voxelotor (Oxbryta™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO171

Split Fill Management*

Description

Voxelotor (Oxbryta) is an orally administered hemoglobin S (HbS) polymerization inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit	
voxelotor (Oxbryta)	Sickle Cell Disease	500 mg tablets	90 tablets/30 days	
		300 mg soluble tablet	10 - <20 kg	60 tablets/30 days
			20 - <40 kg	90 tablets/30 days
			≥40 kg	150 tablets/30 days

Initial Evaluation

I. **Voxelotor (Oxbryta)** may be considered medically necessary when the following criteria are met:
   A. Member is 4 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a hematologist; **AND**
   C. Medication will not be used in combination with crizanlizumab-tmca (Adakveo); **AND**
   D. A diagnosis of **sickle cell disease (SCD)** when the following are met:
      1. Baseline hemoglobin level is ≤ 10.5 g/dL; **AND**
      2. Treatment with both the following have been ineffective, contraindicated, or both are not tolerated:
         i. Hydroxyurea (generic, Siklos, Droxia) for a minimum duration of six months; **AND**
         ii. L-glutamine (available over-the-counter); **AND**
      3. If requesting soluble tablets, member must demonstrate a medical reason they are unable to utilize oral tablets (e.g., weight, difficulty swallowing, oral/motor difficulties, feeding tube administration). Convenience of administration route does not equate to medical necessity

II. Voxelotor (Oxbryta) is considered investigational when used for all other conditions, AND when used in combination with crizanlizumab-tmca (Adakveo).

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy established through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Use of voxelotor (Oxbryta) is **not** in combination with crizanlizumab-tmca (Adakveo); **AND**
IV. Member has exhibited improvement or stability of disease symptoms (e.g., reduced vaso-occlusive crises (VOCs) compared to baseline, increase in hemoglobin levels, maintained increased hemoglobin levels); **AND**
V. If requesting soluble tablets, the member must demonstrate a medical reason they are unable to utilize oral tablets (e.g., weight, difficulty swallowing, oral/motor difficulties, feeding tube administration)

Supporting Evidence

I. Approval for voxelotor (Oxbryta) occurred following the phase 3 pivotal HOPE trial (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS Polymerization). Subjects were between 12 to 65 years of age with confirmed sickle cell disease with documentation of one to 10 vaso-occlusive events within the past 12 months and baseline hemoglobin levels between 5.5 and 10.5 g/dL. Efficacy was based on hemoglobin response rate defined as a hemoglobin increase of >1 g/dL from baseline. The trial reported a response rate of 51.1% (46/90) compared to 6.5% (6/92) in the placebo group ($p < 0.001$).
II. The efficacy in younger pediatric patients was evaluated in the single arm, open label, HOPE-KIDS 1 trial which included patients aged 4 to <12 years old. Patients in the HOPE-KIDS 1 trial had a baseline hemoglobin ≤10.5 g/dL and 80% were on background hydroxyurea therapy. Previous vaso-occlusive event was not required. Similar to the HOPE trial, the primary outcome in HOPE-KIDS 1 was hemoglobin response rate, which was reported as 36% (16/45) (95% CI: 21.6%, 49.5%).
III. Voxelotor (Oxbryta) was approved under accelerated approval based on increase in hemoglobin. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial. There are no data to support an increase in hemoglobin level results in a reduction in vaso-occlusive events, or other complications related to sickle cell disease. Hemoglobin represents one of many factors contributing to vaso-occlusive events. Voxelotor (Oxbryta) approval was based on increase in hemoglobin and all patients included in trials had hemoglobin levels ≤10.5 g/dL, clinical necessity of voxelotor (Oxbryta) in patients with hemoglobin levels >10.5 g/dL is unknown. Per the American Society of Hematology (ASH), for

patients with sickle cell disease receiving simple transfusions, the point of diminishing benefit of arterial oxygen delivery is estimated to be between 10 and 11 g/dL; beyond this point any increase in hemoglobin concentration decreases the arterial oxygen delivery.

