DR.007.D Adakveo® (Crizanlizumab-tcma)

Original Implementation Date : 08/01/2020
Version [D] Date : 05/28/2025
Last Reviewed Date: 05/28/2025

PRODUCT VARIATIONS

This policy only applies to Jefferson Health Plans Medicare Advantage and Jefferson Health Plans Individual and Family Plans product lines.

POLICY STATEMENT

The plan considers Adakveo®(Crizanlizumab-tcma) medically necessary to reduce the frequency of vasoocclusive crises in adult and pediatric patients 16 years or older with sickle cell disease.

FDA APPROVED INDICATIONS

Adakveo® is a monoclonal antibody used to reduce the frequency of vaso-occlusive crises (VOCS) in adult and pediatric patients 16 years or older with sickle cell disease.

OFF-LABEL USE

Authorization for off-labeled use of medication will be evaluated on an individual basis. Review of an off-labeled request by the Medical Staff will be predicated on the appropriateness of treatment and full consideration of medical necessity. For off-label use, Medical Directors will review scientific literature and local practice patterns.

PRIOR AUTHORIZATION CRITERIA

INITIAL CRITERIA

*AUTHORIZATION DURATION: IF **ALL CRITERIA MET**, APPROVE FOR 6 MONTHS*

1. Adults 16 years of age and older; AND
2. Medication is being prescribed by or in consultation with a specialist (e.g., hematologist); or other specialist with expertise in the diagnosis and management of sickle cell disease AND

3. Patients with documented diagnosis of a sickle cell disease (homozygous hemoglobin S [HbSS], sickle hemoglobin C disease [HbSC], sickle β0-thalassemia [HbSβ0-thalassemia], sickle β+-thalassemia [HbSβ+-thalassemia], or other genotypes); AND
    a) Patient has experienced at least two sickle cell-related pain crises in the prior year OR
    b) Patient has experienced at least one vaso-occlusive crisis in the prior year
4. If patient is female and of childbearing potential, has documentation of recent negative pregnancy test; AND
5. Patient has had previous treatment failure, intolerance, or contraindication with hydroxyurea, or is taking hydroxyurea concomitantly with Adakveo®; AND
6. Patient is not receiving concomitant chronic, prophylactic blood transfusion therapy; AND
7. Patient is not receiving concomitant Oxybryta (voxelotor) therapy; AND
8. Adakveo® initial dosing is in accordance with the United States Food and Drug Administration approved labeling

Please note: For members who are new to the plan and are already treated and stable with Adakveo® (records must be attached), the medication will be approved for continuation of treatment.

RENEWAL CRITERIA

1. All initial criteria are met; AND
2. The patient has documented reduction in the frequency of vaso-occlusive crises and has good tolerance and no side effects to the treament with Adakveo®; AND
3. Adakveo® maintenance dosing is in accordance with the United States Food and Drug Administration approved labeling

DOSAGE AND ADMINISTRATION

DOSING RECOMMENDATIONS:

- Recommended administration of Adakveo® 5mg/kg by intravenous infusion over a period of 30 minutes at Week 0, Week 2, and every 4 weeks thereafter.
- If a dose is missed, administer Adakveo® as soon as possible. If Adakveo® is administered within 2 weeks after the missed dose, continue original dosing schedule. If Adakveo is administered more than 2 weeks after the missed dose, continue dosing every 4 weeks thereafter.
- Physicians should reevaluate the treatment with Adakveo at least yearly to assess individual patient's response to treatment and consider discontinuation if not effective.

- Adakveo® may be given with or without hydroxyurea.

- It is recommended to dilute Adakveo® in 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to a total volume of 100 mL for intravenous infusion.
- Administer Adakveo® diluted solution by intravenous infusion over a period of 30 minutes through an IV line which must contain a sterile nonpyrogenic 0.2-micron inline filter, do not mix or co-administer with other drugs through the same intravenous line.
- After administration of Adakveo, flush the line with at least 25 mL of 0.9% Sodium Chloride Injection or 5% Dextrose Injection

This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be considered.

RISK FACTORS/SIDE EFFECTS

Infusion Reactions:
Infusion-related reactions (occurring within 24 hours of infusion) have been reported. Symptoms may include fever, chills, nausea, vomiting, fatigue, dizziness, pruritus, urticaria, sweating, dyspnea, or wheezing. Monitor patients for signs and symptoms of infusion-related reactions. Discontinue Adakveo® infusion for severe reactions and manage as clinically necessary.

Pregnancy:
Adakveo® has the potential to cause fetal harm when administered to pregnant women. Adakveo® should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the fetus.

Lactation:
The development and health benefits of breast-feeding should be considered along with the mother's clinical need for Adakveo and any potential adverse effects on the breastfed child from Adakveo or from the underlying maternal condition

Interferes with Platelet Tests:
Adakveo interferes with automated platelet counts (platelet clumping) in particular when blood samples are collected in tubes containing EDTA, which may lead to unevaluable or falsely decreased platelet counts

Adverse Reactions:
The most common adverse reactions (≥ 10%) were nausea, arthralgia, back pain, abdominal pain, pyrexia and diarrhea

MONITORING

During therapy: Infusion reactions

Run blood samples within 4 hours of blood collection or collect blood samples in tubes containing citrate. When needed, estimate platelet count via peripheral blood smear.

