

Medical Policy Bulletin

Title:

Luspatercept–aamt (Reblozyl®)

Policy #:

MA08.110b

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

BETA THALASSEMIA

Initial Therapy

Luspatercept–aamt (Reblozyl®) is considered medically necessary and, therefore, covered for the treatment of anemia in adult individuals with beta thalassemia who require regular red blood cell (RBC) transfusions, when all of the following criteria, including dosing and frequency, are met:

- Documented diagnosis of β -thalassemia, hemoglobin E/ β -thalassemia, or β -thalassemia combined with alpha-thalassemia confirmed by one of the following tests:
 - Molecular genetic testing that reveals pathogenic variation(s) in the *HBB* gene causing β -thalassemia
 - Hemoglobin electrophoresis
- There is documentation the individual is transfusion-dependent, requiring regular RBC transfusions (i.e., at least six units of red blood cell [RBC] in the previous 24 weeks and no transfusion-free period for ≥ 35 days during that period).
- Treatment will not be combined with a gene therapy used to treat β -thalassemia.
- Dosing and Frequency: 1 mg/kg as a subcutaneous injection every three weeks. If a reduction in RBC transfusion burden is not achieved after at least 2 consecutive doses (6 weeks), luspatercept–aamt (Reblozyl®) will be covered up to a maximum dose of 1.25 mg/kg every three weeks.

Continuation Therapy

Continuation of luspatercept–aamt (Reblozyl®) is considered medically necessary and, therefore, covered for individuals who have demonstrated a documented reduction in the number of transfusions compared to baseline.

MYELODYSPLASTIC SYNDROMES

Initial Therapy

Luspatercept–aamt (Reblozyl®) is considered medically necessary and, therefore, covered for the treatment of anemia in adult individuals with myelodysplastic syndromes (MDS) when all of the following criteria, including dosing and frequency, are met:

- Documented diagnosis of myelodysplastic syndromes (MDS) with all of the following components:
 - The individual has one of the following MDS subtypes with ring sideroblasts according to World Health Organization criteria (i.e., with either $\geq 15\%$ ring sideroblasts or $\geq 5\%$ ring sideroblasts if *SF3B1* variation is present, and with $< 5\%$ bone marrow blasts):
 - MDS with ring sideroblasts (MDS-RS)
 - Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)
 - The individual has lower-risk disease according to one of the following scales:
 - International Prognostic Scoring System (IPSS): low or intermediate-1 risk
 - Revised International Prognostic Scoring System (IPSS-R): very low, low, or intermediate risk
 - WHO-Based Prognostic Scoring System (WPSS): very low, low, or intermediate risk
 - The individual does not have MDS with chromosome 5q deletion (del[5q]) [i.e., the individual's MDS is non-del(5q)]
- There is documentation that the individual is transfusion-dependent, requiring regular RBC transfusions (i.e., ≥ 2 units every 8 weeks)
- The individual has a documented failure, contraindication, intolerance, or is unlikely to respond to erythropoiesis-stimulating agents (ESA) (i.e., serum erythropoietin level is > 200 U/L in those who had not previously been treated with erythropoiesis-stimulating agents)
- Dosing and Frequency: 1 mg/kg as a subcutaneous injection every three weeks. If individual is not RBC transfusion-free after at least 2 consecutive doses, an increased dose of 1.33 mg/kg every three weeks will be covered. If individual is still not RBC transfusion-free after at least 2 more consecutive doses, an increased maximum dose of 1.75 mg/kg every three weeks will be covered.

Continuation Therapy

Continuation of luspatercept–aamt (Reblozyl®) is considered medically necessary and, therefore, covered for individuals who have demonstrated at least one of the following, compared to baseline:

- increase in RBC transfusion independence (transfusion-free period)
- reduction in transfusion burden (the amount of units required with each red-cell transfusion)

NOT MEDICALLY NECESSARY

Continuation therapy with luspatercept–aamt (Reblozyl®) in individuals with beta thalassemia is considered not medically necessary and, therefore, not covered for individuals who do not experience a decrease in transfusion burden after 5 doses (two doses at 1 mg/kg and three doses at 1.25 mg/kg). The available published peer-reviewed literature does not support its use in the treatment of this disease.

