Utilization Review Policy 220

POLICY: Adakveo® (crizanlizumab-tmca injection, for intravenous use)

EFFECTIVE DATE: 5/1/2020
LAST REVISION DATE: 01/15/2025

COVERAGE CRITERIA FOR: All UCare Plans

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]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Adakveo. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills

required for evaluation and diagnosis of patients treated with Adakveo as well as the monitoring required for adverse events and long-term efficacy, approval requires Adakveo to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Adakveo is recommended in those who meet the following criteria:

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); OR

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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Adakveo is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.

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
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
Annual Revision	No criteria changes.	01/15/2025
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025