Clinical Policy: Ivabradine (Corlanor)
Reference Number: CP.PMN.70
Effective Date: 11.01.15
Last Review Date: 02.21
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Ivabradine (Corlanor®) is a hyperpolarization-activated cyclic nucleotide-gated channel blocker.

FDA Approved Indication(s)
Corlanor 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 (LVEF) ≤ 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;
- 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Corlanor is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Heart Failure (must meet all):
      1. Diagnosis of chronic heart failure;
      2. Prescribed by or in consultation with a cardiologist;
      3. Age ≥ 6 months;
      4. LVEF ≤ 35% for adults or ≤ 45% for pediatrics;
      5. Member is in sinus rhythm with a resting heart rate of one of the following (a, b, c, or d):
         a. Age 6 to 12 months: ≥ 105 beats per minute;
         b. Age 1 to 3 years: ≥ 95 beats per minute;
         c. Age 3 to 5 years: ≥ 75 beats per minute;
         d. Age 5 years and older: ≥ 70 beats per minute;
      6. Failure of two of the following beta-blockers recommended for heart failure at up to maximally indicated doses, each used for ≥ 30 days, unless clinically significant adverse effects are experienced or all are contraindicated: bisoprolol, carvedilol (immediate- or extended-release), extended-release metoprolol succinate;
7. Member has used one of the aforementioned beta blockers for ≥ 30 days within the past 60 days, unless clinically significant adverse effects are experienced or all are contraindicated;
8. Dose does not exceed 15 mg (2 tablets or 15 mL) per day.

**Approval duration:**
- HIM – 12 months
- Medicaid/Commercial – Length of Benefit

**B. Other diagnoses/indications**
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

**II. Continued Therapy**
**A. Heart Failure** (must meet all):
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Corlanor for heart failure and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 15 mg (2 tablets or 15 mL) per day.

**Approval duration:**
- HIM – 12 months
- Medicaid/Commercial – Length of Benefit

**B. Other diagnoses/indications** (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 12 months (whichever is less);** or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**
**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**
*Appendix A: Abbreviation/Acronym Key*
- DCM: dilated cardiomyopathy
- FDA: Food and Drug Administration
- LVEF: left ventricular ejection fraction
### Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta-Blockers Recommended for Heart Failure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bisoprolol (Zebeta®)</td>
<td><strong>Heart Failure</strong>&lt;sup&gt;†&lt;/sup&gt; Initially, 1.25 mg PO QD for 48 hours, then 2.5 mg QD for the first month, then 5 mg QD.</td>
<td>10 mg/day</td>
</tr>
<tr>
<td>carvedilol (Coreg®, Coreg CR®)</td>
<td><strong>Heart Failure</strong> Immediate-release: Initially, 3.125 mg PO BID for 2 weeks. Dosage may be subsequently increased to 6.25, 12.5, and then 25 mg PO BID over successive intervals of at least 2 weeks. Extended-release: Initially, 10 mg PO QD for 2 weeks. Dosage may be subsequently increased to 20, 40, and then 80 mg PO QD over successive intervals of at least 2 weeks.</td>
<td>Immediate-release: 100 mg/day Extended-release: 80 mg/day</td>
</tr>
<tr>
<td>metoprolol succinate extended release (Toprol XL®)</td>
<td><strong>Heart Failure</strong> 25 mg PO QD for 2 weeks in patients with NYHA class II heart failure, or 12.5 mg PO QD in patients with more severe heart failure. Double the dose every 2 weeks as tolerated, up to the target dosage of 200 mg PO QD.</td>
<td>200 mg/day</td>
</tr>
</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

<sup>†</sup>Off-label indication

### Appendix C: Contraindications/Boxed Warnings

- **Contraindication(s):**
  - 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
- **Boxed warning(s):** none reported
V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure</td>
<td>Adult and pediatric patients ≥ 40 kg: Initially 2.5 mg (pediatrics and vulnerable adults) or 5 mg PO BID. After 2 weeks of treatment, adjust dose based on heart rate. The maximum dose is 7.5 mg BID.</td>
<td>15 mg/day</td>
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<tr>
<td></td>
<td>Pediatric patients &lt; 40 kg: Initially 0.05 mg/kg PO BID. Adjust dose at 2-week intervals by 0.05 mg/kg based on heart rate.</td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability

- Tablets: 5 mg, 7.5 mg
- Oral solution: 5 mg/5 mL

VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Converted to new template. Added age restriction and DDI contraindication as the interactions are severe per PI/safety approach; Modified max dose requirement to include specific quantity limit. Updated references.</td>
<td>08.07.17</td>
<td>11.17</td>
</tr>
<tr>
<td>3Q 2018 annual review: policies combined for Commercial and Medicaid lines of business; Commercial: added prescriber, age, LVEF, and sinus rhythm; modified requirement related to failure of 2 generic beta-blockers to include only beta-blockers which have been</td>
<td>04.11.18</td>
<td>08.18</td>
</tr>
</tbody>
</table>
Reviews, Revisions, and Approvals

<table>
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<tbody>
<tr>
<td>shown to be effective in reducing mortality (bisoprolol, carvedilol, and</td>
<td>10.30.18</td>
<td>02.19</td>
</tr>
<tr>
<td>metoprolol succinate) in patients with chronic heart failure per 2013 ACCF/AHA guideline for the management of heart failure and duration of trial; Medicaid: removed contraindication requirement related to drug-drug interaction and incorporated the information in Appendix C; references reviewed and updated.</td>
<td></td>
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</tr>
<tr>
<td>1Q 2019 annual review: no significant changes; references reviewed and</td>
<td>03.15.19</td>
<td></td>
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<tr>
<td>updated.</td>
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<tr>
<td>Added HIM line of business due to addition of agent(s) to the HIM formulary with PA</td>
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<tr>
<td>RT4: Added recently FDA-approved pediatric indication extension.</td>
<td>05.06.19</td>
<td></td>
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<tr>
<td>1Q 2020 annual review: no significant changes; references reviewed and</td>
<td>11.26.19</td>
<td>02.20</td>
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<tr>
<td>updated.</td>
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<tr>
<td>1Q 2021 annual review: no significant changes; references to HIM.PHAR.21</td>
<td>10.16.20</td>
<td>02.21</td>
</tr>
<tr>
<td>revised to HIM.PA.154; references reviewed and updated.</td>
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</tr>
</tbody>
</table>

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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CLINICAL POLICY
Ivabradine

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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