Continuation therapy with luspatercept–aamt (Reblozyl®) in individuals with MDS-RS or MDS/MPN-RS-T is considered not medically necessary and, therefore, not covered for individuals who do not experience a decrease in transfusion burden after at least 3 consecutive doses of the maximum dosage of 1.75 mg/kg administered at three-week intervals. The available published peer-reviewed literature does not support its use in the treatment of this disease.

When molecular genetic testing reveals established benign variation(s) or wild-type genotype in the *HBB* gene, luspatercept–aamt (Reblozyl®) is considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support its use in the treatment of this disease.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for luspatercept–aamt (Reblozyl®), including those listed below, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

- Individuals with hemoglobin S/ β -thalassemia or alpha-thalassemia
- Individuals with non-transfusion-dependent beta-thalassemia
- As a substitute for RBC transfusions in those who require immediate correction of anemia

When molecular genetic testing reveals likely pathogenic or variations of unknown significance (VUS) in the *HBB* gene, the use of luspatercept–aamt (Reblozyl®) is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of luspatercept–aamt (Reblozyl®). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of luspatercept–aamt (Reblozyl®) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for luspatercept–aamt (Reblozyl®).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

When coverage of luspatercept–aamt (Reblozyl®) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Guidelines

There is no Medicare coverage determination addressing luspatercept–aamt (Reblozyl®); therefore, the Company policy is applicable.

DRUG INFORMATION

Luspatercept–aamt (Reblozyl®) for individuals with beta thalassemia is administered as a subcutaneous injection every three weeks. Per prescribing information: Assess and review hemoglobin (Hb) results prior to each dose. If an RBC transfusion occurred prior to dosing, use the pretransfusion hemoglobin for dose evaluation. In the absence of transfusions, if hemoglobin increase is greater than 2 g/dL within 3 weeks or the predose Hb is ≥ 11.5 g/dL, reduce the dose or interrupt treatment.

Luspatercept–aamt (Reblozyl®) for individuals with MDS-RS or MDS/MPN-RS-T is administered as a subcutaneous injection every three weeks. Per prescribing information: Prior to each dose, review the individual's hemoglobin (Hb) and transfusion record. In the absence of transfusions, if Hb increase is greater than 2 g/dL within 3 weeks or if the predose Hb is ≥ 11.5 g/dL, reduce the dose or interrupt treatment. If, upon dose reduction, the individual loses response (i.e., requires a transfusion) or hemoglobin 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.

PROGNOSTIC SCORING SYSTEMS FOR MDS

There are three prognostic scoring systems for MDS that use several factors to calculate a risk score to categorize the disease as either Lower-risk MDS (milder disease with slower progression) or Higher-risk MDS (more aggressive

disease). Factors may include the following: percent of blast cells in bone marrow, chromosome changes, number of low blood counts, hemoglobin levels, platelets and neutrophil counts, and presence of severe anemia.

Lower-risk disease is defined in one of the following scoring systems:

- International Prognostic Scoring System (IPSS): low or intermediate-1 risk
- Revised International Prognostic Scoring System (IPSS-R): very low, low, or intermediate risk
- WHO-Based Prognostic Scoring System (WPSS): very low, low, or intermediate risk

Higher-risk disease is defined in one of the following scoring systems:

- International Prognostic Scoring System (IPSS): intermediate-2 or high risk
- Revised International Prognostic Scoring System (IPSS-R): high or very high risk
- WHO-Based Prognostic Scoring System (WPSS): high or very high risk

BENEFIT APPLICATION

Subject to the applicable Evidence of Coverage, luspatercept–aamt (Reblozyl®) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria and Dosing and Frequency Requirements listed in this medical policy are met.

For Medicare Advantage members, certain drugs are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when luspatercept–aamt (Reblozyl®) is covered under a member's medical benefit (Part B benefit). It does not address instances when luspatercept–aamt (Reblozyl®) is covered under a member's pharmacy benefit (Part D benefit).

