Mircera® (methoxy polyethylene glycol-epoetin beta)
(Intravenous/Subcutaneous)

NON-DIALYSIS

Document Number: IC-0244

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I. Length of Authorization

- Coverage will be provided for 45 days and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Mircera 30 mcg prefilled syringe: 1 syringe every 14 days
- Mircera 50 mcg prefilled syringe: 1 syringe every 14 days
- Mircera 75 mcg prefilled syringe: 1 syringe every 14 days
- Mircera 100 mcg prefilled syringe: 1 syringe every 14 days
- Mircera 120 mcg prefilled syringe: 1 syringe every 14 days
- Mircera 150 mcg prefilled syringe: 1 syringe every 14 days
- Mircera 200 mcg prefilled syringe: 1 syringe every 28 days
- Mircera 250 mcg prefilled syringe: 1 syringe every 28 days
- Mircera 360 mcg prefilled syringe: 1 syringe every 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 360 billable units every 28 days

III. Initial Approval Criteria [1]

Coverage is provided in the following condition(s):

Universal Criteria [1-6]

- Lab values are obtained within 30 days of the date of administration (unless otherwise indicated); AND

- Patient has adequate iron stores as demonstrated by serum ferritin ≥ 100 ng/mL (mcg/L) and transferrin saturation (TSAT) ≥ 20% (measured within the previous 3 months for renewal)*; **AND**
- Other causes of anemia (e.g., hemolysis, bleeding, vitamin deficiency, etc.) have been ruled out; **AND**
- Patient does not have uncontrolled hypertension; **AND**

Anemia Due to Chronic Kidney Disease (Non-Dialysis Patients) † [1-6]

- Initiation of therapy Hemoglobin (Hb) < 10 g/dL and/or Hematocrit (Hct) < 30%; **AND**
  - Patient is at least 18 years of age; **OR**
- Patient is converting from another erythropoietin stimulating agent (ESA) (i.e., epoetin or darbepoetin) after their hemoglobin level was stabilized with an ESA; **AND**
  - Patient is at least 3 months of age

† FDA Approved Indications; ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,5]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Previous dose was administered within the past 60 days; **AND**
- Disease response with treatment as defined by improvement in anemia compared to pretreatment baseline; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: pure red cell aplasia, severe allergic reactions (anaphylaxis, angioedema, bronchospasm, etc.), severe cutaneous reactions (erythema multiforme, Stevens-Johnson Syndrome [SJS]/Toxic Epidermal Necrolysis [TEN], etc.), severe cardiovascular events (stroke, myocardial infarction, congestive heart failure, thromboembolism, etc.), uncontrolled hypertension, seizures, etc.; **AND**

Anemia Due to Chronic Kidney Disease (Non-Dialysis Patients):

- **Pediatric patients (3 months to 17 years of age):** Hemoglobin (Hb) < 12 g/dL and/or Hematocrit (Hct) < 36%
- **Adult patients**: Hemoglobin (Hb) <11 g/dL and/or Hematocrit (Hct) <33%

* Intravenous iron supplementation may be considered when evaluating iron status
• Functional iron deficiency (i.e., adequate iron stores with an insufficient supply of available iron) may occur in patients with chronic diseases, cancer, and/or in those currently receiving ESAs. • Iron is not generally recommended in anemic patients with a Ferritin >500 ng/mL.

- Anemic patients with a Ferritin ≤500 ng/mL AND TSAT <50% may derive benefit from IV iron therapy in conjunction with ESA.

