Luspatercept

Overview

This policy supports medical necessity review for luspatercept (Reblozyl®).

Medical Necessity Criteria

Luspatercept (Reblozyl) is considered medically necessary when ONE of the following is met (1 or 2):

1. **Beta-Thalassemia.** Individual meets ALL of the following criteria (A, B, C, and D):
   A. Individual is 18 years of age or older
   B. Treatment of anemia with a documented diagnosis of Beta-Thalassemia
   C. Individual requires regular red blood cell transfusions
   D. The medication is being prescribed by or in consultation with a hematologist.
2. **Myelodysplastic Syndrome or Myelodysplastic/Myeloproliferative Neoplasm.** Individual meets **ALL** of the following criteria (A, B, C, D, E, F, G, H, and I):
   
   A. Individual is 18 years of age or older
   
   B. Treatment of anemia with a documented diagnosis of **EITHER** of the following (i or ii):
      
      i. Myelodysplastic syndromes with ring sideroblasts (MDS-RS)
      
      ii. Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis associated anemia (MDS/MPN-RS-T)
   
   C. Individual has very low- to intermediate-risk myelodysplastic syndrome (determined by the Revised International Prognostic Scoring System [IPSS-R score less than or equal to 5.0; see Appendix])
   
   D. Individual does **not** have a confirmed mutation with deletion 5q (del 5q)
   
   E. Individual currently requires blood transfusions, defined as at least two red blood cell units over the previous 8 weeks
   
   F. Individual meets **ONE** of the following (i or ii):
      
      i. Individual has had an inadequate response to a trial of an erythropoiesis stimulating agent (ESA) for at least 6 weeks, unless intolerant
      
      ii. Serum erythropoietin level is greater than 500 mU/L
   
   G. Pretreatment hemoglobin level is < 10.0 g/dL
   
   H. Luspatercept (Reblozyl) will **not** be used in combination with an erythropoiesis stimulating agent (ESA)
   
   I. The medication is being prescribed by or in consultation with a hematologist or oncologist.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

**Reauthorization Criteria**

Luspatercept (Reblozyl) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response including the following:

1. According to the prescriber, the individual has experienced a clinically meaningful decrease in transfusion burden.

**Authorization Duration**

Initial approval duration:

- Beta-Thalassemia: up to 4 months
- MDS-RS or MDS/MPN-RS-T: up to 6 months

Reauthorization approval duration:

- Beta-Thalassemia: up to 12 months
- MDS-RS or MDS/MPN-RS-T: up to 12 months

**Conditions Not Covered**

Luspatercept (Reblozyl) is considered experimental, investigational or unproven for **ANY** other use.

**Coding / Billing Information**

Note:  1) This list of codes may not be all-inclusive.
       2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.
Covered when medically necessary when used to report Luspatercept (Reblozyl):

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0896</td>
<td>Injection, luspatercept-aamt, 0.25 mg</td>
</tr>
</tbody>
</table>

**Background**

**OVERVIEW**

Reblozyl is an erythroid maturation agent indicated for the following conditions:

- **Beta-thalassemia**, for treatment of adults with anemia who require regular red blood cell (RBC) transfusions.
- **Myelodysplastic syndromes with ring sideroblasts (MDS-RS) or myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) associated anemia**, for those failing an erythropoiesis stimulating agent and requiring two or more RBC units over 8 weeks in adult patients with very low- to intermediate-risk disease.

Safety and efficacy have not been established in patients < 18 years of age.

**Disease Overview**

Beta-thalassemia, an inherited blood disorder, is characterized by reduced levels of functional hemoglobin. Patients with a severe form (beta-thalassemia major) become symptomatic due to low hemoglobin level (e.g., increased cardiac effort, tachycardia, poor growth) or ineffective erythropoiesis (e.g., bone changes, massive splenomegaly). Even with treatment, severe complications may arise due to iron overload secondary to increased intestinal absorption and frequent blood transfusions. The frequency of symptomatic patients with beta-thalassemia is estimated at approximately 1 in 100,000 individuals in the general population but is less common in the US.

Myelodysplastic syndromes are cancers in which cells in the bone marrow do not mature and become healthy blood cells. Patients with MDS with refractory anemia and ring sideroblasts have too few RBCs in the blood with too much iron inside the cell. However, the number of white blood cells and platelets are normal. Supportive therapy may include transfusions and use of erythropoiesis-stimulating agents (ESAs). ESAs may be given to increase the number of mature RBCs made by the body and to lessen the effects of anemia.

