Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Luspatercept (Reblozyl)	MP-RX-FP-76-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B DRUG

Service Description

This document addresses the use of Luspatercept (Reblozyl) , a drug approved by the Food and Drug Administration (FDA) for the treatment of anemia in adults with beta thalassemia (β-thalassemia) and myelodysplastic syndrome (MDS) or myelodysplastic/myeloproliferative neoplasms (MDS/MPN) require regular red blood cell transfusions.

Background Information

The FDA approved indications for Reblozyl include:

- Anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions
- Anemia failing an erythropoiesis stimulating agent and requiring 2 or more RBC units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

The National Comprehensive Cancer Network (NCCN) gives a 2A category recommendation for the use of Reblozyl in MDS-RS with ring sideroblasts greater than or equal to 15% (or ring sideroblasts 5% to 14% with an SF3B1 mutation).

Beta thalassemia is an inherited blood disorder caused by mutations in the beta-globin (HBB) gene. These mutations result in defective red blood cells (RBC) that have little or no hemoglobin, the iron-containing protein that is responsible for oxygen transport. People who inherit just one HBB gene mutation (thalassemia minor or thalassemia trait) are usually asymptomatic. People who inherit two defective genes develop beta thalassemia with moderate anemia that can be managed with intermittent RBC transfusions (beta thalassemia intermedia) or severe anemia that is transfusion-dependent (beta thalassemia major, also called Cooley's anemia). Hemoglobin E beta thalassemia (E/β-thalassemia) and hemoglobin S beta thalassemia (S/β-thalassemia, also known as sickle beta thalassemia) are related disorders that occur when beta thalassemia is combined with another gene mutation or abnormality.

Myelodysplastic syndromes (MDS) are conditions that can occur when the body no longer makes enough healthy, normal blood cells in the bone marrow. This leads to a low number of one or more types of blood cells. A shortage of red blood cells (anemia) is the most common finding. MDS is also known as a form of blood cancer. Several types of MDS exist, based on how many types of blood cells are affected along with

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other factors. About one-third of MDS patients can progress to a rapidly growing cancer of bone marrow cells called acute myeloid leukemia (AML). The World Health Organization (WHO) provides classifications for myeloid neoplasms and acute leukemias. It classifies MDS into 6 main types, primarily based on how the cells in the bone marrow look under the microscope. MDSRS is not a common subtype of MDS and rarely turns into AML. Some patients present with clinical features that overlap between MDS and myeloproliferative neoplasms (MPN), which have their own WHO classifications. The mixed diagnosis indicates that the patient has abnormal blood cells combined with proliferation of cells. It is rarer than MDS and estimated incidence is more difficult to define. Key clinical features of MDS/MPN-RS-T include anemia and elevated platelet counts.

Reblozyl is a first in class drug, and classified as a erythroid maturation agent. While Reblozyl may reduce the transfusion burden, it does not completely eliminate the need for RBC transfusions. The goal of treatment in these patients focuses on symptom control, quality of life improvement, reduction or elimination of RBC transfusions and toxicity minimization. Per labeling, Reblozyl is to be administered by a healthcare professional as a subcutaneous injection. At this time, Reblozyl is not recommended for pediatric use due to findings from toxicity studies in juvenile animals.

Approved Indications

A. Anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions.

B. Anemia failing an erythropoiesis stimulating agent and requiring 2 or more RBC units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

Other Uses: N/A

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J0896	Injection, luspatercept-aamt, 0.25 mg (Reblozyl) (Effective 7/1/2020)

ICD-10	Description
D56.1	Beta Thalassemia
D56.5	Hemoglobin E-Beta thalassemia
D46.Z	Other myelodysplastic syndromes
D46.9	Myelodysplasia NOS

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Luspatercept (Reblozyl)

A. Prescriber Specialties: N/A

B. Criteria For Initial Approval: β-thalassemia

Initial requests for Reblozyl (luspatercept) for β-thalassemia may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**

II. Individual has a diagnosis of beta thalassemia or hemoglobin E beta (E/β)-thalassemia; **AND**

III. Documentation is provided that individual required regular red blood cell transfusions at initiation, defined as both of the following (NCT02604433):
   a. Individual received six to twenty (6-20) RBC units in the last 24 weeks; **AND**
   b. Individual had no transfusion-free period greater than 35 days in the last 24 weeks; **AND**

