Reblozyl® (luspatercept-aamt)
(Subcutaneous)

Document Number: IC-0503

Last Review Date: 04/01/2026
Date of Origin: 12/03/2019
Dates Reviewed: 12/2019, 04/2020, 07/2020, 10/2020, 04/2021, 04/2022, 04/2023, 10/2023, 04/2024, 05/2025, 04/2026

I. Length of Authorization [1,12]

- Beta Thalassemia:
  - Initial: Prior authorization validity will be provided initially for 15 weeks (5 initial doses).
  - Renewal: Prior authorization validity may be renewed every 12 months (365 days).
- Anemia Due to Myelodysplastic Syndromes:
  - Initial: Prior authorization validity will be provided initially for 21 weeks (7 initial doses).
  - Renewal: Prior authorization validity may be renewed every 6 months (180 days).
- Anemia Due to Myeloproliferative Neoplasms (MPN) – Myelofibrosis:
  - Initial: Prior authorization validity will be provided initially for 24 weeks (8 initial doses).
  - Renewal: Prior authorization validity may be renewed every 6 months (180 days).

II. Dosing Limits

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

- Beta Thalassemia: 600 billable units every 21 days
- Myelodysplastic Syndromes and Myeloproliferative Neoplasms: 800 billable units every 21 days

III. Initial Approval Criteria [1]

Prior authorization validity is provided in the following conditions:

- Member is at least 18 years of age, unless otherwise specified**; **AND**

Universal Criteria [1]

- 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 for at least 3 months after treatment; **AND**
- Member 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 red blood cell (RBC) transfusions in members requiring immediate correction of anemia; **AND**
- Member has a pre-dose Hemoglobin (Hgb) < 11.5 g/dL* obtained within 7 days of the date of administration (unless otherwise specified); **AND**

***Note**: If Hgb is ≥ 11.5 g/dL, the dose must be delayed until the Hb is ≤ 11 g/dL. If an RBC transfusion occurred prior to dosing, the pretransfusion Hgb must be considered for dosing purposes.*

Beta Thalassemia † Φ [1,4,8]

- Member has a documented diagnosis of beta thalassemia (excludes isolated alpha-thalassemia and hemoglobin S/ß-thalassemia variants) as outlined by the following:
  - Member diagnosis is confirmed by *HBB* sequence gene analysis showing biallelic pathogenic variants; **OR**
  - Member has severe microcytic hypochromic anemia, absence of iron deficiency, anisopoikilocytosis with nucleated red blood cells on peripheral blood smear, and hemoglobin analysis that reveals decreased amounts or complete absence of hemoglobin A (HbA) and increased HbA_2 with or without increased amounts of hemoglobin F (HbF); **AND**
- Member is RBC transfusion dependent as defined by requiring 6-20 RBC units per 24 weeks; **AND**
- Member 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

***§** Requests for members deemed to have any major end organ damage will be reviewed on a case-by-case basis.*

***Requests for members <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*

Anemia Due to Myelodysplastic Syndromes (MDS) † ‡ Φ [1,5-7]

- Used as a single agent; **AND**
  - Used for the treatment of symptomatic anemia with Myelodysplastic Syndromes (MDS); **AND**
    - Member has lower risk disease (IPSS-R very low, low, or intermediate-risk) without del(5q) mutation; **AND**
      - Member has ring sideroblasts <15% (or ring sideroblasts <5% with an SF3B1 mutation); **AND**
        - Member has serum erythropoietin ≤ 500 mU/mL; **AND**

- ❖ Used as initial treatment; **OR**
- ❖ Used following no response* to or relapse after an erythropoiesis stimulating agent (ESA) alone (despite adequate iron stores); **OR**

– Member has ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation); **AND**

- ➢ Used as initial treatment; **OR**
- ➢ Used following no response* to or relapse after imetelstat

- Used for the treatment of anemia with Myelodysplastic Syndromes/Myeloproliferative (MDS/MPN) Overlap Neoplasm and thrombocytosis with an SF3B1 mutation; **OR**
- Used for the treatment of anemia with MDS/MPN with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T); **AND**
  - Member has required 2 or more RBC units over an 8-week timeframe; **AND**
    - Member is erythropoiesis stimulating agent (ESA) ineligible (i.e. serum erythropoietin > 200 mU/mL and not previously treated with ESA); **OR**
    - Member has had an inadequate response to prior treatment with an ESA (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 equivalent); **OR**
    - Member has a documented contraindication or intolerance to the use of an ESA

