Luspatercept-aamt (Reblozyl®)

NDC CODE(S) 59572-0711-XX REBLOZYL 25MG Solution Reconstituted (CELGENE CORP)
59572-0775-XX REBLOZYL 75MG Solution Reconstituted (CELGENE CORP)

DESCRIPTION

Luspatercept-aamt is a recombinant fusion protein that serves as an erythroid maturation agent. It is a receptor fusion protein consisting of a modified extracellular domain of the human activin receptor type IIB linked to a human IgG1 Fc domain which binds to several endogenous TGF-β superfamily ligands.

In beta thalassemia, abnormally elevated Smad2/3 signaling prevents erythroid maturation through differentiation of late-stage erythroid precursors (normoblasts). It is characterized by reduced synthesis of the hemoglobin subunit beta (hemoglobin beta chain) that results in microcytic hypochromic anemia, an abnormal peripheral blood smear with nucleated red blood cells, and reduced amounts of hemoglobin A (HbA) on hemoglobin analysis. It is thought that luspatercept-aamt decreases abnormally elevated Smad2/3 signaling and improves hematology parameters associated with ineffective erythropoiesis.

POLICY

- Luspatercept-aamt for the treatment of any one of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Chronic anemia of Beta Thalassemia
  - Anemia of Myelodysplastic Syndrome (MDS)
- Luspatercept-aamt for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

Universal Criteria

- Females of reproductive potential have a negative pregnancy test prior to start of therapy and will use an effective method of contraception during treatment and at least for 3 months after treatment; **AND**
- Patient does not have major end organ damage*, defined as any of the following:
  - Liver disease with an ALT > 3x the ULN or history of evidence of cirrhosis; **OR**
  - Heart disease, heart failure NYHA classification 3 or higher, or significant arrhythmia requiring treatment, or recent myocardial infarction within 6 months of treatment; **OR**
  - Lung disease, including pulmonary fibrosis or pulmonary hypertension which are clinically significant i.e., ≥ Grade 3; **OR**
  - Creatinine clearance < 60 mL/min; **AND**

**Note: Request for patients deemed to have any major end organ damage will be reviewed on a case-by-case basis.*

- Patient has not had a deep vein thrombosis or a thrombotic stroke which required medical intervention within 6 months prior to therapy; **AND**
- Other causes of anemia (e.g., hemolysis, bleeding, recent major surgery, vitamin deficiency, etc.) have been ruled out; **AND**
- Reblozyl is not being used as a substitute for RBC transfusions in patients requiring immediate correction of anemia

Beta Thalassemia

- Patient must be 18 years or older*; **AND**
- Patient has a documented diagnosis of beta thalassemia (excludes alpha-thalassemia and hemoglobin S/ß-thalassemia variants) as outlined by the following:
  - Patient diagnosis is confirmed by HBB sequence gene analysis showing biallelic pathogenic variants; **OR**
  - Patient has severe microcytic/hypochromic anemia, anisopoikilocytosis with nucleated red blood cells on peripheral blood smear, and hemoglobin analysis that reveals decreased amounts or complete absence of hemoglobin A and increased amounts of hemoglobin F; **AND**
- Patient is red blood cell (RBC) transfusion dependent as defined by requiring 6-20 RBC units per 24 weeks; **AND**
- Patient has a baseline Hemoglobin (Hb) < 11.5 g/dL (if Hb is 11.5 g/dL or higher, the dose must be delayed until the Hb is 11 g/dL or less) *(*Note: If an RBC transfusion occurred prior to dosing, the pretransfusion Hgb must be considered for dosing purposes. Lab values are obtained within 7 days of the date of administration)*; **AND**

**Note: Request for patients <18 years will be considered on a case by case basis for those with high transfusion burden and symptomatic iron overload, history of alloimmunization, or history of transfusion reactions*

Myelodysplastic Syndrome

- Patient must be 18 years or older; **AND**
- Patient has required 2 or more red blood cell units over an 8 week timeframe; **AND**
- Patient has a diagnosis of one of the following:
  - Myelodysplastic syndrome with ring sideroblasts (MDS-RS); **OR**
  - Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T; **AND**
- Patient has very low to intermediate risk disease defined as any one of the following:
  - IPSS-R: very low, low, or intermediate; **OR**
  - IPSS: low/intermediate-1; **OR**
  - WPSS: very low, low, or intermediate; **AND**
- Patient has symptomatic anemia with ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation); **AND**
  - Serum erythropoietin >200 mU/mL; **OR**
  - Patient has had an inadequate response to prior treatment with an erythropoiesis-stimulating agent (i.e. epoetin alpha >40,000 units/week for at least 8 doses or darbepoetin alpha >500 mcg every 3 weeks for at least 4 doses); **OR**
  - Patient has a documented contraindication or intolerance to the use of an erythropoiesis-stimulating agent