However, services that are identified in this policy as experimental/investigational or not medically necessary are not eligible for coverage or reimbursement by the Company.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Luspatercept–aamt (Reblozyl®) was approved by the FDA on November 8, 2019 for the treatment of anemia in adult individuals with beta thalassemia who require regular red blood cell (RBC) transfusions. (Limitations of use: Luspatercept–aamt (Reblozyl®) is not indicated for use as a substitute for RBC transfusions in individuals who require immediate correction of anemia). Supplemental approvals for luspatercept–aamt (Reblozyl®) have since been issued by the FDA. The safety and effectiveness in pediatric individuals have not been established, and based on findings in juvenile animals, is not recommended for use in the pediatric population.

Description

LUSPATERCEPT-AAMT (REBLOZYL®)

Luspatercept–aamt (Reblozyl®) was approved by the US Food and Drug Administration (FDA) on November 8, 2019 for the treatment of anemia in adult individuals with beta thalassemia who require regular red blood cell (RBC) transfusions. Luspatercept–aamt (Reblozyl®) is not indicated for use as a substitute for RBC transfusions in individuals who require immediate correction of anemia. A supplemental approval was granted on April 3, 2020 for the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell units over 8 weeks in adults 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).

Luspatercept–aamt (Reblozyl®) is a recombinant fusion protein that causes erythroid maturation. Luspatercept–aamt (Reblozyl®) binds to and inhibits several endogenous transforming growth factor (TGF)- β superfamily ligands involved in late stage erythropoiesis, thereby diminishing abnormally elevated Smad2/3 signaling and enhancing RBC production and preventing anemia.

BETA THALASSESMIA

Beta thalassemia is a relatively rare inherited blood disorder in the United States, but its incidence of symptomatic cases is estimated to be approximately 1 in 100,000 individuals in the general population. Many states in the United States diagnose infants with a hemoglobin disorder through newborn screenings, although most states do not routinely test for thalassemia. Beta thalassemia is caused by variations in the *HBB* gene (usually in an autosomal recessive pattern) that provides instructions for making the beta-globin protein, a component (subunit) of hemoglobin.

A lack of beta-globin leads to a shortage of functional hemoglobin, the iron-containing protein in red blood cells (RBC) that carries oxygen to cells throughout the body, creating a shortage of mature RBC. This shortage of mature red blood cells leads to anemia and other associated health problems, such as organ damage or abnormal blood clots, in those with beta thalassemia.

Beta thalassemia has three main forms, minor, intermedia, and major, which indicate the severity of the disease. Individuals with beta thalassemia minor (trait) are usually asymptomatic and individuals often are unaware that they have the condition. Individuals with thalassemia intermedia are typically diagnosed later in life, exhibit a wide variability in symptoms and severity (less severe phenotype than thalassemia major), and may only require periodic blood transfusions (non-transfusion-dependent thalassaemia). The most severe form of beta thalassemia is thalassemia major (also known as Cooley's anemia), diagnosed within the first two years of life, and require life-long, regular blood transfusions to replenish their red blood cell supply. In beta thalassemia major, there is minimal to no beta globin chain production and consequently little to no adult hemoglobin (HbA). Beta thalassemia major is caused by homozygosity or compound heterozygosity for beta⁰ thalassemia mutations or, in rare cases, beta⁺ thalassemia mutations with extremely low production of beta globin chains. The other major cause is compound heterozygosity for hemoglobin E (ie, HbE/beta thalassemia); HbE is a beta⁺ type of mutation. Worldwide, individuals with HbE/beta-thalassaemia represent approximately 50% of those affected with severe beta thalassaemia.

Over time, an influx of iron-containing hemoglobin from chronic blood transfusions can lead to a buildup of iron in the body, resulting in liver, heart, and hormone problems. Individuals are required to undergo chelation therapy to remove the excess iron from the body. The only available curative option is a hematopoietic stem cell transplant.

