PRIOR AUTHORIZATION POLICY

POLICY: Sickle Cell Disease – Oxbryta Prior Authorization Policy
- Oxbryta® (voxelotor tablets, tablets for oral suspension – Global Blood Therapeutics)

REVIEW DATE: 01/03/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Oxbryta, a hemoglobin S (or sickle hemoglobin) polymerization inhibitor, is indicated for the treatment of **sickle cell disease** in patients ≥ 4 years of age.[1]

Clinical Efficacy

All of the included patients in the pivotal study (HOPE; 12 to 64 years of age) had at least one sickle cell-related crisis in the previous 12-month period.[2] In addition, baseline hemoglobin level was < 10.5 g/dL for these patients. Approximately 65% of patients were receiving concomitant hydroxyurea therapy. Efficacy was based on hemoglobin response, which was defined as a > 1 g/dL increase from baseline to Week 24 in hemoglobin level. The response rate was significantly higher in the Oxbryta group compared with placebo. The annualized incidence rate of vasoocclusive crisis was lower for the Oxbryta group compared with placebo; however, the difference was not statistically significant. In general, clinical benefits of treatment for sickle cell disease include reduction in the number of vaso-occlusive crises, delay in time to sickle cell-related crises and reduction in the number of days in the hospital.[3]

Use of Oxbryta in pediatric patients 4 to < 12 years of age was evaluated in an open-label Phase 2 study.[1,4] There was no eligibility requirement regarding prior vasoocclusive crises. Patients also had baseline hemoglobin level < 10.5 g/dL.

Guidelines

The American Society of Hematology guidelines for sickle cell disease: management of acute and chronic pain associated with sickle cell disease (2020) was published before approval of Oxbryta and the guidelines do not mention Oxbryta.[5] The National Institutes of Health – National Heart, Lung, and Blood Institute issued the Evidence-Based Management of Sickle Cell Disease, Expert Panel Report in 2014.[3] These guidelines were published prior to the approval of Oxbryta. Hydroxyurea has been shown to reduce the frequency of painful episodes, the incidence of acute coronary syndrome events, and the need for transfusions and hospitalizations. Hydroxyurea is recommended for use in most patients with sickle cell disease; however, it is not recommended for use in pregnant female or women who are breastfeeding. Females and males of reproductive potential are advised to use effective contraception during and after treatment with hydroxyurea.[3,6,7] Hydroxyurea can also cause myelosuppression and treatment should not be initiated in patients with depressed bone marrow function.[6]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Oxbryta. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Oxbryta as well as the monitoring required for adverse events and long-term efficacy, approval requires Oxbryta to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Oxbryta® (voxelotor tablets, tablets for oral suspension – Global Blood Therapeutics)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Sickle Cell Disease.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patients meets one of the following: (a or b):
       - **a)** Patient is ≥ 4 years of age and < 12; OR
       - **b)** Patient is ≥ 12 years of age and has had at least one sickle cell-related crisis in the previous 12-month period; AND
     - **ii.** Patient's baseline hemoglobin level was ≤ 10.5 g/dL (before initiating Oxbryta therapy); AND
     - **iii.** Patient meets one of the following criteria (a, b, or c):

a) Patient is currently receiving a hydroxyurea product; OR
b) According to the prescriber, patient has tried a hydroxyurea product and has experienced inadequate efficacy or significant intolerance; OR
c) According to the prescriber, patient is not a candidate for hydroxyurea therapy; AND
Note: Examples of patients who are not candidates for hydroxyurea therapy include patients who are pregnant or who are planning to become pregnant and patients with an immunosuppressive condition (such as cancer).

iv. The medication is prescribed by or in consultation with a physician who specializes in sickle cell disease (e.g., a hematologist).

B) Patient is Currently Receiving Oxbryta. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
i. Patient is ≥ 4 years of age; AND
ii. According to the prescriber, patient is receiving clinical benefit from Oxbryta therapy; AND
Note: Examples of clinical benefit include reduction in the number of vaso-occlusive crises/sickle cell-related crises; delay in time to sickle cell-related crises; and reduction in the number of days in the hospital.
iii. The medication is prescribed by or in consultation with a physician who specializes in sickle cell disease (e.g., a hematologist).

CONDITIONS NOT COVERED

Oxbryta® (voxelotor tablets, tablets for oral suspension – Global Blood Therapeutics)
is(are) considered experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Oxbryta™ tablets and tablets for oral suspension [prescribing information]. San Francisco, CA: Global Blood Therapeutics; October 2022.
2. Vichinsky E, Hoppe CC, Ataga KI, et al. A phase 3 randomized trial of voxelotor in sickle cell disease. *N Engl J Med*. 2019;381:509-519.
3. The National Institutes of Health – National Heart, Lung, and Blood Institute Evidence-Based Management of Sickle Cell Disease, Expert Panel Report 2014. Available at: https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf. Accessed on December 5, 2023.
4. 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. Pediatri Blood Cancer. 2022;69(8):e29716.
5. Brandow AM, Carroll CP, Creary S, et al. American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain. *Blood Adv*. 2020;4:2656-2701
6. Droxia® capsules [prescribing information]. Princeton, NJ: Bristol-Myers Squibb;July 2021.
7. Siklos® tablets [prescribing information]. Bryn Mawr, PA: Medunik; November 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date

Annual Revision	No criteria changes.	12/07/2022
Annual Revision	No criteria changes.	01/03/2024