



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 12/12/2024

Adakveo® (crizanlizumab-tmca)

HCPCS: J0791

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. FDA approved indication
 - b. FDA approved age
 - c. Prescribed by or in consultation with a hematologist
 - d. Patient has experienced 2 or more sickle cell-related crises in the past 12 months
 - e. Trial and failure for at least 6 months, contraindication, OR intolerance to hydroxyurea
 - f. Must not be using long-term red blood cell transfusion therapy
 - g. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity limit: Align with FDA recommended dosing
 - b. Initial Authorization Period: One year at a time
 - c. Renewal Criteria: Patient has experienced a decrease in the number of sickle cell-related crises

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Sickle cell disease (SCD) is a recessive hemolytic anemia caused by a mutation in the β -globin gene. It is characterized by the formation of sickle hemoglobin (HbS). HbS is less soluble and less elastic than fetal hemoglobin (HbF) or normal adult hemoglobin (HbA). The disease involves multicellular adhesion between sickled red blood cells, white blood cells, platelets, and endothelial cells resulting in vaso-occlusive crises (VOCs). VOCs are the hallmark of SCD and are experienced by approximately 70% of patients. They are recurring, unpredictable, painful events that decrease organ function with complications including stroke, pneumonia, vision loss, pulmonary hypertension, leg ulcers, and sepsis. VOCs are often treated as an emergency requiring acute care and are the number one reason patients with SCD visit the emergency room or are hospitalized.
- Hydroxyurea is a ribonucleotide reductase inhibitor which increases the amount of circulating HbF in the body and has been a mainstay of therapy. It also has been shown to lower the number of circulating leukocytes and reticulocytes altering the expression of adhesion molecules; raise red blood cell (RBC) volume; and improve cellular deformability and rheology, all of which contribute to a decrease in VOCs. The 2014 National Heart, Lung, and Blood Institute Evidence-Based Management of Sickle Cell Disease Guidelines recommend the use of hydroxyurea for the following patient populations:
 - In adults with SCD who have three or more sickle cell-associated moderate to severe pain crises in a 12-month period
 - In adults with SCD who have sickle cell-associated pain that interferes with daily activities and quality of life
 - In adults with SCD who have a history of severe and/or recurrent acute coronary syndrome
 - In adults with SCD who have severe symptomatic chronic anemia that interferes with daily activities or quality of life
 - In infants 9 months of age and older, children, and adolescents with SCD, offer treatment with hydroxyurea regardless of clinical severity to reduce complications
 - In adults and children with SCD who have chronic kidney disease and are taking erythropoietin
- The guidelines recommend starting hydroxyurea at a dose of 15 mg/kg/day for adults and increasing the dose by 5 mg/kg/day every 8 weeks to a maximum dose of 35 mg/kg/day. A clinical response to therapy may take 3 – 6 months. Therefore, a 6 month trial on the maximum tolerated dose is required prior to considering discontinuation due to treatment failure, whether due to lack of adherence or failure to respond to therapy.
- Adakveo is a monoclonal antibody that is indicated to reduce the frequency of VOCs in adults and pediatric patients aged 16 years and older with sickle cell disease. It binds to P-selectin and blocks interactions between endothelial cells, platelets, RBCs, and leukocytes. P-selectin plays a role in the formation of the multicellular aggregates that lead to VOCs.
- The efficacy of Adakveo was evaluated in the SUSTAIN trial, a randomized, multicenter, placebo-controlled, double-blind trial of 198 patients with sickle cell disease of any genotype and a history of 2 - 10 VOCs in the previous 12 months. Patients were excluded if they were receiving long-term red blood cell transfusions. The primary endpoint was the annual rate of VOCs leading to a healthcare visit. Acute chest syndrome, hepatic sequestration, splenic sequestration, and priapism (requiring a visit to a medical facility) were also considered VOCs. Patients receiving Adakveo 5 mg/kg, had a lower median annual rate of VOC compared to those receiving placebo (1.63 vs. 2.98, p-value = 0.01) indicating a 45.3% lower rate with Adakveo. Thirty-six percent of patients treated with Adakveo did not

experience a VOC compared to 17% in the placebo arm. The median time to first VOC from randomization was 4.1 months vs. 1.4 months in the Adakveo and placebo arm, respectively.

