Pharmacy Policy

Erythropoiesis Stimulating Agents

Policy Number: 9.161
Version Number: 13.0
Version Effective Date: 05/02/2017

Product Applicability □ All Plan+ Products

Well Sense Health Plan
☒ New Hampshire Medicaid
☒ NH Health Protection Program
☐ ________________

Boston Medical Center HealthNet Plan
☒ MassHealth
☒ Qualified Health Plans/ConnectorCare/Employer Choice Direct
☒ Senior Care Options
☐ ________________

Note: Disclaimer and audit information is located at the end of this document.

Policy Summary
The Plan will authorize coverage of erythropoiesis stimulating agents when appropriate criteria are met.

Description of Item or Service
Erythropoiesis stimulating agents (ESAs) include erythropoietin (Procrit®, Epogen®), darbepoietin (Aranesp®), and methoxy polyethylene glycol-epoetin beta (Mircera®). Erythropoietin and darbepoietin are glycoproteins that are produced with recombinant DNA technology. Both of these proteins mimic the effects of endogenous erythropoietin produced by the kidneys. Both endogenous and recombinant human erythropoietin stimulates the division and differentiation of committed erythroid progenitors in the bone marrow. Mircera® is an erythropoietin receptor activator with greater activity in vivo as well as increased half-life in contrast to erythropoietin.

FDA indications for currently available erythropoiesis stimulating agents are listed in the table below:

FDA Approved Indications for Erythropoiesis Stimulating Agents (ESA)

<table>
<thead>
<tr>
<th>ESA</th>
<th>FDA Approved Indication</th>
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</thead>
</table>

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### Erythropoiesis Stimulating Agents

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythropoietin, darbepoietin, methoxy polyethylene glycol-epoetin beta</td>
<td>Treatment of anemia associated with chronic kidney disease (includes those on dialysis and not on dialysis)</td>
</tr>
<tr>
<td>Erythropoietin, darbepoietin</td>
<td>Treatment of anemia in patients on myelosuppressive chemotherapy where there is a minimum of at least two additional months of planned chemotherapy</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>Treatment of anemia in Zidovudine-treated HIV-infected patients</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>Reduction of allogeneic RBC transfusion in patients undergoing noncardiac, nonvascular surgery</td>
</tr>
</tbody>
</table>

Well accepted off-label indications for erythropoietin include treatment of anemia of chronic disease (i.e. rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel diseases), anemia associated with myelodysplastic disease, and treatment of anemia in patients with Hepatitis C that are receiving ribavirin therapy.

Safety concerns around the ESAs have resulted in black box warnings mandated by the FDA. In patients with chronic kidney disease (CKD), it was shown that there was a greater risk of death, serious cardiovascular events and stroke when an ESA was administered to target hemoglobin values >11g/dL. No trial has identified a hemoglobin level, ESA dose, or dosing strategy that does not increase these risks. Therefore, for patients with CKD, it is recommended to use the lowest ESA dose sufficient to reduce the need for red blood cell (RBC) transfusions. In general, the risk of blood transfusion is considered to be low when hemoglobin value is >10g/dL. Specifically, for CKD patients on dialysis, the FDA recommendation is to initiate ESA therapy when hemoglobin is <10g/dL with a target of 10-11g/dL; and for CKD patients not on dialysis, the recommendation is to initiate ESA therapy when hemoglobin is <10g/dL and reduce or interrupt ESA dose when ESA exceeds 10g/dL. Certain younger or healthier CKD patients without co-morbidities may still be symptomatic at hemoglobin values are less than <12g/dL and require ESA therapy to maintain their hemoglobin at this level if the benefit outweighs the risk.

Due to the risk associated with use of ESAs in cancer patients, it is recommended that ESAs only be used to treat anemia secondary to chemotherapy for the shortest duration and discontinued at completion of the chemotherapy regimen. An ESA may be initiated when Hgb levels are <10g/dl and clinical benefit outweighs risk of thromboembolism. ESAs are not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure.

Although the ESAs are useful for preventing the need for blood transfusions for some patients, their impact on patient quality of life is an area of controversy. It is recommended that the lowest dose needed to avoid red blood cell transfusions be used.

In light of the serious safety concerns associated with use of ESAs, and the limited data available to demonstrate improvements in quality of life, the risk vs. benefit for initiating ESA therapy must be carefully considered based on individual patient characteristics.

