Original Effective Date: 03/01/2018
Current Effective Date: 06/27/2024
Last P&T Approval/Version: 04/24/2024
Next Review Due By: 04/2025
Policy Number: C12651-A

Endari (L-glutamine) NC

PRODUCTS AFFECTED

Endari (L-glutamine oral powder)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Sickle Cell Disease

REQUIRED MEDICAL INFORMATION:
All uses of Endari (L-glutamine oral powder) are considered not medically necessary for all indications, including but not limited to Sickle Cell Disease (SCD), due to insufficient evidence of therapeutic value since long term clinical benefit has not been established. Data from one clinical trial in a small number of people with SCD demonstrated fewer events than placebo group, but efficacy and clinical benefit, including effect on SCD outcomes and organ complications, has not been established. No long term data is available. This coverage policy is subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

Molina Healthcare will continue to evaluate and update this policy as relevant clinical evidence becomes available to determine whether Endari (L-glutamine oral powder) provides the impact on health outcomes or patient management.
Generic prescription hydroxyurea or over-the-counter (OTC), commercially available or powder for pharmaceutical compounding, L-glutamine, are available and recommended based on the limited evidence of Endari as discussed below. (Please see benefits for applicable coverage)

CONTINUATION OF THERAPY:
NA

DURATION OF APPROVAL:
NA

PRESCRIBER REQUIREMENTS:
NA

AGE RESTRICTIONS:
NA

QUANTITY:
NA

PLACE OF ADMINISTRATION:
NA

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Amino Acids

FDA-APPROVED USES:
Indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years and older.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
NA

OTHER SPECIAL CONSIDERATIONS:
The use of Endari (L-glutamine oral powder) is not covered for all indications due to insufficient evidence to establish clinical effectiveness or superiority over standard L-glutamine dietary supplements. There is no high-quality evidence and no head-to-head studies from published clinical trials and peer-reviewed literature evaluating the clinical safety and efficacy of this pharmaceutical grade L-glutamine oral powder versus over-the-counter L-glutamine, which is separately available as

a nutritional supplement and widely available without a prescription at drugstores across the United States, although in much smaller doses than those the FDA recommends for sickle cell disease.

There is also limited evidence from published clinical trials and lack of data supporting the long-term benefits, side-effect profile, or risks associated with pharmaceutical grade L-glutamine (Endari) over the various L-glutamine dietary supplements. In addition, there is also no head-to-head studies with hydroxyurea, the only previous drug treatment available for the management of SCD. Hydroxyurea is the preferred agent in the treatment of SCD.

At this time, there are no guidelines relevant to L-glutamine (Endari) for SCD and no consensus from clinical experts to suggest that Endari is equivalent to or should replace hydroxyurea therapy. Currently, it may be considered as add-on therapy in patients ages 5 years and older who have at least two sickle cell crises a year, despite maximally tolerated hydroxyurea doses, or as monotherapy for patients unable to tolerate hydroxyurea.

Endari does not treat the underlying cause of SCD and has shown modest benefits in the reduction of sickle cell acute crisis (median 3 vs. median 4) and hospitalizations for sickle cell pain (median 2 vs. median 3). Furthermore, there are no head-to-head studies with hydroxyurea, the only previous drug treatment available for the management of SCD. At the present time, the role of Endari may be considered as add-on therapy since approximately two-thirds of the participants in both arms (63%) also had been receiving hydroxyurea on a stable dose for at least three months and continued hydroxyurea during the pivotal phase 3 trial therefore, L-glutamine should not replace hydroxyurea therapy at this time.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:

REFERENCES

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cell disease. Approved Drugs. July 7, 2017; Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approved-l-glutamine- powder-treatment-sickle-cell-disease Accessed January 2020.
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11. Brandow, A. M., Carroll, C. P., Creary, S., Edwards-Elliott, R., Glassberg, J., Hurley, R. W., . . . Lang, E. (2020). American Society of Hematology 2020 Guidelines for Sickle Cell Disease: Management of acute and chronic pain. Blood Advances, 4(12), 2656-2701. doi:10.1182/bloodadvances.2020001851
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SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q2 2024
REVISION- Notable Revisions: Required Medical Information Place of Administration Other Special Considerations References	Q2 2023
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file