Effective Date: 02/01/2020
Last P&T Approval/Version: 01/26/2022
Next Review Due By: 01/2023
Policy Number: C18002-A

Reblozyl (luspatercept-aamt)

PRODUCTS AFFECTED

Reblozyl (luspatercept-aamt)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Anemia in adult patients with beta thalassemia, anemia

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy wasapproved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-bycase basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. BETA THALASSEMIA:
1. Documentation of diagnosis of β-thalassemia or HemoglobinE/β-thalassemia NOTE: Not to be used in patients with sickle beta thalassemia or alpha thalassemia
   AND
2. Documentation member has a performance status of Eastern Cooperative Oncology Group (ECOG) of 0 or 1.
   AND

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3. Documentation member requires regular blood transfusions (6-20 RBC units per 24 weeks) Documentation of pre-treatment transfusion burden required.
   AND
4. Prescriber attests that member will continue to receive best supportive care (RBC transfusions; iron-chelating agents; use of antibiotic, antiviral, and antifungal therapy; and/or nutritional support, as needed)
   AND
5. Documentation that patients (pre-transfusion if done) hemoglobin is ≤ 11g/dL
   AND
6. Prescriber attests females of reproductive potential have a negative pregnancy test prior to start oftherapy and will use an effective method of contraception during treatment and at least for 3 months after treatment

B. ANEMIA:

1. Documented diagnosis of myelodysplastic syndrome OR documented diagnosis of myelodysplastic/myeloproliferative neoplasm
   AND
2. Member has documented lower risk disease as defined as one of the following: (i) Revised International Prognostic Scoring System (IPSS-R): Very Low, Low, Intermediate (Score 0 to ≤ 4.5); (ii) IPSS: Low/Intermediate-1 (Score 0 to 1), OR (iii) WHO-Based Prognostic Scoring System (WPSS): Very Low, Low, Intermediate (Score 0 to 2)
   AND
3. Documentation of ONE of the following: Ring sideroblasts ≥ 15% OR Ring sideroblasts ≥ 5% with an SF3B1 mutation
   AND
4. Documentation of member's pretreatment hemoglobin ≤ 11g/dL
   AND
5. Documentation member is requiring 2 or more red blood cell (RBC) units over 8weeks
   AND
6. Documentation of one of the following: (i) Serum erythropoietin >500 mU/mL OR (ii) Both of the following: Serum erythropoietin ≤500 mU/mL AND member has had an inadequate response
   epoetin alpha >40,000 units/week for at least 8 doses or darbepoetin alpha >500 mcg every 3 weeks for at least 4 doses); OR member has a documented contraindication or intolerance to the use of an erythropoiesis-stimulating agent
   AND
7. Prescriber attests 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

CONTINUATION OF THERAPY:

A. BETA THALASSEMIA:

1. Documentation that member has had a decrease in RBC transfusion burden from pre- treatment
   AND
2. Documentation member has been adherent to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
   AND
3. Member has not experienced any intolerable adverse effects or drug toxicity

B. ANEMIA:

1. Member has previously received Reblozyl for the treatment of symptomatic anemia associated with myelodysplastic syndromes;
   AND
2. Documentation that the member no longer requires pRBC transfusions (transfusion

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independence); and Reblozyl is prescribed by, or in consultation with, a hematologist, or other specialist with expertise in the diagnosis and management of myelodysplastic syndromes.
AND

3. Documentation member has been adherent to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
AND
4. Member has not experienced any intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 9 weeks, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified hematologist

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
maximum dose of 1.25 mg/kg subcutaneous every 21 days

Maximum Quantity Limits – << based on FDA label>>

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Reblozyl (luspatercept-aamt). For information on site of care, see:
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Hematopoietic Growth Factors

FDA-APPROVED USES:
Treatment of anemia in adult patients with beta thalassemia who 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 syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)
D46.1 Refractory anemia with ring sideroblasts
D46.20 Refractory anemia with excess of blasts, unspecified
D46.21 Refractory anemia with excess of blasts 1
D46.22 Refractory anemia with excess of blasts2
D46.B Refractory cytopenia with multilineage dysplasia and ring sideroblasts