### Policy

The Plan may authorize coverage of erythropoiesis stimulating agents for members meeting the following criteria:

**Policy Applicability by Product**

<table>
<thead>
<tr>
<th>Medication</th>
<th>BMC HealthNet Plan</th>
<th>Well Sense Health Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aranesp</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

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Prior Authorization

A prior authorization request will be required for all pharmacy prescriptions or medical benefit claims for Aranesp, Epogen, Procrit, and Mircera. These requests will be granted approval when the criteria below are met.

Aranesp®, Epogen®, Procrit®

Initial Therapy

Documentation of the following:
1. One of the following clinical conditions:
   - Chronic Kidney Disease (with or without dialysis) to reduce the need for red blood cell transfusions
   - Chemotherapy-induced anemia in non-myeloid malignancy (current or history of chemotherapy within the last 30 days)
   - Anemia secondary to zidovudine treatment for HIV*
   - Myelodysplastic Disease*
   - Anemia secondary to peginterferon/ribavirin treatment for Hepatitis C*
   - Anemia of chronic disease* (must include underlying condition); AND

2. Lab findings confirming Hgb level < 10 g/dL (within the last 30 days); AND
3. Lab findings confirming serum ferritin ≥100 ng/mL or transferrin saturation of ≥ 20% (within the last 90 days); OR

Documentation of the following:
1. An indication of intended high-risk surgery (must be elective, non-cardiac, and non-vascular); AND
2. Lab findings confirming Hgb level between 10 - 13 g/dL within the last 30 days; AND
3. Lab findings confirming serum ferritin ≥100 ng/mL or transferrin saturation of ≥ 20% within the last 90 days.

Continuation of Therapy

Documentation of the following:
1. One of the following clinical conditions:
   - Chronic Kidney Disease (with or without dialysis) to reduce the need for red blood cell transfusions
   - Chemotherapy-induced anemia in non-myeloid malignancy (current or history of chemotherapy within the last 30 days)
   - Anemia secondary to zidovudine treatment for HIV*
   - Myelodysplastic Disease*
   - Anemia secondary to peginterferon/ribavirin treatment for Hepatitis C*
   - Anemia of chronic disease* (must include underlying condition); AND

2. Lab findings confirming Hgb level ≤ 12 g/dL (within the last 30 days); AND
3. Lab findings confirming serum ferritin ≥100 ng/mL or transferrin saturation of ≥ 20% (within the last 90 days); AND
4. Clinical response evidenced by an increase in hemoglobin, or decreased need for blood transfusion

*Applies to Epogen and Procrit only

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Mircera®

**Initial Therapy**
Documentation of the following:
1. A diagnosis of Chronic Kidney Disease with or without dialysis; **AND**
2. Lab findings confirming Hgb level < 10 g/dL (within the last 30 days); **AND**
3. Lab findings confirming serum ferritin ≥100 ng/mL or transferrin saturation of ≥ 20% (within the last 90 days); **AND**
4. An inadequate response, intolerance to a trial of erythropoietin or darbepoetin.

**Continuation of Therapy**
Documentation of the following:
1. A diagnosis of Chronic Kidney Disease on dialysis; **AND**
2. Lab findings confirming Hgb level ≤ 12 g/dL (within the last 30 days); **AND**
3. Lab findings confirming serum ferritin ≥100 ng/mL or transferrin saturation of ≥ 20% (within the last 90 days); **AND**
4. Clinical response evidenced by an increase in hemoglobin, or decreased need for blood transfusion

**Approval Duration**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Approval duration &amp; notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Anemia of Chronic Kidney Disease</td>
<td>(6) months intervals</td>
</tr>
<tr>
<td>- Anemia secondary to zidovudine treatment of HIV,</td>
<td>(3) months intervals</td>
</tr>
<tr>
<td>- Anemia secondary to peginterferon/ribavirin treatment for Hepatitis C</td>
<td></td>
</tr>
<tr>
<td>- Anemia of chronic disease</td>
<td></td>
</tr>
<tr>
<td>- Myelodysplastic disease</td>
<td></td>
</tr>
<tr>
<td>- Chemotherapy-induced anemia</td>
<td>(8) weeks intervals or less based on scheduled completion of chemotherapy</td>
</tr>
<tr>
<td>- Pre-Surgery</td>
<td>(1) month interval</td>
</tr>
</tbody>
</table>

**Applicable Coding:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0881, J0882</td>
<td>darbepoetin (Aranesp)</td>
</tr>
<tr>
<td>J0885, J0886</td>
<td>epoetin alfa (Procrit, Epogen)</td>
</tr>
<tr>
<td>J0887, J0888</td>
<td>methoxy polyethylene glycol-epoetin beta (Mircera)</td>
</tr>
</tbody>
</table>