***Note:** No response defined as a lack of ≥1.5 gm/dL rise in hemoglobin OR lack of a decrease in RBC transfusion requirement by 3 to 6 months of treatment.*

Anemia Due to Myeloproliferative Neoplasms (MPN) – Myelofibrosis ‡ [5,11]

- Member has anemia with symptomatic splenomegaly and/or constitutional symptoms; **AND**
  - Used in combination with ruxolitinib; **OR**
- Member has anemia with no splenomegaly or constitutional symptoms; **AND**
  - Used as a single agent; **OR**
- Member has anemia with splenomegaly and constitutional symptoms well controlled on current JAK inhibitor; **AND**
  - Used in combination with JAK inhibitor

† FDA Approved Indications; **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1,5-8,12]

Prior authorization validity can be renewed based on the following criteria:

- Member continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Member will not receive doses < 21 days apart; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: thromboembolic events, severe hypertension, extramedullary hematopoietic masses in members with beta thalassemia, etc.; **AND**

Beta Thalassemia

- Member is experiencing disease response as evidenced by a decrease in the number of RBC transfusions from baseline; **OR**
- For new starts: Member 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**
- Member experienced a response followed by a lack/loss of response and requires a dose increase to 1.25 mg/kg (from 1 mg/kg)

Anemia Due to Myelodysplastic Syndromes (MDS)

- Member is experiencing disease response as evidenced by a decrease in the number of RBC transfusions from baseline; **OR**
- For ESA-naïve members:
  - For new starts: Member is not RBC transfusion-free OR has a Hgb concentration < 10 g/dL with hemoglobin increase < 1 g/dL since last dose after at least 2 consecutive, initial (1 mg/kg) doses (6 weeks) and requires a dose increase to 1.33 mg/kg; **OR**
  - Member is not RBC transfusion-free OR has a Hgb concentration < 10 g/dL with hemoglobin increase < 1 g/dL since last dose after at least 2 consecutive, 1.33 mg/kg doses (6 weeks) and requires a dose increase to 1.75 mg/kg; **OR**
- For ESA-refractory or intolerant members:
  - For new starts: Member is not RBC transfusion-free after at least 2 consecutive, initial (1 mg/kg) doses (6 weeks) and requires a dose increase to 1.33 mg/kg; **OR**
  - Member is not RBC transfusion-free after at least 2 consecutive, 1.33 mg/kg doses (6 weeks) and requires a dose increase to 1.75 mg/kg; **OR**
- Member experienced a response followed by a lack/loss of response and requires a dose increase by one dose level from the level in which response was lost (not to exceed a dose of 1.75 mg/kg)

Anemia Due to Myeloproliferative Neoplasms (MPN) – Myelofibrosis

- Member is experiencing disease response from baseline (e.g. decrease in the number of RBC transfusions from baseline, ≥ 1.5 g/dL hemoglobin increase without RBC transfusions from baseline, reduction in anemia-related fatigue symptoms, etc.); **OR**
- For new starts: Member has not achieved disease response after at least 2 consecutive, initial (1 mg/kg or 1.33 mg/kg) doses (6 weeks) and requires a dose increase by one dose level from the initial level (1.33 mg/kg or 1.75mg/kg); **OR**

- Member experienced a response followed by a lack/loss of response and requires a dose increase by one dose level from the level in which response was lost (not to exceed a dose of 1.75 mg/kg)