PEER-REVIEWED LITERATURE

Summary

The safety and efficacy of luspatercept-aamt (Reblozyl®) was evaluated in a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial (BELIEVE) in adults (n=336) with a documented diagnosis of β-thalassemia (77% of participants), hemoglobin E/β-thalassemia, or β-thalassemia combined with alpha-thalassemia who required regular red blood cell transfusions (6-20 red blood cell [RBC] units in the 24 weeks prior to randomization and no transfusion-free period for ≥ 35 days during that period). Participants were randomized 2:1 to luspatercept-aamt (Reblozyl®) 1 mg/kg subcutaneously every 21 days plus best supportive care (BSC) (n=224) or placebo plus BSC (n=112) administered subcutaneously once every 21 days, as long as a reduction in transfusion requirement was observed or until unacceptable toxicity resulted. All participants were eligible to receive best supportive care, which included RBC transfusions; iron-chelating agents; use of antibiotic, antiviral, and antifungal therapy; and/or nutritional support, as needed. The BELIEVE trial excluded those with hemoglobin S/β-thalassemia or alpha-thalassemia or who had major organ damage (liver disease, heart disease, lung disease, renal insufficiency). Those with recent deep vein thrombosis or stroke or recent use of ESA, immunosuppressant, or hydroxyurea therapy were also excluded.

The baseline transfusion burden 12 weeks prior to randomization was approximately a median of 6.12 transfusion (minimum 3, maximum 14). The primary outcome of this trial was the proportion of participants achieving RBC transfusion burden reduction (≥33% reduction from baseline) with a reduction of at least 2 units from Week 13 to Week 24. Twenty-one percent of those who were in the luspatercept-aamt (Reblozyl®) group achieved at least a 33% reduction in transfusions compared to 4.5% of the individuals who received a placebo (p<0.0001). Thromboembolic events were reported more frequently in those treated with luspatercept-aamt (Reblozyl®) (3.6%), compared to placebo (0.9%).

MYELODYSPLASTIC SYNDROMES

Myelodysplastic syndromes (MDS) are a group of cancers caused by variation(s) in gene(s) and are characterized by ineffective hematopoiesis and progressive cytopenias. The hematopoietic stem cells become abnormal and either stop replicating, or they create defective (dysplasia, die early, etc.) new blood cells. The defective cells overcrowd the bone marrow causing even fewer healthy blood cells to be created or survive and enter the bloodstream. MDS affects all three lines of blood cells, causing symptomatic anemia (dyspnea, fatigue, weakness), infection, and bleeding. MDS predominating affects the elderly male population and has the risk of progression to an aggressive cancer, acute myeloid leukemia. There are many types of MDS classified by the following features: percent of blast cells in bone marrow, chromosome changes, number of low blood counts, hemoglobin levels, platelets and neutrophil counts, and presence of severe anemia.

The only curative option for MDS are an allogeneic hematopoietic cell transplantation (HCT). Other treatment options for MDS, depending on genetic and other hematologic factors, may include erythropoiesis-stimulating agent (ESA) therapy, red-cell transfusions with iron chelation therapy, lenalidomide, or hypomethylating agents (e.g., azacitidine, decitabine). Individuals with anemia and lower-risk MDS in whom ESA therapy is not effective (serum erythropoietin

levels above 200 U/L) generally become dependent on red-cell transfusions. Treatment goals for those with lower-risk MDS include transfusion independence, improvement in hemoglobin levels, and maintenance of or improvement in quality of life.

PEER-REVIEWED LITERATURE

Summary

The safety and efficacy of luspatercept–aamt (Reblozyl®) to decrease the severity of anemia was evaluated in a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial (MEDALIST) by Fenaux et al 2020, in adults (n=229) with a documented diagnosis of myelodysplastic syndrome (MDS) with ring sideroblasts according to World Health Organization criteria (i.e., with either ≥15% ring sideroblasts or ≥5% ring sideroblasts if an *SF3B1* variation was present, and with <5% bone marrow blasts). About 87% of participants had MDS with ring sideroblasts (MDS-RS), while the remainder were categorized as Myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T). Participants had disease defined according to the IPSS-R as being of very low (10% of participants), low (72% of participants), or intermediate risk (17% of participants) MDS. Participants required regular red blood cell transfusions (≥2 units per 8 weeks during the 16 weeks before randomization), and had an inadequate response to prior treatment with an erythropoiesis-stimulating agent (ESA), be intolerant of ESAs, or have a serum erythropoietin > 200 U/L. The study excluded individuals with MDS with deletion 5q (del 5q), white blood cell count > 13 Gi/L, neutrophils < 0.5 Gi/L, platelets < 50 Gi/L, or with prior use of a disease modifying agent for treatment of MDS. The median age was 71 years (range 26-95). Ninety-one percent of individuals had a variation in the *SF3B1* gene.

