Medical Policy

BlueCross BlueShield of Kansas
An independent licensee of the Blue Cross Blue Shield Association

Title: Endari™ (L-glutamine)

- **Prime Therapeutics will review Prior Authorization requests**
  Prior Authorization Form:
  https://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6595KS-ENDA.pdf

  Link to Drug List (Formulary):
  https://www.bcbsks.com/drugs/

Professional
Original Effective Date: April 1, 2018
Revision Date(s): April 1, 2018; September 1, 2018
Current Effective Date: September 1, 2018

Institutional
Original Effective Date: April 1, 2018
Revision Date(s): April 1, 2018; September 1, 2018
Current Effective Date: September 1, 2018

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the Endari Prior Authorization is to encourage appropriate selection of patients for treatment and dosing according to product labeling, and/or clinical studies, and/or guidelines. The program will not allow approval for patients who have an FDA labeled contraindication to the requested agent. Requests will be reviewed when patient specific documentation is provided.

Target Agent

Endari™ (L-glutamine)

FDA Approved Indications and Dosage[1]

Agent	Indication	Dosage & Administration				
		Weight in Pounds	Per dose in grams	Per day in grams	Packets per dose	Packets per day
Endari™ (L-glutamine)	To reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older	Less than 66	5	10	1	2
		66-143	10	20	2	4
		Greater than 143	15	30	3	6

POLICY

Initial Evaluation

Endari will be approved when ALL of the following are met:

1. The patient has a diagnosis of sickle cell disease
   AND
2. The patient is using the requested agent to reduce the acute complications of sickle cell disease
   AND
3. The patient is 5 years of age or greater
   AND
4. ONE of the following
   a. The patient has tried and received inadequate response to therapy with hydroxyurea therapy
      OR
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to hydroxyurea
   AND
5. The patient does NOT have any FDA labeled contraindication(s) to the requested agent
   AND
6. The requested dose is within the FDA labeled dose

Length of Initial Approval: 12 months

Renewal Evaluation

1. The patient has been previously approved through the Prime Therapeutics prior authorization process for the requested agent
   AND
2. The prescriber has indicated that the patient has seen a reduction in acute complications of sickle cell disease since initiating therapy with Endari
   AND
3. The patient does NOT have any FDA labeled contraindication(s) to the requested agent
   AND
4. The requested dose is within the FDA labeled dose

Length of Renewal Approval: 12 months

Contraindications	
Endari	None

RATIONALE

Guidelines

Hydroxyurea is a mainstay in the management of sickle cell disease. It reduces the incidence of acute painful episodes and hospitalization rates, and prolongs survival.[2,3]

Efficacy[1]

The efficacy of L-glutamine was evaluated in a randomized, double-blind, placebo controlled, multi-center clinical trial with 230 patients. 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 L-glutamine compared to patients who received placebo. The recurrent crisis event time analysis yielded an intensity rate ratio (IRR) value of 0.75 with 95% CI= (0.62, 0.90) and (0.55, 1.01) based on unstratified models using the Andersen-Gill and Lin, Wei, Yang and Ying methods, respectively in favor of L-glutamine, suggesting that over the entire 48- week period, the average cumulative crisis count was reduced by 25% from the L-glutamine group over the placebo group.

Safety[1]

L-glutamine carries no black box warnings or contraindications.

REVISIONS	
04-01-2018	Policy added to the bcbsks.com web site.
09-01-2018	In Policy section: ▪ In Initial Evaluation Item 6 and Renewal Evaluation Item 4 removed quantity limit check and allowance for requests to go above FDA dosing

REVISIONS	
	"The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)"

REFERENCES

1. Endari prescribing information. Emmaus Medical, Inc. July 2017.
2. Overview of the management and prognosis of sickle cell disease. UpToDate. Literature review current through 10/2017. Last updated 10/23/2017. Accessed 11/30/2017
3. Evidence-based management of sickle cell disease; expert panel report 2014. National Heart, Lung, Blood Institute. Available at https://www.nhlbi.nih.gov/health-pro/guidelines/sickle-cell-disease-guidelines