FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosage &amp; Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corlanor® (ivabradine)</td>
<td>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</td>
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<tr>
<td></td>
<td>Starting dose is 5 mg twice daily. After 2 weeks of treatment, adjust dose based on heart rate. The maximum dose is 7.5 mg twice daily.</td>
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<tr>
<td></td>
<td>In patients with conduction defects or in whom bradycardia could lead to hemodynamic compromise, initiate dosing at 2.5 mg twice daily</td>
</tr>
</tbody>
</table>

CLINICAL RATIONALE

Heart Failure

The ACCF/AHA/HFSA (Heart Failure Society of America) state that ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤35%) who are receiving guideline directed evaluation and management (GDEM), 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.  

The ACCF/AHA guideline classifies heart failure by the following in relation to New York Heart Association (NYHA) Functional Classification:

<table>
<thead>
<tr>
<th>ACCF/AHA Stages of HF</th>
<th>ACCF/AHA Stage Description</th>
<th>NYHA Functional Classification</th>
<th>NYHA Functional Classification Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At high risk for HF but without structural heart disease or symptoms of HF</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>Structural heart disease but without signs or symptoms of HF</td>
<td>I</td>
<td>No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF</td>
</tr>
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<td>ACCF/AHA Stages of HF</td>
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<tr>
<td>-----------------------</td>
<td>---------------------------</td>
<td>--------------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>C</td>
<td>Structural heart disease with prior or current symptoms of HF</td>
<td>I</td>
<td>No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>II</td>
<td>Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>III</td>
<td>Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IV</td>
<td>Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest</td>
</tr>
<tr>
<td>D</td>
<td>Refractory HF requiring specialized interventions</td>
<td>IV</td>
<td>Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest</td>
</tr>
</tbody>
</table>

The ACCF/AHA guideline recommends the following algorithm for the treatment of heart failure with reduced ejection fraction (HFrEF) (≤40%) ACCF/AHA Class C and NYHA Class I-IV:

- All patients should receive an angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), or angiotensin receptor/neprilysin inhibitor (ARNI) in addition to a beta blocker
- For volume overloaded NYHA Class II-IV patients, a loop diuretic should be added
- For persistently symptomatic African American NYHA class III-IV patients, hydralazine and isosorbide dinitrate should be added
- For NYHA Class II-IV patients with estimated creatinine >30 mL/min and potassium <5.0 mEq/dL, an aldosterone antagonist should be added

**Safety**

Ivabradine is contraindicated in patients with:
- Acute decompensated heart failure
- Blood pressure less than 90/50 mmHg
- Sick sinus syndrome, sinoatrial block, or 3rd degree AV block, unless a functioning demand pacemaker is present
- Resting heart rate less than 60 bpm prior to treatment
- Severe hepatic impairment
- Pacemaker dependence (heart rate maintained exclusively by the pacemaker)
Concomitant use of strong cytochrome P450 3A4 (CYP3A4) inhibitors

REFERENCES
   https://www.ahajournals.org/doi/pdf/10.1161/CIR.0000000000000509
Hyperpolarization-Activated Cyclic Nucleotide-Gated (HCN) Channel Blocker (Corlanor) Prior Authorization with Quantity Limit

OBJECTIVE
The intent of the Hyperpolarization-Activated Cyclic Nucleotide-Gated (HCN) prior authorization (PA) with Quantity Limit (QL) program is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and according to dosing recommended in product labeling. Corlanor will be approved for use in patients with stable, symptomatic chronic heart failure; who have a baseline or current left ventricular ejection fraction of ≤35%; who are in sinus rhythm with a resting heart rate of ≥70 beats per minute; who is on maximally tolerated dose of beta blocker or the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to beta blockers. The program will approve for doses within the set limit. Doses above the set limit will be approved if the requested quantity is below the FDA limit and cannot be dose optimized or when the quantity is above the FDA limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis. Requests for an HCN agent will be reviewed when patient specific documentation is provided.

TARGET DRUG
Corlanor® (ivabradine)

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit Per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corlanor (ivabradine)</td>
<td>40700035100320M, N, O, or Y</td>
<td>40700035100330M, N, O, or Y</td>
<td>2 tablets</td>
</tr>
</tbody>
</table>

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Corlanor will be approved when ALL of the following are met:
1. The patient has stable, symptomatic chronic heart failure (e.g. NYHA Class II, III, IV; ACCF/AHA Class C, D)
   AND
2. The patient has a baseline OR current left ventricular ejection fraction of ≤35%
   AND
3. Prior to initiating therapy with the requested agent, the patient is in sinus rhythm with a resting heart rate of ≥70 beats per minute
   AND
4. ONE of the following:
   a. The patient is on a maximally tolerated dose of beta blocker (e.g. atenolol, bisoprolol, carvedilol, metoprolol)
   OR
   b. The patient has a history of a documented intolerance, FDA labeled contraindication, or hypersensitivity to a beta blocker (e.g. atenolol, bisoprolol, carvedilol, metoprolol)
   AND
5. The patient does NOT have any FDA labeled contraindication(s) to the requested agent
   AND
6. ONE of the following:
   a. The quantity requested is less than or equal to the program quantity limit
   OR
   b. The quantity (dose) requested is above the program limit, less than or equal to the maximum dose recommended in FDA approved labeling and the prescribed dose cannot be achieved using a lesser quantity of a higher strength
   OR
c. The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

**Length of Approval:** 12 months
Step Therapy Supplement

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

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. 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

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

   OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) 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

Length of Approval: As per program specific criteria