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Limitations

The Plan will not approve coverage of erythropoiesis stimulating agents in the following instances:

1. When the above criteria are not met.
2. When anemia is associated with the treatment of AML (acute myelogenous leukemia), CML Chronic myelogenous leukemia), or erythroid cancers.
3. When anemia is related to the cancer and not chemotherapy-induced or if anemia is only radiotherapy-induced.
4. Hemoglobin is not within 30 days of the authorization request and required iron tests are not within 90 days of the authorization request.

Clinical Background Information and References

2. Kelliher TB, Afdhal NH. Management of the side effects of peginterferon and ribavirin being used for treatment of chronic hepatitis C virus infection. Up to Date®, accessed December 2013; available from: http://www.uptodate.com

<table>
<thead>
<tr>
<th>Original Approval Date</th>
<th>Original Effective Date</th>
<th>Policy Owner</th>
<th>Approved by</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/01/2008</td>
<td>05/08/2008</td>
<td>Pharmacy Services</td>
<td>Pharmacy &amp; Therapeutics (P&amp;T) Committee</td>
</tr>
</tbody>
</table>

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### Policy Revisions History

<table>
<thead>
<tr>
<th>Review Date</th>
<th>Summary of Revisions</th>
<th>Revision Effective Date</th>
<th>Approved by</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/10/2008</td>
<td>Criteria updated to include package labeling changes (ESAs not indicated for cancer patients receiving myelosuppressive therapy when the intended outcome is cure)</td>
<td>01/01/2009</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>11/12/2009</td>
<td>P&amp;T Annual Review, serum ferritin and transferrin saturation criteria added for continuation, Hgb upper limit for continuation lowered to 10 g/dL in members with chemotherapy-induced anemia (formerly 10 -12 g/dL).</td>
<td>03/01/2010</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>11/11/2010</td>
<td>P&amp;T Annual Review, iron requirements changed to allow either adequate serum ferritin or transferrin saturation levels</td>
<td>03/01/2011</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>07/14/2011</td>
<td>Policy applied to Commercial</td>
<td>11/01/2011</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>01/12/2012</td>
<td>P&amp;T Annual Review, Hgb upper limit for continuation lowered to 11g/dL in patients with anemia of chronic kidney disease on dialysis, and 10g/dL in non-dialysis CKD patients.</td>
<td>05/01/2012</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>08/22/2012</td>
<td>Policy applied to NH Medicaid and complied with PDL preferences</td>
<td>12/01/2013</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>01/10/2013</td>
<td>P&amp;T Annual Review, upper limit for Hgb raised to &lt;= 12g/dL for CKD with/without dialysis; increased approval duration for CKD and chemotherapy-induced anemia; revised continuation criteria for epoetin and darbepoetin; added criteria for Omonyts *</td>
<td>05/01/2013</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>12/13/2013</td>
<td>Policy applied to ConnectorCare/Qualified Health Plan (QHP)</td>
<td>01/01/2014</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>01/09/2014</td>
<td>P&amp;T Annual Review, no criteria change required</td>
<td>05/16/2014</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>01/08/2015</td>
<td>P&amp;T Annual Review, no changes required</td>
<td>05/05/2015</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>05/29/2015</td>
<td>NH PDL requirements removed</td>
<td>09/08/2015</td>
<td>P&amp;T Committee</td>
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**Policy Revisions History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
<th>Date</th>
<th>Reviewing Body</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/14/2016</td>
<td>P&amp;T Annual Review, added criteria for Mircera; removed Omontys due to product discontinuation</td>
<td>05/03/2016</td>
<td>P&amp;T Committee NH DHHS</td>
</tr>
<tr>
<td>01/12/2017</td>
<td>P&amp;T Annual Review, no changes required</td>
<td>05/03/2017</td>
<td>P&amp;T Committee NH DHHS</td>
</tr>
</tbody>
</table>

**Next Review Date**

01/11/2018

**Other Applicable Policies**

9.002 Mandatory Generic Substitution Program
9.015 Quantity Limitation Program

**Reference to Applicable Laws and Regulations, If Any**

**Disclaimer Information**

Medical Policies are the Plan’s guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member’s benefit document, and when appropriate, coordinates with the Member’s health care Providers to consider the individual Member’s health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan’s service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member’s benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.

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