Clinical Policy Title:	methoxy polyethylene glycol-epoetin beta
Policy Number:	RxA.208
Drug(s) Applied:	Mircera®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Methoxy polyethylene glycol-epoetin beta (Mircera®) is an erythropoiesis-stimulating agent (ESA). It is indicated for the treatment of anemia associated with chronic kidney disease (CKD) in:

- Adult patients on dialysis and patients not on dialysis.
- Pediatric patients 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.

Limitation(s) of use:

- Mircera® is not indicated and is not recommended for use:
  - In the treatment of anemia due to cancer chemotherapy.
  - As a substitute for red blood cell transfusions in patients who require immediate correction of anemia.
- Mircera® has not been shown to improve symptoms, physical functioning or health-related quality of life.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
methoxy polyethylene glycol-epoetin beta (Mircera®)	Anemia due to CKD	**Adult patients with CKD on or not on dialysis** Initial treatment: 0.6 mcg/kg body weight subcutaneously or intravenously once every two weeks; Maintenance treatment: dose twice that of the every-two-week dose subcutaneously or intravenously once monthly; Conversion from another ESA: Dosed subcutaneously or intravenously once monthly or once every two weeks based on total weekly epoetin alfa or darbepoetin alfa dose at time of conversion;**Pediatric patients with CKD on hemodialysis**	Varies

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Conversion from another ESA: Dosed intravenously once every four weeks based on total weekly epoetin alfa or darbepoetin alfa dose at time of conversion.	

Dosage Forms

- Injection (single-dose prefilled syringe): 30 mcg, 50 mcg, 75 mcg, 100 mcg, 120 mcg, 150 mcg, 200 mcg, or 250 mcg in 0.3 mL solution; 360 mcg in 0.6 mL solution

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Anemia of Chronic Kidney Disease (must meet all)**:**

1. Diagnosis of anemia of CKD;
2. Member meets one of the following (a or b):
   a. Age ≥ 18 years (on or not on dialysis);
   b. Age 5 to 17 years, on dialysis, and will be converting from another ESA agent (e.g., epoetin alfa, darbepoetin alfa);
3. Prescribed by or in consultation with a hematologist or nephrologist;
4. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
5. Pretreatment hemoglobin < 10 g/dL;
6. Failure of Procrit®, unless contraindicated or clinically significant adverse effects are experienced; *Prior authorization is required for Procrit
7. Dosing interval does not exceed one of the following (a or b):
   a. Adults: Subcutaneously or intravenously once every two weeks;
   b. Pediatrics: Intravenously once every four weeks.

Approval Duration

Medicaid: 6 months

Commercial: 6 months

II. Continued Therapy Approval

A. Anemia of Chronic Kidney Disease (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Adequate iron stores as indicated by current (within the last 3 months) serum ferritin level ≥ 100 mcg/L or serum transferrin saturation ≥ 20%;
4. Dosing interval does not exceed one of the following (a or b):

a. Adults: Subcutaneously or intravenously once every two weeks;
b. Pediatrics: Intravenously once every four weeks.

Approval Duration
Medicaid: 6 months
Commercial: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CKD: chronic kidney disease
ESA: erythropoiesis-stimulating agent
FDA: Food and Drug Administration
RBC: red blood cell
PRCA: pure red cell aplasia

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
Procrit®	**Anemia due to CKD** Adults: 50-100 Units/kg Intravenously or Subcutaneously Three times weekly; Pediatrics (age 1 month or older): 50 Units/kg Intravenously or Subcutaneously Three times weekly.	Varies
Epogen®	**Anemia due to CKD** Adults: 50-100 Units/kg Intravenously or Subcutaneously Three times weekly. The intravenous route is recommended for patients on hemodialysis; Pediatrics (ages 1 month or older): 50 Units/kg Intravenously or Subcutaneously Three times weekly.	Varies

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Uncontrolled hypertension;
  - Pure red cell aplasia (PRCA) that begins after treatment with erythropoietin protein drugs;
  - History of serious or severe allergy reactions to Micerna (i.e anaphylaxis, angioedema, bronchospasm, skin rash, and uticaria).

- Boxed Warning(s):
  - ESAs increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence.

APPENDIX D: General Information

- Seizures: Epogen increases the risk for seizures in patients with CKD. Increase monitoring of these patients for changes in seizure frequency or premonitory symptoms.

References

1. Mircera Prescribing Information. Gallen Switzerland; Vifor (International) Inc; June 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125164s078lbl.pdf. Accessed July 12, 2021.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int. 2012;2(Suppl):279-335. Available at: https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-Anemia-Guideline-English.pdf. Accessed July 12, 2021.
3. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2021. Accessed with subscription at: http://www.clinicalkey.com. Accessed July 12, 2021.
4. Mircera. Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed July 12, 2021.
5. Epogen. Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed July 12, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Reformatted age “Age 5 to 17 years” 2. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 3. Initial Therapy criteria & Continued Therapy criteria: Added Approval Duration Medicaid: 6 months; Updated Approval duration for commercial to 6 months 4. Reference reviewed and updated.	06/22/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Continued Therapy Approval Criteria II.A.1. was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance”.	07/12/2021	09/14/2021

3. Appendix A was updated to include abbreviation PRCA. 4. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 5. Appendix B was updated to include alternative brand-name drug Epogen® and its dosing regimen and maximum dose.. 6. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 7. Appendix C contraindications was updated to include "History of serious or severe allergy reactions to Micerna…". 8. Appendix D was updated to include warning and precaution, "Epogen increases the risk for seizures in patients with CKD…". 9. References were reviewed and updated. 10.		