In the double-blind Primary Phase of the trial, participants were randomized (2:1) to receive luspatercept or placebo, administered subcutaneously every 3 weeks for 24 weeks with no crossover allowed. The starting dose of luspatercept was 1 mg/kg. If a new transfusion was necessary after the individuals were considered to have transfusion independence, they could continue receiving luspatercept, with adjustment to a dose of 1.33 mg/kg, and then to 1.75 mg/kg. At Week 25, disease was assessed and those without clinical benefit discontinued luspatercept or placebo and entered follow-up. Those who had clinical benefit without disease progression could enter the double-blind Extension Phase (n=126) and continue receiving luspatercept or placebo until they had unacceptable toxic effects or disease progression, withdrew consent, or met discontinuation criteria. Follow-up will continue for ≥3 years following the last dose.

The primary end point of RBC transfusion independence for 8 weeks or longer during weeks 1 through 24, was seen in 58 individuals (38%) who received luspatercept versus 10 individuals (13%) who received placebo (P<0.001). The results showed that there was a greater reduction in the severity of anemia in transfusion dependent individuals with lower-risk myelodysplastic syndromes with ring sideroblasts who received luspatercept. The most common luspatercept-associated adverse events (of any grade) included fatigue, diarrhea, asthenia, nausea, and dizziness.

OFF-LABEL INDICATION

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

American Hospital Formulary Service (AHFS). Drug Information 2020. luspatercept. [Lexicomp Online Web site]. 12/09/2019. Available at: <http://online.lexi.com/lco/action/home> [via subscription only]. Accessed April 8, 2020.

Angelucci E, Matthes-Martin S, Baronciani D, et al. Hematopoietic stem cell transplantation in thalassemia major and sickle cell disease: indications and management recommendations from an international expert panel. *Haematologica*. 2014 May;99(5):811-20.

Benz EJ. Clinical manifestation and diagnosis of the thalassemias. [UpToDate Web Site]. Updated 01/17/2020. Available at: <http://www.uptodate.com/home> [via subscription only]. Accessed April 13, 2020.

Cappellini MD, Viprakasit V, Taher AT, et al.; BELIEVE Investigators. A Phase 3 Trial of Luspatercept in Patients with Transfusion-Dependent Beta-Thalassemia. *N Engl J Med*. 2020 Mar 26;382(13):1219-1231.

Elsevier's Clinical Pharmacology Compendium. luspatercept. 03/13/2020. [Clinical Key Web site]. Available

at: <https://www.clinicalkey.com/pharmacology/> [via subscription only]. Accessed April 8, 2020.

Fenaux P, Platzbecker U, Mufti GJ, et al. Luspatercept in patients with lower-risk myelodysplastic syndromes. *N Engl J Med* 2020;382:140-51, study and supplement.

Langhi D, Ubiali, EMA, Marques JFC, et al. Guidelines on Beta-thalassemia major – regular blood transfusion therapy: Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular: project guidelines: Associação Médica Brasileira – 2016. *Rev Bras Hematol Hemoter*. 2016 Oct-Dec; 38(4): 341–345.

Lexi-Drugs Compendium. luspatercept. 04/02/2020. [Lexicomp Online Web site]. Available at: <http://online.lexi.com/lco/action/home> [via subscription only]. Accessed April 8, 2020.

Olivieri NF, Pakbaz Z, Vichinsky E. Hb E/beta-thalassaemia: a common & clinically diverse disorder. *Indian J Med Res*. 2011;134(4):522–531.

National Comprehensive Cancer Network (NCCN). *NCCN Clinical Practice Guidelines in Oncology Myelodysplastic Syndromes*. V.2.2020. 02/28/2020. [NCCN Web site]. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf [via free subscription]. Accessed April 8, 2020.

National Comprehensive Cancer Network (NCCN). *NCCN Drugs & Biologics Compendium*. Luspatercept–aamt (Reblozyl®). [NCCN Web site]. 2020. Available at: https://www.nccn.org/professionals/drug_compendium/content/ [via subscription only]. Accessed April 8, 2020.

National Comprehensive Cancer Network (NCCN). *NCCN Guidelines for Patients - Myelodysplastic Syndromes*. 2018. [NCCN Web site]. Available at: https://www.nccn.org/professionals/physician_gls/default.aspx [via free subscription]. Accessed April 10, 2020.

