF but without structural heart disease or symptoms of HF	None	None

B	Structural heart disease but without signs or symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF
C	Structural heart disease with prior or current symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF
		II	Slight limitation of physical activity. Comfort able at rest, but ordinary physical activity results in symptoms of HF
		III	Marked limitation of physical activity. Comfort able at rest, but less than ordinary activity causes symptoms of HF
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest
D	Refractory HF requiring specialized interventions	IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest

Dilated Cardiomyopathy (DCM)	Dilated cardiomyopathy (DCM) is a clinical diagnosis characterized by left ventricular or biventricular dilation and impaired contraction that is not explained by abnormal loading conditions (for example, hypertension and valvular heart disease) or coronary artery disease. Mutations in several genes can cause DCM, including genes encoding structural components of the sarcomere and desmosome. Nongenetic forms of DCM can result from different etiologies, including inflammation of the myocardium due to an infection (mostly viral); exposure to drugs, toxins or allergens; and systemic endocrine or autoimmune diseases. The heterogeneous etiology and clinical presentation of DCM make a correct and timely diagnosis challenging. Echocardiography and other imaging techniques are required to assess ventricular dysfunction and adverse myocardial remodeling. Immunological and histological analyses of an endomyocardial biopsy sample are indicated when inflammation or infection is suspected. As DCM eventually leads to impaired contractility, standard approaches to prevent or treat heart failure are the first-line treatment for patients with DCM. Cardiac resynchronization therapy and implantable cardioverter–defibrillators may be required to prevent life-threatening arrhythmias.(4)

Efficacy	Ivabradine is a hyperpolarization-activated cyclic nucleotide-gated channel blocker that reduces the spontaneous pacemaker activity of the cardiac sinus node by selectively inhibiting the I current, resulting in heart rate reduction with no effect on ventricular repolarization and no effects on myocardial contractility. It gained its indication for heart failure in adult patients via the systolic heart failure treatment with the I_f inhibitor ivabradine trial (SHIFT). This was a randomized, double-blind trial comparing Corlanor and placebo in 6558 patients with stable NYHA class II to IV heart failure, left ventricular ejection fraction less than or equal to 35%, and resting heart rate greater than or equal to 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, with fluid retention and symptoms of congestion minimized. SHIFT demonstrated that Corlanor reduced the risk of the combined endpoint of hospitalization for worsening heart failure or cardiovascular death based on a time-to-event analysis. Because Corlanor was effective in improving outcomes in patients with dilated cardiomyopathy (DCM) in SHIFT, the effect on heart rate was considered a reasonable basis to infer clinical benefits in pediatric patients with DCM. Thus, Corlanor was evaluated for its effect on heart rate in a multi-center, randomized, double-blind, placebo-controlled trial in children with symptomatic DCM. The study collected data from 116 patients 6 months to less than 18 years old with DCM in sinus rhythm, NYHA/Ross class II to IV heart failure, and left ventricular ejection fraction less than or equal to 45%. A statistically significant reduction in heart rate was observed with Corlanor compared to placebo at the end of the titration period (-23 plus or minus 11 bpm vs. -2 plus or minus 12 bpm respectively).(1)
Safety	Ivabradine is contraindicated in patients with: • Acute decompensated heart failure • Clinically significant hypotension • Sick sinus syndrome, sinoatrial block, or 3rd degree AV block, unless a functioning demand pacemaker is present • Clinically significant bradycardia • Severe hepatic impairment • Pacemaker dependence (heart rate maintained exclusively by the pacemaker) • Concomitant use of strong cytochrome P450 3A4 (CYP3A4) inhibitors(1)

REFERENCES

Number	Reference
1	Corlanor prescribing information. Amgen Inc. August 2021.
2	2013 ACCF/AHA Guideline for the Management of Heart Failure. Accessed at http://circ.ahajournals.org/.
3	2022 ACC/AHA/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. Available at: https://www.acc.org/guidelines/hubs/heart-failure
4	Heinz-Peter S, Fairweather D, Calforio AL, et. al. Dilated cardiomyopathy. *Nat Rev Dis* Primers. 2018; 5(1): 32. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5574280/

