Drug Coverage Policy

Effective Date.....7/15/2024
Coverage Policy Number.....IP0475
Policy Title.....Endari for Individual and Family Plans

Sickle Cell Disease – Endari for Individual and Family Plans

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

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 and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

OVERVIEW
Endari 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.

Guidelines
The American Society of Hematology guidelines for sickle cell disease: management of acute and chronic pain associated with sickle cell disease (2020) does address Endari's place in therapy.[2] The National Institutes of Health – National Heart, Lung, and Blood Institute issued the Evidence-Based Management of Sickle Cell Disease, Expert Panel Report in 2014.[3] The use of L-glutamine products in sickle cell disease is not mentioned (guidelines were published before the approval of Endari). Hydroxyurea has been shown to reduce the frequency of painful episodes, the incidence of acute coronary syndrome events, and the need for transfusions and hospitalizations.

Medical Necessity Criteria

Endari 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 the following criteria (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 is met for the product(s) as listed in the below table.

Individual and Family Plans:

Product	Criteria
Endari (L-glutamine oral powder)	**ONE** of the following: 1. Failure, contraindication, or intolerance to **ONE** of the following: a. hydroxyurea b. Droxia 2. According to the prescriber, the patient is not a candidate for a hydroxyurea product (e.g., a patient who is planning to become pregnant; a pregnant patient; or a patient with an immunosuppressive condition [such as cancer])

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

References

1. Endari™ oral powder [prescribing information]. Torrance CA: Emmaus Medical; October 2020.
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.
3. The National Institutes of Health – National Heart, Lung, and Blood Institute Evidence-Based Management of Sickle Cell Disease, Expert Panel Report 2014. Available at: https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf. Accessed on December 5, 2023.

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

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