Luspatercept-aamt (Reblozyl®)

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Description of Procedure or Service

Luspatercept-aamt (Reblozyl®) is an erythroid maturation agent that is indicated for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions.

Beta thalassemia is an inherited hematologic disorder characterized by reduced hemoglobin production, resulting in a decrease in oxygen transported to cells throughout the body. Clinical manifestations of beta thalassemia include hemolytic anemia and impaired iron handling. Supportive treatment for beta thalassemia patients often consists of lifelong chronic blood transfusions for survival, together with treatment for iron overload caused by frequent transfusions.

Luspatercept-aamt (Reblozyl®) is a recombinant fusion protein that was approved by the U.S. Food and Drug Administration (FDA) in November 2019 for the treatment of anemia in patients with beta thalassemia requiring regular RBC transfusions. Luspatercept induces erythroid maturation by binding several endogenous TGF-β superfamily ligands, thus diminishing Smad2/3 signaling. In beta thalassemia, decreasing abnormally elevated Smad2/3 signaling is thought to improve hematology parameters associated with ineffective erythropoiesis.

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for luspatercept-aamt (Reblozyl) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member’s Benefit Booklet for availability of benefits. Member’s benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Luspatercept-aamt (Reblozyl) is covered
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**Initial Therapy**

Luspatercept-aamt (Reblozyl) is considered medically necessary for the treatment of anemia in adult patients (≥18 years old) with beta thalassemia when the following criteria are met:

1. The patient has a confirmed diagnosis of beta thalassemia (including Hemoglobin E/beta thalassemia and beta thalassemia with mutation and/or multiplication of alpha globin); AND
2. The patient requires regular red blood cell (RBC) transfusions (defined as at least 6 RBC units within the 24 weeks prior to initiation and no transfusion-free period ≥35 days during that time); AND
3. Luspatercept is prescribed by or in consultation with a hematologist or specialist in treating beta thalassemia; AND
4. The patient does not have a diagnosis of Hemoglobin (sickle) S/beta thalassemia or alpha thalassemia (e.g., Hemoglobin H); AND
5. The patient does not have major organ damage (e.g., liver disease, heart disease, lung disease, or renal insufficiency)

Initial authorization: 6 months

**Continuation Therapy**

Continuation of treatment with luspatercept-aamt (Reblozyl) beyond 6 months after initiation of therapy, and every 12 months thereafter, is considered medically necessary for the treatment of beta thalassemia when the following criteria are met:

1. The patient is currently receiving luspatercept and continues to meet initial criteria; AND
2. The patient has demonstrated a reduction in RBC transfusion burden following luspatercept treatment

**When Luspatercept-aamt (Reblozyl) is not covered**

Luspatercept-aamt (Reblozyl) is considered investigational and therefore not covered when the above criteria are not met.

Luspatercept-aamt is considered investigational and therefore not covered when used as a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia.

Luspatercept-aamt is considered investigational and therefore not covered for any other diagnoses, including Hemoglobin (sickle) S/beta thalassemia and alpha thalassemia (e.g., Hemoglobin H).

**Policy Guidelines**

The recommended starting dose of Reblozyl is 1 mg/kg given as a subcutaneous injection once every 3 weeks. Reblozyl should be administered by a healthcare professional. Hemoglobin (Hgb) should be assessed and reviewed prior to each administration. If a red blood cell (RBC) transfusion occurred prior to dosing, dosing considerations should be based on the pretransfusion
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Hgb. If the pre-dose Hgb is ≥ 11.5 g/dL and the Hgb is not influenced by recent transfusion, the Reblozyl dose should be delayed until the Hgb is ≤ 11 g/dL.

If a reduction in RBC transfusion burden is not achieved after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose, the Reblozyl dose should be increased to, but not exceeding, the maximum dose of 1.25 mg/kg. If a patient experiences a response followed by a lack of or lost response to Reblozyl, the patient should be assessed for causative factors (e.g., a bleeding event). Reblozyl should be discontinued if a patient does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose, or if unacceptable toxicity occurs at any time.

According to the manufacturer’s safety information for Reblozyl, the most common adverse reactions (>10% incidence) include headache, bone pain, arthralgia, fatigue, cough, abdominal pain, diarrhea, and dizziness. Patients with beta thalassemia have an increased risk of thrombosis/thromboembolism, thus patients receiving Reblozyl should be monitored for signs and symptoms of thromboembolic events and treatment initiated promptly in these events. Hypertension may develop in patients receiving Reblozyl treatment. Blood pressure should be monitored during treatment and anti-hypertensive therapy initiated if needed. Reblozyl may cause fetal harm, and females of reproductive potential receiving Reblozyl should use effective contraception.

Clinical Trial Evidence

The efficacy and safety of luspatercept was assessed in a randomized, multicenter, double-blind, placebo-controlled, multicenter trial of 336 adult patients with beta thalassemia (including Hemoglobin E/beta thalassemia and beta thalassemia with mutation and/or multiplication of alpha globin) requiring regular RBC transfusions (6-20 RBC units per 24 weeks) with no transfusion-free period greater than 35 days during the 24-week period (BELIEVE trial; NCT02604433). Patients were randomized 2:1 to receive luspatercept (n=224) or placebo (n=112) subcutaneously once every 3 weeks as long as a reduction in transfusion requirement was observed or until unacceptable toxicity. All patients within the trial were permitted to receive best supportive care, including RBC transfusions; iron-chelating agents; antibiotic, antiviral, and antifungal therapy; and/or nutritional support, as needed. Patients with hemoglobin S/beta thalassemia or alpha thalassemia, or who had major organ damage (liver disease, heart disease, lung disease, renal insufficiency) were excluded from the trial. Other exclusion criteria included patients with recent deep vein thrombosis or stroke, or recent use of ESAs, immunosuppressants, or hydroxyurea therapy. The primary efficacy endpoint was based on the proportion of patients achieving a reduction in RBC transfusion burden (≥33% reduction from baseline) with at least a 2-unit reduction from week 13 to week 24. Luspatercept compared with placebo significantly increased the proportion of patients with a 33% or greater reduction in RBC transfusion burden (with a reduction of at least 2 units) from weeks 13 to 24 (21.4% vs 4.5%; p<0.0001).

The following information is derived from FDA prescribing information, as peer reviewed published trial results have not been identified.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: C9399, J3490, J3590
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BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources


Medical Director review 2/2020

Policy Implementation/Update Information

2/11/20 New policy developed. Reblozyl is considered medically necessary for the treatment of anemia in adult patients (≥18 years old) with beta thalassemia when specified medical criteria and guidelines are met. Added HCPCS codes C9399, J3490, and J3590 to Billing/Coding section. References added. Medical Director review 2/2020. (krc)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.