MEDICAL MUTUAL®

Drug Policy

Policy:	Endari (L-glutamine oral powder)	Annual Review Date: 12/19/2024 Last Revised Date: 12/19/2024

OVERVIEW

Endari is indicated to reduce the acute complications of sickle cell disease (SCD) in adults and pediatric patients ≥ 5 years of age. L-glutamine is an essential amino acid and serves as a precursor of nucleic acids and nucleotides including the pyridine nucleotides (nicotinamide adenine dinucleotide [NAD] and reduced nicotinamide adenine dinucleotide [NADH]). These pyridine nucleotides play key roles in the regulation and prevention of oxidative damage in red blood cells (RBCs) and studies have shown that oxidative phenomena may play a significant role in the pathophysiology of SCD.

POLICY STATEMENT

This policy involves the use of Endari. Prior authorization is recommended for pharmacy benefit coverage of Endari. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Endari as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Endari be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Endari is recommended in those who meet the following criteria:

1. <u>Sickle Cell Disease (SCD)*</u>

Criteria. *Patient must meet the following criteria (A, B, C, D <u>and</u> E):*

A) The patient is ≥ 5 years of age; AND
B) Endari is prescribed by, or in consultation with, a physician who specializes in SCD (e.g., a hematologist); AND
C) Patient had an adequate trial of hydroxyurea unless the patient has a contraindication to hydroxyurea per the prescribing physician; AND
D) History of trial of non-prescription L-glutamine supplementation.
E) If brand Endari is being requested, the patient meets both of the following criteria (a and b):
a. Patient has tried generic L-glutamine; AND

b. Brand Endari is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

F) If patient is continuing therapy, provider attest to a positive response to therapy such as: decreased hospitalizations, decrease in sickle cell crisis, decrease in acute pain events, etc.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 365 days (1 year)
B) *Extended Approval:* 365 days (1 year)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Endari has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

***Documentation Requirements:**

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Endari™ oral powder [prescribing information]. Torrance CA: Emmaus Medical, Inc; July 2017.
2. FDA Briefing document, Oncologic Drugs Advisory Committee Meeting: L-glutamine. Available at: https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/OncologicDrugsAdvisoryCommittee/UCM559734.pdf. Accessed on October 16, 2017.
3. Piel FB, Steinberg MH. Sickle cell disease. *N Engl J Med*. 2017;376:1561-1573.
4. Azar S, Wong TE. Sickle cell disease – a brief update. *Med Clin North Am*. 2017;101:375-393.
5. glutamine. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 06 November 2019. Accessed on 19 November 2019.