Drug Coverage Policy

Effective Date.....5/1/2026
Coverage Policy Number IP0475
Policy Title.....L-glutamine for Individual and Family Plans

Sickle Cell Disease – L-glutamine for Individual and Family Plans

- Endari™ (L-glutamine oral powder – Emmaus Medical, generic)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW
L-glutamine oral powder, an amino acid, is indicated to **reduce the acute complications of sickle cell disease** in patients ≥ 5 years of age.[1]

L-glutamine is an essential amino acid and serves as a precursor of nucleic acids and nucleotides including the pyridine nucleotides (nicotinamide adenine dinucleotide and reduced nicotinamide adenine dinucleotide).[1,2] These pyridine nucleotides play key roles in the regulation and prevention of oxidative damage in red blood cells and studies have shown that oxidative phenomena may play a significant role in the pathophysiology of sickle cell disease.

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POLICY STATEMENT
Prior Authorization is required for benefit coverage of L-glutamine oral powder. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with L-glutamine oral powder as well as the monitoring required for adverse events and long-term efficacy, approval requires L-glutamine oral powder to be prescribed by or in consultation with a physician who specializes in the condition being treated.

L-glutamine oral powder is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Sickle Cell Disease.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 5 years of age; AND
   B) The medication is prescribed by or in consultation with a physician who specializes in sickle cell disease (e.g., a hematologist).
   C) Preferred product criteria are met for the product(s) as listed in the below table.

Individual and Family Plans:

Product	Criteria
Endari (L-glutamine oral powder)	The patient has tried the bioequivalent generic product, L-glutamine oral powder **[may require prior authorization]** AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which would result , per the prescriber, in a significant allergy or serious adverse reaction.

Conditions Not Covered

L-glutamine oral powder for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Endari™ oral powder [prescribing information]. Torrance CA: Emmaus Medical; June 2025.
2. 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;4:2656-2701.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** coverage policy title from *L-glutamine Oral Powder for Individual and Family Plans* to *Sickle Cell Disease – Endari for Individual and Family Plans.* **Added** *Preferred Product Criterion* for *the patient who is not a candidate for a hydroxyurea product.*	7/1/2024
Selected Revision	Generic L-glutamine oral powder was added to the policy. Policy name was changed from Sickle Cell Disease – Endari to Sickle Cell Disease – L-glutamine.	2/15/2025
Annual Revision	No criteria changes.	4/15/2025
Selected Revision	**Updated** Preferred Product Table for Individual and Family Plans **from** requiring a trial of hydroxyurea or Droxia **to** requiring a trial of the generic product.	1/1/2026
Annual Revision	No criteria changes.	5/1/2026

The policy effective date is in force until updated or retired.