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in the Initial Approval Criteria; **AND**
- Patient will not receive doses < 21 days apart; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: thromboembolic events, severe hypertension, etc.; **AND**
- Other causative factors (e.g., a bleeding event) have been ruled out; **AND**
- Reblozyl is not being used as a substitute for RBC transfusions in patients requiring immediate correction of anemia; **AND**

- Hemoglobin (Hb) <11.5 g/dL (if Hb is 11.5 g/dL or higher, the dose must be delayed until the Hb is 11 g/dL or less) *(*Note: If an RBC transfusion occurred prior to dosing, the pretransfusion Hgb must be considered for dosing purposes. Lab values are obtained within 7 days of the date of administration)*; **AND**

Beta Thalassemia

- Patient is experiencing disease response as evidenced by a decrease in the number of RBC transfusions; **OR**
- For new starts: Patient has not achieved a reduction in RBC transfusion burden after at least 2 consecutive, initial (1 mg/kg), doses (6 weeks) and requires a dose increase to 1.25 mg/kg; **OR**
- Patient experienced a response followed by a lack/loss of response and requires a dose increase to 1.25 mg/kg (from 1 mg/kg)

Myelodysplastic Syndrome

- Patient is experiencing disease response as evidenced by a decrease in the number of RBC transfusions; **OR**
- For new starts: Patient has not achieved a reduction in RBC transfusion burden after at least 2 consecutive, initial (1 mg/kg), doses (6 weeks) and requires a dose increase to 1.33 mg/kg; **OR**
- Patient has not achieved a reduction in RBC transfusion burden after at least 2 consecutive, 1.33 mg/kg doses (6 weeks) and requires a dose increase to 1.75 mg/kg; **OR**
- Patient experienced a response followed by a lack/loss of response and requires a dose increase to 1.33 mg/kg (from 1 mg/kg)

**Note:* *Discontinue Reblozyl if a patient does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose level or if unacceptable toxicity occurs at any time.*

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Beta Thalassemia	The recommended starting dose is 1 mg/kg once every 3 weeks by subcutaneous injection. ▫ Dose increases for insufficient response: If a patient does not achieve a reduction in RBC transfusion burden after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose, increase the Reblozyl dose to 1.25 mg/kg. Do not increase the dose beyond the maximum dose of 1.25 mg/kg.
Myelodysplastic Syndrome	The recommended starting dose is 1 mg/kg once every 3 weeks by subcutaneous injection. ▫ Dose increases for insufficient response: If a patient is not RBC transfusion free after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose, increase the Reblozyl dose to 1.33 mg/kg. If a patient is not RBC transfusion free after at least 2 consecutive doses (6 weeks) at the 1.33 mg/kg starting dose, increase the Reblozyl dose to 1.75 mg/kg. Do not increase the dose beyond the maximum dose of 1.75 mg/kg. *Note: If, upon a dose modification (i.e., dose reduction), a patient loses response (i.e. requires a transfusion) or Hgb concentration drops by 1 g/dL or more in 3 weeks in the absence of transfusion, increase the dose by one dose level. Wait a minimum of 6 weeks between dose increases.*
▫ If a planned administration of Reblozyl is delayed or missed, administer Reblozyl as soon as possible and continue dosing as prescribed, with at least 3 weeks between doses. ▫ Assess and review hemoglobin (Hgb) results prior to each administration. If an RBC transfusion occurred prior to dosing, the pretransfusion Hgb must be considered for dosing purposes. ▫ Dose decreases/interruptions: If Hgb increase is >2 g/dL or the pre-dose Hgb is >11.5 g/dL and the Hgb level is not influenced by recent transfusion, reduce the dose or interrupt treatment until the Hgb is <11 g/dL.	

- **Reblozyl should be reconstituted and administered by a healthcare professional.**

LENGTH OF AUTHORIZATION

- Beta Thalassemia: Coverage will be provided initially for 15 weeks (5 initial doses) and may be renewed annually thereafter.

- Myelodysplastic Syndrome: Coverage will be provided initially for 21 weeks (7 initial doses) and may be renewed every 6 months thereafter.

DOSING LIMITS

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

- 600 billable units every 21 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) luspatercept-aamt. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2021.
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7. Fenaux P, Platzbecker U, Mufti GJ, et al. Luspatercept in Patients with Lower-Risk Myelodysplastic Syndromes. January 9, 2020. N Engl J Med 2020; 382:140-151 DOI: 10.1056/NEJMoa1908892.
8. Cappellini MD, Viprakasit V, Taher AT, et al. A Phase 3 Trial of Luspatercept in Patients With Transfusion-Dependent β-Thalassemia. N Engl J Med, 382 (13), 1219-1231; 2020 Mar 26. PMID: 32212518. DOI: 10.1056/NEJMoa1910182
9. Lexicomp Online. (2021, February). AHFS DI. Luspatercept-aamt. Retrieved April 16, 2021 from Lexicomp Online with AHFS.
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EFFECTIVE DATE 8/31/2021

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