References:

1. Adakveo [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; June 2024.
2. Ataga KI, Kutlar A, Kanter J, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. *New Engl J Med.* 2017; 376 (5): 429 – 439.
3. Ogedegbe HO. Sickle cell disease: an overview. *Laboratory Medicine.* 2002; 33(7): 515 – 543.
4. Yale SH, Nagib N, & Guthrie T. Approach to the vaso-occlusion crisis in adults with sickle cell disease. *Am Fam Physician.* 2000; 61(5): 1349 – 1356.
5. Kanter J & Kruse-Jarres R. Management of sickle cell disease from childhood through adulthood. *Blood Rev.* 2013; 27(6): 279 – 287.
6. Brousseau DC, Panepinto JA, Nimmer M, et al. The number of people with sickle-cell disease in the United States: national and state estimates. *Am J Hematol.* 2010; 85(1): 77 – 78.
7. 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/publications/56-364NFULL.pdf>. Accessed on: October 4, 2020.

Policy History												
#	Date	Change Description										
1.8	Effective Date: 12/12/2024	Annual review of criteria was performed, no changes were made										
1.7	Effective Date: 12/14/2023	Annual review of criteria was performed, no changes were made										
1.6	Effective Date: 12/01/2022	Annual review of criteria was performed, no changes were made										
1.5	Effective Date: 12/09/2021	Annual review of criteria was performed, no changes were made										
1.4	Effective Date: 12/03/2020	Updated to include a trial and failure of hydroxyurea, the trial and failure of preferred products statement, and updated the approval duration to 1 year										
1.3	Effective Date: 03/16/2020	UM medical management system update for MAPPO and BCNA <table border="1" data-bbox="485 615 1365 825"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>Yes</td> </tr> <tr> <td>BCN</td> <td>Yes</td> </tr> <tr> <td>MAPPO</td> <td>Yes</td> </tr> <tr> <td>BCNA</td> <td>Yes</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
BCNA	Yes											
1.2	Effective Date: 02/01/2020	UM medical management system update for BCBS <table border="1" data-bbox="485 892 1365 1102"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>Yes</td> </tr> <tr> <td>BCN</td> <td>Yes</td> </tr> <tr> <td>MAPPO</td> <td>No</td> </tr> <tr> <td>BCNA</td> <td>No</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	No											
BCNA	No											
1.1	Effective Date: 01/02/2020	UM medical management system update for BCN <table border="1" data-bbox="485 1169 1365 1379"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>No</td> </tr> <tr> <td>BCN</td> <td>Yes</td> </tr> <tr> <td>MAPPO</td> <td>No</td> </tr> <tr> <td>BCNA</td> <td>No</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	Yes	MAPPO	No	BCNA	No
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	No											
BCN	Yes											
MAPPO	No											
BCNA	No											
1.0	Effective Date: 12/05/2019	New full drug review										

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Adakveo® (crizanlizumab-tmca) J0791



This form is to be used by participating physicians to obtain coverage for Adakveo. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

PATIENT INFORMATION

PHYSICIAN INFORMATION

Name	Name
ID Number	Specialty
D.O.B. <input type="checkbox"/> Male <input type="checkbox"/> Female	Address
Diagnosis	City /State/Zip
Drug Name	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Is this request for: Initiation Continuation *Date patient started therapy:* _____
- Site of administration? Provider office/Home infusion Other: _____
 Hospital outpatient facility (**go to #3**) *Reason for Hospital Outpatient administration:* _____
- Please specify location of administration if hospital outpatient infusion:** _____
- Please provide the NPI number for the place of administration:** _____
- Initiation AND Continuation of therapy:**
 - What is the patient's diagnosis?
 Sickle cell disease
 Other, Please specify: _____
 - Please specify the number of sickle cell-related crises the patient experienced in the past 12 months: _____
 - Please provide the dates of the patient's last two sickle-cell related crises: _____
 - Has the patient tried hydroxyurea for at least 6 months and failed therapy?
 Yes, Please specify how the patient failed hydroxyurea therapy (for example: side effects, lack of efficacy, etc.): _____
 No
 - Is the patient currently on and will they continue to be on long-term red blood cell transfusion therapy? Yes No
- Continuation of therapy:**
 - Has the patient experienced a decrease in the number of sickle cell-related crises? Yes No

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name

Physician Signature

Date

Step 2: Checklist	<input type="checkbox"/> Form Completely Filled Out <input type="checkbox"/> Attached chart notes	<input type="checkbox"/> Pertinent test results
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

Confidentiality notice: This transmission contains confidential information belonging to the sender that is legally privileged. This information is intended only for use of the individual or entity named above. The authorized recipient of this information is prohibited from disclosing this information to any other party. If you are not the intended recipient, you are hereby notified that any disclosure, copying, distribution or action taken in reliance on the contents of this document is strictly prohibited. If you have received this in error, please notify the sender to arrange for the return of this document.