STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

# Adakveo (crizanlizumab-tmca)
## PAM–025

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|---|---|---|---|
| **Iowa Medicaid Program:** | Prior Authorization | **Effective Date:** | 01/01/2021 |
| **Revision Number:** | 4 | **Last Rev Date:** | 07/19/2024 |
| **Reviewed By:** | Medicaid Medical Director | **Next Rev Date:** | 07/18/2025 |
| **Approved By:** | Medicaid Clinical Advisory Committee | **Approved Date:** | 12/23/2020 |

## Overview

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|---|---|
| Medication:[1] | crizanlizumab-tmca |
| Brand Name: | Adakveo® |
| Pharmacologic Category: | Sickle Cell Disease Agents; P-selectin blocker |
| FDA-Approved Indication(s): | Reduce the frequency of vaso-occlusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease |
| How Supplied: | 100 mg/10 mL (10 mg/mL) single-dose vial |
| Dosage and Administration: | • IV infusion: 5 mg/kg at weeks 0 and 2, then every 4 weeks thereafter<br>• Provider should reevaluate the treatment at least yearly to assess response to treatment and consider discontinuation if no perceived benefit is achieved. |
| Benefit Category: | Medical |

## Descriptive Narrative

Sickle cell disease (SCD) affects about 100,000 persons in the United States and primarily affects African Americans, Latinos, and other minorities. It results in a host of acute and chronic complications including vaso-occlusive pain, organ damage, hemolytic anemia, countless disease complications, and shortened survival. Persons with this genetic disorder have an average life expectancy of 40 to 60 years.

Sickle hemoglobin (Hb S, alpha2:beta$^S$2) is a result of a specific point mutation in the gene *HBB*, which encodes hemoglobin beta chains. It substitutes valine for the normal glutamic acid at the seventh amino acid (*HBB* p.glu7val). SCD is an autosomal recessive trait. For the disease to manifest, there must be homozygosity for Hb S or compound heterozygosity for Hb S and beta thalassemia or a different *HBB* variant that interacts with Hb S.[2]

Episodes of acute pain (previously called "sickle cell crises") are one of the most common types of vaso-occlusive events in SCD and the most common reason for seeking medical attention. Vaso-occlusive pain in SCD is intense, although there can be significant variability in the severity and frequency of acute painful episodes. Pain can co-occur with (and mask) other potentially life-threatening complications of SCD, and so treatment should be accompanied by additional evaluations as appropriate for these complications.[3]

After an acute vaso-occlusive pain episode resolves, it is prudent to ensure that appropriate measures have been taken to decrease the likelihood of future vaso-occlusive pain events and to reduce the intensity of chronic pain. For children and adults with Hb SS or Hb S-beta$^0$-thalassemia, hydroxyurea is the main preventing therapy for decreasing the incidence rate of acute vaso-occlusive pain. Hydroxyurea has the greatest long-term evidence for benefit in reducing acute painful episodes as well as reducing other vaso-occlusive complications of SCD such as acute chest syndrome and in some cases stroke, decreasing the requirement for blood transfusions, and improving survival. If hydroxyurea is not tolerated or is ineffective, treatment with Adakveo® is an option for patients who are 16 years of age or older.[4]

## Guidelines

Guidelines for the management of sickle cell disease are published by the American Society of Hematology (ASH) as five separate guidelines:

1. Guidelines for sickle cell disease: Management of acute and chronic pain (2020).[5]
2. Guidelines for sickle cell disease: Cerebrovascular disease (2020).[6]
3. Guidelines for sickle cell disease: Transfusion support (2020).[7]
4. Guidelines for sickle cell disease: Cardiopulmonary and kidney disease (2019).[8]
5. Guidelines for sickle cell disease: Stem cell transplantation (2021).[9]

A 6th guideline is planned: Hydroxyurea Dosing and Monitoring for Sickle Cell Disease. ASH is currently accepting invitations for nominations, including self-nominations, for individuals to serve on the Dosing and Monitoring of Hydroxyurea for Sickle Cell Disease guideline panel.[10]

## Criteria

Prior authorization is required.

Adakveo® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of sickle cell disease (any genotype); **AND**
2. Member is 16 years of age or older; **AND**
3. The member has experienced two or more vaso-occlusive crises (VOCs) within the previous 12 months prior to initiation of therapy; **AND**
4. One of the two following conditions are met (a or b):
    a. The member is currently receiving and will continue to receive hydroxyurea in conjunction with Adakveo®; **OR**
    b. The member has a documented history of treatment failure, intolerance, or contraindication to hydroxyurea; **AND**
5. Adakveo® will not be used in conjunction with Oxbryta® (voxelotor); **AND**
6. Prescribed by, or in consultation with, a hematologist; **AND**
7. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 5 mg/kg at weeks 0 and 2, then every 4 weeks thereafter; **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which the regimen prescribed does not align with FDA-approved labeling.

