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Section:	Prescription Drugs	**Effective Date:**	July 1, 2025
Subsection:	Hematological Agents	**Original Policy Date:**	December 6, 2019
Subject:	Reblozyl	**Page:**	1 of 5

Last Review Date: June 12, 2025

Reblozyl

Description

Reblozyl (luspatercept-aamt)

Background
Reblozyl (luspatercept-aamt) is a recombinant fusion protein that binds several endogenous TGF-β superfamily ligands, thereby diminishing Smad2/3 signaling. Reblozyl promotes erythroid maturation through differentiation of late-stage erythroid precursors (normoblasts). In a model of β-thalassemia, Reblozyl decreased abnormally elevated Smad2/3 signaling and improved hematology parameters associated with ineffective erythropoiesis (1).

Regulatory Status
FDA-approved indications: Reblozyl is an erythroid maturation agent indicated for the treatment of: (1)

- Anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions.
- Anemia without previous erythropoiesis stimulating agent use (ESA-naïve) in adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS) who may 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/ myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

Limitations of Use: Reblozyl is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia (1).

Thromboembolic events have been reported in patients taking Reblozyl. These events may include deep vein thromboses, pulmonary embolus, portal vein thrombosis, and ischemic strokes. Thromboprophylaxis may be considered in patients with beta thalassemia at increased risk for thromboembolic events (1).

Hypertension has also been reported in patients treated with Reblozyl. Blood pressure should be monitored prior to each administration. Extramedullary hematopoietic masses (EHM) have also been observed. EHM are clumps of blood cell precursors that form when tissues other than bone marrow produce blood cells. In cases of patients with EHM and serious complications, Reblozyl should be discontinued (1).

Reblozyl may cause fetal harm when administered to a pregnant woman. Pregnant women should be advised of the potential risk to a fetus. Females of reproductive potential should use an effective method of contraception during treatment with Reblozyl and for at least 3 months after the final dose (1).

Hemoglobin (Hgb) should be assessed and reviewed prior to each administration. If a RBC transfusion occurred prior to dosing, the pretransfusion Hgb must be considered for dosing purposes (1).

The safety and effectiveness of Reblozyl in pediatric patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Reblozyl may be considered **medically necessary** if the conditions indicated below are met.

Reblozyl may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Anemia associated with beta thalassemia
    a. Patient requires regular red blood cell (RBC) transfusions

2. Anemia with very low- to intermediate-risk myelodysplastic syndromes (MDS)
    a. **NO** previous erythropoiesis stimulating agent use (ESA-naïve)

3. Anemia associated with **ONE** of the following disorders:
    a. Very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS)
    b. Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)

    AND ALL of the following:
    a. Patient requires 2 or more RBC units over 8 weeks
    b. Patient has failed an erythropoiesis stimulating agent

AND ALL of the following for **ALL** diagnoses:
a. Hemoglobin will be assessed and reviewed prior to each administration
b. Blood pressure will be monitored prior to each administration

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Reblozyl (luspatercept-aamt) is a recombinant fusion protein that binds several endogenous TGF-β superfamily ligands, thereby diminishing Smad2/3 signaling. Reblozyl promotes erythroid maturation through differentiation of late-stage erythroid precursors (normoblasts). In a model of β-thalassemia, Reblozyl decreased abnormally elevated Smad2/3 signaling and improved hematology parameters associated with ineffective erythropoiesis. The safety and effectiveness of Reblozyl in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Reblozyl while maintaining optimal therapeutic outcomes.

References

1. Reblozyl [package insert]. Summit, NJ: Celgene Corporation; May 2024.

Policy History

Date	Action
December 2019	Addition to PA
March 2020	Annual review
April 2020	Addition of indication: Anemia with MDS-RS or MDS/MPN-RS-T. Also changed hemoglobin requirement to “hemoglobin will be assessed and reviewed prior to each administration”
June 2020	Annual review
September 2021	Annual review
September 2022	Annual editorial review and reference update
December 2022	Annual review and reference update
September 2023	Annual review
October 2023	Per PI update, added indication of MDS-associated anemia in patients that are ESA-naïve
December 2023	Annual review
June 2024	Annual review
June 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 12, 2025 and is effective on July 1, 2025.