MEDICAL MUTUAL®

Drug Policy

Policy:	**201510**	**Initial Effective Date: 04/30/2015**
Code(s):	**HCPCS J0888**	**Annual Review Date: 09/20/2018**
SUBJECT:	Mircera® (methoxy polyethylene glycol-epoetin beta injection)	**Last Revised Date: 12/28/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Overview

Mircera is a an erythoid stimulating agent (ESA) that is approved for the following indications:[1]

1) Treatment of anemia with chronic kidney disease (CKD) in adult patients on dialysis and adult patients not on dialysis; AND
2) Treatment of anemia associated with CKD in 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.

Mircera is available as single-dose prefilled syringes in the following strengths: 30 mcg/0.3 mL, 50 mcg/0.3 mL, 75 mcg/0.3 mL, 100 mcg/0.3 mL, 120 mcg/0.3 mL, 150 mcg/0.3 mL, 200 mcg/0.3 mL, 250 mcg/0.3 mL, and 360 mcg/0.6 mL.

Policy Statement

This policy involves the use of Mircera. Prior authorization is recommended for medical benefit coverage of Mircera. Approval is recommended for those who meet the conditions of coverage in the **Criteria**, **Dosing**, **Initial/Extended Approval**, **Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. The requirement that the patient meet the Criteria for coverage of the requested medication applies to the initial authorization only. **Waste Management** applies for all covered conditions. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy. *The site of care medical necessity criteria applies to initial therapy and reauthorizations under the medical benefit.

Recommended Authorization Criteria

Coverage of Mircera is recommended in those who meet the following criteria listed below.

Food and Drug Administration (FDA)-Approved Indications

1. **<u>Anemia in Chronic Kidney Disease (CKD) for Patients Who are on Dialysis</u> <u>– No prior approval needed for this indication.</u>**

Approve Mircera if the patient meets the following criteria (a, b, c, d, <u>and</u> e):

a) For initial therapy, Hb is < 10.0 g/dL for adults and ≤ 11.0 g/dL for children; OR
For patients currently receiving an erythroid stimulating agents (e.g., Aranesp, epoetin alfa, or Mircera), Hb is ≤ 11.5 g/dL for adults and ≤ 12.0 g/dL for children or If the Hb is > 12g/dL but the patient has had a previous beneficial response to therapy, the provider must have a protocol for dose reduction and withholding doses if subsequest Hb values exceed 12g/dL.; AND

b) The patient is currently receiving iron therapy or iron stores are adequate (e.g., Mircera prescribing information recommends supplemental iron therapy when serum ferritin is < 100 mcg/L or when serum transferrin saturation is < 20%); AND

c) Patient is aged ≥ 5 years; AND

d) Patient's hypertension is well controlled; AND

e) Site of care medical necessity is met*.

Mircera is indicated for the treatment of anemia associated with CKD in adult patients on dialysis and in pediatric patients 5 to 17 years of age on dialysis who are converting from another ESA after their hemogolobin level was stabilized with the ESA.[1] The prescribing information for Mircera recommends that therapy should be initiated for adult patients with CKD on dialysis when the Hb is < 10.0 g/dL and if the Hb level approaches or exceeds 11.0 g/dL, reduce or interrupt the Mircera dose. The Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines for anemia in CKD, published in 2012, state that for adults with CKD on dialysis ESA therapy should be used to avoid having the Hb concentration fall below 9.0 g/dL by initiating ESA therapy when the Hb is between 9.0 to 10.0 g/dL.[2] In general, ESAs should not be used to maintain Hb concentrations above 11.5 g/dL in adult patients with CKD. For pediatric patients with CKD, the Hb concentration in which ESAs should be initiated in the individual patient should be considered with awareness of the potential benefits and potential harms. In all pediatric patients with CKD receiving ESA therapy the selected Hb concentration should be in the range of 11.0 to 12.0 g/dL. For adult patients with CKD on ESA therapy who are not receiving iron supplementation, a trial of intravenous iron (or oral iron therapy in patients with CKD not on dialysis) is recommended when transferrin saturation is < 30% and ferritin is ≤ 500 mcg/L. For all pediatric patients with CKD receiving ESA therapy who are not receiving iron supplementation, oral iron (or intravenous iron in patients with CKD who are on dialysis) should be administered to maintain transferrin saturation > 20% and ferritin > 100 mcg/L. During the initiation of ESA therapy, KDIGO guidelines recommend to measure Hb concentrations at least monthly. During the maintenance phase of ESA therapy for patients with CKD on dialysis, measure Hb concentrations at least monthly. KDIGO recommends to evaluate iron status (transferrin saturation and ferritin) at least every 3 months during ESA therapy, including the decision to start or continue iron therapy.