V. Dosage/Administration [1,12]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Beta Thalassemia</td><td>The recommended starting dose is 1 mg/kg once every 3 weeks by subcutaneous injection.
Titrate the dose based on response (see table below).
Do not increase the dose beyond the maximum dose of 1.25 mg/kg.
Discontinue Reblozyl if no response as described in the table below, or if unacceptable toxicity occurs at any time.
<table><tr><th colspan="2">Dose Increases for Insufficient Response</th></tr><tr><td>If after at least 2 consecutive doses (6 weeks) at 1 mg/kg, the member:
Has no reduction in RBC transfusion burden</td><td>Increase the dose to 1.25 mg/kg every 3 weeks</td></tr><tr><td>If after at least 3 consecutive doses (9 weeks) at 1.25 mg/kg, the member:
Has no reduction in RBC transfusion burden</td><td>Discontinue treatment</td></tr></table></td></tr>
<tr><td>Anemia Due to Myelodysplastic Syndromes (MDS)</td><td>The recommended starting dose is 1 mg/kg once every 3 weeks by subcutaneous injection.
Titrate the dose based on response (see tables below for ESA-naïve and ESA-refractory or intolerant members).
Do not increase the dose more frequently than every 6 weeks (2 doses) or beyond the maximum dose of 1.75 mg/kg.
Discontinue Reblozyl if no response as described in the table below, or if unacceptable toxicity occurs at any time.
<u>Note</u>: If, upon a dose reduction, the member 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.
<table><tr><th colspan="2">Dose Increases for Insufficient Response for <u>ESA-Naïve Members</u></th></tr><tr><td>If after at least 2 consecutive doses (6 weeks) at 1 mg/kg, the member:
Is not RBC transfusion-free, or
Has a Hgb concentration < 10 g/dL with Hb increase < 1 g/dL since last dose</td><td>Increase the dose to 1.33 mg/kg every 3 weeks</td></tr><tr><td>If after at least 2 consecutive doses (6 weeks)</td><td>Increase the dose to 1.75</td></tr></table></td></tr>
</table>

	at 1.33 mg/kg, the member: • Is not RBC transfusion-free, or • Has a Hgb concentration < 10 g/dL with Hb increase < 1 g/dL since last dose	mg/kg every 3 weeks
	If after at least 3 consecutive doses (9 weeks) at 1.75 mg/kg, the member: • Has no reduction in RBC transfusion burden including no increase from baseline Hgb	• Discontinue treatment

Dose Increases for Insufficient Response for ESA- Refractory or Intolerant Members	
If after at least 2 consecutive doses (6 weeks) at 1 mg/kg, the member: • Is not RBC transfusion-free	• Increase the dose to 1.33 mg/kg every 3 weeks
If after at least 2 consecutive doses (6 weeks) at 1.33 mg/kg, the member: • Is not RBC transfusion-free	• Increase the dose to 1.75 mg/kg every 3 weeks
If after at least 3 consecutive doses (9 weeks) at 1.75 mg/kg, the member: • Has no reduction in RBC transfusion burden including no increase from baseline Hgb	• Discontinue treatment

Anemia Due to Myeloproliferative Neoplasms (MPN) – Myelofibrosis	The recommended starting dose is 1 mg/kg to 1.33 mg/kg once every 3 weeks by subcutaneous injection. – Dose increases for insufficient response: If a member is not having beneficial response after at least 2 consecutive doses (6 weeks) at the current dose level, increase the Reblozyl dose to 1.33 mg/kg (in those on 1 mg/kg) or 1.75mg/kg (in those on 1.33 mg/kg). Do not increase the dose more frequently than every 6 weeks (2 doses) or beyond the maximum dose of 1.75 mg/kg.
– Dose decreases/interruptions: In the absence of transfusions, if Hgb increase is >2 g/dL within 3 weeks or if the pre-dose Hgb is ≥11.5 g/dL, reduce the dose or interrupt treatment until the Hgb is ≤11 g/dL. – Reblozyl should be reconstituted and administered by a healthcare professional.	

VI. Billing Code/Availability Information

HCPCS Code:

- J0896 – Injection, luspatercept-aamt, 0.25 mg; 1 billable unit = 0.25 mg

NDC(s):

- Reblozyl 25 mg single-dose vial: 59572-0711-xx

- Reblozyl 75 mg single-dose vial: 59572-0775-xx

VII. References

1. Reblozyl [package insert]. Summit, NJ; Celgene, Inc: February 2026. Accessed March 2026.
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12. Gerds AT, Harrison C, Kiladjian JJ, et al. Safety and efficacy of luspatercept for the treatment of anemia in patients with myelofibrosis: Results from the ACE-536-MF-001 study [abstract]. J Clin Oncol 2023;41:7016-7016.
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Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C93.10	Chronic myelomonocytic leukemia not having achieved remission
C94.40	Acute panmyelosis with myelofibrosis not having achieved remission
C94.41	Acute panmyelosis with myelofibrosis, in remission
C94.42	Acute panmyelosis with myelofibrosis, in relapse
C94.6	Myelodysplastic disease, not elsewhere classified
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1

D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.Z	Other myelodysplastic syndromes
D47.1	Chronic myeloproliferative disease
D47.4	Osteomyelofibrosis
D56.1	Beta thalassemia
D75.81	Myelofibrosis

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
15	KY, OH	CGS Administrators, LLC