Myelodysplastic/myeloproliferative neoplasms are diseases of the blood and bone marrow with features of myelodysplastic syndromes as well as myeloproliferative neoplasms (e.g., a greater than normal number of blood stem cells become one or more types of blood cells and the total number of blood cells slowly increases). In the pivotal study evaluating Reblozyl for MDS/MPN, patients with deletion 5q were excluded from enrollment. All patients were required to have disease refractory to ESAs (unless endogenous erythropoietin level was elevated), and the median pretransfusion hemoglobin level was 7.6 g/dL (range, 5 to 10 g/dL).

**Dosing Information**

For all indications, the starting dose is 1 mg/kg given subcutaneously once every 3 weeks. Assess and review hemoglobin levels and transfusion record prior to each dose. Discontinue if a patient does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of three doses) at the maximum dose level. For beta thalassemia, the maximum recommended dose is 1.25 mg/kg given once every 3 weeks. For MDS and MDS/MPN, the maximum dose is 1.75 mg/kg given once every 3 weeks.

**Guidelines**

Guidelines do not address Reblozyl for treatment of beta-thalassemia. Standards of Care Guidelines for Thalassemia (2012) are published by the Children’s Hospital and Research Center of Oakland. Life-long blood transfusions and iron chelation are the main treatments for beta-thalassemia. Transfusions are usually needed every 3 to 4 weeks and are recommended to maintain the pre-transfusion Hb level above 9 to 10 g/dL and post-transfusion Hb level should not exceed 14 g/dL. Blood transfusions are given to improve anemia as well as
suppress ineffective erythropoiesis. Most serious growth, bone, and neurologic complications are prevented with regular transfusions. Once transfusions are started, transfusion-related complications become a major source of morbidity. Hydroxyurea is described as an experimental agent for beta-thalassemia. The Thalassaemia International Federation (2014) also recommends transfusions and iron chelation for treatment of beta-thalassemia. These guidelines state that transfusions are usually administered every 2 to 5 weeks and are recommended to maintain the pre-transfusion Hb level above 9 to 10.5 g/dL and post-transfusion Hb level below 14 to 15 g/dL. The primary goal of chelation therapy is to maintain safe levels of body iron bybalancing iron from blood transfusion with iron excretion by chelation. Despite literature suggesting hydroxyurea may be beneficial in certain patients with beta-thalassemia, use is not recommended outside of a clinical trial.

The National Comprehensive Cancer Network (NCCN) guidelines for MDS (version 2.2022 – November 15, 2021) recommend Reblozyl in patients symptomatic anemia due to MDS, in patients without del(5q), who have no response to ESAs (defined by rise in hemoglobin level or decrease in transfusion burden) following 6 to 8 weeks of treatment. Reblozyl is also a treatment option for patients who have serum erythropoietin levels > 500 mU/mL. Reblozyl is also a treatment option for MDS/MPN with ring sideroblasts and thrombocytosis.

Appendix
The revised International Prognostic Scoring System (IPPS-R) shows the same disease factors as IPSS, but in a more detailed way. The following five disease factors are: Blasts, Cytogenetics, Hemoglobin, Absolute neutrophil count, Platelet count.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Prognostic Factors Scored</th>
<th>Risk Groups Based on Total IPPS-R Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blasts in bone marrow (percent)</strong></td>
<td>• Less than or equal to 2 = 0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Greater than 2 to less than 5 = 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 5 to 10 = 2</td>
<td></td>
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<tr>
<td></td>
<td>• Greater than 10 = 3</td>
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<tr>
<td><strong>Cytogenetics</strong></td>
<td>• -Y,del(11q) = 0</td>
<td>Very Low = 1.5 or lower</td>
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<tr>
<td></td>
<td>• Normal, del(5q), del(12p), del(20q), double including del(5q) = 1</td>
<td>Low = 2 to 3</td>
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<tr>
<td></td>
<td>• Del(7q), +8, +19, i(17q), any other single or double including -7/del(7q), complex: 3 abnormalities = 3</td>
<td></td>
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<tr>
<td></td>
<td>• Greater than 3 abnormalities = 4</td>
<td></td>
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<tr>
<td><strong>Cytopenias</strong></td>
<td>Hemoglobin level (g/dL)</td>
<td>Intermediate = 3.5 to 4.5</td>
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<tr>
<td></td>
<td>• Equal to or greater than 10 = 0</td>
<td>High = 5 to 6</td>
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<td></td>
<td>• 8 to less than 10 = 1</td>
<td>Very High = 6.5 or greater</td>
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<tr>
<td></td>
<td>• Less than 8 = 1.5</td>
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<tr>
<td></td>
<td>Platelet count (x 10⁹/L of blood)</td>
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</tr>
<tr>
<td></td>
<td>• Equal to or greater than 100 = 0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 50 to less than 100 = 0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Less than 50 = 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neutrophil count ([ANC] x 10⁹/L of blood)</td>
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</tr>
<tr>
<td></td>
<td>• Equal to or greater than 0.8 = 0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Less than 0.8 = 0</td>
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