Original Effective Date: 01/09/2020
Current Effective Date: 09/01/2024
Last P&T Approval/Version: 07/31/2024
Next Review Due By: 07/2025
Policy Number: C17965-A

Oxbryta (voxelotor)

PRODUCTS AFFECTED

Oxbryta (voxelotor)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Sickle Cell Disease

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. SICKLE CELL DISEASE:
1. Documented diagnosis of sickle cell disease with one of the following genotypes: Homozygous hemoglobin S, Hemoglobin Sβ0-thalassemia, Hemoglobin Sβ+-thalassemia or Hemoglobin SC
   AND
2. Documentation member has had at least 1 episode of vaso-occlusive crisis (VOC)

in the past 12 months
AND

3. Member is concurrently receiving hydroxyurea OR has a labeled contraindication** or serious side effects to hydroxyurea
   *** NOTE: *Myelosuppression and hydroxyurea treatment failure: Myelosuppression is dose-dependent and reversible and does not qualify for treatment failure. NIH guidelines recommend a 6-month trial on the maximum tolerated dose prior to considering discontinuation due to treatment failure, whether due to lack of adherence or failure to respond to therapy. A lack of increase in mean corpuscular volume (MCV) and/or fetal hemoglobin (HbF) levels is not indication to discontinue therapy.*
   AND
4. Documentation of member specific treatment goals, which include monitoring parameters and metric that will be used to determine efficacy (e.g., documentation of hemoglobin level, baseline value of number/severity of vaso occlusive crisis per 3 months) [DOCUMENTATION REQUIRED]

CONTINUATION OF THERAPY:

A. SICKLE CELL DISEASE:

1. Documentation that member has made progress or has met the treatment goals established prior to the beginning of therapy (e.g., an increase in Hb level from baseline of at least 1 g/dL, decrease in frequency/severity of vaso-occlusive crisis) [DOCUMENTATION REQUIRED]
   AND
2. Documentation member has been adherent to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
4. Prescriber attests Oxbryta continues to be prescribed concurrently with hydroxyurea, unless contraindicated or clinically significant adverse effects are experienced

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified hematologist or physician specializing in the treatment of Sickle Cell Disease (SCD). [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

4 years of age and older

QUANTITY:

12 years of age and older: 1,500mg (three tablets) taken once a day
4 years to less than 12 years:
10kg to less than 20kg: 600mg per day,
20kg to less than 40kg: 900 mg per day,
40 kg or greater: 1,500mg per day

Maximum Quantity Limits –

12 years of age and older: 2500mg daily if taken with strong CYP3A4 inducer; 2000mg daily if taken with a moderate CYP3A4 inducer
4 years to less than 12 years:

10kg to less than 20kg: 900mg daily if taken with strong CYP3A4 inducer; 900mg daily if taken with a moderate CYP3A4 inducer
20kg to less than 40kg: 1500mg daily if taken with strong CYP3A4 inducer; 1200mg daily if taken with a moderate CYP3A4 inducer
40kg or greater: 2500mg daily if taken with strong CYP3A4 inducer; 2100mg daily if taken with a moderate CYP3A4 inducer

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:
Hemoglobin S (HbS) Polymerization Inhibitor

FDA-APPROVED USES:
Indicated for the treatment of sickle cell disease in adults and pediatric patients 4 years of age and older
This indication is approved under accelerated approval based on increase in hemoglobin (Hb). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Oxbryta was evaluated for SCD in the randomized, double-blind, placebo-controlled, multicenter Hemoglobin Oxygen Affinity Modulation (HOPE) trial (NCT03036813). In this study, 274 patients were randomized to daily oral administration of Oxbryta 1,500 mg (N=90), Oxbryta 900 mg (N=92), or placebo (N=92). Patients were included if they had from 1 to 10 VOC events within 12 months prior to enrollment and baseline hemoglobin ≥5.5 to ≤10.5 g/dL. Eligible patients taking stable doses of hydroxyurea for at least 90 days could continue hydroxyurea therapy throughout the study.

Randomization was stratified by patients already receiving hydroxyurea (yes, no), geographic region (North America, Europe, other), and age (12 to <17 years, 18-65 years). The trial excluded patients who received RBC transfusions within 60 days and erythropoietin within 28 days of enrollment, had renal insufficiency or uncontrolled liver disease, or were pregnant or lactating.

