



Louisiana

L-Glutamine (Endari™)

Policy # 00604

Original Effective Date: 05/16/2018

Current Effective Date: 05/16/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider L-glutamine (Endari™)† for the treatment of sickle cell disease to be **eligible for coverage**.

Patient Selection Criteria

Coverage eligibility for L-glutamine (Endari) will be considered when all of the following criteria are met:

- Patient is 5 years of age or older; AND
- Patient has a diagnosis of sickle cell disease; AND
- Patient has had at least 2 documented episodes of sickle cell crisis within the previous 12 months; AND
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient is currently adherent to daily hydroxyurea therapy or has a contraindication to the use of hydroxyurea.
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of L-glutamine (Endari) when the patient has not had at least 2 documented episodes of sickle cell crisis in the previous year or when the patient is not adherent to daily hydroxyurea therapy to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of L-glutamine (Endari) when the patient is younger than 5 years of age or does not have a diagnosis of sickle cell disease to be **investigational.***

Background/Overview

Endari contains the amino acid L-glutamine which is theorized to reduce the acute complications of sickle cell disease by protecting sickled red blood cells from oxidative damage. It should be administered twice

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daily at a dose based on patient's weight as indicated in the package insert. Each 5 gram powder packet should be dissolved in 8 ounces of cold or room temperature beverage or food prior to administration.

Sickle Cell Disease

Sickle cell disease is a group of inherited red blood cell disorders in which the hemoglobin is abnormal and leads to "sickling" of the red blood cells. This reduces the ability of the blood to transport oxygen to the body and can result in blocked blood vessels and tissue ischemia which manifest as various complications. Complications of sickle cell disease include acute vaso-occlusive crises, severe anemia, splenic sequestration, acute chest syndrome, stroke, retinal damage, priapism, joint problems, and others. Patients with sickle cell disease have a shorter life expectancy than race-matched peers and often have a low quality of life due to frequent crises. The only other drug currently approved to prevent painful crises in sickle cell disease is hydroxyurea (Droxia®)†. The 2014 National Institutes of Health- National Heart, Lung, and Blood Institute Evidence-based management of sickle cell disease guidelines recommend hydroxyurea therapy in adult patients with three or more sickle cell-associated moderate to severe pain crises in a 12-month period, who have sickle-cell associated pain that interferes with daily activities and quality of life, who have severe and/or recurrent acute chest syndrome, or who have severe symptomatic chronic anemia. The guidelines also recommend hydroxyurea for infants ≥ 9 months of age, children, and adolescents with sickle cell anemia to reduce complications.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Endari was approved in July 2017 to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Efficacy of Endari in sickle cell disease was evaluated in a randomized, double-blind, placebo-controlled, multi-center clinical trial which included 230 patients with sickle cell anemia who had 2 or more painful crises within 12 months prior to enrollment. Patients who had been stabilized on hydroxyurea for at least 3 months continued their therapy throughout the study. Study patients received Endari or placebo for a treatment duration of 48 weeks followed by 3 weeks of tapering.

Efficacy was demonstrated by a reduction in the number of sickle cell crises through week 48 and prior to the start of tapering among patients that received Endari compared to patients who received placebo. A sickle cell crisis was defined as a visit to an emergency room/medical facility for sickle cell disease-related pain which was treated with a parenterally administered narcotic or ketorolac. In addition, the occurrence of

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chest syndrome, priapism, and splenic sequestration were considered sickle cell crises. Treatment with Endari resulted in fewer hospitalizations due to sickle cell pain at week 48 (median of 2 vs 3 for placebo), fewer cumulative days in the hospital (median 6.5 vs 11), and a lower incidence of acute chest syndrome (8.6% vs 23.1%).

References

1. Endari oral powder [package insert]. Torrance CA. Emmaus Medical, Inc. July 2017.
2. The National Institutes of Health—National Heart, Lung, and Blood Institute Evidence-Based Management of Sickle Cell Disease, Expert Panel Report 2014. Available at: <http://www.nhlbi.nih.gov/health-topics/evidence-based-managment-sickle-cell-disease>. Accessed January 2, 2018.

Policy History

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Current Effective Date: 05/16/2018

05/03/2018 Medical Policy Committee review

05/16/2018 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 05/2019

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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