Clinical Policy: Crizanlizumab-tmca (Adakveo)

Reference Number: CP.PHAR.449
Effective Date: 03.01.20
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Crizanlizumab-tmca (Adakveo®) is a selectin blocker.

FDA Approved Indication(s)

Adakveo is indicated to reduce the frequency of vasoocclusive crises (VOC) in adults and pediatric patients aged 16 years and older with sickle cell disease (SCD).

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 Adakveo 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 ≥ 16 years;
3. Prescribed by or in consultation with a hematologist;
4. Hb level ≥ 4 g/dL;
5. Member meets one of the following (a or b; *see Appendix D*):
   a. Documentation supports that member has been adherent to hydroxyurea treatment for at least the past 6 months AND both of the following (i and ii):
      i. Hydroxyurea was dosed at the maximum tolerated dose for ≥ 6 months;
      ii. Member has experienced ≥ 1 VOC within the past 6 months;
   b. Member has experienced ≥ 2 VOC within the past 12 months AND one of the following (i, ii, or ii):
      i. Member has contraindication to hydroxyurea (e.g., severe myelosuppression*);
      ii. Documentation of a clinically significant intolerance* to hydroxyurea (e.g., worsening kidney function, severe cutaneous toxicity, pancreatitis);
      **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.

iii. Provider attestation for both of the following (1 and 2):
   1) Member's past adherence to hydroxyurea for ≥ 6 months at the maximum tolerated dose;
   2) Member experienced ≥ 1 VOC while on the maximum tolerated dose;

6. Failure of L-glutamine at up to maximally tolerated doses, unless contraindicated or clinically significant adverse effects are experienced;*
   **For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395*
7. Documentation of baseline incidence of VOC over the last twelve months;
8. Adakveo is prescribed concurrently with hydroxyurea, unless contraindicated or clinically significant adverse effects are experienced;
9. Adakveo is not prescribed concurrently with Oxbryta®;
10. Dose does not exceed 5 mg/kg doses on Day 1 and Day 15, followed by 5 mg/kg every 4 weeks.

Approval duration: 6 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by a documented improvement in the incidence of VOC from baseline;

3. Adakveo is prescribed concurrently with hydroxyurea, unless contraindicated or clinically significant adverse effects are experienced;
4. Adakveo is not prescribed concurrently with Oxbryta;
5. If request is for a dose increase, new dose does not exceed 5 mg/kg every 4 weeks.

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 crises

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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)

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
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, and members can restart hydroxyurea when values have recovered.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
SCD	Administer 5 mg/kg by intravenous infusion on Week 0, Week 2, and every 4 weeks thereafter.	5 mg/kg

VI. Product Availability
Single-dose vial for injection: 100 mg/10 mL (10 mg/mL)

VII. References

1. Adakveo Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2024. Available at https://www.novartis.com/us-en/sites/novartis_us/files/adakveo.pdf. Accessed November 18, 2024.
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. Ataga K, Kutlar A, Kanter J, et al. Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease. *N Engl J Med*. 2017 Feb 2;376(5):429-439.
4. Kutlar A, Kanter J, Liles DK, et al. Effect of Crizanlizumab on pain crises in subgroups of patients with sickle cell disease: A SUSTAIN study analysis. *Am J Hematol*. 2019;94:55-61.
5. Micromedex® Healthcare Series [Internet database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Accessed November 18, 2024.
6. 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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0791	Injection, crizanlizumab-tmca, 5 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; added coding implications; references reviewed and updated.	10.26.20	02.21
Corrected optional criteria that required at least 2 VOC to requiring at least 1 VOC within the past 6 months while on hydroxyurea.	02.16.21	05.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.15.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.27.22	
1Q 2023 annual review: no significant changes; references reviewed and updated.	10.31.22	02.23
1Q 2024 annual review: no significant changes; references reviewed and updated.	10.31.23	02.24
1Q 2025 annual review: no significant changes; references reviewed and updated.	11.18.24	02.25
For hydroxyurea trial, added that documentation supports adherence to hydroxyurea for at least the past 6 months, examples of	07.14.25	08.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
hydroxyurea contraindications and intolerances, and a bypass option requiring provider attestation of past adherence to hydroxyurea for ≥ 6 months at the maximum tolerated dose and ≥ 1 VOC while on the maximum tolerated dose; removed ICD-10-CM Codes section. For Endari, added step therapy bypass for IL HIM per IL HB 5395.		

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.