Drug Coverage Policy

Effective Date..... 4/15/2025
Coverage Policy Number IP0120
Policy Title..... Adakveo

Sickle Cell Disease – Adakveo

- Adakveo® (crizanlizumab-tmca intravenous infusion– Novartis)

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 Healthcare Coverage Policy

OVERVIEW
Adakveo, a monoclonal antibody, is indicated to **reduce the frequency of vasoocclusive crises** due to **sickle cell disease** in patients ≥ 16 years of age.[1]

Clinical Efficacy
All of the patients included in the 52-week pivotal study (SUSTAIN) had a history of two to ten vasoocclusive crises in the previous 12 months.[2] Concomitant use of hydroxyurea was allowed during the study and approximately 60% of patients were on concomitant hydroxyurea therapy. At Week 52, compared with placebo, the annual rate of pain crises was significantly lower and the time to first and second sickle cell-related pain crises was significantly delayed in the Adakveo

group. In addition, treatment with Adakveo decreased the annual rate of hospitalized days, compared with placebo.

Dosing Information
Adakveo is given by intravenous infusion over a period of 30 minutes at Week 0, Week 2, and every 4 weeks thereafter; the dose is 5 mg/kg.[1]

Guidelines/Recommendations
Hydroxyurea is the cornerstone of therapeutic management of sickle cell disease.[3] Hydroxyurea significantly reduces vasoocclusive crises, acute chest syndrome, and the need for blood transfusions; all of which results in lower morbidity and mortality rates.

The American Society of Hematology guidelines for sickle cell disease: management of acute and chronic pain associated with sickle cell disease (2020) does not address the use of Adakveo.[4] 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.[5] These guidelines were published prior to the approval of Adakveo. 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 females or women who are breastfeeding. Females and males of reproductive potential are advised to use effective contraception during and after treatment with hydroxyurea.[5-7] Hydroxyurea can also cause myelosuppression and treatment should not be initiated in patients with depressed bone marrow function.[6-8]

Medical Necessity Criteria

Adakveo is considered medically necessary when the following criteria are met:

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.** Patient is ≥ 16 years of age; AND
     - **ii.** Patient has had at least one sickle cell-related crisis in the previous 12-month period; AND
     - **iii.** Patient meets ONE of the following (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 Adakveo. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 16 years of age; AND
     - **ii.** According to the prescriber, patient is receiving clinical benefit from Adakveo therapy; AND

Note: Examples of clinical benefit include reduction in the number of vasoocclusive 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).

Dosing. Approve the following dosing regimens (A and B):

A) Up to 5 mg/kg given by intravenous infusion at Weeks 0 and 2; AND

B) Up to 5 mg/kg given by intravenous infusion for up to once every 4 weeks.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding 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.

References

1. Adakveo® intravenous infusion [prescribing information]. East Hanover, NJ: Novartis; June 2024.
2. Ataga KI, Kutlar J, Kanter K, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. *N Engl J Med*. 2017;376(5):429-439.
3. López Rubio M and Argüello Marina M. The current role of hydroxyurea in the treatment of sickle cell anemia. *J Clin Med*. 2024;13(21)L6404.
4. 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.
5. 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 January 8, 2025.
6. Droxia® capsules [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; July 2021.
7. Siklos® tablets [prescribing information]. Bryn Mawr, PA: Medunik; November 2023.
8. Xromi oral solution [prescribing information]. Franklin, TN: Rare Disease Therapeutics; April 2024.

Revision Details

Type of Revision	Summary of Changes	Date

Annual Revision	**Policy Name Change: Updated** Policy Name from "Crizanlizumab-tmca" to "Sickle Cell Disease – Adakveo." **Initial Therapy: Replaced** the requirement "vaso-occlusive crisis (VOC)" in the previous 12-month period" with "sickle cell-related crisis". **Added** a note detailing examples of patients ineligible for hydroxyurea therapy. **Patient is Currently Receiving Adakveo: Added** note with examples of clinical benefit. **Conditions Not Covered: Removed** "Concomitant Oxbryta Therapy."	08/01/2024
Annual Revision	No criteria changes.	4/15/2025

The policy effective date is in force until updated or retired.