Medical Policy:
Reblozyl (luspatercept-aamt) subcutaneous injection

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.205	January 11, 2024	February 7th, 2020

Definitions

Reblozyl is an erythroid maturation agent. Luspatercept-aamt is a receptor fusion protein consisting of a modified extracellular domain of the human activin receptor type IIB linked to a human IgG1 Fc domain with a calculated molecular mass of approximately 76 kD. Luspatercept is produced in Chinese hamster ovary cells by recombinant DNA technology.

Length of Authorization

Beta Thalassemia: Coverage will be provided initially for 15 weeks (5 initial doses) and may be renewed annually thereafter.

Myelodysplastic Syndrome: Coverage will be provided initially for 21 weeks (7 initial doses) and may be renewed every 6 months thereafter.

Dosing Limits [Medical Benefit]

1.25mg/kg every 3 weeks (Anemia related to beta-thalassemia)- 600 billable units every 21 days

1.75mg/kg every 3 weeks (Myelodysplastic syndromes associated anemia) - 800 billable units every 21 days

Guideline

I. Initial Approval Criteria

Reblozyl *may be considered medically necessary if one of the below conditions are met* ***AND*** *use is consistent with the medical necessity criteria that follows:*

1. **Anemia related to beta-thalassemia**
    A. Patient is 18 years of age and older; **AND**
    B. According to the prescriber, the patient requires regular red blood cell transfusions as defined by meeting both of the following (i and ii):
        i. Patient has received at least 6 units of packed red blood cells within the preceding 24 weeks; **AND**
        ii. Patient has not had any transfusion-free period > 35 days within the preceding 24 weeks; **AND**
    C. The patient has Hgb less than or equal to 11 g/dL (If the pre-dose Hgb is greater than or equal to 11.5 g/dL and the Hgb level is not influenced by recent transfusion, delay dosing until the Hgb is less than or equal to 11 g/dL); **AND**
    D. Patient has not received Zynteglo (betibeglogene autotemcel intravenous infusion) in the past; **AND**
    E. The medication is being prescribed by or in consultation with a hematologist.

2. Myelodysplastic/Myeloproliferative Neoplasm
    A. Patient is ≥ 18 years of age; **AND**
    B. According to the prescriber, the patient has myelodysplastic/myeloproliferative neoplasm and meets both of the following (i and ii):
        i. Ring sideroblast positivity; **AND**
        Note: This is defined as ring sideroblasts ≥ 15% or ring sideroblasts ≥ 5% with an SF3B1 mutation.
        ii. Thrombocytosis defined as platelet count ≥ 450 x 10^9/L; **AND**
    C. Patient has very low- to intermediate-risk disease, as determined by the prescriber; **AND**
    Note: This is determined using the International Prognostic Scoring System (IPSS).
    D. Patient does not have a confirmed mutation with deletion 5q [del(5q)]; **AND**
    E. Patient currently requires blood transfusions, defined as at least two red blood cell units over the previous 8 weeks; **AND**
    F. Pretreatment hemoglobin level is < 10.0 g/dL; **AND**
    G. Reblozyl will not be used in combination with an erythropoiesis stimulating agent; **AND**
    H. The medication is being prescribed by or in consultation with an oncologist or hematologist.

3. Myelodysplastic Syndromes Associated Anemia
    A. Patient is 18 years of age or older; **AND**
    B. According to the prescriber, the patient has myelodysplastic syndromes and meets one of the following (i or ii):
        i. Ring sideroblast positivity; **OR**
        Note: This is defined as ring sideroblasts ≥ 15% or ring sideroblasts ≥ 5% with an SF3B1 mutation.
        ii. Serum erythropoietin level is ≤ 500 mU/mL; **AND**

C. Patient has very low- to intermediate-risk myelodysplastic syndromes, as determined by the prescriber; **AND**
Note: This is determined using the International Prognostic Scoring System (IPSS).
D. Patient does not have a confirmed mutation with deletion 5q [del(5q)]; **AND**
E. Patient currently requires blood transfusions, defined as at least two red blood cell units over the previous 8 weeks; **AND**
F. Pretreatment hemoglobin level is < 10.0 g/dL; **AND**
G. will not be used in combination with an erythropoiesis stimulating agent; **AND**
H. The medication is being prescribed by or in consultation with an oncologist or hematologist