V. Dosage/Administration [1]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Anemia due to Chronic Kidney Disease in ADULT patients – Non-dialysis §</td><td>
<u>Initial Dose in patients who are not currently receiving treatment with an ESA:</u>
Administer 1.2 mcg/kg subcutaneously once every 28 days. Alternatively, a starting dose of 0.6 mcg/kg body weight once every two weeks as a single intravenous or subcutaneous injection.
<u>Initial Dose for patients converting from another ESA:</u>
<table>
<tr><th rowspan="2">Previous Weekly Epoetin alfa Dose (units/week)</th><th rowspan="2">Previous Weekly Darbepoetin alfa Dose (mcg/week)</th><th colspan="2">Mircera Dose</th></tr>
<tr><td>Once Monthly (mcg/month)</td><td>Once Every 2 Weeks (mcg/every 2 weeks)</td></tr>
<tr><td>less than 8000</td><td>less than 40</td><td>120</td><td>60</td></tr>
<tr><td>8000 to 16000</td><td>40 to 80</td><td>200</td><td>100</td></tr>
<tr><td>more than 16000</td><td>more than 80</td><td>360</td><td>180</td></tr>
</table>
<u>Maintenance Dose:</u>
Once Hb has stabilized, administer once monthly using a dose that is twice that of the every-two-week dose and subsequently titrate as necessary. Most commonly the dose ranges from 120 to 360 mcg every 28 days.
</td></tr>
<tr><td>Anemia due to Chronic Kidney Disease in PEDIATRIC patients 3 months to 17 years of age – Non-dialysis ¥</td><td>
Administer once every 4 weeks as an intravenous or subcutaneous injection to pediatric patients 3 month to 17 years of age. The starting dose is calculated based on the total weekly ESA dose at the time of conversion (see table below).
<table>
<tr><th>Previous Weekly Epoetin alfa or Epoetin beta Dose (units/week)</th><th>Previous Weekly Darbepoetin alfa Dose (mcg/week)</th><th>Mircera Dose Once every 4 weeks (mcg)</th></tr>
<tr><td>less than 1300 units</td><td>less than 6 mcg</td><td>30</td></tr>
<tr><td>1300 units to less than 2000 units</td><td>6 mcg to less than 9 mcg</td><td>50</td></tr>
<tr><td>2000 units to less than 2700 units</td><td>9 mcg to less than 12 mcg</td><td>75</td></tr>
<tr><td>2700 units to less than 3500 units</td><td>12 mcg to less than 15 mcg</td><td>100</td></tr>
<tr><td>3500 units to less than 4200 units</td><td>15 mcg to less than 19 mcg</td><td>120</td></tr>
<tr><td>4200 units to less than 5500 units</td><td>19 mcg to less than 24 mcg</td><td>150</td></tr>
<tr><td>5500 units to less than 7000 units</td><td>24 mcg to less than 31 mcg</td><td>200</td></tr>
<tr><td>7000 units to less than 9500 units</td><td>31 mcg to less than 42 mcg</td><td>250</td></tr>
<tr><td>greater than or equal to 9500 units</td><td>greater than or equal to 42 mcg</td><td>360</td></tr>
</table>
<u>NOTE:</u>
– Pre-filled syringes are not designed for administration of partial doses. Pediatric patients requiring a dose of less than 30 mcg of Mircera should not be treated with Mircera.
</td></tr>
</table>

	– In patients less than 6 years of age, maintain the same route of administration as the previous ESA when switching from another ESA to Mircera.

§ Dose Adjustments and Discontinuation Guidance for ADULT patients:

- Do not increase the dose more frequently than once every 4 weeks. Decreases in dose can occur more frequently. Avoid frequent dose adjustments.
- If the hemoglobin rises rapidly (e.g., more than 1 g/dL in any 2-week period), reduce the dose by approximately 25% to the closest dose achievable with the prefilled syringes to reduce rapid responses.
- If the hemoglobin continues to rise following a dose reduction, discontinue Mircera until the hemoglobin level begins to decrease, at which point therapy should be restarted with a dose that is approximately 25% below the previously administered dose.
- For patients who do not respond adequately, if the hemoglobin has not increased by more than 1 g/dL after 4 weeks of therapy, increase the dose by approximately 25% to the closest dose achievable with the prefilled syringes.
- For patients who do not respond adequately over a 12-week escalation period, increasing the dose further is unlikely to improve response and may increase risks. Use the lowest dose that will maintain a hemoglobin level sufficient to reduce the need for RBC transfusions. Evaluate other causes of anemia. Discontinue Mircera if responsiveness does not improve.

¥ Dose Adjustments and Discontinuation Guidance for PEDIATRIC patients 3 months to 17 years of age:

- If a dose adjustment is required to maintain the hemoglobin concentration above 10 g/dl and within the target range, refer to the table below for the dose adjustment based on hemoglobin response.
- Dose adjustments should not be made more often than once every 4 weeks

Hemoglobin Assessment	Compared with the Previous Mircera Dose
Hb decreases by more than 1.0 g/dL compared with baseline Hb	Increase dose by approximately 25% to the closest dose achievable with the prefilled syringes
Hb is less than 10 g/dL and greater than or equal to 9 g/dL (Hb < 10.0 and ≥ 9.0 g/dL)	Increase dose by approximately 25% to the closest dose achievable with the prefilled syringes
Hb is less than 9 g/dL (Hb < 9.0 g/dL)	Increase dose by approximately 50% to the closest dose achievable with the prefilled syringes
Hb increases by more than 1.0 g/dL compared with the baseline Hb	Decrease dose by approximately 25% to the closest dose achievable with the prefilled syringes
Hb is increasing and is approaching 12 g/dL or Hb is greater than or equal to 12 g/dL (Hb ≥ 12 g/dL)	Decrease dose by approximately 25% to the closest dose achievable with the prefilled syringes
If Hb exceeds 12 g/dL and continues to increase following a dose reduction	Stop doses until Hb is less than 12.0 g/dL. Resume dose at approximately 25% below previous dose to the closest dose achievable with the prefilled syringes at next scheduled dosing day.

