Jefferson Health Plans

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

Original Implementation Date : 8/1/2020
Version [C] Date : 11/1/2023
Last Reviewed Date: July 2024

PRODUCT VARIATIONS

This policy only applies to Jefferson Health Plans Medicare and Individual and Family (ACA) product lines.

POLICY STATEMENT

Jefferson Health Plans 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 vasoocclusive crises 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); 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
    I. Patient has experienced at least two sickle cell-related pain crises 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, intolerance, or contraindication with hydroxyurea, or is taking 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: 5 mg/kg by intravenous infusion on week 0, week 2 and every 4 weeks thereafter.
9. 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 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: dose does not exceed 5 mg/kg every 4 weeks

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.
- Adakveo® may be given with or without hydroxyurea.

- 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, do not mix or co-administer with other drugs through the same intravenous line.

- 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.

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

MONITORING

During therapy: Infusion reactions.

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 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® is a registered trademark of the American Medical Association.

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

HCPCS Code	Description
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
D57.1	Sickle-cell disease without crisis
D57.20	Sickle-cell/Hb-C disease without crisis
D57.211	Sickle-cell/Hb-C disease without crisis
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 with acute chest syndrome
D57.412	Sickle-cell thalassemia with splenic sequestration
D57.419	Sickle-cell thalassemia, unspecified
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, 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 by Jefferson Health Plans to assist in administering plan benefits and constitute neither offers 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
2024 annual review. Updated references.	C	11/1/2023
2023 annual review. Added Renewal Criteria. Updated References	C	11/1/2023
2022 annual review. No changes.	B	1/1/2021
Version B. This policy only applies to Jefferson Health Plans Medicare LOB. No other changes for 2021.	B	1/1/2021
New Drug Policy.	A	8/1/2020

REFERENCES

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2. IPD Analytics. New Drug Review Adakveo® (crizanlizumab-tcma). 2019.

3. Brawley OW, Cornelius LJ, Edwards LR, Northington Gamble V, Green BL, Inturrisi C, James AH, Laraque D, Mendez M, Montoya CJ, Pollock BH, Robinson L, Scholnik AP, Schori M. National Institutes of Health Consensus Development Conference Statement: hydroxyurea treatment for sickle cell disease. Ann Intern Med. 2008; 148:932-8.

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7. Crizanlizumab. Up-To-Date Online. Accessed: June 2024.

8. Study of Dose Confirmation and Safety of Crizanlizumab in Pediatric Sickle Cell Disease Patients. Clinicaltrials.gov website https://clinicaltrials.gov/ct2/show/NCT03474965?term=crizanlizumab&draw=2&rank=1. Accessed July 11, 2023

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