Pharmacy Policy Bulletin

Title: Sickle Cell Disease Agents

Policy #: Rx.01.206

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for L-glutamine (Endari®) and voxelotor (Oxbryta®) as provided under the member's prescription drug benefit.

Description:

Sickle cell disease (SCD) is caused by a point mutation in the beta-globin gene, resulting in defective hemoglobin, which is less soluble than normal fetal or adult hemoglobin. The red blood cells become sickled in shape causing hemolytic anemia and vaso-occlusion, which can lead to acute and chronic pain, and tissue ischemia. SCD refers to any of the syndromes in which the sickle mutation is co-inherited with a mutation at the other beta globin allele that reduces normal beta globin production. It includes sickle cell anemia, sickle beta thalassemia, and hemoglobin sickle cell disease.

Endari® is an amino acid indicated to reduce the acute complications of sickle cell disease in adults and pediatric patients 5 years of age and older.

The mechanism of action of the amino acid L-glutamine in treating sickle cell disease (SCD) is not fully understood. 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.

Voxelotor (Oxbryta®) is a hemoglobin S polymerization inhibitor that binds to HbS with a 1:1 stoichiometry and exhibits preferential partitioning to red blood cells (RBCs). By increasing the affinity of Hb for oxygen, voxelotor demonstrates dose-dependent inhibition of HbS polymerization. Nonclinical studies suggest that voxelotor may inhibit RBC sickling, improve RBC deformability, and reduce whole blood viscosity. Oxbryta® is indicated for the treatment of sickle cell disease in adults and pediatric patients 12 years of age and older.

Policy:

INITIAL CRITERIA L-glutamine (Endari®) is approved when ALL of the following are met:

1. Diagnosis of sickle cell disease; and
2. Member is 5 years of age or older; and
3. Member has had 2 or more painful sickle cell crises within the past 12 months; and
4. Prescribed by or in consultation with a hematologist/oncologist, and
5. Documentation of ONE of the following:
   a. Concurrent hydroxyurea therapy; or
   b. Inadequate response or inability to tolerate hydroxyurea

Initial authorization duration: 12 months

CONTINUATION CRITERIA L-glutamine (Endari®) is re-approved when there is documentation of positive clinical response to therapy from baseline (e.g., reduction in the number of sickle cell crises, fewer hospitalizations due to sickle cell pain, etc.).

Continuation authorization duration: 2 years

INITIAL CRITERIA Voxelotor (Oxbryta®) is approved when ALL of the following are met:

1. Diagnosis of sickle cell disease; and
2. No concurrent therapy with crizanlizumab-tmca (Adakveo®); and
3. Member is 12 years of age or older; and
4. Member had at least one vaso-occlusive crisis (VOC) event within the past 12 months (e.g., acute painful crisis, acute chest syndrome); and
5. Hemoglobin level that is between 5.5g/dL and 10.5g/dL prior to therapy initiation; and
6. Inadequate response or inability to tolerate hydroxyurea (i.e. Siklos, Droxia); and
7. Prescribed by or in consultation with a hematologist/oncologist.

Initial authorization duration: 12 months

CONTINUATION CRITERIA Voxelotor (Oxbryta®) is re-approved when there is documentation of positive clinical response to Oxbryta® therapy (e.g., an increase in hemoglobin level of greater than or equal to 1 g/dL from baseline, decreased annualized incidence rate of VOCs)

Continuation authorization duration: 2 years

Black Box Warning as shown in the drug Prescribing Information:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Endari® (L-glutamine oral powder) [prescribing information]. Torrance, CA: Emmaus Medical, Inc.; July 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208587s000lbl.pdf. Accessed September 30, 2021.

Oxbryta® (voxelotor) [prescribing information]. South San Francisco, CA: Global Blood Therapeutics, Inc., November 2019. Available at: https://hcp.oxbryta.com/pdf/prescribing-information.pdf. Accessed September 30, 2021.

Vichinsky Elliott P. Overview of the clinical manifestations of sickle cell disease. UpToDate. Accessed September 30, 2021.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Endari®	L-glutamine
Oxbryta®	Voxelotor

Cross References:

Off-Label Use Rx.01.33

Policy Version Number:	5.00
P&T Approval Date:	September 23, 2021
Policy Effective Date:	January 01, 2022
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