IV. Individual has a baseline hemoglobin (Hgb) level less than or equal to 11 g/dL.

C. Criteria For Continuation of Therapy: β-thalassemia

Continuation requests for Reblozyl (luspatercept) for β-thalassemia may be approved if the following criteria are met:

I. Documentation is provided that individual demonstrates continued need for treatment and has confirmation of response to treatment as evidenced by a decrease in transfusion burden from baseline; **AND**

II. Hemoglobin level is not greater than 11 g/dL.

A. Criteria For Initial Approval: MDS-RS or MDS/MPN-RS-T

Initial requests for Reblozyl (luspatercept) for MDS-RS or MDS/MPN-RS-T may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**

II. Individual has one of the following (A or B):

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A. Documentation is provided that individual has a diagnosis very low to intermediate risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) greater than or equal to 15% (or ring sideroblasts 5% to 14% with an SF3B1 mutation) (Label, NCCN 2A); **AND**

1. Individual meets one of the following criteria:

a. Serum erythropoietin (EPO) level of greater than 500 mU/mL; **OR**

b. Serum EPO level of less than or equal to 500 mU/mL following no response to combination treatment with erythropoiesis-stimulating agent (ESA) and granulocyte-colony stimulating factor (G-CSF); **OR**

B. Individual has a diagnosis of myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) with all of the following:

1. Ring sideroblasts greater than or equal to 15% (WHO 2017), and documentation is provided; **AND**
2. Thrombocytosis (defined as platelets greater than or equal to 450 x109/L) (WHO 2017); **AND**
3. Insufficient response to ESAs; **AND**

III. Documentation is provided that individual has required regular red blood cell transfusions of two (2) or more RBC units over eight (8) weeks in the last 16 weeks; **AND**

IV. Individual has a baseline hemoglobin (Hgb) level less than or equal to 11 g/dL.

D. Criteria For Continuation: MDS-RS or MDS/MPN-RS-T

I. Documentation is provided that individual demonstrates continued need for treatment and has confirmation of response to treatment as evidenced by a decrease in transfusion burden from baseline; **AND**

II. Hemoglobin level is not greater than 11.0 g/dL.

E. Authorization Duration

I. Initial Request: 6 months
II. Continuation Requests: 12 months

B. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive)

Reblozyl (luspatercept) for **β-thalassemia** may not be approved for the following:

I. Individual has a diagnosis of sickle beta thalassemia (S/β-thalassemia); **OR**

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II. Individual has a diagnosis of alpha (α)-thalassemia; **OR**
III. Individual has a platelet count greater than 1000 x 10^9/L; **OR**
IV. History of deep vein thrombosis (DVT) or stroke within the last 24 weeks; **OR**
V. Use beyond 9 weeks of treatment (i.e., administration of consecutive 3 doses) in the absence of response (response defined as decrease in transfusion burden from baseline) at maximum dose level (i.e., 1.25 mg/kg every 3 weeks).

Reblozyl (luspatercept) for MDS-RS or MDS/MPN-RS-T may not be approved for the following:

i. Individual has unresolved iron deficiency (defined as serum ferritin less than or equal to 15µg/L, or transferrin saturation less than or equal to 20%) (NCT02631070); OR
ii. Use beyond 9 weeks of treatment (i.e., administration of consecutive 3 doses) in the absence of response (response defined as decrease in transfusion burden from baseline) at maximum dose level (i.e., 1.75 mg/kg every 3 weeks).

Requests for Reblozyl (luspatercept) may not be approved when the above criteria are not met and for all other indications.

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Limits or Restrictions

A. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Limit
Reblozyl (luspatercept) 25mg, 75mg vials	1.75 mg/kg per 3 weeks
Exceptions	
N/A	

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Reference Information

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10. NCCN Clinical Practice Guidelines in Oncology™. © 2022 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on June 25, 2022. a. Myelodysplastic Syndromes. Version 3.2022. Revised January 13, 2022.
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13. Orazi A, et al. Myelodysplastic Syndromes/Myeloproliferative Neoplasms, Chapter 5, in Swerdlow S. Campo E, Harris NL, et al (Eds). World Health Organization Classification and Tumours of Haematopoietic and Lymphoid Tissues, Revised 4th edition. Volume 2. IARC Press, Lyon, 2017, 82-96.
14. Thalassemia. Cooley's Anemia Foundation. Available at https://www.thalassemia.org/learn-about-thalassemia/about-thalassemia/. Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Revised: 8/18/23