

## Corporate Medical Policy

### Crizanlizumab-tmca (Adakveo<sup>®</sup>)

<b>File Name:</b>	crizanlizumab_adakveo
<b>Origination:</b>	2/2020
<b>Last CAP Review:</b>	3/2020
<b>Next CAP Review:</b>	3/2021
<b>Last Review:</b>	3/2020

#### Description of Procedure or Service

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Crizanlizumab-tmca (Adakveo<sup>®</sup>) is a selectin blocker that is indicated to reduce the frequency of vasoocclusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease.

Sickle cell disease (SCD) is an inherited hematologic disorder in which red blood cells are abnormally shaped in a crescent or sickle form, which restricts the flow in blood vessels and limits delivery of oxygen to tissue. This characteristic presence of sickle hemoglobin (HbS) is associated with chronic hemolysis, recurrent severe pain episodes (i.e. sickle cell-related pain crises or vasoocclusive crises), organ damage, and premature death. Vasoocclusive crises (VOCs) are the clinical hallmark of SCD, as well as the primary cause of healthcare encounters and increased risk of mortality in SCD patients. The key interventions to reduce VOCs include long-term treatment with hydroxyurea or regular blood transfusions. However, hydroxyurea is not completely effective in VOC prevention, and chronic transfusions create high patient burden. Crizanlizumab is one of the first targeted therapies approved to treat painful VOCs in SCD patients.

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.

**Related Pharmacy Policy:**  
Oxbryta<sup>™</sup>

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

#### Policy

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**BCBSNC will provide coverage for crizanlizumab-tmca (Adakveo<sup>®</sup>) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.**

#### Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit

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design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## **When Crizanlizumab-tmca (Adakveo) is covered**

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### **Initial Therapy**

Crizanlizumab-tmca (Adakveo) is considered medically necessary in adult and pediatric patients ( $\geq 16$  years of age) with sickle cell disease to reduce the frequency of vasoocclusive crises (VOCs) when the following criteria are met:

1. The patient has a confirmed diagnosis of sickle cell disease of any genotype (e.g. HbSS, HbSC, HbS/beta<sup>0</sup>-thalassemia, HbS/beta<sup>+</sup>-thalassemia); AND
2. The patient has had at least two vasoocclusive crisis (VOC) events in the last 12 months prior to initiation, as documented by a treating physician; AND
3. The patient has a baseline hemoglobin (Hgb) level  $\geq 4.0$  g/dL; AND
4. The patient is currently taking hydroxyurea, or has tried and failed or has a clinical contraindication/intolerance to hydroxyurea; AND
5. The patient will not be taking crizanlizumab concomitantly with voxelotor (Oxbryta); AND
6. Crizanlizumab is prescribed by or in consultation with a hematologist or specialist in sickle cell disease

Initial authorization: 6 months

### **Continuation Therapy**

Continuation of treatment with crizanlizumab-tmca (Adakveo) beyond 6 months after initiation of therapy, and every 12 months thereafter, is considered medically necessary for the treatment of sickle cell disease when the following criteria are met:

1. The patient is currently receiving crizanlizumab and continues to meet initial criteria; AND
2. The patient has improvement of disease as demonstrated by a decrease in the frequency of vasoocclusive crisis (VOC) events

## **When Crizanlizumab-tmca (Adakveo) is not covered**

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Crizanlizumab-tmca (Adakveo) is considered **investigational** and therefore not covered when the above criteria are not met.

## **Policy Guidelines**

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The recommended dose of Adakveo is 5 mg/kg administered as a 30-minute intravenous infusion given at week 0, week 2, and every 4 weeks thereafter. Adakveo should be administered by a healthcare professional and may be given with or without hydroxyurea.

According to the manufacturer's safety information for Adakveo, the most common adverse reactions ( $>10\%$  incidence) include nausea, joint pain, back pain, and fever. Infusion-related reactions may be observed following Adakveo administration. In addition, interference with

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automated platelet counts (platelet clumping) has been observed following Adakveo administration.

Vasooclusive crisis (VOC) events leading to a healthcare visit, as defined within the SUSTAIN trial, are acute episodes of pain with no cause other than a vasooclusive event that require a medical facility visit and treatment with oral or parenteral opioids, or parenteral NSAIDs. Acute chest syndrome, hepatic sequestration, splenic sequestration, and priapism requiring a medical facility visit are also considered to be VOC events.

## Clinical Trial 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/beta<sup>0</sup>-thalassemia, HbS/beta<sup>+</sup>-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 were observed in study participants regardless of SCD genotype and/or hydroxyurea use.

## **Billing/Coding/Physician Documentation Information**

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable codes: J0791*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## **Scientific Background and Reference Sources**

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# Crizanlizumab-tmca (Adakveo®)

Novartis Pharmaceuticals Corporation. Adakveo (crizanlizumab-tmca) injection, for intravenous use. Highlights of prescribing information. November 2019. Available at: <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/adakveo.pdf>. Last accessed January 2020.

U.S. Food and Drug Administration. FDA approves first targeted therapy to treat patients with painful complication of sickle cell disease. November 2019. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-targeted-therapy-treat-patients-painful-complication-sickle-cell-disease>. Last accessed January 2020.

Institute for Clinical and Economic Review (ICER). Crizanlizumab, Voxelotor, and L-Glutamine for Sickle Cell Disease: Effectiveness and Value. Draft Evidence Report January 23, 2020. 2020. Available at: [https://icer-review.org/wp-content/uploads/2019/08/ICER\\_SCD\\_Draft\\_Evidence\\_Report\\_012320-1.pdf](https://icer-review.org/wp-content/uploads/2019/08/ICER_SCD_Draft_Evidence_Report_012320-1.pdf). Last accessed February 2020.

Ataga KI, Kutlar A, Kanter J, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. N Engl J Med 2017;376:429-39. Available at: [https://www.nejm.org/doi/10.1056/NEJMoa1611770?url\\_ver=Z39.88-2003&rfr\\_id=ori:rid:crossref.org&rfr\\_dat=cr\\_pub%3dwww.ncbi.nlm.nih.gov](https://www.nejm.org/doi/10.1056/NEJMoa1611770?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dwww.ncbi.nlm.nih.gov). Last accessed January 2020.

Medical Director review 2/2020

Specialty Matched Consultant Advisory Panel 3/2020

## **Policy Implementation/Update Information**

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- 2/11/20 New policy developed. Crizanlizumab-tmca (Adakveo) is considered medically necessary in adult and pediatric patients ( $\geq 16$  years of age) with sickle cell disease to reduce the frequency of vasoocclusive crises (VOCs) when specified medical criteria and guidelines are met. Added HCPCS codes C9399, J3490, and J3590 to Billing/Coding section. References added. Medical Director review 2/2020. (krc)
- 3/31/20 Added HCPCS code C9053 to Billing/Coding section effective 4/1/2020. Specialty Matched Consultant Advisory Panel review 3/18/2020. No change to policy statements. (krc)
- 6/30/20 Added HCPCS code J0791 to Billing/Coding section effective 7/1/2020 and deleted codes C9053, C9399, J3490, and J3590 termed 6/30/2020. (krc)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.