Dosing in Patients with CKD who are on Dialysis. *Dosing must meet the following (A, B OR C):*

A) For adults who are not currently treated with an ESA, the dose is 0.6 mcg/kg body weight given as a single intravenous (IV) or subcutaneous (SC) injection once every 2 weeks. After the hemoglobin has stabilized, Mircera may be given once monthly using a dose that is twice that of the once every 2-week dose and subsequently titrated as needed; OR

B) For adults converting from epoetin alfa or darbepoetin alfa to Mircera, Mircera can be given once every 2 weeks or once monthly to patients whose hemoglobin has been stabilized by treatment with an ESA. The Mircera dose, given as a single IV or SC injection, should be based on the total weekly ESA dose at the time of conversion. If

the previous weekly dose of epoetin alfa was < 8,000 units/week or the previous weekly darbepoetin alfa dose was < 40 mcg/week, the Mircera dose should be 120 mcg once monthly or 60 mcg once every 2 weeks; if the previous weekly dose of epoetin alfa was 8,000 to 16,000 units/week or the previous weekly darbepoetin alfa dose was 40 to 80 mcg/week, the Mircera dose is 200 mcg once monthly or 100 mcg once every 2 weeks; if the previous weekly epoetin alfa dose was > 16,000 units/week or the previous darbepoetin alfa dose was > 80 mcg/week, the Mircera dose is 360 mcg once monthly or 180 mcg once every 2 weeks; OR

C) For pediatric patients with CKD on hemodialysis, administer Mircera IV once every 4 weeks to pediatric patients (5 to 17 years of age) whose hemoglobin levels has been stabilized by therapy with an ESA as follows: 1) for patients previously on epoetin alfa, administer four-times the previously weekly epoetin alfa dose (units) divided by 125; 2) for patients previously on darbepoetin alfa, administer four-times the previous weekly darbepoetin alfa dose (mcg) divided by 0.55.

Initial Approval/Extended Approval.

A) *Initial Approval*. Initial approval is for 6 months if Hb is < 10.0 g/dL for adults and ≤ 11.0 g/dL for children.

B) *Extended Approval*. Extended approval is at 6-month intervals if the Hb is ≤ 11.5 g/dL for adults and ≤ 12.0 g/dL for children and the patient responds to therapy. Response is defined as Hb has increased, Hb has stayed the same and not decreased further, RBC transfusions are not required, and/or the number of RBC transfusions has decreased. For patients not responding, discontinue Mircera and evaluate and treat for other causes of anemia.

Duration of Therapy in Patients with CKD who are on Dialysis. Indefinite as long as the patient has CKD and is receiving dialysis.

Labs/Diagnostics. *Patient must meet the following criteria (A AND B)*:

A) Monitor Hb at therapy initiation and at 6-month intervals; AND

B) Iron stores (for example, serum iron, total iron binding capacity, serum ferritin, percent transferrin saturation [TSAT], bone marrow biopsy) must be evaluated at therapy initiation and at 6-month intervals, unless the patient is currently receiving iron therapy.

2. Anemia in Chronic Kidney Disease (CKD) for Patients Who are Not on Dialysis.[1] Approve Mircera if the patient meets the following criteria (a, b, c, d, and e).

a) For initial therapy, Hb is < 10.0 g/dL; OR
For patients currently receiving an ESA (e.g., Aranesp, epoetin alfa, or Mircera),, Hb is ≤ 11.5 g/dL or If the Hb is > 12g/dL but the patient has had a previous beneficial response to therapy, the provider must have a protocol for dose reduction and withholding doses if subsequest Hb values exceed 12g/dL. ; AND

b) The patient is currently receiving iron therapy or iron stores are adequate (e.g., Mircera prescribing information recommends supplemental iron therapy when serum ferritin is < 100 mcg/L or when serum transferrin saturation is < 20%); AND

c) Patient is aged ≥ 18 years; AND

d) Patient's with hypertension are well controlled; AND

e) Site of care medical necessity is met*.

Mircera is indicated for the treatment of anemia due to CKD in adults not on dialysis.[1] The safety and efficacy of Mircera in pediatric patients have not been established for the treatment of anemia in patients with CKD who are not yet on dialysis. The prescribing information for Mircera recommends for patients with CKD not on dialysis, Mircera should be initiated when the Hb is < 10.0 g/dL and other considerations apply (e.g., patient is likely to need transfusions). If the Hb exceeds 10.0 g/dL, reduce or interrupt the Mircera dose and use the lowest dose sufficient to reduce the need for RBC transfusions.[1] Clinical practice guidelines for anemia in CKD from KDIGO recommend against ESA therapy for adult patients with CKD who are not on dialysis when Hb levels are ≥ 10.0 g/dL.[2] For adult patients with CKD who are not on dialysis with Hb levels < 10.0 g/dL, the decision whether to initiate ESA therapy should be individualized based on many factors (e.g., prior response to iron therapy, the risk of needing a transfusion, presence of symptoms). In general, ESAs should not be used to maintain Hb concentrations above 11.5 g/dL in adult patients with CKD. For adult patients with CKD on ESA therapy who are not receiving iron supplementation, a trial of IV iron (or oral iron therapy in patients with CKD not on dialysis) is suggested when transferrin saturation is < 30% and ferritin is ≤ 500 mcg/L. KDIGO guidelines recommend during the initiation of ESA therapy to measure Hb concentrations at least monthly. For patients with CKD not on dialysis during the maintenance phase of ESA therapy, measure Hb concentration at least every 3 months. KDIGO recommends evaluating iron status (transferrin saturation and ferritin) at least every 3 months during ESA therapy, including the decision to start or continue iron therapy.[2]

