Effective Date **1/1/2023**
Next Review Date… **1/1/2024**
Coverage Policy Number **IP0475**

L-glutamine Oral Powder for Individual and Family Plans

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Related Coverage Resources

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. 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

This policy supports medical necessity review for L-glutamine oral powder, 5 gram packet (Endari™) for Individual and Family Plans.

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

Medical Necessity Criteria

L-glutamine (Endari) is considered medically necessary when the following are met:

1. **Sickle Cell Disease.** Individual meets **ALL** of the following criteria (A, B, and C):
   A. Individual is 5 years of age or older
   B. The medication is prescribed by or in consultation with a physician who specializes in sickle cell disease (e.g., a hematologist).

C. Individual meets the preferred covered alternative(s) criteria as indicated in the table below

Coverage varies across plans and requires the use of preferred products. Refer to the customer's benefit plan document for coverage details.

Individual and Family Plan Non-Covered Products and Covered Alternative(s):

Non-Covered Product	Criteria
Endari (L-glutamine oral powder, 5 gram packet)	The individual has had an inadequate response, contraindication, or is intolerant to **ONE** of the following: A. Hydroxyurea B. Droxia

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.

Reauthorization Criteria

L-glutamine (Endari) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

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.

Disease Overview
Sickle cell disease, a multisystem disorder, is the most common condition caused by a single gene mutation.[3] In the US, population estimates suggest that a total of 100,000 persons have the disease. Approximately 300,000 babies are born with sickle cell anemia each year and it is estimated that the number could be as high as 400,000 by 2050.

Sickle cell disease is characterized by the presence of abnormal erythrocytes damaged by the sickle hemoglobin gene – this variant of the normal adult hemoglobin can be inherited from both parents or from one parent along with another variant, such as hemoglobin C or with β-thalassemia.[3] Complications of sickle cell disease include vaso-occlusion (which can result in pain and organ failure), hemolytic anemia, and large-vessel vasculopathy

(cerebrovascular disease, pulmonary hypertension, ischemic organ damage, hyposplenism, renal failure, bone disease, liver failure).

Guidelines
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.[4] 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.

References

1. Endari™ oral powder [prescribing information]. Torrance CA: Emmaus Medical; October 2020.
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 November 19, 2021.
3. Piel FB, Steinberg MH. Sickle cell disease. *N Engl J Med*. 2017;376:1561-1573.
4. 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 November 19, 2021.