IV. Acute complications and symptoms occur intermittently in sickle cell disease and throughout its course. These complications include vaso-occlusive pain crises (VOCs), acute chest syndrome, aplastic crisis, hemolytic crisis, and the pooling of blood within bodily organs. Vaso-occlusive crises (VOCs) include stroke, severe pain, kidney and other organ and/or tissue damage for which there is no other explanation than vaso-occlusive crisis. Transfusion protocol is considered the most effective therapy for secondary stroke prophylaxis. If this is contraindicated or ineffective, hydroxyurea is introduced.

V. Hydroxyurea: Generic hydroxyurea is considered first-line in the treatment of sickle cell disease. Typically offered to patients with three or greater sickle cell-associated moderate-to-severe crises within the last 12 months. Has been shown to be disease modifying at reducing the rate of pain episodes, stroke, transfusion requirement, and mortality. Has been shown to reduce the number of VOCs and hospitalizations. The majority of subjects in the HOPE and HOPE-KIDS 1 trials were established on hydroxyurea at baseline.

VI. L-glutamine: Typically considered in patients who have at least two VOCs per year, despite maximally tolerated hydroxyurea dose, and considered against cost. Was approved to reduce acute complications of sickle cell disease (VOCs). Monotherapy is considered in patients who do not tolerate hydroxyurea. Over-the-counter products are available as well as in a prescription product L-glutamine (Endari)

VII. Both hydroxyurea and L-glutamine have evidence to support disease-modifying activity and the reduction of VOC or complications related to disease.

VIII. In children 12 years and older, as well as in adults, voxelotor (Oxbryta) is dosed as 1,500 mg daily. Children ages 4 to less than 12 years old follow weight-based dosing as noted in the table below.

Dosing in Children 4 to <12 years old:	
Weight	**Dose**
10 – 19 kg	600 mg once daily
20 – 39 kg	900 mg once daily
≥40 kg*	1,500 mg once daily

*Medical necessity for 300 mg soluble tablets is required for members weighing 40 kg or greater; as the recommended dose (1,500 mg daily) can be obtained with the 500 mg oral tablet, providing a significant price differential (~2.5x difference).

Investigational or Not Medically Necessary Uses

I. There is currently limited to no data to support the safety and efficacy of concomitant use of voxelotor (Oxbryta) with crizanlizumab-tmca (Adakveo).

References

1. Oxbryta [Package Insert]. Global Blood Therapeutics. San Francisco, CA. December, 2021
2. Vichinsky E, Hoppe CC, Ataga KI et al. A phase 3 randomize trial of voxelotor in sickle cell disease. N Engl J Med. 2019; 381: 509-19.
3. Buchanan GR, Yawn BP, Afenyi-Annan AN et al. Evidence-based management of sickle cell disease: expert panel report. National Heart, Lung, and Blood Institute. 2014.
4. Center for Drug Evaluation and Research. Application Number 213137Orig1s000 Summary Review. Summary Review for Regulatory Action: NDA213137. Updated November 25, 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/213137Orig1s000Multidiscipline.pdf
5. Estepp JH, Kalpatthi R, Woods G, et al. Safety and efficacy of voxelotor in pediatric patients with sickle cell disease aged 4 to 11 years. Pediatr Blood Cancer. 2022;69(8):e29716.
6. Howard J, Ataga KI, Brown RC, et al. Voxelotor in adolescents and adults with sickle cell disease (Hope): long-term follow-up results of an international, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Haematol. 2021;8(5):e323-e333.
7. DeBaun MR, Jordan LC, King AA, et al. American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults. Blood Advances. 2020;4(8):1554-1588.

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated member age requirement to 4 years of age and older. Removal of prior VOC requirement. Added requirement of baseline Hb ≤ 10.5 g/dL. Addition of medical necessity requirement for use of 300 mg soluble tablets over 500 mg tablet.	**08/2022**
Policy created	02/2020