Medical Policy:

Adakveo® (crizanlizumab-tmca) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.204	February 11, 2025	

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Adakveo (crizanlizumab-tmca) is a humanized IgG2 kappa monoclonal antibody that binds to P-selectin and blocks interactions with P-selectin glycoprotein ligand 1. The up-regulation of P-selectin in endothelial cells results in adhesion of sickle erythrocytes to the endothelium, causing vaso-occlusion. By binding to P-selectin, Adakveo (Crizanlizumab-tmca) inhibits interactions between endothelial cells, platelets, red blood cells, and leukocytes that are involved in the pathogenesis of vaso-occulsion, which may result in decreased platelet aggregation, maintenance of blood flow, and minimized sickle cell-related pain crises.

Adakveo (Crizanlizumab-tmca) is indicated to reduce the frequency of vasoocclusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease.

Length of Authorization

Coverage will be provided for 12 months and may be renewed.

Guideline

I. INITIAL APPROVAL CRITERIA

1. **Reduce The Frequency Of Vaso-Occlusive Crises (VOCs)**

Adakveo (crizanlizumab-tmca) may be considered medically necessary when all of the below conditions are met:

A. Patient is 16 years of age or older; **AND**
B. Diagnosis of sickle cell disease defined as any genotype (HbSS, HbSC, HbS/beta^{0}thalassemia, HbS/beta$^+$-thalassemia, and others); **AND**
C. Patient had an insufficient response to a minimum 3-month trial of hydroxyurea (unless contraindicated or intolerant); **AND**
D. Patient experienced one or more vaso-occlusive crises (VOC) in the previous year despite adherence to hydroxyurea therapy

Note: VOC is defined as an event prompting either a visit or outreach to the provider which results in a diagnosis of VOC being made necessitating subsequent interventions such as narcotic pain management, non-steroidal anti-inflammatory therapy, hydration, etc.

Limitations/Exclusions

Therapy will not be used in conjunction with voxelotor (Oxbryta) or L-glutamine (Endari); **AND**

A. Patient has not received prior treatment with gene therapy **OR**

Note: Examples of gene therapy include lovotibeglogene autotemcel, exagamglogene autotemce

B. Patient failed to respond or lost response to treatment with prior gene therapy

Note: Examples of gene therapy include lovotibeglogene autotemcel, exagamglogene autotemcel)

II. RENEWAL CRITERIA

Adakveo (crizanlizumab-tmca) may be renewed when all of the below conditions are met:l.

A. Patient continues to meet initial approval criteria; **AND**
B. Absence of unacceptable toxicity from the drug (e.g. severe infusion-related reactions); **AND**
C. Disease stabilization or improvement (e.g. reduction in frequency of VOCs).

Dosing/Administration

Indication	Dose
All indications	5 mg/kg by intravenous infusion over 30 minutes at week 0, week 2, and every 4 weeks thereafter.

Applicable Procedure Codes

Code	Description
J0791	Injection, crizanlizumab-tmca, 5 mg (Adakveo). J-Code effective date: 07/01/2020

Applicable NDCs

Code	Description
00078-0883-XX	Adakveo 100 mg/10 mL single-dose vial

ICD-10 Diagnoses

Code	Description

D57.00	Hb-SS disease with crisis unspecified
D57.01	Hb-SS disease with acute chest syndrome
D57.02	Hb-SS disease with splenic sequestration
D57.03	Hb-SS disease with cerebral vascular involvement
D57.04	Hb-SS disease with crisis with other specified complication
D57.09	Hb-SS disease with crisis with other specified complication
D57.1	Sickle-cell disease without crisis
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
D57.213	Sickle-cell/Hb-C disease with cerebral vascular involvement
D57.214	Sickle-cell/Hb-C disease with crisis with other specified complication
D57.218	Sickle-cell/Hb-C disease with crisis with other specified complication
D57.219	Sickle-cell/Hb-C disease with crisis unspecified
D57.3	Sickle-cell trait
D57.40	Sickle-cell thalassemia without crisis
D57.411	Sickle-cell thalassemia with acute chest syndrome
D57.412	Sickle-cell thalassemia with splenic sequestration
D57.413	Sickle-cell thalassemia, unspecified, with cerebral vascular involvement
D57.414	Sickle-cell thalassemia, unspecified, with crisis with other specified complication
D57.418	Sickle-cell thalassemia, unspecified, with crisis with other specified complication
D57.419	Sickle-cell thalassemia with crisis unspecified
D47.42	Sickle-cell thalassemia beta zero without crisis
D57.431	Sickle-cell thalassemia beta zero with acute chest syndrome
D57.432	Sickle-cell thalassemia beta zero with splenic sequestration
D57.433	Sickle-cell thalassemia beta zero with cerebral vascular involvement
D57.434	Sickle-cell thalassemia beta zero with crisis with other specified complication
D57.438	Sickle-cell thalassemia beta zero with crisis with other specified complication
D57.439	Sickle-cell thalassemia beta zero with crisis unspecified
D57.44	Sickle-cell thalassemia beta plus without crisis
D57.451	Sickle-cell thalassemia beta plus with acute chest syndrome
D57.452	Sickle-cell thalassemia beta plus with splenic sequestration
D57.453	Sickle-cell thalassemia beta plus with cerebral vascular involvement
D57.454	Sickle-cell thalassemia beta plus with crisis with other specified complication
D57.458	Sickle-cell thalassemia beta plus with crisis with other specified complication
D57.459	Sickle-cell thalassemia beta plus with crisis 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
D57.813	Other sickle-cell disorders with cerebral vascular involvement
D57.814	Other sickle-cell disorders with crisis with other specified complication
D57.819	Other sickle-cell disorders with crisis, unspecified

