Reference number(s)
4717-A

Standard Medicare Part B Management Reblozyl

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Reblozyl	luspatercept-aamt

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

- Treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions
- Treatment of 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
- Treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell 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)

Compendial Use[4]

Myelofibrosis-associated anemia

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Limitations of Use:

Reblozyl is not indicated for use as a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia.

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

Anemia with Beta Thalassemia

The following documentation must be available, upon request, for all submissions for initial therapy requests:

- Pretreatment or pretransfusion hemoglobin (Hgb) level
- Either of the following:
  - Hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) results OR molecular genetic testing results, or
  - Chart notes or medical record documentation stating diagnosis of beta thalassemia (β-thalassemia) or hemoglobin E/β-thalassemia was previously confirmed by hemoglobin electrophoresis or HPLC results, OR molecular genetic testing[D]

Anemia of Myelodysplastic Syndrome or Myelodysplastic/Myeloproliferative Neoplasm

The following documentation must be available, upon request, for all submissions for initial therapy requests: Pretreatment or pretransfusion hemoglobin (Hgb) level

Exclusions[1]

Coverage will not be provided for treatment of anemia with beta thalassemia in members with hemoglobin S/β-thalassemia or alpha-thalassemia.

Coverage Criteria

Anemia with Beta Thalassemia[1-4,6]

Authorization of 16 weeks may be granted for treatment of anemia with beta thalassemia in members 18 years of age or older when all of the following criteria are met:

- The member has symptomatic anemia evidenced by a pretreatment or pretransfusion Hgb level less than or equal to 11 grams per deciliter (g/dL).

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- The member has a diagnosis of beta thalassemia (β-thalassemia) or hemoglobin E/β-thalassemia (β-thalassemia with mutation and/or multiplication of alpha globin is allowed) confirmed by one of the following:
    - Hemoglobin electrophoresis or high-performance liquid chromatography (HPLC)
    - Molecular genetic testing
- The member required at least 6 red blood cell (RBC) units to be transfused in the previous 24 weeks.

Note: If a red blood cell (RBC) transfusion occurred prior to dosing, the pretransfusion hemoglobin (Hgb) level must be considered for dosing purposes.

Anemia of Myelodysplastic Syndrome or Myelodysplastic/Myeloproliferative Neoplasm[1,5]

Authorization of 24 weeks may be granted for treatment of anemia of myelodysplastic syndrome or myelodysplastic/myeloproliferative neoplasm in members 18 years of age or older when all of the following criteria are met:

- The member has any of the following:
    - Very low- to intermediate-risk myelodysplastic syndrome
    - Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)
    - Myelodysplastic/myeloproliferative neoplasm with SF3B1 variant and thrombocytosis (MDS/MPN-SF3B1-T)
- The member has symptomatic anemia evidenced by a pretreatment or pretransfusion Hgb level less than or equal to 11 g/dL.
- The member has been receiving regular red blood cell (RBC) transfusions as defined by greater than or equal to 2 units per 8 weeks.

Myelofibrosis-associated Anemia[4]

Authorization of 12 months may be granted for treatment of myelofibrosis-associated anemia.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with Reblozyl.
- Reblozyl is being used to treat an indication listed in the coverage criteria.
- The member is receiving benefit from therapy. Benefit is defined as meeting both of the following criteria:
    - Achieving or maintaining red blood cell transfusion burden reduction.
    - No evidence of unacceptable toxicity from Reblozyl.

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Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Reblozyl.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- A phase 3 trial of luspatercept in patients with transfusion-dependent β-thalassemia
- Luspatercept in patients with lower-risk myelodysplastic syndromes
- 2021 Thalassaemia International Federation guidelines for the management of transfusion-dependent thalassemia
- NCCN Guideline: Myelodysplastic syndromes
- NCCN Guideline: Myelofibrosis

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Reblozyl are covered in addition to myelofibrosis-associated anemia.

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using hemoglobin electrophoresis, high-performance liquid chromatography (HPLC), or molecular genetic testing is supported by the 2021 Thalassemia International Federation guidelines for the management of transfusion-dependent thalassemia. The diagnosis of thalassemias relies on using red blood cell indices, hemoglobin analysis, and assessing the clinical severity of anemia. Molecular genetic testing may be useful for predicting the clinical phenotype and enabling presymptomatic diagnosis of at-risk family members and prenatal diagnosis.

According to the UpToDate database, the diagnostic evaluation of a thalassemia depends on the personal and family history and available laboratory results. Genetic testing is used for precise diagnosis and is especially important in carrier detection, prenatal testing, and genetic counseling. Genetic testing can be done by gene sequencing or a number of other methods. If genetic testing is not available, hemoglobin can be analyzed using a number of protein chemistry methods. The most commonly used methods are HPLC and various hemoglobin electrophoresis techniques.

Support for using Reblozyl to treat myelofibrosis-associated anemia can be found in the National Comprehensive Cancer Network's guideline for myeloproliferative neoplasms. The NCCN Guideline for myeloproliferative neoplasms supports the use of Reblozyl for myeloproliferative-associated anemia with or without symptomatic splenomegaly and/or constitutional symptoms.

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6. Farmakis D, Porter J, Taher A, Cappellini MD, Angastiniotis M, Eleftheriou A. 2021 Thalassaemia International Federation guidelines for the management of transfusion-dependent thalassemia. *Hemasphere*. 2022;6(8):e732.

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