Reblozyl® (luspatercept-aamt) (Subcutaneous)

I. Length of Authorization

- Coverage will be provided initially for 15 weeks (6 initial doses) and may be renewed annually thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:
   - Reblozyl 25 mg single-dose vial: 2 vials every 21 days
   - Reblozyl 75 mg single-dose vial: 2 vials every 21 days

B. Max Units (per dose and over time) [HCPCS Unit]:
   - 150 mg every 21 days

III. Initial Approval Criteria\(^1,2,3,4\)

Coverage is provided in the following conditions:

**Beta Thalassemia †**

- Patient must be 18 years or older*: 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
- 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 has a documented diagnosis of beta thalassemia (excludes alpha-thalassemia and hemoglobin S/β-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 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 ie, ≥ 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**
- 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**
- Other causes of anemia (e.g., hemolysis, bleeding, recent major surgery, vitamin deficiency, etc.) have been ruled out

† FDA approved indications

### IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- 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**
- 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**
  - 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); **AND**

- Other causative factors (*e.g.*, *a bleeding event*) have been ruled out

*Note:* Discontinue therapy if the patient does not experience a decrease in transfusion burden after 15 weeks of treatment (administration of 6 doses) at the maximum dose level or if unacceptable toxicity occurs at any time

### V. Dosage/Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta Thalassemia</td>
<td>The recommended starting dose is 1 mg/kg once every 3 weeks by subcutaneous injection.</td>
</tr>
</tbody>
</table>

- 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.
- If the pre-dose Hgb is greater than or equal to 11.5 g/dL and the Hgb level is not influenced by recent transfusion, delay dosing until the Hgb is less than or equal to 11 g/dL.
- **Dose increase:** 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.
- **Continuation:** If a patient experienced a response followed by a lack of or lost response, initiate a search for causative factors (*e.g.*, *a bleeding event*). If typical causes for a lack or loss of hematologic response are excluded, follow dosing recommendations for management of patients with an insufficient response to therapy.
- **Discontinuation:** Discontinue therapy 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.
- Reblozyl should be reconstituted and administered by a healthcare professional.

### VI. Billing Code/Availability Information

**Jcode:**

- J3590 – Unclassified biologic

**NDC:**

- Reblozyl 25 mg single-dose vial: 59572-0711-xx
- Reblozyl 75 mg single-dose vial: 59353-0775-xx

### VII. References


**Appendix 1 – Covered Diagnosis Codes**

<table>
<thead>
<tr>
<th>ICD-10</th>
<th>ICD-10 Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D56.1</td>
<td>Beta thalasemia</td>
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**Appendix 2 – Centers for Medicare and Medicaid Services (CMS)**

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 Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

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

**Medicare Part B Administrative Contractor (MAC) Jurisdictions**

<table>
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<tr>
<th>Jurisdiction</th>
<th>Applicable State/US Territory</th>
<th>Contractor</th>
</tr>
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<tbody>
<tr>
<td>E (1)</td>
<td>CA, HI, NV, AS, GU, CNMI</td>
<td>Noridian Healthcare Solutions, LLC</td>
</tr>
<tr>
<td>F (2 &amp; 3)</td>
<td>AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ</td>
<td>Noridian Healthcare Solutions, LLC</td>
</tr>
<tr>
<td>5</td>
<td>KS, NE, IA, MO</td>
<td>Wisconsin Physicians Service Insurance Corp (WPS)</td>
</tr>
<tr>
<td>6</td>
<td>MN, WI, IL</td>
<td>National Government Services, Inc. (NGS)</td>
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<tr>
<td>H (4 &amp; 7)</td>
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<tr>
<td>8</td>
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<td>First Coast Service Options, Inc.</td>
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<td>Palmetto GBA, LLC</td>
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<tr>
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<td>Novitas Solutions, Inc.</td>
</tr>
<tr>
<td>K (13 &amp; 14)</td>
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<td>National Government Services, Inc. (NGS)</td>
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<td>15</td>
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<td>CGS Administrators, LLC</td>
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