The majority of patients had HbSS or HbS/β-thalassemia genotype (90%) and were receiving background hydroxyurea therapy (65%). The median age was 24 years (range: 12 to 64 years); 46 (17%) patients were 12 to < 17 years of age, and 42% were male. Median baseline Hb was 8.5 g/dL (5.9 to 10.8 g/dL). Forty- two percent (n=115) of patients had 1 VOC event and 58% (n=159 had 2 to 10 events within 12 months prior to enrollment. Rates of hydroxyurea use by study arm were 58% (1,500 mg), 63% (900 mg),

and 58% (placebo).

Efficacy was based on Hb response rate defined as a Hb increase of >1 g/dL from baseline to Week 24 in patients treated with Oxbryta 1,500 mg versus placebo. The response rate for Oxbryta 1,500 mg was 51.1% (46/90) compared to 6.5% (6/92) in the placebo group (p<0.001). No outlier subgroups were observed.

Significant improvements were also seen in measures of hemolysis. There was a 29.1% reduction in indirect bilirubin in the Oxbryta 1,500 mg group and a 20.3% reduction in the 900 mg group, versus a reduction of only 3.2% in the placebo group. In addition, the reduction in reticulocytes was most notable in the 1,500 mg group (-19.9%), versus a reduction of 1.3% in the 900 mg group and an increase of 4.5% in the placebo group.

Oxbryta and VOCs the number of VOCs per person per year was 2.77 in the 1,500 mg Oxbryta group, 2.76 in the 900 mg Oxbryta group, and 3.19 in the placebo group. For patients who had had at least two crises in the past year, the incidence rate was 2.88 in the 1,500 mg group, 3.39 in the 900 mg group, and 3.5 in the placebo group. Compared to placebo, Oxbryta decreased the frequency of VOCs by less than 1 per year, which is not deemed statistically significant.
Oxbryta and RBC Transfusion The percentage of patients who underwent RBC transfusions during the study were similar in all three groups; 33% in the 1,500 mg Oxbryta group, 32% in the 900 mg Oxbryta group, and 25% in the placebo group. Most transfusions were performed due to acute VOCs.

Adverse Reactions There were no significant differences in adverse reactions between the Oxbryta and placebo groups. The most common adverse reactions, occurring in 10% or more of patients, were headache and diarrhea. The rates of grade 3 or higher adverse reactions and discontinuations were similar among the groups. Serious adverse reactions occurred in 3% (3/88) of patients receiving Oxbryta 1,500 mg, which included headache, drug hypersensitivity, and pulmonary embolism occurring in 1 member each. Permanent discontinuation due to an adverse reaction (Grades 1-4) occurred in 5% (4/88) of patients who received Oxbryta 1,500 mg. Dosage modifications (dose reduction or dosing interruption) due to an adverse reaction occurred in 41% (36/88) of patients who received Oxbryta. Most frequent adverse reactions requiring dosage interruption occurring in more than one member who received Oxbryta 1,500 mg included diarrhea, headache, rash, and vomiting. The safety profiles observed in pediatric patients 12 to 17 years of age were similar to those seen in adult patients.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Oxbryta (voxelotor) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Oxbryta (voxelotor) include: prior drug hypersensitivity to voxelotor or excipients (generalized rash, urticaria, mild shortness of breath, mild facial swelling, and eosinophilia).

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Oxbryta TABS 300MG, 500MG
Oxbryta TBSO 300MG

REFERENCES

1. Oxbryta (voxelotor) [prescribing information]. South San Francisco, CA: Global Blood Therapeutics Inc; August 2023.
2. Vichinsky E, Hoppe CC, Ataga KI, et al; HOPE Trial Investigators. A phase 3 randomized trial of voxelotor in sickle cell disease. N Engl Med. 2019;381(6):509-519.doi: 10.1056/NEJMoa1903212
3. Metcalf B, Chuang C, Dufu K, Patel MP, Silva-Garcia A, Johnson C, Lu Q, Partridge JR, Patskovska L, Patskovsky Y, Almo SC, Jacobson MP, Hua L, Xu Q, Gwaltney SL 2nd, Yee C, Harris J, Morgan BP, James J, Xu D, Hutchaleelaha A, Paulvannan K, Oksenberg D, Li Z. Discovery of GBT440, an Orally Bioavailable R-State Stabilizer of Sickle Cell Hemoglobin. ACSMed Chem Lett. 2017 Jan 23;8(3):321-326. doi: 10.1021/acsmedchemlett.6b00491. eCollection2017 Mar 9.
4. Sickle Cell Disease Clinical Guidelines | CDC. (2020). Retrieved 2 January 2020, from https://www.cdc.gov/ncbddd/sicklecell/recommendations.html

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information FDA-Approved Uses References	Q3 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity Drug Class FDA-Approved Uses Contraindications/Exclusions/Discontinuation References	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Quantity Available Dosage Form	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file