Limitations/Exclusions

Reblozyl is not considered medically necessary when any of the following selection criteria is met:

1. When it is being used as a substitute for RBC transfusions in patients who require immediate correction of anemia.

II. Renewal Criteria

1. Patient continues to meet initial approval criteria; **AND**
2. The need for regular RBC transfusions has been decreased as indicated by prescriber; **AND**
3. Patient will not receive doses < 21 days apart; **AND**
4. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: thromboembolic events, severe hypertension, extramedullary hematopoietic masses in patients with beta thalassemia, etc.

Dosage/Administration

	Dose
Beta Thalassemia	The recommended starting dose of Reblozyl is 1 mg/kg once every 3 weeks by subcutaneous injection. If a patient does not achieve a reduction in RBC transfusion burden after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose, increase the Revlozyl dose to 1.25 mg/kg. Do not increase the dose beyond the maximum dose of 1.25 mg/kg.
Myelodysplastic Syndromes	The recommended starting dose of Reblozyl is 1 mg/kg once every 3 weeks by subcutaneous injection. **Dose Increases for Insufficient Response at Initiation of Treatment** Not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at the 1 mg/kg starting dose • Increase the dose to 1.33 mg/kg every 3 weeks Not RBC transfusion-free after at least 2 consecutive doses (6 weeks) at 1.33 mg/kg • Increase the dose to 1.75 mg/kg every 3 weeks No reduction in RBC transfusion burden after at least 3 consecutive doses (9 weeks) at 1.75 mg/kg

	– **Discontinue treatment** **Dose Modifications for Predose Hemoglobin Levels or Rapid Hemoglobin Rise** Predose hemoglobin is greater than or equal to 11.5 g/dL in the absence of transfusions • Interrupt treatment • Restart when the hemoglobin is no more than 11 g/dL Increase in hemoglobin greater than 2 g/dL within 3 weeks in the absence of transfusions and -current dose is 1.75 mg/kg, then reduce dose to 1.33 mg/kg -current dose is 1.33 mg/kg, then reduce dose to 1 mg/kg -current dose is 1 mg/kg, then reduce dose to 0.8 mg/kg -current dose is 0.8 mg/kg, then reduce dose to 0.6 mg/kg -current dose is 0.6 mg/kg, then **Discontinue treatment**

Applicable Procedure Codes

Code	Description
J0896	Injection, luspatercept-aamt, 0.25 mg (Reblozyl). J-Code effective date: 07/01/2020

Applicable NDCs

Code	Description
59572-0775-01	Reblozyl (luspatercept-aamt) PDS 75MG
59572-0711-01	Reblozyl (luspatercept-aamt PDS 25MG

ICD-10 Diagnoses

Code	Description
C93.10	Chronic myelomonocytic leukemia not having achieved remission
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasiaand ring sideroblasts
D46.4	Refractory anemia, unspecified
D46.Z	Other myelodysplastic syndromes
D46.9	Myelodysplastic syndrome, unspecified
D56.1	Beta-thalassemia

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/11/2024	Annual Review: Initial Criteria: Anemia related to beta-thalassemia

