Adakveo

I. Generic Name:

a. Crizanlizumab

II. Brand Name:

a. Adakveo

III. Medication Class:

a. P-selectin inhibitor : monoclonal antibody that binds to P-selectin and block interaction with ligands including P-selectin glycoprotein ligand 1, inhibition of interaction between endothelial cells, platelets, red blood cells, and leukocytes may result in decreased platelet aggregation, maintenance of blood flow and minimization of sickle cell related pain crises

IV. FDA Approved Uses:

a. Sickle cell disease (SCD): To reduce the frequency of vaso-occlusive crises in adults and pediatric patients 16 years of age and older

V. Application of Criteria:

a. The following criteria apply to Illinois Medicaid, Michigan Medicaid, and Meridian Choice (HIX)

VI. Criteria for Use:

a. Member must be 16 years of age or older
b. Prescribed by a hematologist/oncologist
c. Current chart notes with plan of care recommending treatment with Adakveo
d. Clear documentation of severity and frequency of vaso-occlusive pain crises (VOCs)
e. Documentation that the patient has had 2 or more episodes of VOCs requiring an emergent intervention (ED visit or admission) within the past 12 months
f. Documentation of adequate trial and failure and compliance to appropriate maximum tolerated dose of Hydroxyurea
g. Documentation of adequate trial and failure and compliance to appropriate maximum tolerated dose of Endari (L-Glutamine)
h. Documentation of adequate trial and failure and compliance to combination treatment with Hydroxyurea and Endari at maximum tolerated doses
i. Current CBC documenting Hemoglobin (Hgb) level greater than or equal to 4.0 g/dL

j. Related lab work/test results such as neonatal genetic screening, high-performance liquid chromatography (HPLC), iso-electric focusing (IEF), direct DNA testing, or gel electrophoresis supporting the diagnosis of one of the following genotypes:
   A. (Refer to Table 1): Please note that hemoglobin electrophoresis testing after transfusion of red cells can result in an incorrect diagnosis. In such cases, sickle cell diagnosis should utilize DNA testing or be postponed for at least four months after transfusion.
   B. Homozygous sickle cell (HbSS) disease
   C. Sickle-cell Beta+ thalassemia (SC-Beta+)
   D. Sickle-cell Beta0 thalassemia (SC-Beta0)
   E. Hemoglobin SC (HbSc) disease

VII. Required Medical Information:

a. Proper diagnosis and documentation of an FDA approved indication
b. Current progress notes detailing the diagnosis with plan of care
c. Documentation of dose, date ranges of therapy, and clinical outcomes for all medications previously tried and failed
d. Complete chart notes documenting disease history
e. Related lab work/test results
f. Charts showing compliance to previous therapy and office visits

VIII. Contraindications:

a. Hypersensitivity to Adakveo or any component of the formulation

IX. Not Approved If:

a. Request is for Adakveo as combination therapy used concurrently with either Endari (L-Glutamine) or Oxbryta (voxelotor)
b. Patient shows non-compliance with previous treatment based on progress notes and/or pharmacy claims/fill history for required step therapies
c. Patient shows any contraindications to the use of Adakveo as outlined in the FDA approved prescribing information
d. Request is for a non-FDA approved indication or dose

X. Length of Authorization:

a. Initial: 3 months
b. Continuation: up to 6 months

XI. Dosing:

a. Initial dose: 5mg/kg IV once every 2 weeks for 2 doses
b. Maintenance dose: 5mg/kg IV once every 4 weeks thereafter

XII. Criteria for Continuation of Therapy:

a. Initial therapy was tolerated
b. Demonstrated improvement in disease (reduction in the number of frequent VOCs)
c. Patient must be compliant with taking all medication as prescribed
d. Patient must not be experiencing any severe adverse reaction while taking the medication
e. Office visit every 3-6 months with verified compliance and improvement or stability on drug

XII. Criteria for Discontinuation of Therapy:

a. Patient is non-compliant with pharmacologic or non-pharmacologic therapy
b. No demonstrable clinically significant improvement after initiation and stabilization of drug therapy
c. Patient is non-responsive to FDA-approved usual maximum dosing

XIII. References:

1. Crizanlizumab: Facts and Comparisons. Wolters Kluwer Health. November 2019.
2. Adakveo (crizanlizumab-tmca) Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2019.
3. Yawn BP, Buchanan GR, Afenyi-annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA. 2014; 312 (10):1033-48.
4. Ryan K, Bain BJ, Worthington D, et al. Significant haemoglobinopathies: guidelines for screening and diagnosis. Br J Haematol. 2010; 149 (1):35-49.
5. Torres L, Conran N. Emerging pharmacotherapeutic approaches for the management of sickle cell disease. Expert Opin Pharmacother. 2019; 20(2):173-186.
6. 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.
7. Kutlar A, Kanter J, Liles DK, et al. Effect of crizanlizumab on pain crises in subgroups of patients with sickle cell disease: A SUSTAIN study analysis. Am J Hematol. 2019; 94 (1):55-61.

Adakveo

Table 1. Hemoglobin patterns in common hemoglobinopathies

				Older children (>5 years, adolescents, and adults)				
Phenotype	**Genotype**	Neonatal Screen	Age = 6 weeks screening	**HbA (%)**	**HbA2 (%)**	**HbF (%)**	**HbS (%)**	**HbC (%)**
Normal	AA	FA	FA or AF	95 – 98	2 – 3	< 2	0	0
HbSS disease	**SS**	**FS**	**FS**	**0**	**< 3.5**	**5 - 15 (or higher)**	**85 – 95**	**0**
SC-Beta+	**SBeta+**	**FSA or FS**	**FSA**	**3 – 30**	**> 3.5**	**2- 10**	**65 – 90**	**0**
SC-Beta0	**SBeta0**	**FS**	**FS**	**0**	**> 3.5**	**2 - 15**	**80 – 92**	**0**
HbSc disease	**SC**	**FSC**	**FSC**	**0**	**< 3.5**	**1 – 5 (or higher)**	**45 – 50**	**45 – 50**
Beta thalassemia trait	A/(Beta or Beta+)	FA	FA	90 – 95	> 3.5	1 – 3	0	0
Sickle cell trait	AS	FAS	FAS	50 – 60	< 3.5	< 2	35 – 45 (lower if concomitant alpha thalassemia)	0

PHARMACY BENEFITS MANAGER

meridianRx

P.XXX Approval Criteria

Adakveo

Approved by: _____ Date: _____
CMO

Initial Approval:	
Revised:	
Annual Review:	
Next Review Date:	