Clinical Policy Title:	l-glutamine
Policy Number:	RxA.366
Drug(s) Applied:	Endari®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

L-glutamine (Endari®) is an amino acid indicated to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
l-glutamine (Endari®)	Sickle cell disease	Weight > 65 kg: 15 g (3 packets) orally twice daily Weight 30 to 65 kg: 10 g (2 packets) orally twice daily Weight < 30 kg: 5 g (1 packet) orally twice daily	30 g/day (maximum dose based on weight)

Dosage Forms

- Oral powder: 5 g

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Sickle Cell Disease (must meet all)**:**

1. Diagnosis of sickle cell disease;
2. Age ≥ 5 years;
3. Failure of hydroxyurea at up to maximally tolerated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 30 grams per day based on weight.

Approval duration

Commercial: 12 months

Medicaid: 12 months

II. Continued Therapy Approval

A. Sickle Cell Disease (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 30 grams per day based on weight.

Approval duration

Commercial: 12 months

Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
SCD: Sickle Cell Disease
RBC: Red Blood Cell
NAD: Nicotinamide Adenine Dinucleotide
NADH: Nicotinamide Adenine Dinucleotide Hydrogen

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Hydroxyurea (Droxia))	15 mg/kg PO once daily	35 mg/kg/day

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Oxidative stress phenomena are involved in the pathophysiology of SCD. Sickle red blood cells (RBCs) are more susceptible to oxidative damage than normal RBCs, which may contribute to the chronic hemolysis and vaso-occlusive events associated with SCD. The pyridine nucleotides, NAD+ and its reduced form NADH, play roles in regulating and preventing oxidative damage in RBCs. L-glutamine may improve the NAD redox potential in sickle RBCs through increasing the availability of reduced glutathione.

References

1. Endari® Prescribing Information. Torrance, CA: Emmaus Medical Inc; October 2020. Available at: https://www.endarirx.com/pi . Accessed May 31, 2021.
2. Droxia Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; February 2021 Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=740e054b-faac-7c27-f06d-a56efb699355&type=display . Accessed May 31, 2021.

3. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA 2014;312(10):1033-48.
4. U.S. Department of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute. The Management of Sickle Cell Disease (NIH Publication No. 02-2117). (2002). Retrieved from https://www.nhlbi.nih.gov/files/docs/guidelines/sc_mngt.pdf.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Continued Therapy Approval Criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 3. References were updated.	07/12/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…" 3. Appendix A was updated to include abbreviations SCD, RBC, NAD, NADH. 4. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 5. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic	05/31/2021	09/14/2021

only". 6. Appendix B was updated to remove Hydrea. 7. Appendix D was updated to include “Oxidative stress phenomena are involved in the pathophysiology of SCD…” 8. References were reviewed and updated.		