		Further defined "Requires regular blood transfusions" as According to the prescriber, the patient requires regular red blood cell transfusions as defined by meeting both of the following (i and ii): Patient has received at least 6 units of packed red blood cells within the preceding 24 weeks; AND Patient has not had any transfusion-free period > 35 days within the preceding 24 weeks; AND Patient has not received Zynteglo (betibeglogene autotemcel intravenous infusion) in the past; AND The medication is being prescribed by or in consultation with a hematologist." Renamed "Anemia failing an erythropoiesis stimulating agent" indication to: "Myelodysplastic/Myeloproliferative Neoplasm. " and updated all criteria as follows: A. Patient is ≥ 18 years of age; AND B. According to the prescriber, the patient has myelodysplastic/myeloproliferative neoplasm and meets both of the following (i and ii): i. Ring sideroblast positivity; AND ii. Thrombocytosis defined as platelet count ≥ 450 x 10^9/L; AND C. Patient has very low- to intermediate-risk disease, as determined by the prescriber; AND D. Patient does not have a confirmed mutation with deletion 5q [del(5q)]; AND E. Patient currently requires blood transfusions, defined as at least two red blood cell units over the previous 8 weeks; AND F. Pretreatment hemoglobin level is < 10.0 g/dL; AND G. Reblozyl will not be used in combination with an erythropoiesis stimulating agent; AND H. The medication is being prescribed by or in consultation with an oncologist or hematologist. Myelodysplastic Syndromes Associated Anemia: Reworded and separated the following "Patient has anemia without previous erythropoiesis stimulating agent use (ESA-naïve) with very low- to intermediate-risk myelodysplastic syndromes (MDS) who may require regular red blood cell (RBC) transfusions." To: "According to the prescriber, the patient has myelodysplastic syndromes and meets one of the following (i or ii): Ring sideroblast positivity; OR Serum erythropoietin level is ≤ 500 mU/mL; AND Patient has very low- to intermediate-risk myelodysplastic syndromes, as determined by the prescriber; AND Patient does not have a confirmed mutation with deletion 5q [del(5q)]; AND Patient currently requires blood transfusions, defined as at least two red blood cell units over the previous 8 weeks; AND Pretreatment hemoglobin level is < 10.0 g/dL; AND Reblozyl will not be used in combination with an erythropoiesis stimulating agent; AND The medication is being prescribed by or in consultation with an oncologist or hematologist" Renewal Criteria: added: "Patient will not receive doses < 21 days apart; AND Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: thromboembolic events, severe hypertension, extramedullary hematopoietic masses in patients with beta thalassemia, etc."
EmblemHealth & ConnectiCare	9/20/2023	Updated length of authorization: from: "Coverage will be provided for 12 months and may be renewed." To "Beta Thalassemia: Coverage will be provided initially for 15 weeks (5 initial doses) and may be renewed annually thereafter. Myelodysplastic Syndrome: Coverage will be provided initially for 21 weeks (7 initial doses) and may be renewed every 6 months thereafter."

		Add indication and criteria: Myelodysplastic Syndromes Associated Anemia; Updating dosing chart name from "the 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)." to "Myelodysplastic Syndromes Associated Anemia"
EmblemHealth & ConnectiCare	1/11/2023	Transfer to New Template; Added codes C93.10, D46.0, D46.20, removed code D56.5
EmblemHealth & ConnectiCare	6/10/2020	Added J-Code (J0896): Injection, luspatercept-aamt, 0.25 mg (Reblozyl). J-Code effective date: 07/01/2020
EmblemHealth & ConnectiCare	04/13/2020	Added Max Billable Units: 1.75mg/kg every 3 weeks (Anemia failing an erythropoiesis stimulating agent) Updated dosing for Anemia failing an erythropoiesis stimulating agent) per FDA Label: Dose Increases for Insufficient Response at Initiation of Treatment & Dose Modifications for Predose Hemoglobin Levels or Rapid Hemoglobin Rise
EmblemHealth & ConnectiCare	04/10/2020	Updated indications per FDA Label to include: Added: Anemia failing an erythropoiesis stimulating agent Added the following Applicable Diagnosis Codes: D46.1 • Refractory anemia with ring sideroblasts D46.A • Refractory cytopenia with multilineage dysplasia D46.B • Refractory cytopenia with multilineage dysplasia and ring sideroblasts D46.4 • Refractory anemia, unspecified D46.Z • Other myelodysplastic syndromes D46.9 • Myelodysplastic syndrome, unspecified
EmblemHealth & ConnectiCare	02/07/2020	New Medical Policy

References

1. Reblozyl [package insert]. Celgene Corporation Summit, NJ 07901 and Acceleron Pharma, Inc. Cambridge, MA 02139; 2019.
2. Luspatercept-aamt. IBM Micromedex® DRUGDEX®. IBM Watson Health, Greenwood Village, Colorado, USA January 2020.