RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	crizanlizumab-tmca
Policy Number:	RxA.586
Drug(s) Applied:	Adakveo®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Crizanlizumab-tmca (Adakveo®) is a selectin blocker used to reduce the frequency of vasoocclusive crises (VOC) in adults and pediatric patients aged 16 years and older with sickle cell disease (SCD).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
crizanlizumab-tmca (Adakveo®)	SCD	Administer 5 mg/kg by intravenous infusion over a period of 30 minutes on Week 0, Week 2, and every 4 weeks thereafter.	5 mg/kg

Dosage Forms

- Single-dose vial for injection: 100 mg/10 mL (10 mg/mL)

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Sickle Cell Disease (must meet all)**:**

1. Diagnosis of SCD with any genotype;
2. Age 16 years of age or older;
3. Prescribed by or in consultation with a hematologist;
4. Member meets one of the following (a or b):
   a. Member has experienced at least 2 VOC within the past 6 months while on hydroxyurea at up to maximally indicated doses (see *Appendix D)*;
   b. Member has intolerance* or contraindication to hydroxyurea and has experienced at least 2 VOC within the past 12 months (see *Appendix D)*;

**Myelosuppression and hydroxyurea treatment failure: Myelosuppression is dose-dependent and reversible and does not qualify for treatment failure. NIH guidelines recommend a 6 month trial on the maximum tolerated dose prior to considering discontinuation due to treatment failure, whether due to*

lack of adherence or failure to respond to therapy. A lack of increase in mean corpuscular volume (MCV) and/or fetal hemoglobin (HbF) levels is not indication to discontinue therapy

5. Documentation of baseline incidence of VOC over the last twelve months;
6. Adakveo® is prescribed concurrently with hydroxyurea, unless contraindicated or clinically significant adverse effects are experienced;
7. Adakveo® is not prescribed concurrently with Oxbryta®;
8. Dose does not exceed 5 mg/kg doses on Day 1 and Day 15, followed by 5 mg/kg every 4 weeks.

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Sickle Cell Disease (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by a documented improvement in the incidence of VOC from baseline;
3. Adakveo® is prescribed concurrently with hydroxyurea, unless contraindicated or clinically significant adverse effects are experienced;
4. Adakveo® is not prescribed concurrently with Oxbryta®;
5. If request is for a dose increase, new dose does not exceed 5 mg/kg every 4 weeks.

Approval duration:
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
SCD: Sickle cell disease
Hb: Haemoglobin
VOC: Vaso-occlusive crises

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
hydroxyurea (Droxia®)	*Age ≥ 18 years* Initial: 15 mg/kg/day PO single dose; based on blood counts, may increase by 5 mg/kg/day every 12 weeks to a max 35 mg/kg/day	35 mg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
hydroxyurea (Siklos®)	<u>*Age ≥ 2 years*</u> Initial: 20 mg/kg/day PO once daily; based on blood counts, may increase by 5 mg/kg/day every 8 weeks or if a painful crisis occurs	35 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- A VOC is defined as a previously documented episode of acute painful crisis or acute chest syndrome (ACS) for which there was no explanation other than VOC that required prescription or healthcare professional-instructed use of analgesics for moderate to severe pain.
- <u>Myelosuppression and hydroxyurea treatment failure:</u> Myelosuppression is dose dependent and reversible and does not qualify for treatment failure. NIH guidelines recommend a 6 month trial on the maximum tolerated dose prior to considering discontinuation due to treatment failure, whether due to lack of adherence or failure to respond to therapy. A lack of increase in mean corpuscular volume (MCV) and/or fetal hemoglobin (HbF) levels is not indication to discontinue therapy.
- <u>Hydroxyurea dose titration:</u> Members should obtain complete blood counts (CBC) with white blood cell (WBC) differential and reticulocyte counts at least every 4 weeks for titration. The following lab values indicate that it is safe to increase dose.
  - Absolute neutrophil count (ANC) in adults ≥ 2,000/uL, or ANC ≥ 1,250/uL in younger patients with lower baseline counts
  - Platelet counts ≥ 80,000/uL

  If neutropenia or thrombocytopenia occurs: hydroxyurea dosing is held, CBC and WBC differential are monitored weekly, members can restart hydroxyurea when values have recovered.

References

1. Adakveo® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2019. Available https://www.novartis.us/sites/www.novartis.us/files/adakveo.pdf . Accessed August 18, 2020.
2. 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;94:55-61.
3. Ataga K, Kutlar A, Kanter J, et al. Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease. N Engl J Med. 2017 Feb 2;376(5):429-439.
4. 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 Sep 10;312(10):1033-48.
5. Micromedex® Healthcare Series [Internet database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Accessed August 18, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Line of business policy applies was updated to All lines of business 3. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 4. APPENDIX B: Was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements". 5. References were updated. 6. Removed "Hb level ≥ 4 g/dL" from the initial approval criteria.	12/03/2020	12/07/2020