Clinical Policy: L-glutamine (Endari)
Reference Number: CP.PMN.116
Effective Date: 08.22.17
Last Review Date: 11.19
Line of Business: Commercial, Medicaid

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

Description
L-glutamine (Endari®) is an amino acid.

FDA Approved Indication(s)
Endari is indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.

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 Endari is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Sickle Cell Disease (must meet all):
      1. Diagnosis of sickle cell disease;
      2. Age ≥ 5 years;
      3. Failure of hydroxyurea at up to maximally tolerated doses, unless contraindicated or clinically significant adverse effects are experienced;
      4. Dose does not exceed 30 grams per day based on weight.
      Approval duration:
      Medicaid – 12 months
      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, and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Sickle Cell Disease (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, new dose does not exceed 30 grams per day based on weight.
Approval duration:
Medicaid – 12 months
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 6 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, 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, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   FDA: Food and Drug Administration

   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>hydroxyurea (Hydrea®, Droxia®)</td>
<td>15 mg/kg PO QD</td>
<td>35 mg/kg/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.

Appendix C: Contraindications/Boxed Warnings
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>Sickle cell disease</td>
<td>Weight &gt; 65 kg: 15 g (3 packets) PO BID</td>
<td>30 g/day (maximum dose based on weight)</td>
</tr>
<tr>
<td></td>
<td>Weight 30 to 65 kg: 10 g (2 packets) PO BID</td>
<td></td>
</tr>
</tbody>
</table>
L-glutamine

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight &lt; 30 kg</td>
<td>5 g (1 packet) PO BID</td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability
Oral powder: 5 g

VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td>08.22.17</td>
<td>11.17</td>
</tr>
<tr>
<td>No significant changes; per SDC, added Commercial line of business; added redirection to hydroxyurea.</td>
<td>04.12.18</td>
<td></td>
</tr>
<tr>
<td>4Q 2018 annual review: no significant changes added continued therapy approval duration for commercial; references reviewed and updated.</td>
<td>08.14.18</td>
<td>11.18</td>
</tr>
<tr>
<td>4Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>08.22.19</td>
<td>11.19</td>
</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.
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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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