Drug Policy:

Reblozyl™ (luspatercept-aamt)

POLICY NUMBER UM ONC_1392	SUBJECT Reblozyl™ (luspatercept-aamt)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATES COMMITTEE REVIEWED 04/08/20, 08/12/20, 11/11/20, 10/13/21, 11/15/21, 05/11/22, 10/12/22, 07/12/23, 10/11/23, 12/13/23, 12/12/24	APPROVAL DATE December 12, 2024	EFFECTIVE DATE December 27, 2024	COMMITTEE APPROVAL DATES 04/08/20, 08/12/20, 11/11/20, 10/13/21, 11/15/21, 05/11/22, 10/12/22, 07/12/23, 10/11/23, 12/13/23, 12/12/24	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Evolent Specialty Services Clinical Guideline Review Committee		
NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

Evolent clinical guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses clinical guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this clinical guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their plan customer service representative for specific coverage information.

I. PURPOSE

To define and describe the accepted indications for Reblozyl (luspatercept-aamt) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, AND

2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. Beta Thalassemia Anemia

1. Reblozyl (luspatercept-aamt) is being used for ALL of the following conditions:
   a. The member has beta thalassemia anemia who require regular red blood cell (RBC) transfusions defined as 6-20 RBC units within the last 6 months, including the last 30 days
   b. Initiate if hemoglobin (Hgb) is less than or equal to 11 gm/dL
   c. Continue if Hgb is less than or equal to 11 gm/dL OR the total number of RBC transfused is not reduced after at least 2 consecutive doses
   d. TREATMENT DISCONTINUATION: Reblozyl should be discontinued if the member has an inadequate response to a therapeutic trial: Less than 1 gm/dl increase in Hgb and/or the member is still transfusion dependent (defined as requiring a prbc transfusion every 8 weeks after 24 weeks of therapy and/or requiring a red blood cell transfusion every 12 weeks after 48 weeks of therapy).

C. Myelodysplastic Syndromes (MDS)

1. INITIAL LINE OF THERAPY FOR MDS:

   Reblozyl(luspatercept-aamt) may be used as monotherapy in Low Risk MDS if all of the following criteria are met:

   a. IPSS-R Risk Types: Very Low, Low or Intermediate risk; with or without Ring Sideroblasts; < 5% blasts in the bone marrow
   b. RBC transfusion dependent defined as follows: Need for 2-6 pRBC units/8 weeks prior to starting therapy
   c. Baseline serum erythropoietin (EPO) level of < 500 Units/L
   d. No prior therapy with an ESA (erythropoiesis stimulating agent)
   e. Members do not have the deletion 5q (del 5q) mutation as their only cytogenetic alteration.

2. SUBSEQUENT LINE OF THERAPY FOR MDS

   Reblozyl (luspatercept-aamt) may be used as monotherapy, as subsequent line of therapy for Low Risk MDS when all the following criteria are met:

   a. Member has Lower Risk MDS with symptomatic anemia, specifically either MDS with ring sideroblasts greater than or equal to 15% OR MDS with ring sideroblasts greater than or equal to 5% + SF3B1 mutation AND
   b. Serum erythropoietin level greater than 500 mU/ml OR
   c. Serum erythropoietin level less than 500 mU/ml AND failure of a trial of therapy (generally 3-6 months) with an ESA- Erythropiesis Stimulating Agent (epoetin alfa greater than or equal to 40,000 IU/week or darbepoetin alpha greater than or equal to 500 mcg/3 weeks) AND the member required 2 or more RBC units over 8 weeks.
   d. Members do not have the deletion 5q (del 5q) mutation as their only cytogenetic alteration.
   e. TREATMENT DISCONTINUATION: Reblozyl should be discontinued if the member has an inadequate response to a therapeutic trial: Less than 1 gm/dl increase in Hgb and/or the member is still transfusion dependent (defined as requiring a prbc transfusion every 8

weeks after 24 weeks of therapy and/or requiring a red blood cell transfusion every 12 weeks after 48 weeks of therapy).

III. EXCLUSION CRITERIA

A. Concurrent use of an erythropoiesis-stimulating agent, cytotoxic agents, or immunosuppressants.

B. Dosing exceeds single dose limit of Reblozyl (luspatercept-aamt) 1.25 mg/kg for Beta Thalassemia Anemia and 1.75 mg/kg for MDS.

C. Investigational use of Reblozyl (luspatercept-aamt) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. CODING INFORMATION

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

V. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

VI. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VII. ATTACHMENTS

A. None

VIII. REFERENCES

A. Cappellini MD, et al. BELIEVE Clinical Trial. A Phase 3 Trial of Luspatercept in Patients with Transfusion-Dependent β-Thalassemia. N Engl J Med. 2020 Mar 26;382(13):1219-1231.

B. Fenaux P, et al. MEDALIST Clinical Trial. Luspatercept in Patients with Lower-Risk Myelodysplastic Syndromes. N Engl J Med. 2020 Jan 9;382(2):140-151.

C. Platzbecker et al. COMMANDS trial. *Lancet* 2023; 402: 373–85 Published Online June 10, 2023 https://doi.org/10.1016/ S0140-6736(23)00874-7.

D. Reblozyl information. Celgene Summit, NJ 2024.

E. Clinical Pharmacology Elsevier Gold Standard 2024.

F. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2024.

G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.

H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2024.

I. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

J. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.