Revision History

Company(ies)	DATE	REVISION

<table>
<tr><td>EmblemHealth & ConnectiCare</td><td>2/10/2025</td><td>Removed Limitations: Adakveo (crizanlizumab-tmca) is not considered medically necessary when any of the below conditions are met:: A. Dosing exceeds single dose limit of Adakveo (crizanlizumab-tmca) 5 mg/kg. B. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable. Replaced with A.Patient has not received prior treatment with gene therapy OR Note: Examples of gene therapy include lovotibeglogene autotemcel, exagamglogene autotemce
Patient failed to respond or lost response to treatment with prior gene therapy
Note: Examples of gene therapy include lovotibeglogene autotemcel, exagamglogene autotemcel)

Removed from initial approval: Prior history of one or more sickle cell-related pain crises in the previous 12 months; AND Patient is currently receiving a hydroxyurea product; OR Patient had an insufficient response to a minimum 3-month trial of hydroxyurea (unless contraindicated or intolerant.) Added in Patient had an insufficient response to a minimum 3-month trial of hydroxyurea (unless contraindicated or intolerant); AND Patient experienced one or more vaso-occlusive crises (VOC) in the previous year despite adherence to hydroxyurea therapy Note: VOC is defined as an event prompting either a visit or outreach to the provider which results in a diagnosis of VOC being made necessitating subsequent interventions such as narcotic pain management, non-steroidal anti-inflammatory therapy, hydration, etc.</td></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>4/30/2024</td><td>Annual review: No criteria changes</td></tr>
<tr><td>EmblemHealth & ConnectiCare</td><td>8/11/2023</td><td>Annual Review:
Reduce The Frequency Of Vaso-Occlusive Crises (VOCs) Initial Criteria:
Removed “Prior history of 2 or more sickle cell-related pain crises in the previous 12 months; AND” Replaced with “Prior history of one or more sickle cell-related pain crises in the previous 12 months; AND”
Removed “If receiving hydroxyurea, treatment must be prescribed for at least 6 months; AND on a stable dose of hydroxyurea for at least 3 months.”
Added “Patient is currently receiving a hydroxyurea product; OR
Patient had an insufficient response to a minimum 3-month trial of hydroxyurea (unless contraindicated or intolerant)”
Added codes:
<table>
<tr><td>D57.03</td><td>Hb-SS disease with cerebral vascular involvement</td></tr>
<tr><td>D57.09</td><td>Hb-SS disease with crisis with other specified complication</td></tr>
<tr><td>D57.213</td><td>Sickle-cell/Hb-C disease with cerebral vascular involvement</td></tr>
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</table></td></tr>
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			involvement
		D57.438	Sickle-cell thalassemia beta zero with crisis with other specified complication
		D57.439	Sickle-cell thalassemia beta zero with crisis unspecified
		D57.44	Sickle-cell thalassemia beta plus without crisis
		D57.451	Sickle-cell thalassemia beta plus with acute chest syndrome
		D57.452	Sickle-cell thalassemia beta plus with splenic sequestration
		D57.453	Sickle-cell thalassemia beta plus with cerebral vascular involvement
		D57.458	Sickle-cell thalassemia beta plus with crisis with other specified complication
		D57.459	Sickle-cell thalassemia beta plus with crisis unspecified
		D57.813	Other sickle-cell disorders with cerebral vascular involvement
		D57.818	Other sickle-cell disorders with crisis with other specified complication
EmblemHealth & ConnectiCare	3/17/2022	Transferred policy to new template	
EmblemHealth & ConnectiCare	6/10/2020	Added J-Code (J0791) Injection, crizanlizumab-tmca, 5 mg (Adakveo). J-Code effective date: 07/01/2020	

References

1. Adakveo [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; November 2019.
2. Sins JWR, Mager DJ, Syrin CA, et al. Pharmacotherapeutical strategies in the prevention of acute, vaso-occlusive pain in sickle cell disease: a systematic review. *Am J Hematol*. 2017;1(19):1598-1616.
3. Piel FB, Steinberg MH. Sickle cell disease. *N Engl J Med*. 2017;376:1561-1573.
4. The National Institutes of Health – 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/media/docs/sickle-cell-disease-report%20020816_0.pdf. Accessed on January 23, 2020.
5. Reprixys Pharmaceutical Corporation. Study to Assess Safety and Impact of SelG1 With or Without Hydroxyurea Therapy in Sickle Cell Disease Patients With Pain Crises (SUSTAIN). In: ClinicalTrials.gov [Internet]. National Library of Medicine (US). [cited 2020 Jan 22]. Available at: https://www.clinicaltrials.gov/ct2/show/NCT01895361?term=01895361&draw=2&rank=1. Search term: NCT01895361.
6. Ataga KI, Kutlar J, Kanter K, et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. *N Engl J Med*. 2017;376(5):429-439.
7. Micromedex® Healthcare Series; Thomson Micromedex, Greenwood Village, Co. 2019.