VI. Billing Code/Availability Information

HCPCS Code:

- J0888 – Injection, epoetin beta, 1 microgram, (for non-ESRD use); 1 billable unit = 1 mcg

NDC(s):

- Mircera 30 mcg/0.3 mL single-dose prefilled syringe: 59353-0400-xx
- Mircera 50 mcg/0.3 mL single-dose prefilled syringe: 59353-0401-xx
- Mircera 75 mcg/0.3 mL single-dose prefilled syringe: 59353-0402-xx
- Mircera 100 mcg/0.3 mL single-dose prefilled syringe: 59353-0403-xx
- Mircera 120 mcg/0.3 mL single-dose prefilled syringe: 59353-0407-xx
- Mircera 150 mcg/0.3 mL single-dose prefilled syringe: 59353-0404-xx
- Mircera 200 mcg/0.3 mL single-dose prefilled syringe: 59353-0405-xx

- Mircera 250 mcg/0.3 mL single-dose prefilled syringe: 59353-0406-xx
- Mircera 360 mcg/0.6 mL single-dose prefilled syringe: 59353-0408-xx

VII. References

1. Mircera [package insert]. St. Gallen, Switzerland; Vifor (International) Inc. April 2024. Accessed May 2024.
2. Levin NW, Fishbane S, Cañedo FV, et al. MAXIMA study investigators. Intravenous methoxy polyethylene glycol-epoetin beta for haemoglobin control in patients with chronic kidney disease who are on dialysis: A randomised non-inferiority trial (MAXIMA). Lancet 370: 1415–1421, 2007.
3. Sulowicz W, Locatelli F, Ryckelynck JP, et al. PROTOS Study Investigators. Once-monthly subcutaneous C.E.R.A. maintains stable hemoglobin control in patients with chronic kidney disease on dialysis and converted directly from epoetin one to three times weekly. Clin J Am Soc Nephrol 2: 637–646, 2007.
4. Fischbach M, Wühl E, Reigner SCM, et al. Efficacy and Long-Term Safety of C.E.R.A. Maintenance in Pediatric Hemodialysis Patients with Anemia of CKD [published correction appears in Clin J Am Soc Nephrol. 2019;14(6):907] Clin J Am Soc Nephrol. 2018;13(1):81-90.
5. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. Kidney Int Suppl. 2012;2(suppl):279-335. https://kdigo.org/guidelines/anemia-in-ckd/. Published August 2012.
6. Mikhail, A., Brown, C., Williams, J.A. et al. Renal association clinical practice guideline on Anaemia of Chronic Kidney Disease. *BMC Nephrol* 18**,** 345 (2017).Upd 2020. https://doi.org/10.1186/s12882-017-0688-1.
7. Pamletto GBA. Local Coverage Article (LCA): Billing and Coding: Erythropoiesis Stimulating Agents (ESA) (A58982). Centers for Medicare & Medicaid Services, Inc. Updated on 02/16/2024 with effective dates 03/01/2024. Accessed April 2024.
8. Wisconsin Physicians Service Insurance Corporation. Local Coverage Article (LCA): Billing and Coding: Erythropoiesis Stimulating Agents (ESA) (A56795). Centers for Medicare & Medicaid Services, Inc. Updated on 05/23/2023 with effective dates 06/01/2023. Accessed April 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D63.1	Anemia in chronic kidney disease
I12.9	Hypertensive chronic kidney disease with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I13.0	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease

I13.10	Hypertensive heart and chronic kidney disease without heart failure, with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
N18.30	Chronic kidney disease, stage 3 (moderate), unspecified
N18.31	Chronic kidney disease, stage 3a
N18.32	Chronic kidney disease, stage 3b
N18.4	Chronic kidney disease, stage 4 (severe)
N18.5	Chronic kidney disease, stage 5

Dual coding requirements:

- Anemia due to CKD (not on dialysis): must bill D63.1 AND I12.9, I13.0, I13.10, N18.30, N18.31, N18.32, N18.4, or N18.5

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
J,M	A58982	Palmetto GBA
5,8	A56795	Wisconsin Physicians Service Insurance Corp (WPS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC