Clinical Policy Title:	Luspatercept-aamt
Policy Number:	RxA.628
Drug(s) Applied:	Reblozyl®
Original Policy Date:	05/21/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Luspatercept-aamt is indicated for the treatment of anemia in adult patients with beta thalassemia who require regular RBC transfusions.

Luspatercept-aamt is indicated for the treatment of anemia failing an erythropoiesis stimulating agent and requiring 2 or more red blood cell units over 8 weeks in adults with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

Limitations of use: Luspatercept-aamt is not indicated as a substitute for RBC transfusions in patients who require immediate correction of anemia.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
luspatercept-aamt (Reblozyl®)	Anemia, after erythropoiesis stimulating agent failure, requiring 2 or more RBC units over 8 weeks – MDS-RS or MDS/MPN-RS-T	Prior to each dose, review Hb; if an RBC transfusion occurred prior to dosing, use the pre-transfusion Hb for dose evaluation. Initial, 1 mg/kg subQ once every 3 weeks; if patient is not transfusion-free after at least 2 consecutive doses (6 weeks) at any dose level, increase dose. To titrate, increase to 1.33 mg/kg every 3 weeks, then to MAX dose If pre-dose Hb is 11.5 g/dL or greater in the absence	1.75 mg/kg every 3 weeks

Drug Name	Indication	Dosing Regimen	Maximum Dose
		of transfusions, delay dosing until Hb is 11 g/dL or lower	
luspatercept (Reblozyl®)	Anemia - beta Thalassemia	Prior to each dose, review Hb; if an RBC transfusion occurred prior to dosing, use the pre-transfusion Hb for dose evaluation. Initial, 1 mg/kg subQ once every 3 weeks; if reduction in RBC transfusion burden is not achieved after at least 2 consecutive doses (6 weeks), increase to MAX dose. If pre-dose Hb is 11.5 g/dL or greater in the absence of transfusions, delay dosing until Hb is 11 g/dL or lower	1.25 mg/kg every 3 weeks

Dosage Forms

- Lyophilized Powder for reconstitution: 25mg/vial, 75mg/vial

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Beta Thalassemia (must meet all):

1. Diagnosis of anemia from beta thalassemia or Hemoglobin E/beta-thalassemia (may include beta-thalassemia with mutation and/or multiplication of alpha globin).
2. Member's diagnosis should not be Hemoglobin S/β-thalassemia or alpha (α)-thalassemia (e.g., Hemoglobin H);
3. Prescribed by or in consultation with a hematologist or a specialist who treats beta thalassemia;
4. Age ≥ 18 years;
5. Prescriber attests that pre-dose hemoglobin levels will be reviewed for each administration (pre-dose Hgb ≤ 11 g/dL is required prior to every dose);
6. Member does not have any of the following conditions:
   a. Platelet counts less than or equal to 1000×10^9/L;
   b. Recent deep vein thrombosis or stroke;
   c. Major organ damage (liver/heart/lung disease, renal insufficiency);
   d. Active hepatitis C (HCV) infection, or active infectious hepatitis B (HBV), or known positive human immunodeficiency virus (HIV) not receiving antiretroviral therapy;

7. Member is on regular red blood cell transfusions and meets the following (a and b):
   a. minimum of 6 RBC units in the 24 weeks prior to the request;
   b. no transfusion-free period for ≥ 35 days during that 24 week period;
8. Dose requested does not exceed 1.25 mg/kg every 3 weeks.

Approval Duration:
Commercial: 6 months
Medicaid: 6 months

B. MDS-RS or MDS/MPN-RS-T (must meet all):
1. Diagnosis of anemia from very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T);
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Prescriber attests that pre-dose hemoglobin levels will be reviewed for each administration (pre-dose Hgb ≤ 11 g/dL is required prior to every dose);
5. Member must meet the following (a or b):
   a. Current (within the last 3 months) serum erythropoietin (EPO) > 500 mU/mL;
   b. Current (within the last 3 months) serum EPO ≤ 500 mU/mL and documented failed single therapy with erythropoiesis-stimulating agents (ESA)* (e.g. epoetin alfa, darbepoetin alfa), or combination therapy granulocyte-colony stimulating factors(G-CSF)* (e.g. filgrastim, filgrastim-sndz, tbo-filgrastim) unless contraindicated or clinically significant adverse effects are experienced with ESAs or G-CSFs;
   **ESAs or G-CSFs may require prior authorization*
6. Member has not used any of the following within 5 weeks of the request:
   a. Anticancer cytotoxic chemotherapeutic treatment (e.g. anthracyclines, vinca alkaloids, alkylating agents, antimetabolites);
   b. Corticosteroids (e.g. prednisone, dexamethasone, methylprednisolone, hydrocortisone) except for members on a stable or decreasing dose for ≥ 1 week prior to treatment with Reblozyl® for medical conditions other that MDS;
   c. Iron-chelating agents (e.g. deferoxamine, Deferasirox, deferiprone), except for members on a stable or decreasing dose for at least 8 weeks prior to treatment with Reblozyl®;
   d. Other RBC hematopoietic growth factors (e.g. Interleukin-3);
7. Member is on regular red blood cell transfusions requiring 2 or more red blood cell units over 8 weeks;
8. Dose requested does not exceed 1.75 mg/kg every 3 weeks.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Beta thalassemia (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (e.g. decrease in transfusion burden);
3. If request is for dose increase, dose does not exceed 1.25 mg/kg every 3 weeks;

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. **MDS-RS or MDS/MPN-RS-T** (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (e.g. decrease in transfusion burden);
3. If request is for dose increase, dose does not exceed 1.75 mg/kg every 3 weeks.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
ESA: Erythropoiesis-stimulating agents
G-CSF: granulocyte-colony stimulating factors
RBC: red blood cell
EPO: Erythropoietin
MDS-RS: Myelodysplastic syndromes with ring sideroblasts
MDS/MPN-RS-T: myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Availability
Epoetin alfa (Epogen®)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, and 10,000 units/mL • Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL
Epoetin alfa (Procrit®)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, and 40,000 units/mL • Multiple-dose vial containing benzyl alcohol: 20,000 units/2 mL and 20,000 units/mL
Epoetin alfa-epbx (Retacrit®)	• Single-dose vial: 2,000 units/mL, 3,000 units/mL, 4,000 units/mL, 10,000 units/mL, 40,000 units/mL
Darbapoetin alfa (Aranesp®)	• Single-dose vials: 25 mcg, 40 mcg, 60 mcg, 100 mcg, 200 mcg, 300 mcg • Single dose prefilled syringes: 10 mcg/0.4 mL, 25 mcg/0.42 mL, 40 mcg/0.4 mL, 60 mcg/0.3 mL, 100 mcg/0.5 mL, 150 mcg/0.3 mL, 200 mcg/0.4 mL, 300 mcg/0.6 mL, and 500 mcg/mL

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):

- None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Health care professionals are advised to monitor the member's blood pressure prior to each administration and manage new-onset hypertension or exacerbations of pre-existing hypertension using anti-hypertensive agents.
- Members who receive Reblozy®l should be monitored for thromboembolic events and institute treatment promptly. Reblozyl® may cause fetal harm when administered to a pregnant woman.
- Advise females of reproductive potential to use an effective method of contraception during treatment with Reblozyl® and for at least 3 months after the final dose.

References

1. Reblozyl (luspatercept-aamt) subcutaneous injection prescribing information. Celgene Corporation, Summit, NJ, 2020. April 2020. Available at: https://packageinserts.bms.com/pi/pi_reblozyl.pdf. Accessed January 22, 2021.
2. Cappellini MD, Viprakasit V, Taher AT, et al. (BELIEVE Investigators); A Phase 3 Trial of Luspatercept in Patients with Transfusion-Dependent β-Thalassemia. N Engl J Med. 2020 Mar 26;382(13):1219-1231. doi: 10.1056/NEJMoa1910182. Accessed January 22, 2021.
3. Reblozyl Micromedex Solutions Truven Health Analytics, Inc. Ann Arbor, MI; 2020, March 17. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed January 22, 2021.
4. Myelodysplastic Syndromes. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf (Version 3.2021). In: National Comprehensive Cancer Network Guidelines. Available at www.NCCN.org. Accessed January 22, 2021.
5. Management and prognosis of beta thalassemia. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, Mar, 2020. Accessed with subscription at: http://uptodate.com. Accessed January 22, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	05/04/2020	05/21/2020
Policy was reviewed: 1. Clinical policy title was updated. 2. Line of Business Policy Applies to was updated to "All lines of business". 3. APPENDIX B language updated to ''Below are suggested therapeutic alternatives….''. 4. Approval duration for continued therapy was updated to 12 months from 6 months. 5. References were reviewed and updated.	01/22/2021	03/09/2021