Endari
Prior Authorization
Program Summary

This program applies to FocusRx and KeyRx.
The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.
Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dosage &amp; Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endari™ (L-glutamine) Oral powder</td>
<td>To reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older</td>
<td>Orally twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weight in Pounds</td>
</tr>
<tr>
<td>Less than 66</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>66-143</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Greater than 143</td>
<td></td>
<td>15</td>
</tr>
</tbody>
</table>

CLINICAL RATIONALE

Guidelines
Hydroxyurea is a mainstay in the management of sickle cell disease. It reduces the incidence of acute painful episodes and hospitalization rates, and prolongs survival.2,3

Efficacy
The efficacy of L-glutamine was evaluated in a randomized, double-blind, placebo controlled, multi-center clinical trial with 230 patients. Efficacy was demonstrated by a reduction in the number of sickle cell crises through Week 48 and prior to the start of tapering among patients that received L-glutamine compared to patients who received placebo. The recurrent crisis event time analysis yielded an intensity rate ratio (IRR) value of 0.75 with 95% CI= (0.62, 0.90) and (0.55, 1.01) based on unstratified models using the Andersen-Gill and Lin, Wei, Yang and Ying methods, respectively in favor of L-glutamine, suggesting that over the entire 48-week period, the average cumulative crisis count was reduced by 25% from the L-glutamine group over the placebo group.

Safety
L-glutamine carries no black box warnings or contraindications.

REFERENCES
Endari Prior Authorization

TARGET™ AGENT
Endari (L-glutamine)

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endari (L-glutamine)</td>
<td>82801020003020</td>
<td>M, N, O, Y</td>
</tr>
<tr>
<td>5 g packet</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Initial Evaluation

Target agent will be approved when ALL of the following are met:

1. The patient has a diagnosis of sickle cell disease
   AND
2. The patient is using the requested agent to reduce the acute complications of sickle cell disease
   AND
3. The patient is 5 years of age or over
   AND
4. ONE of the following
   a. The patient has tried and had an inadequate response to hydroxyurea
   OR
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to hydroxyurea
   AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
6. The requested quantity (dose) does not exceed the maximum FDA labeled dose

Length of Initial Approval: 12 months

Renewal Evaluation

Target agent will be approved when ALL of the following are met:

1. The patient has been previously approved through the Prime Therapeutics Prior Authorization process for the requested agent
   AND
2. The patient has had clinical benefit with the requested agent (i.e., reduction in acute complications of sickle cell disease since initiating therapy with the requested agent)
   AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
4. The requested quantity (dose) does not exceed the maximum FDA labeled dose

Length of Renewal 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