Dosing in Patients with CKD who are not on Dialysis. *Dosing must meet the following:*

A) For adults, initiate therapy for patients who are not currently treated with an ESA at 0.6 mcg/kg body weight given as a single IV or SC injection once every 2 weeks. Once the hemoglobin has stabilized, administer once monthly using a dose that is twice that of the every 2-week dose. Titrate as needed.

Initial Approval/Extended Approval.

A) *Initial Approval*. Initial approval is for 6 months if Hb is < 10.0 g/dL for adults.

B) *Extended Approval*. Extended approval is at 6-month intervals if the Hb is ≤ 11.5 g/dL for adults and the patient responds to therapy. Response is defined as Hb has increased, Hb has stayed the same and not decreased further, RBC transfusions are not required, and/or the number of RBC transfusions has decreased. For patients not responding, discontinue Mircera and evaluate and treat for other causes of anemia.

Duration of Therapy in Patients with CKD who are not on Dialysis: Indefinite as long as the patient has CKD.

Labs/Diagnostics. *Patients must meet the following criteria (A AND B)*:

A) Monitor Hb at therapy initiation and at 6-month intervals; AND

B) Iron stores (for example, serum iron, total iron binding capacity, serum ferritin, TSAT, bone marrow biopsy) must be evaluated at therapy initiation and at 6-month intervals, unless the patient is currently receiving iron therapy.

Waste Management for All Indications.

Prefilled syringes are available in many different strengths. The dose should be calculated and the number of syringes needed assessed.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Mircera has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Anemia Associated with Cancer in Patients Receiving Myelosuppressive Cancer Chemotherapy.** Mircera is not indicated and not recommended for the treatment of anemia due to cancer chemotherapy.[1] In a dose-ranging trial of Mircera involving patients (n = 153) who were undergoing chemotherapy for non-small cell lung cancer, the trial was terminated prematurely because more deaths occured among patients receiving Mircera compared with another ESA (Aranesp).

2. **To Enhance Athletic Performance.** Mircera is not recommended for approval because this indication is excluded from coverage in a typical pharmacy benefit.

3. **Anemia in Patients due to Acute Blood Loss.** Use of Mircera is not appropriate in these types of situations.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Mircera® solution for injection [prescribing information]. Basking Ridge, NJ: Vifor Pharma; June 2018.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. *Kidney Inter*. 2012;2(Suppl):279-335. Available at: http://www.kdigo.org/clinical_practice_guidelines/pdf/KDIGO-Anemia%20GL.pdf. Accessed on June 18, 2018.
3. Locatelli F, Choukroun G, Truman M, et al. Once-monthly continuous erythropoietin receptor activator (C.E.R.A.) in patients with hemodialysis-dependent chronic kidney disease: pooled data form Phase III trial. *Adv Ther*. 2016;33:610-625.
4. Saglimbene VM, Palmer SC, Ruospo M, et al. Continuous erythropoiesis receptor activator (CERA) for the anemia of chronic kidney disease. *Cochrane Database Syst Rev*. 2017 Aug 7;8:CD009904.

5. Fischbach M, Wuhl E, Reigner SCM, et al. Efficacy and long-term safety of C.E.R.A. maintenance in pediatric hemodialysis patients with anemia of CKD. *Clin J Am Soc Nephrol*. 2018;13(1):81-90.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

***MMO Site of Care Medical Necessity Criteria:**

- Medications in this policy will be administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless *at least one* of the following are met†:

    1. Age less than 18* years; or
    2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
    3. History of a severe adverse event from previous administration of the prescribed medication; or
    4. Requested medication is being administered as follows:
        - part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
        - administered with dialysis; or
    5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or
    6. Up to 1 dose of medication or re-initiation after at least 12 months; or
    7. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility based location.

* Effective 01/01/2019, age criterion applies to 18 years of older. Age at original effective date (03/01/2016) was 21 years or older.
†This criterion does not apply to Medicare or Medicare Advantage members.

Prior approval is required for HCPCS Codes J0888.

HCPCS Code(s):	
J0888	Injection, epoetin beta, 1 microgram (for non-ESRD use)