Adakveo® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation that member has experienced a positive clinical benefit to treatment with Adakveo® (as evidenced by a reduction in the frequency of vaso-occlusive crises [VOC] from baseline); **AND**
3. Prescribed by, or in consultation with, a hematologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 5 mg/kg every 4 weeks; **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which the regimen prescribed does not align with FDA-approved labeling.

## Approval Duration and Quantity Limits

| | Initial Authorization | Subsequent Authorization(s) |
|---|---|---|
| Approval Duration | 12 months | 12 months |
| Quantity Limits | 5 mg/kg at weeks 0 and 2, then<br>5 mg/kg every 4 weeks thereafter | 5 mg/kg every 4 weeks |

## Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

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

| ICD-10 | Description |
|---|---|
| D57.00-D57.819 | Sickle cell disease |

| NDC (Strength) | Labeler | Dosage | Pkg Size | Pkg Qty | Units/ Pkg |
|---|---|---|---|---|---|
| 00078-0883-61 (single-dose vial, 100 mg/10 mL) | Novartis Pharmaceuticals Corporation (00078) | 5 mg | 1 | EA | 20 |

## Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

## References


[1] Adakveo® prescribing information (06/2024). Novartis Pharmaceuticals Corporation: East Hanover, NJ. Available online at www.hcp.novartis.com. Accessed July 8, 2024.

[2] Steinberg MH. Pathophysiology of sickle cell disease. Tirnauer JS, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 1, 2024.

[3] Vichinsky EP. Overview of the clinical manifestations of sickle cell disease. Tirnauer JS, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 1, 2024.

[4] Vichinsky EP. Disease-modifying therapies to prevent pain and other complications of sickle cell disease. Tirnauer JS, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 1, 2024.

[5] Brandow AM, Carroll CP, et al. American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain. *Blood Adv* 2020; 4 (12): 2656–2701. PMID 32559294.

[6] DeBaun MR, Jordan LC, et al. American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults. *Blood Adv* 2020; 4 (8): 1554-1588. PMID 32298430.

[7] Chou ST, Alsawas M, et al. American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support. *Blood Adv* 2020; 4(2): 327-255. PMID 31985807.

[8] Liem RI, Lanzkron S, et al. American Society of Hematology 2019 guidelines for sickle cell disease: cardiopulmonary and kidney disease. *Blood Adv* 2019; 3(23): 3867-3897. PMID 31794601.

[9] Kanter J, Liem RI, et al. American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation. Blood Adv. 2021 Sep 28;5(18):3668-3689. PMID 34581773.

[10] ASH Clinical Practice Guidelines on Sickle Cell Disease. Hydroxyurea Dosing and Monitoring for SCD: invitation for panel nominations. Available online at www.hematology.org/education/clinicians/guidelines-and-quality-care/clinical-practice-guidelines/sickle-cell-disease-guidelines. Accessed June 1, 2024.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

## Criteria Change History

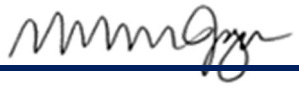
| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| [mm/dd/yyyy] | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| [mm/dd/yyyy] | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 07/19/2024 | CAC | Annual review. Overview table: added "Provider should reevaluate the treatment at least yearly to assess response to treatment and consider discontinuation if no perceived benefit is achieved." (language approved by FDA June 26, 2024). Descriptive Narrative: added information on vaso-occlusive pain in sickle cell disease and options for treatment. Guidelines: added guidelines on stem cell transplantation, as well as information on a sixth guideline planned for hydroxyurea dosing and monitoring in SCD. Added dosing information into criteria. Updated references. | 4 |
| **Signature** William (Bill) Jagiello, DO | |  | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 07/21/2023 | CAC | Annual review. Updated references. | 3 |
| **Signature** William (Bill) Jagiello, DO | |  | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 07/15/2022 | CAC | Added overview of sickle cell genetics to Descriptive Narrative. Added criteria language "The regimen/dosing prescribed is within the FDA-approved labeling." Added dosing information to Approval Duration/Quantity Limits section. Initial authorization duration changed from every 6 months to every 12 months. Format updated. | 2 |
| **Signature** William (Bill) Jagiello, DO | |  | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 07/16/2021 | CAC | Criteria implementation. | 1 |
| **Signature** William (Bill) Jagiello, DO | |  | |

CAC = Medicaid Clinical Advisory Committee