



PREFERRED SPECIALTY MANAGEMENT POLICY

POLICY: Sickle Cell Disease – L-glutamine Preferred Specialty Management Policy

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

REVIEW DATE: 08/20/2025 effective 10/01/2025

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 ACCCOMPANIED 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.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

L-glutamine oral powder, an amino acid, is indicated to **reduce the acute complications of sickle cell disease** in patients \geq 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. Studies have shown that oxidative phenomena may play a significant role in the pathophysiology of sickle cell disease.

POLICY STATEMENT

This Preferred Specialty Management program has been developed to encourage the use of a Preferred Product. For all medications (Preferred and Non-Preferred), the patient is required to meet the respective standard *Prior Authorization Policy* criteria. The program also directs the patient to try one Preferred Product prior to the approval of a Non-Preferred Product. Requests for the Non-Preferred Product will also be reviewed using the exception criteria (below). If the patient meets the standard *Sickle Cell Disease – L-glutamine Prior Authorization Policy* criteria but has not tried a Preferred Product, approval for a Preferred Product will be authorized. All approvals are provided for 1 year in duration.

Documentation: Documentation will be required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, and prescription receipts.

Preferred Product: generic L-glutamine oral powder
Non-Preferred Product: Endari oral powder (brand)

Sickle Cell Disease – L-glutamine Preferred Specialty Management Policy non-preferred product(s) is(are) covered as medically necessary when the following non-preferred product exception criteria is(are) met. Any other exception is considered not medically necessary.

NON-PREFERRED PRODUCT EXCEPTION CRITERIA

Non-Preferred Product	Exception Criteria
Endari	<ol style="list-style-type: none">1. Approve for 1 year if the patient meets ALL of the following (A, B, <u>and</u> C):<ol style="list-style-type: none">A) Patient meets the standard <i>Sickle Cell Disease – L-glutamine Prior Authorization Policy</i> criteria; ANDB) Patient has tried generic L-glutamine oral powder [documentation required]; ANDC) Patient cannot continue to use the generic L-glutamine oral powder due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand and bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction [documentation required].2. If the patient has met the standard <i>Sickle Cell Disease – L-glutamine Prior Authorization Policy</i> criteria (1A), but has <u>not</u> met exception criteria (1B) and/or (1C) above for brand Endari: approve generic L-glutamine oral powder.

REFERENCES

1. Endari™ oral powder [prescribing information]. Torrance CA: Emmaus Medical; October 2020.

3 Pages - Cigna National Formulary Coverage - Policy:Sickle Cell Disease – L-glutamine Preferred Specialty Management Policy

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	Effective 10/01/2025	08/20/2025

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