Reblozyl (luspatercept)

Override(s)	Approval Duration
Prior Authorization	For β-thalassemia, myelodysplastic syndromes with ring sideroblasts (MDS-RS), myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T), myelodysplastic syndromes (MDS) in ESA-naïve individuals: Initial Requests: 6 months Continuation Requests: 1 year

Medications	Dosing Limit
Reblozyl 25 mg, 75 mg vial	1.75 mg/kg per 3 weeks

APPROVAL CRITERIA

Initial requests for Reblozyl (luspatercept) for β-thalassemia may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of beta thalassemia or hemoglobin E beta (E/β)-thalassemia; **AND**
III. Documentation is provided that individual required regular red blood cell transfusions at initiation, defined as *both* of the following (NCT02604433):
    A. Individual received six to twenty (6-20) RBC units in the last 24 weeks; **AND**
    B. Individual had no transfusion-free period greater than 35 days in the last 24 weeks; **AND**
IV. Individual has a baseline hemoglobin (Hgb) level 11 g/dL or less.

Continuation requests for Reblozyl (luspatercept) for β-thalassemia may be approved if the following criteria are met:

I. Documentation is provided that individual demonstrates continued need for treatment and has confirmation of response to treatment as evidenced by a decrease in transfusion burden from baseline; **AND**
II. Hemoglobin level 11.0 g/dL or less.

Reblozyl (luspatercept) for β-thalassemia may not be approved for the following:

I. Individual has a diagnosis of sickle beta thalassemia (S/β-thalassemia); **OR**
II. Individual has a diagnosis of alpha (α)-thalassemia; **OR**
III. Individual has a platelet count greater than 1000 x 10^9/L; **OR**
IV. History of deep vein thrombosis (DVT) or stroke within the last 24 weeks; **OR**

V. Use beyond 9 weeks of treatment (i.e., administration of consecutive 3 doses) in the absence of response (response defined as decrease in transfusion burden from baseline) at maximum dose level (i.e., 1.25 mg/kg every 3 weeks).

Initial requests for Reblozyl (luspatercept) MDS-RS or MDS/MPN-RS-T or ESA-naïve MDS may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has one of the following (A, B, or C):
    A. Documentation is provided that individual has a diagnosis very low to intermediate risk MDS-RS greater than or equal to 15% (or ring sideroblasts 5% to 14% with an SF3B1 mutation) (Label, NCCN 2A); **AND**
        1. Individual meets *one* of the following criteria:
            a. Serum erythropoietin (EPO) level of greater than 500 mU/mL; **OR**
            b. Serum EPO level of less than or equal to 500 mU/mL following no response to combination treatment with erythropoiesis-stimulating agent (ESA) *and* granulocyte-colony stimulating factor (G-CSF); **OR**
    B. Individual has a diagnosis of MDS/MPN-RS-T with *all* of the following:
        1. Ring sideroblasts greater than or equal to 15% (WHO 2017), and documentation is provided; **AND**
        2. Thrombocytosis (defined as platelets greater than or equal to 450 $x10^9$/L) (WHO 2017); **OR**
    C. Individual has a diagnosis of MDS; **AND**
        1. Individual is ESA-naïve; **AND**
        2. Documentation is provided that individual has serum EPO level less than 500 U/L; **AND**
III. Documentation is provided that individual has required regular red blood cell transfusions of two (2) or more RBC units over eight (8) weeks in the last 16 weeks; **AND**
IV. Individual has a baseline hemoglobin (Hgb) level 11 g/dL or less.

Continuation requests for Reblozyl (luspatercept) for MDS-RS or MDS/MPN-RS-T may be approved if the following criteria are met:

I. Documentation is provided that individual demonstrates continued need for treatment and has confirmation of response to treatment as evidenced by a decrease in transfusion burden from baseline; **AND**
II. Hemoglobin level is 11.0 g/dL or less.

Reblozyl (luspatercept) for MDS-RS or MDS/MPN-RS-T or MDS may not be approved for the following:

I. Individual has had an inadequate response to ESAs and one of the following:
    A. Individual has unresolved iron deficiency (defined as serum ferritin 15 µg/L or less, or transferrin saturation 20% or less) (NCT02631070); **OR**

B. Use beyond 9 weeks of treatment (i.e., administration of consecutive 3 doses) in the absence of response (response defined as decrease in transfusion burden from baseline) at maximum dose level (i.e., 1.75 mg/kg every 3 weeks); **OR**

II. Individual is ESA-naïve and one of the following (Platzbecker, et al.):
   A. Individual has unresolved iron deficiency (defined as serum ferritin less than 100 µg/L); **OR**
   B. Individuals has uncontrolled hypertension.

Requests for Reblozyl (luspatercept) may not be approved when the above criteria are not met and for all other indications.

Key References:

1. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016; 127-2391-2405.
2. Beta Thalassemia. National Organization for Rare Disorders. Available at https://rarediseases.org/rare-diseases/thalassemia-major/.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2021. URL: http://www.clinicalpharmacology.com. Updated periodically.
4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 14, 2021.
5. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
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7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2021; Updated periodically.
8. Myelodysplastic Syndromes. American Cancer Society. Available at https://www.cancer.org/cancer/myelodysplastic-syndrome.html.
9. Myeloproliferative Neoplasms—Health Professional Version. National Cancer Institute. Available at https://www.cancer.gov/types/myeloproliferative.
10. NCCN Clinical Practice Guidelines in Oncology™. © 2021 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on July 14, 2021.
    a. Myelodysplastic Syndromes. Version 3.2021. Revised January 15, 2021.
11. NCT02604433. ClinicalTrials.gov. U.S. National Library of Medicine. Available at https://clinicaltrials.gov/ct2/show/NCT02604433?term=nct02604433&draw=2&rank=1.
12. NCT02631070. ClinicalTrials.gov. U.S. National Library of Medicine. Available at https://clinicaltrials.gov/ct2/show/NCT02631070?term=nct02631070&draw=2&rank=1.
13. Orazi A, et al. Myelodysplastic Syndromes/Myeloproliferative Neoplasms, Chapter 5, in Swerdlow S. Campo E, Harris NL, et al (Eds). World Health Organization Classification and Tumours of Haematopoietic and Lymphoid Tissues, Revised 4th edition. Volume 2. IARC Press, Lyon, 2017, 82-96.
14. Thalassemia. Cooley's Anemia Foundation. Available at https://www.thalassemia.org/learn-about-thalassemia/about-thalassemia/.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.