Clinical Policy: Voxelotor (Oxbryta)

Reference Number: CP.PHAR.451
Effective Date: 03.01.20
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Voxelotor (Oxbryta™) is a hemoglobin S (HbS) polymerization inhibitor.

FDA Approved Indication(s)

Oxbryta is indicated for the treatment of sickle cell disease (SCD) in adults and pediatric patients 4 years of age and older.

This indication is approved under accelerated approval based on the increase in hemoglobin (Hb). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Oxbryta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of SCD with one of the following genotypes (a, b, c, or d):
   a. Homozygous hemoglobin S;
   b. Hemoglobin $S\beta^0$-thalassemia;
   c. Hemoglobin $S\beta^+$-thalassemia;
   d. Hemoglobin SC;
2. Age ≥ 4 years;
3. Prescribed by or in consultation with a hematologist;
4. Hb level ≥ 5.5 and ≤ 10.5 g/dL;
5. Member meets one of the following (a or b):
   a. Member has experienced at least 1 vaso-occlusive crisis (VOC) within the past 6 months while on hydroxyurea at up to maximally indicated doses (*see Appendix D*);
   b. Member has intolerance* or contraindication to hydroxyurea and has experienced at least 1 VOC within the past 12 months (*see Appendix D*);
   **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.

6. If request is for tablets for oral suspension: documentation supports inability to swallow tablets;
7. For age ≥ 5 years: Failure of L-glutamine at up to maximally tolerated doses, unless contraindicated or clinically significant adverse effects are experienced;
8. For age ≥ 16 years: Failure of a 6-month trial of Adakveo®, unless contraindicated or clinically significant adverse effects are experienced;
9. Failure of blood transfusion(s), unless contraindicated or clinically significant adverse effects are experienced (e.g., cutaneous ulcers, iron overload);
10. Oxbryta is prescribed concurrently with hydroxyurea, unless contraindicated or clinically significant adverse effects are experienced;
11. Oxbryta is not prescribed concurrently with Adakveo;
12. Dose does not exceed 1,500 mg (3 tablets) per day.

Approval duration: 2 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by an increase in Hb level from baseline of at least 1 g/dL;
3. Oxbryta is prescribed concurrently with hydroxyurea, unless contraindicated or clinically significant adverse effects are experienced;
4. Oxbryta is not prescribed concurrently with Adakveo;
5. If request is for a dose increase, new dose does not exceed 1,500 mg (3 tablets) per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
Hb: hemoglobin
SCD: sickle cell disease
VOC: vaso-occlusive crisis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
hydroxyurea (Droxia®)	*Age ≥ 18 years* Initial: 15 mg/kg/day PO single dose; based on blood counts, may increase by 5 mg/kg/day every 12 weeks to a max 35 mg/kg/day	35 mg/kg/day
hydroxyurea (Siklos®)	*Age ≥ 2 years* Initial: 20 mg/kg/day PO QD; based on blood counts, may increase by 5 mg/kg/day every 8 weeks or if a painful crisis occurs	35 mg/kg/day
L-glutamine (Endari®)	Weight > 65 kg: 15 g (3 packets) PO BID Weight 30 to 65 kg: 10 g (2 packets) PO BID Weight < 30 kg: 5 g (1 packet) PO BID	30 g/day (maximum dose based on weight)
Adakveo® (crizanlizumab-tmca)	*Age ≥ 16 years* 5 mg/kg IV infusion at week 0, week 2, and every 4 weeks thereafter	5 mg/kg

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

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): prior drug hypersensitivity to Oxbryta or excipients
- Boxed warning(s): none reported

Appendix D: General Information

- A VOC is defined as a previously documented episode of acute painful crisis or acute chest syndrome (ACS) for which there was no explanation other than VOC that required prescription or healthcare professional-instructed use of analgesics for moderate to severe pain.

- 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.
- Hydroxyurea dose titration: Members should obtain complete blood counts (CBC) with white blood cell (WBC) differential and reticulocyte counts at least every 4 weeks for titration. The following lab values indicate that it is safe to increase dose.
  - Absolute neutrophil count (ANC) in adults ≥ 2,000/uL, or ANC ≥ 1,250/uL in younger patients with lower baseline counts
  - Platelet counts ≥ 80,000/uL

  If neutropenia or thrombocytopenia occurs: hydroxyurea dosing is held, CBC and WBC differential are monitored weekly, members can restart hydroxyurea when values have recovered.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
SCD	*Age ≥ 12 years* 1,500 mg PO QD with or without food. *Age 4 to < 12 years* Weight ≥ 40 kg: 1500 mg PO QD Weight 20 kg to < 40 kg: 900 mg PO QD Weight 10 kg to < 20 kg: 600 mg PO QD	1,500 mg/day

VI. Product Availability

Tablet: 500 mg, 300 mg (for oral suspension)

VII. References

1. Oxbryta Prescribing Information. South San Francisco, CA: Global Blood Therapeutics, Inc.; December 2021. Available at: https://www.oxbryta.com/. Accessed January 10, 2022.
2. 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 Sep 10;312(10):1033-48.
3. Vichinsky E, Hoppe CC, Ataga KI, et al. A phase 3 randomized trial of voxelotor in sickle cell disease. *N Engl J Med*. 2019 Aug 8;381(6):509-519.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Accessed November 14, 2021.
5. Brandow A, Carroll C, Creary S, et al. American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain. *Blood Advances*. 2020;4(12):2656-2701.

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

The following is a list of diagnosis codes that support coverage for the applicable covered procedure code(s).

ICD-10-CM Code	Description
D57.0*	Hb-SS disease with crisis
D57.1	Sickle-cell disease without crisis
D57.2*	Sickle-cell/Hb-C disease
D57.4*	Sickle-cell thalassemia

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	12.10.19	02.20
Added redirections to blood transfusions and a 6 month trial of Adakveo; finalized HIM line of business; reduced initial approval duration to 2 months from 6 months, and continued therapy approval duration to 6 months from 12 months.	03.04.20	05.20
Added requirement for L-glutamine trial per April SDC and prior clinical guidance.	04.22.20	
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.26.20	02.21
1Q 2022 annual review: references reviewed and updated; RT4: updated to reflect pediatric age extension (4-11 years), new dose formulation of tablet for oral suspension, and added criterion for documentation of inability to swallow tablet.	01.10.22	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.