CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Luspatercept-aamt (Reblozyl®)

Version: 1.0

EFFECTIVE DATE: 5/5/2025

NantHealth® | Eviti®

Please note the following:

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For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Luspatercept-aamt (Reblozyl®)

Discussion

Luspatercept-aamt is a recombinant fusion protein that binds several endogenous transforming growth factor (TGF-β) superfamily ligands. Luspatercept-aamt promoted erythroid maturation through differentiation and increasing the percentage of late-stage erythroid precursors (normoblasts) in vivo and increased erythroid precursors in humans, thereby increasing erythropoiesis.[1,2]

Clinically significant adverse reactions include thrombosis/thromboembolism, hypertension, and extramedullary hematopoietic. The most common (>10%) adverse reactions were fatigue, headache, musculoskeletal pain, arthralgia, dizziness/vertigo, nausea, diarrhea, cough, abdominal pain, dyspnea, COVID-19, edema peripheral, hypertension, and hypersensitivity.[1]

Luspatercept-aamt is approved by the Food and Drug Administration (FDA) for myelodysplastic syndromes.[1] The National Comprehensive Cancer Network (NCCN) endorses luspatercept-aamt for the following cancer types: myelodysplastic syndromes and myeloproliferative neoplasms.[3,4]

Definitions

- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.[5]
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.[6]

Policy

Coverage will be considered for FDA approved indications and for NCCN category 1, 2A, or 2B recommendations when the following criteria are met:

Myelodysplastic Syndromes

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. 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; OR
4. Anemia failing an erythropoiesis stimulating agent and requiring 2 or more RBC units over 8 weeks in 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)

Note: It is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia[1]; OR

For **NCCN** required criteria coverage:

5. Lower risk disease associated with symptomatic anemia with no del(5q), with or without other cytogenetic abnormalities with ring sideroblasts <15% (or ring sideroblasts <5% with an SF3B1 mutation) with serum erythropoietin ≤500 mU/mL for one of the following:
   a) Single agent
   b) Following no response to or relapse after an erythropoiesis-stimulating agent (ESA) alone (despite adequate iron stores); OR
6. Lower risk disease associated with symptomatic anemia with no del(5q), with or without other cytogenetic abnormalities with ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation) for one of the following:
   a) Single agent
   b) Following no response to or relapse after imetelstat

   Note: Lower risk defined as IPSS-R (Very Low, Low, Intermediate); OR

Myelodysplastic Syndromes - Myeloproliferative Neoplasms (MDS/MPN) Overlap Neoplasms

For **NCCN** required criteria coverage:

7. MDS/MPN with SF3B1 mutation and thrombocytosis as a single agent option for treatment of anemia.[3]

Myeloproliferative Neoplasms - Myelofibrosis

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Management of myelofibrosis-associated anemia with one of the following:
   a) Ongoing symptomatic splenomegaly and/or constitutional symptoms, to be given in combination with ruxolitinib
   b) No splenomegaly or constitutional symptoms
   c) Splenomegaly and constitutional symptoms well controlled on current JAK inhibitor, to be given in combination with a JAK inhibitor.[4]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Coding (CPT®, ICD-10, and HCPCS)

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
D46	Myelodysplastic syndromes
D47.1	Chronic myeloproliferative disease
D75.81	Myelofibrosis
J0896	Injection, luspatercept-aamt

Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	5/5/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	5/5/2025
6	Revision Changes:	

References

[1] Luspatercept-aamt (Reblozyl) [Package Insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761136s010lbl.pdf. Accessed March 26, 2025.

[2] Patel B, Moosavi L. Luspatercept. In: StatPearls. Treasure Island (FL): StatPearls Publishing; October 14, 2024. https://pubmed.ncbi.nlm.nih.gov/32809470/. Accessed April 23, 2025.

[3] National Comprehensive Cancer Network. NCCN Guidelines: Myelodysplastic Syndromes. https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed March 26, 2025.

[4] National Comprehensive Cancer Network. NCCN Guidelines: Myeloproliferative Neoplasms. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed March 26, 2025.

[5] National Comprehensive Cancer Network. https://www.nccn.org/home. Accessed April 23, 2025.

[6] U.S. Food & Drug Administration. https://www.fda.gov/about-fda/what-we-do. Accessed April 23, 2025.