Reference number(s)
3416-A

STANDARD MEDICARE PART B MANAGEMENT

ADAKVEO (crizanlizumab-tmca)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

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

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

Sickle cell disease, to reduce the frequency of vasoocclusive crises
Authorization of 12 months may be granted for use in reducing the frequency of vasoocclusive crises (VOCs) in members 16 years of age or older with sickle cell disease, when both of the following criteria are met:
A. The member has experienced at least one vasoocclusive crisis within the previous 12 months.
B. The member meets either of the following:
    1. Member has sickle hemoglobin C (HbSC) or sickle β^+-thalassemia (HbSβ^+) genotype
    2. Member has homozygous hemoglobin S (HbSS) or sickle β^0-thalassemia (HbSβ^0) genotype AND meets any of the following:
        i. Has experienced, at any time in the past, an inadequate response or intolerance to a trial of hydroxyurea.
        ii. Has a contraindication to hydroxyurea.
        iii. Will be using Adakveo with concurrent hydroxyurea therapy.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with Adakveo.
B. Adakveo is being used to treat an indication enumerated in Section II.

C. The member is receiving benefit from therapy. Benefit is defined as reduction in the frequency of vasoocclusive crises, or maintenance of such reduction, since initiating therapy with Adakveo.

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Adakveo.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. Evidence-based management of Sickle Cell Disease (NHLBI)
4. Guidelines for the use of hydroxycarbamide in children and adults (2018 British Society for Haematology)
5. Hydroxyurea (hydroxycarbamide) for sickle cell disease (Cochrane Review)

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Adakveo are covered.

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for requiring a trial and inadequate response, intolerance, or contraindication to hydroxyurea can be found in the National Heart, Lung, and Blood Institute (NHLBI) recommendations, the 2018 British Society of Haematology Guidelines, and a Cochrane Review.

The 2014 expert panel report from the NHLBI recommends treatment with hydroxyurea in adults with sickle cell anemia (SCA) who have had three or more moderate to severe sickle cell pain crises in the last 12 months, pain that interferes with daily activities and quality of life, history of severe and/or recurrent acute chest syndrome (ACS), severe symptomatic chronic anemia, and in infants nine months of age and older, children, and adolescents regardless of severity, to reduce complications. The report notes that SCA refers to HbSS or HbSbeta0 thalassemia, while SCD refers to all genotypes including SCA in addition to compound heterozygous disorders such as HbSC and HbSbeta+thalassemia. For individuals with HbSC and HBSbeta+thalassemia who have recurrent pain, the report recommends consideration of hydroxyurea in consultation with a sickle cell expert.

The 2018 British Society for Haematology guidelines for the use of hydroxyurea in SCD recommend the following for patients with HbSS or HbSbeta0 thalassemia:

- In infants who are nine to 42 months of age, hydroxyurea should be offered regardless of clinical severity to reduce sickle cell complications
- In children older than 42 months of age, adolescents and adults, hydroxyurea should be offered in view of the impact on reduction of mortality
- Adults and children should be treated with hydroxyurea if they have had three or more moderate to severe pain crisis in a 12-month period, have sickle cell pain that interferes with daily activities and quality of life, and have a history of severe and/or recurrent ACS.

For children and adults with genotypes other than HbSS or HbSbeta0 thalassemia, the guideline recommends consideration of hydroxyurea in those who have recurrent episodes of acute pain, ACS, or hospitalization.

A Cochrane Review by Rankine-Mullings and Nevitt included nine randomized controlled trials that evaluated the use of hydroxyurea in SCD. The RCTs enrolled a total of 1,104 adults and children with SCD (HbSS, HbSC or HbSbeta0 thalassemia genotypes). The authors found there is evidence that hydroxyurea may be effective in decreasing the frequency of pain episodes and other acute complications in adults and children with HbSS or HbSbeta0 thalassemia genotypes, and in preventing life-threatening neurological events in those at risk of primary stroke. The authors noted that evidence of the effects of hydroxyurea on individuals with the HbSC genotype is limited.

VI. REFERENCES

1. Adakveo [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2021.
2. 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(5):429-439.
3. Evidence-Based Management of Sickle Cell Disease. Expert Panel Report, 2014. National Institutes of Health. Available at https://www.nhlbi.nih.gov/health-topics/evidence-based-management-sickle-cell-disease. Accessed November 8, 2022.
4. Qureshi A, Kaya B, Pancham S, et al. Guidelines for the use of hydroxycarbamide in children and adults with sickle cell disease: A British Society for Haematology Guideline. *Br J Haematol*. 2018; 181(4):460-475.
5. Rankine-Mullings AE, Nevitt SJ. Hydroxyurea (hydroxycarbamide) for sickle cell disease. Cochrane Database Syst. Rev. 2022; 9(9):CD002202.