OVERVIEW
Mircera, an erythropoiesis stimulating agent (ESA), is indicated for the treatment of anemia associated with chronic kidney disease (CKD) in adult patients on dialysis and adults not on dialysis. Mircera is also indicated for use in pediatric patients 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin (Hb) level was stabilized with an ESA. Mircera is not indicated and is not recommended for: 1) the treatment of anemia due to cancer chemotherapy; and 2) as a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia. Mircera is given by subcutaneous (SC) or intravenous (IV) injection. The safety and efficacy of Mircera have not been established in pediatric patients of any age for SC administration; for the treatment of anemia in patients with CKD on peritoneal dialysis; for the treatment of anemia in patients with CKD who are not yet on dialysis; and for patients whose Hb level has not been previously stabilized by treatment with an ESA. The prescribing information for Mircera recommends that therapy should be initiated for patients with CKD on dialysis when the Hb level is < 10.0 g/dL and if the Hb level approaches or exceeds 11.0 g/dL, reduce or interrupt the dose of Mircera. 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.

Guidelines
The Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines for anemia in CKD (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 and 10.0 g/dL. The guidelines recommend against ESA therapy for adult patients with CKD who are not on dialysis when Hb levels are ≥ 10.0 g/dL. 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 pediatric patients with CKD, the Hb concentration in which ESAs should be initiated in the individual patient should be considered while being aware 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. Iron supplementation can improve response to ESA therapy. Baseline and periodic monitoring (e.g., iron, total iron-binding capacity, transferrin saturation, or ferritin levels) and instituting iron replacement when needed may be useful in limiting the need for ESAs, maximizing symptomatic improvement in patients, and determining the reason for failure to adequately respond to ESAs. Iron deficiency can occur following continued ESA use and, therefore, iron supplementation is required in most patients to maintain an optimal response.

Safety
Mircera has a Boxed Warning that ESAs increase the risk of death, myocardial infarction (MI), stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence. For patients with CKD, controlled trials have demonstrated that patients experienced greater risks for death, serious adverse cardiovascular (CV) reactions, and stroke when given ESAs to target a Hb level > 11.0
g/dL. No trial has identified a Hb target level, ESA dose, or dosing strategy that negates such risks. Use the lowest Mircera dose necessary to reduce the need for RBC transfusions. For use in cancer, ESAs shorten overall survival and/or increase the risk of tumor progression or recurrence in clinical studies involving patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers.

**POLICY STATEMENT**
Prior authorization is recommended for medical benefit coverage of Mircera in patients with conditions other than CKD who are on dialysis. The intent of this policy is to provide recommendations for uses other than anemia in patients with CKD who are on dialysis. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Mircera as well as the monitoring required for adverse events and long-term efficacy, approval requires Mircera to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**RECOMMENDED AUTHORIZATION CRITERIA**
Coverage of Mircera is recommended in those who meet one of the following criteria.

**FDA-Approved Indications**

1. **Anemia in Patients with Chronic Kidney Disease who are on Dialysis.** Approve for 3 years.

2. **Anemia in Patients with Chronic Kidney Disease who are not on Dialysis.** Approve for 1 year if the patient meets the following criteria (A or B):
   A) **Initial Therapy.** Approve if the patient meets the following criteria (i, ii, and iii):
      i. The patient has a hemoglobin < 10.0 g/dL; AND
      ii. The patient is ≥ 18 years of age; AND
      iii. The patient meets one of the following (a or b):
         a) The patient is currently receiving iron therapy; OR
         b) The patient has adequate iron stores according to the prescriber; OR
   B) **Patient is currently receiving an erythropoiesis-stimulating agent (ESA).** Note: Examples of erythropoiesis-stimulating agents include an epoetin alfa product (e.g., Epogen, Procrit, or Retacrit), a darbepoetin alfa product (e.g., Aranesp), or a methoxy polyethylene glycol-epoetin beta product (e.g., Mircera). Approve if the patient meets the following criteria (i, ii, and iii):
      i. The patient has a hemoglobin < 11.5 g/dL; AND
      ii. The patient is ≥ 18 years of age; AND
      iii. The patient meets one of the following (a or b):
         a) The patient is currently receiving iron therapy; OR
         b) The patient has adequate iron stores according to the prescriber.

   **Dosing.** Approve the following dosing regimens (A or B):
   A) Approve if the dose meets the following (i and ii):
      i. Each dose is ≤ 180 mcg; AND
ii. Each dose is given no more frequently than once every 2 weeks; OR

B) Approve if the dose meets the following (i and ii):
   i. Each dose is ≤ 360 mcg; AND
   ii. Each dose is given no more frequently than once monthly.

**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.
   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 premature because more deaths occurred 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.

**REFERENCES**

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
<th>Approval Date</th>
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<tbody>
<tr>
<td>New Policy.</td>
<td>Not applicable.</td>
<td>07/25/2018</td>
</tr>
<tr>
<td>Annual revision</td>
<td>The following changes were made:</td>
<td>07/24/2019</td>
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<tr>
<td></td>
<td>1. <strong>Anemia in CKD for Patients Who are on Dialysis</strong>: The approval duration was changed from 6 months to 1 year. For the criteria that requires the patient have a specified Hb value, changed the wording of “adults” to “patients ≥ 18 years of age”. For the criteria that requires children to have a specified Hb value, changed the wording of “children” to “patients &lt; 18 years of age”. For the criteria that addresses patients who are currently receiving an ESA, changed from citing examples of the ESA products in criteria to providing a list of ESAs in a note. The example cited that the “Mircera prescribing information recommends supplemental iron therapy when serum ferritin is &lt; 100 mcg/L or when serum transferrin saturation is &lt; 20%” was deleted. Initial approval and extended approval as a separate section was removed, including criteria that required a response to therapy in for extended approval. Dosing was revised to reflect maximum doses and intervals; the route of administration was removed (see policy). The “Duration of Therapy” and “Labs/Diagnostics” sections were also deleted.</td>
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<td></td>
<td>2. <strong>Anemia in CKD for Patients Who are Not on Dialysis</strong>: The approval duration was changed from 6 months to 1 year. For the criteria that requires the patient have a specified Hb value, changed the wording of “adults” to “patients ≥ 18 years of age”. For the criteria that requires children to have a specified Hb value, changed the wording of “children” to “patients &lt; 18 years of age”. For the criteria that addresses patients who are currently receiving an ESA, changed from citing examples of the ESA products in criteria to providing a list of ESAs in a note. The example cited that the “Mircera prescribing information recommends supplemental iron therapy when serum ferritin is &lt; 100 mcg/L or when serum transferrin saturation is &lt; 20%” was deleted. Initial approval and extended approval as a separate section was removed, including criteria that required a response to therapy in for extended approval. Dosing was revised to reflect maximum doses; the route of administration was removed; (see policy). The “Duration of Therapy” and “Labs/Diagnostics” sections were also deleted.</td>
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<td>3. <strong>Waste Management for All Indications</strong>: This section was removed from the policy.</td>
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<tr>
<td>Selected revision</td>
<td><strong>Anemia in CKD for Patients Who are on Dialysis.</strong> Existing criteria and dosing were removed. This indication is no longer a targeted indication for this policy. All requests for anemia in CKD for patients who are on dialysis changed to approve for 1 year.</td>
<td>9/11/2019</td>
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<tr>
<td>Selected revision</td>
<td>For <strong>Anemia in Patients with Chronic Kidney Disease who are on Dialysis</strong>, the approval duration was changed from 1 year to 3 years.</td>
<td>11/06/2019</td>
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