National Institutes of Health. Clinical trials: An Efficacy and Safety Study of Luspatercept (ACE-536) Versus Placebo in Adults Who Require Regular Red Blood Cell Transfusions Due to Beta (β) Thalassemia (BELIEVE). (NCT02604433). [ClinicalTrials Web site]. last updated 12/27/20. Available at: <https://clinicaltrials.gov/ct2/show/NCT02604433> . Accessed April 10, 2020.

National Institutes of Health. Clinical trials: A Study of Luspatercept (ACE-536) to Treat Anemia Due to Very Low, Low, or Intermediate Risk Myelodysplastic Syndromes (MEDALIST) (NCT02631070). [ClinicalTrials Web site]. last updated 12/04/2019. Available at: <https://clinicaltrials.gov/ct2/show/NCT02631070?term=NCT02631070&draw=2&rank=1> . Accessed March 19, 2020.

National Institutes of Health (NIH). Genetics Home Reference. HBB gene. Reviewed 07/2015. Available at: <https://ghr.nlm.nih.gov/gene/HBB> . Accessed April 10, 2020.

National Institutes of Health (NIH). Genetics Home Reference. Beta thalassemia. Reviewed 09/2015. Available at: <https://ghr.nlm.nih.gov/condition/beta-thalassemia>. Accessed April 13, 2020.

National Organization of Rare Diseases (NORD). *Beta thalassemia*. Updated 2018. Available at: <https://rarediseases.org/rare-diseases/thalassemia-major/>. Accessed April 13, 2020.

Piga A, Perrotta S, Gamberini MR, et al. Luspatercept improves hemoglobin levels and blood transfusion requirements in a study of patients with β -thalassemia. *Blood*. 2019. Mar 21;133(12):1279-1289.

Reblozyl® (luspatercept–aamt). [prescribing information]. Cambridge, MA: Celgene Corp.; 04/2020. Available at: <https://www.reblozylpro.com/>. Accessed April 8, 2020.

Truven Health Analytics. Micromedex® DrugDex® Compendium. Luspatercept–aamt (Reblozyl®). 04/08/2020. Greenwood Village, CO. [Micromedex® Solutions Web site]. Available at: <http://www.micromedexsolutions.com/micromedex2/librarian> [via subscription only]. Accessed April 13, 2020.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Luspatercept–aamt (Reblozyl®) prescribing information and approval letter [FDA Web site]. 04/2020. Available at: <https://www.accessdata.fda.gov/scripts/cder/daf/>. Accessed April 8, 2020.

Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

MEDICALLY NECESSARY

D46.1 Refractory anemia with ring sideroblasts

D46.9 Myelodysplastic syndrome, unspecified

D56.1 Beta thalassemia

D56.5 Hemoglobin E-beta thalassemia

HCPCS Level II Code Number(s)

THE FOLLOWING CODE(S) ARE USED TO REPRESENT LUSPATERCEPT--AAMT (REBLOZYL®)

J0896 Injection, luspatercept-aamt, 0.25 mg

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.110b:

06/29/2022	This policy has been reissued in accordance with the Company's annual review process.
05/19/2021	This policy has been reissued in accordance with the Company's annual review process.
07/01/2020	This policy has been identified for the HCPCS code update, effective 07/01/2020. The following NOC codes have been removed from this policy and are replaced by the following HCPCS code: REMOVED: C9399 Unclassified drugs or biologicals J3590 Unclassified biologics

	REPLACED WITH: J0896 Injection, luspatercept-aamt, 0.25 mg
--	--

Revisions From MA08.110a:

06/08/2020	<p>This version of the policy will become effective 06/08/2020.</p> <p>This policy was updated to communicate the Company's coverage position for the new indication of Myelodysplastic Syndromes (MDS), represented by the following ICD-10 codes:</p> <p>D46.1 Refractory anemia with ring sideroblasts D46.9 Myelodysplastic syndrome, unspecified</p>
------------	---

Revisions From MA08.110:

03/09/2020	The following new policy has been developed to communicate the Company's coverage criteria for luspatercept-aamt (Reblozyl®).
------------	---

Version Effective Date:
07/01/2020
Version Issued Date:
07/02/2020
Version Reissued Date:
06/29/2022