Pharmacy Policy Bulletin: J-0671 Endari (L-glutamine) – Commercial and Healthcare Reform	
Number: J-0671	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.)** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0671-012	**Original Date:** 12/08/2017
Effective Date: 12/20/2024	**Review Date:** 12/04/2024

Drugs Product(s):	• Endari (L-glutamine)
FDA-Approved Indication(s):	• To reduce the acute complications of sickle cell disease (SCD) in adults and pediatrics 5 years of age and older

Background:	• The mechanism of action of Endari in SCD is not completely understood. Endari is thought to increase the availability of reduced glutathione, which sickle red blood cells use to generate anti-oxidant molecules, resulting in regulation and prevention of oxidative damage in red blood cells. • SCD is a group of inherited red blood cell disorders. The red blood cells are C-shaped that are hard and sticky. The sickle cells die early causing a constant shortage of red blood cells. When the sickle cells travel through small blood vessels, they get stuck and clog blood flow and oxygen supply to the tissues causing pain, infection, acute chest syndrome and/or stroke. A vaso-occlusive crisis (VOC) is the hallmark acute complication for a person with SCD and manifests as acute severe pain most commonly in the extremities, chest, and back. Once a VOC occurs, vigorous IV hydration and analgesics are needed. • Acute complications of SCD include VOCs, fever, acute renal failure, priapism, hepatobiliary complications, acute anemia, splenic sequestration, acute chest syndrome (ACS), acute stroke, multisystem organ failure, and acute ocular conditions. • American Society of Hematology guidelines for sickle cell disease suggest that patients with ACS should be considered for transplantation when they have recurrent ACS despite optimal standard of care (hydroxyurea, L-glutamine, crizanlizumab, and chronic transfusion therapy). The guidelines also state that hydroxyurea, L-glutamine, and crizanlizumab reduce the rate of acute pain episodes. • Prescribing Considerations: ○ Endari may be given with or without hydroxyurea.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Endari (L-glutamine) may be approved when all of the following criteria are met **(A. through F.)**:

- **A.** The member is 5 years of age or older.
- **B.** The member has a diagnosis of SCD. (ICD-10: D57)
- **C.** The member has a history of at least two (2) sickle cell acute complications (e.g., VOCs, acute anemia, acute chest syndrome, etc.) within the previous 12 months.
- **D.** The member has experienced therapeutic failure or intolerance to one (1) over-the-counter L-glutamine product.
- **E.** The member meets one (1) of the following criteria **(1. or 2.)**:
  - **1.** The member has experienced therapeutic failure, contraindication, or intolerance to plan-preferred hydroxyurea.
  - **2.** The member is using Endari in addition to hydroxyurea.
- **F.** If the request is for brand Endari, the member has experienced therapeutic failure or intolerance to generic prescription L-glutamine.

II. Reauthorization

When a benefit, reauthorization of Endari (L-glutamine) may be approved when all of the following criteria are met **(A. and B.):**

- **A.** The prescriber attests that the member has experienced a therapeutic response defined as one (1) of the following **(1. or 2.)**:
  - **1.** Stability in sickle cell acute complications (e.g., VOCs, acute anemia, acute chest syndrome, etc.)
  - **2.** Decrease in the number of sickle cell acute complications (e.g., VOCs, acute anemia, acute chest syndrome, etc.)
- **B.** If the request is for brand Endari, the member has experienced therapeutic failure or intolerance to generic prescription L-glutamine.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indication should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Endari [package insert]. Torrance, CA: Emmaus Medical, Inc.; October 2020.
2. Niihara Y, Miller ST, Kanter J, et al. A Phase 3 Trial of l-Glutamine in Sickle Cell Disease. *N Engl J Med*. 2018;379(3):226-235.
3. National Heart, Lung, and Blood Institute. Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014. Available at: https://www.nhlbi.nih.gov/health-topics/evidence-based-management-sickle-cell-disease. Accessed October 7, 2024.
4. Kanter J, Liem RI, Bernaudin F, et al. American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation. *Blood Adv.* 2021;5(18):3668–3689.
5. Brandow AM, Carroll CP, Creary S, et al. American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain. *Blood Adv*. 2020;4(12):2656–2701.