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Corlanor	ivabradine hcl oral soln	5 MG/5ML	M ; N ; O ; Y	N		
Corlanor	Ivabradine HCl Tab ; ivabradine hcl tab	5 ; 5 MG ; 7.5 ; 7.5 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Corlanor	Ivabradine HCl Oral Soln 5 MG/5ML (Base Equiv)	5 MG/5ML	600	mL	30	DAYS			
Corlanor	Ivabradine HCl Tab 5 MG (Base Equiv)	5 ; 5 MG	60	Tablets	30	DAYS			
Corlanor	Ivabradine HCl Tab 7.5 MG (Base Equiv)	7.5 ; 7.5 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Corlanor	ivabradine hcl oral soln	5 MG/5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Corlanor	Ivabradine HCl Tab ; ivabradine hcl tab	5 ; 5 MG ; 7.5 ; 7.5 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Corlanor	Ivabradine HCl Oral Soln 5 MG/5ML (Base Equiv)	5 MG/5ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Corlanor	Ivabradine HCl Tab 5 MG (Base Equiv)	5 ; 5 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Corlanor	Ivabradine HCl Tab 7.5 MG (Base Equiv)	7.5 ; 7.5 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
All target agents are eligible for continuation of therapy

      1. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR**
      2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR**

   B. BOTH of the following:
      1. The patient has stable, symptomatic heart failure (e.g., NYHA Class II, III, IV; ACCF/AHA Class C, D) **AND**
      2. ONE of the following:
         A. ALL of the following:
            1. The patient has heart failure due to dilated cardiomyopathy (DCM) **AND**
            2. The patient is in sinus rhythm with an elevated heart rate **OR**
         B. ALL of the following:
            1. The patient has a baseline OR current left ventricular ejection fraction of less than or equal to 35% **AND**
            2. Prior to initiating therapy with the requested agent, the patient is in sinus rhythm with a resting heart rate of greater than or equal to 70 beats per minute **AND**
            3. ONE of the following:
               A. The patient will be using standard CHF therapy (e.g., beta blockers, ACE inhibitors) in combination with the requested agent **OR**
               B. The patient has an intolerance, hypersensitivity or FDA labeled contraindication to ALL standard CHF therapy (e.g., beta blockers, ACE inhibitors) that is not expected to occur with the requested agent **OR**
               C. The patient's medication history includes use of standard CHF therapy (e.g., beta blockers, ACE inhibitors) **OR**
               D. BOTH of the following:
                  1. The prescriber has stated that the patient has tried standard CHF therapy (e.g., beta blockers, ACE inhibitors) **AND**
                  2. Standard CHF therapy (e.g., beta blockers, ACE inhibitors) was discontinued due to lack of effectiveness or an adverse event **OR**
               E. The patient is currently being treated with the requested agent as indicated by ALL of the following:

Module	Clinical Criteria for Approval
	1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** F. The prescriber has provided documentation that standard CHF therapy (e.g., beta blockers, ACE inhibitors) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. If the requested agent is being used for heart failure (not due to DCM), ONE of the following: A. The patient will be using standard CHF therapy (e.g., beta blockers, ACE inhibitors) in combination with the requested agent **OR** B. The patient has an intolerance, hypersensitivity, or FDA labeled contraindication to ALL standard CHF therapy (e.g., beta blockers, ACE inhibitors) that is not expected to occur with the requested agent **OR** C. The patient's medication history includes use of standard CHF therapy (e.g., beta blockers, ACE inhibitors) **OR** D. BOTH of the following: 1. The prescriber has stated that the patient has tried standard CHF therapy (e.g., beta blockers, ACE inhibitors) **AND** 2. Standard CHF therapy (e.g., beta blockers, ACE inhibitors) was discontinued due to lack of effectiveness or an adverse event **OR** 3. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 4. The prescriber has provided documentation that standard CHF therapy (e.g., beta blockers, ACE inhibitors) cannot be used due to a documented

Module	Clinical Criteria for Approval
	medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the FDA maximum labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of approval:** 12 months