Drug and Biologic Coverage Policy

Effective Date 4/15/2023
Next Review Date… 4/15/2024
Coverage Policy Number IP0115

Luspatercept for Non-Oncology Uses

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Related Coverage Resources

Oncology Medications (CP1403)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for luspatercept (Reblozyl®).

The use of luspatercept for oncology indications are addressed in a separate coverage policy. Please refer to the related coverage policy link above (Oncology Medications).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Initial Approval Criteria

Luspatercept (Reblozyl) is considered medically necessary for the treatment of beta-thalassemia when the individual meets ALL of the following criteria:

1. 18 years of age or older
2. Treatment of anemia with a documented diagnosis of beta-thalassemia

3. Requires regular red blood cell transfusions as defined by meeting **BOTH** of the following:
    a. Received at least six units of packed red blood cells in the previous 24 weeks
    b. Has not had any transfusion-free period greater than 35 days within the previous 24 weeks
4. Has not received Zynteglo (betibeglogene autotemcel intravenous infusion) in the past 12 months
5. Medication is being prescribed by or in consultation with a hematologist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy

Continuation of luspatercept (Reblozyl) is considered medically necessary for the treatment of beta-thalassemia when initial criteria are met AND there is documentation of beneficial response (including that the individual has experienced a clinically meaningful decrease in transfusion burden).

Authorization Duration

Initial approval duration: up to 4 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Coding / Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Covered when medically necessary when used to report Luspatercept (Reblozyl):

HCPCS Codes	Description
J0896	Injection, luspatercept-aamt, 0.25 mg

Background

OVERVIEW
Reblozyl, an erythroid maturation agent, is indicated for the following conditions:[1]

- **Beta thalassemia**, for treatment of adults with anemia who require regular red blood cell (RBC) transfusions.
- **Myelodysplastic syndromes** with ring sideroblasts (MDS-RS) or **myelodysplastic/myeloproliferative neoplasm** with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) associated anemia, for adults with very low- to intermediate-risk disease who have failed an erythropoiesis-stimulating agent (ESA) and require two or more RBC units over 8 weeks.

Clinical Efficacy
Beta Thalassemia
In the BELIEVE trial (published), all patients required regular RBC transfusions at baseline, defined as at least six units of packed RBCs in the preceding 24 weeks, with no transfusion-free intervals > 35 days in that timeframe.[2] A response to Reblozyl was defined as a 33% reduction in transfusion requirement from pretreatment baseline and a reduction in transfusion requirements of at least 2 units RBC during Weeks 13 through 24 compared with pretreatment baseline.

MDS and MDS/MPN-RS-T
In the MEDALIST trial (published), patients were required to have ring sideroblasts according to World Health Organization (WHO) criteria (i.e., ≥ 15% or ≥ 5% if *SF3B1* mutation was present).[3] Patients with deletion 5q were excluded from enrollment. All patients were required to have disease refractory to ESAs (unless endogenous erythropoietin level was elevated), and the median pretransfusion hemoglobin level was 7.6 g/dL (range 5 to 10 g/dL). Regarding response criteria, an erythroid response was defined as a reduction in RBC transfusion of ≥ 4 units per 8 weeks in patients with pretreatment baseline transfusion burden of ≥ 4 units per 8 weeks. For patients with a pretreatment baseline transfusion burden of < 4 units per 8 weeks, a response was defined as an increase in hemoglobin of ≥ 1.5 g/dL over a period of 8 weeks compared with pretreatment baseline. In the pivotal MEDALIST trial publication, which primarily involved patients with MDS, improvements in hemoglobin from baseline were sustained through at least Week 25. It is notable that the MDS disease course may evolve over time and potentially lead to loss of response of previously effective agents; thus, close follow-up is appropriate to verify that therapeutic response is maintained.

Guidelines
The Thalassaemia International Federation published guidelines for the management of transfusion-dependent thalassemia (2021).[4]

- **Chelation therapy** was cited as an effective treatment modality in improving survival, decreasing the risk of heart failure, and decreasing morbidities from transfusional-induced iron overload. The optimal chelation regimen should be individualized and will vary among patients and their clinical status.
- **Allogeneic hematopoietic stem cell transplant (HSCT)** should be offered to patients with beta thalassemia at an early age, before complications due to iron overload have developed if a human leukocyte antigen (HLA) identical sibling is available. In some clinical circumstances, a matched unrelated donor can be adequate.
- **Reblozyl** can be considered for patients ≥ 18 years of age who require regular RBC transfusions.
- **Zynteglo™** (betibeglogene autotemcel intravenous infusion), a gene therapy, may be an option for selected patients when available. Examples include young patients (12 to 17 years of age) with a β^+ genotype who do not have an HLA-compatible sibling donor. Also, Zynteglo can be considered in patients 17 to 55 years of age with a β^+ genotype who do not have severe comorbidities and are at risk or ineligible to undergo allogeneic HSCT but can otherwise undergo an autologous gene therapy procedure with an acceptable risk.

References

1. Reblozyl [prescribing information]. Summit; NJ and Cambridge, MA: Celgene/Acceleron; April 2020.
2. National Organization for Rare Disorders (NORD). Beta thalassemia. Available at: https://rarediseases.org/rare-diseases/thalassemia-major//. Accessed on December 6, 2021.
3. Standards of Care Guidelines for Thalassemia – 2012. Children's Hospital and Research Center Oakland. Available at: https://thalassemia.com/documents/SOCGuidelines2012.pdf. Accessed December 6, 2021.
4. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT) [Internet]. 3rd edition. Nicosia (CY): Thalassaemia International Federation; 2014. Available at: https://www.ncbi.nlm.nih.gov/books/NBK269382/. Accessed on December 6, 2021.
5. National Cancer Institute, National Institutes of Health. Myelodysplastic syndromes treatment. Updated September 20, 2021. Accessed on December 6, 2021. Available at: https://www.cancer.gov/types/myeloproliferative/patient/myelodysplastic-treatment-pdq.
6. The NCCN® Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (Version 2.2022 – November 15, 2021). 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org/clinical.asp. Accessed on December 6, 2021.