BLACK BOX WARNING

N/A

BACKGROUND

Sickle cell disease (SCD) is an inherited group of disorders characterized by the presence of hemoglobin S (HbS), either from homozygosity for the sickle mutation in the beta globin chain of hemoglobin (HbSS) or from compound heterozygosity of a sickle beta globin mutation with another beta globin mutation (e.g., sickle-beta thalassemia). The hallmarks of SCD are Vaso-occlusive phenomena and hemolytic anemia.

Crizanlizumab-tmca (Adakveo®) is a humanized IgG2 kappa monoclonal antibody that was approved by the U.S. Food and Drug Administration (FDA) in November 2019. It works by binding to P-selectin and blocking interaction with its ligands, including P-selectin glycoprotein ligand 1(PSGL-1) on the surface of activated endothelium and platelets, causing a blockage of interactions between endothelial cells, platelets, red blood cells, and leukocytes.

CLINICAL EVIDENCE

The efficacy of crizanlizumab was evaluated in a 52-week, randomized, placebo-controlled, double-blind, multicenter, phase 2 study of 198 patients with sickle cell disease (SUSTAIN trial. NCT01895361). Patients included in the trial were 16 to 65 years of age, had sickle cell disease. (SCD) of any genotype (HbSS, HbSC, HbS/beta0-thalassemia, HbS/beta+-thalassemia, and others) and a history of 2 to 10 VOCs in the previous 12 months as determined by medical history or by patient's recall (crises included the occurrence of appropriate symptoms, a visit to a specific medical facility and/or healthcare professional, and receipt of pain medication).

Patients undergoing long-term red blood cell transfusion therapy or with a hemoglobin level less than 4 g/dL were excluded from the trial. Patients were randomized 1:1:1 to receive high dose crizanlizumab 5 mg/kg (n=67), low dose crizanlizumab 2.5 mg/kg (n=66), or placebo (n=65) as a 30-minute intravenous infusion on week 0, week 2, and every 4 weeks thereafter for the duration of 52-week treatment. Patients received crizanlizumab with or without hydroxyurea and were

permitted to receive periodic transfusions and pain medications (i.e., acetaminophen, NSAIDs, and opioids) as needed. Sixty-two percent (62%) of enrolled patients were receiving hydroxyurea at baseline. Patients receiving hydroxyurea at study entry had to have been taking the drug for at least 6 months and on a stable dose for at least the most recent 3 months. Hydroxyurea could not be initiated during the trial for patients not receiving the drug at study entry. The primary efficacy endpoint was the annual rate of sickle cell-related pain crises (VOCs) leading to a healthcare visit in the high-dose crizanlizumab group versus placebo. SCD patients in the high dose crizanlizumab group had a statistically significant lower median annual rate of VOC compared to patients in the placebo group (1.63 vs. 2.98; p=0.01), indicating a 45.3% lower rate with high dose crizanlizumab. Reductions in VOC frequency was observed in study participants regardless of SCD genotype and/or hydroxyurea use.

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT Code	Description
J0791	Injection, crizanlizumab-tmca, 5 mg

HCPCS Code	Description
N/A	n/a

ICD 10 Code	Description
D57.00	Hb-SS disease with crisis, unspecified
D57.001	Hb-SS disease with acute chest syndrome
D57.002	Hb-SS disease with splenic sequestration
D57.1	Sickle-cell disease without crisis

ICD 10 Code	Description
D57.20	Sickle-cell/Hb-C disease without crisis
D57.211	Sickle-cell/Hb-C disease with acute chest syndrome
D57.212	Sickle-cell/Hb-C disease with splenic sequestration
D57.219	Sickle-cell/Hb-C disease with splenic unspecified
D57.40	Sickle-cell thalassemia without crisis
D57.411	Sickle-cell thalassemia unspecified with acute chest syndrome
D57.412	Sickle-cell thalassemia unspecified with splenic sequestration
D57.419	Sickle-cell thalassemia, unspecified with crisis
D57.80	Other sickle-cell disorders, without crisis
D57.811	Other sickle-cell disorders with acute chest syndrome
D57.812	Other sickle-cell disorders with splenic sequestration
D57.819	Other sickle-cell disorders with crisis, unspecified

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making. Policy Bulletins are developed to assist in administering plan benefits and constitute neither offer of coverage nor medical advice. This Policy Bulletin may be updated and therefore is subject to changes.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
2025 Annual Review. Additions to Prior Authorization Criteria, Dosage and Administration, Risk Factors/Side Effects and Monitoring Sections. References updated.	D	05/28/2025
2024 annual review. Updated references.	C	11/01/2023
2023 annual review. Added Renewal Criteria. Updated References	C	11/01/2023
2022 annual review. No changes.	B	01/01/2021
Version B. This policy only applies to Jefferson Health Plans Medicare LOB. No other changes for 2021.	B	01/01/2021
New Drug Policy.	A	08/01/2020

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6. Joshua J Field, MD Elliot P Vichinsky, MD, Up To Date: Overview of preventive/ outpatient care in sickle cell disease, last update May 02, 2025.

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