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COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Disease State and Treatment Beta thalassemia is part of a group of rare, inherited blood disorders caused by a genetic defect in hemoglobin, characterized by reduced levels of functional hemoglobin. Hemoglobin is an iron-containing protein in red blood cells that carries oxygen to cells throughout the body. Low levels of hemoglobin lead to a lack of oxygen in many parts of the body and anemia, which can cause pale skin, weakness, fatigue, and more serious complications. Organ damage (e.g. renal disease, cardiomyopathy, diabetes) can result. There are three main forms of beta thalassemia – minor, intermedia, and major, terms which indicate the severity of the disease.
Individuals with the minor form, also known as beta thalassemia trait, may experience minor anemia, but they usually do not have symptoms and often are unaware that they have the condition. Individuals with the intermedia form experience a wide range of symptoms, and the severity falls in the broad range between the major and minor forms. Beta thalassemia major, also known as Cooley's anemia, is the severest form of the disorder. Individuals with beta thalassemia major often require regular blood transfusions (about every 2–4 weeks) and lifelong, ongoing medical care. These Individuals are at risk for iron overload, or too much iron in the body, due to the chronic blood transfusions and require medicines to remove extra iron from their bodies (called chelation). People with beta thalassemia are also at an increased risk of developing blood clots.
Hematologists treat patients with beta thalassemia. There are CDC funded Thalassemia Treatment Centers throughout the country.

Reblozyl Efficacy and Safety
The approval of Reblozyl for beta thalassemia, which received a Priority Review designation from the FDA, is based on the results of the clinical trial BELIEVE evaluating patients with beta thalassemia who required RBC transfusions. BELIEVE is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial in which (n=336) patients with beta thalassemia requiring regular red blood cell transfusions(defined as 6-20 RBC units per 24 weeks) with no transfusion-free period greater than 35 days during that period were randomized 2:1 to Reblozyl (n=224) or placebo (n=112). All patients 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.
Reblozyl was administered subcutaneously once every 3 weeks as long as a reduction in transfusion requirement was observed or until unacceptable toxicity. Key eligibility criteria included adult patients with beta thalassemia (with the exception of sickle beta thalassemia) without major organ damage or recent DVT stroke, platelet counts less than or equal to 1000 x 109 /L or recent use of ESA. In addition, patients on immunosuppressants or hydroxyurea therapy were also excluded. Patients received a starting dose of Reblozyl 1 mg/kg subcutaneous injection every 3 weeks. The median duration of treatment was similar between the Reblozyl and placebo arms (63.3 weeks vs. 62.1 weeks, respectively). Per protocol, patients in the Reblozyl and placebo arms were to remain on therapy for at least 48 weeks in the double-blind phase of the trial. Among patients receiving Reblozyl, 94% were exposed for 6 months or longer and 72% were exposed for greater than one year. The median age of patients who received Reblozyl was 30 years (range: 18, 66); 59% female; 54% White, and 36% Asian.

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Results

The trial achieved a clinically meaningful and statistically significant improvement in the primary endpoint. Twenty-one percent of the patients who received Reblozyl achieved at least a 33% reduction in transfusion burden (with a reduction of at least 2 units) during weeks 13–24 after randomization compared to 4.5% of the patients who received a placebo. The transfusion reduction meant that the member needed fewer transfusions over 12 consecutive weeks while taking Reblozyl. While the study also met key secondary endpoints, including transfusion burden reduction of at least 33% (with a reduction of at least 2 units), during weeks 37 to 48, which was achieved in 19.6% (n=44) of patients in the Reblozyl arm and 3.6% (n=4) in the placebo arm, it still indicates that 80.4% of patients did not meet the secondary endpoint. Other efficacy endpoints included transfusion burden reduction of greater-than or equal to 50% (with a reduction of at least 2units) during weeks 13-24 and weeks 37-48. A greater-than or equal to 50% reduction in transfusion burden was observed in 7.6% of patients (n=17) receiving Reblozyl vs. 1.8% of patients(n=2) in the placebo arm at weeks 13- 24

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Reblozyl (luspatercept-aamt) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy.

Discontinue REBLOZYL if a member does not experience a decrease in transfusion burden after 9 weeks of treatment (administration of 3 doses) at the maximum dose level.

OTHER SPECIAL CONSIDERATIONS:

None

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

HCPCS CODE	DESCRIPTION
J0896	Injection, luspatercept-aamt, 0.25 mg

AVAILABLE DOSAGE FORMS:

REBLOZYL 25 mg/vial (NDC 59572-0711-01)
REBLOZYL 75 mg/vial (NDC 59572-0775-01)

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