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P&T Date: 08/07/2025

Rytelo™ (imetelstat)

HCPCS: J0870

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Must have anemia requiring at least 4 units of red blood cells over an 8 week period
   d. World Health Organization (WHO)/French American British (FAB) classification that meets IPSS classification of low or intermediate-1 risk disease
   e. Must be refractory, intolerant, or ineligible to receive an erythropoietin stimulating agent (ESA) unless serum erythropoietin is greater than 500 mU/mL defined as at least one of the following:
      i. Documentation of non-response or response that is no longer maintained to prior ESA-containing regimen of either recombinant human erythropoietin > 40,000 IU/week for at least 8 doses or equivalent OR darbepoetin alpha > 500 µg every 3 weeks for at least 4 doses or equivalent
      ii. Documentation of discontinuation of prior ESA-containing regimen at any time after introduction due to intolerance or an adverse event
   f. Must not have myelodysplastic syndrome (MDS) associated with del 5q cytogenetic abnormality
   g. Must not have secondary MDS known to have arisen as the result of chemical injury or treatment with chemotherapy and/or radiation for other diseases
   h. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in WyoBlue Advantage's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center

for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Rytelo is an oligonucleotide telomerase inhibitor indicated for the treatment of adult patients with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia requiring 4 or more red blood cell (RBC) units over 8 weeks who have not responded to, have lost response to, or are ineligible for erythropoiesis-stimulating agents (ESA).

- MDS are a group of blood cancers that occur as a result of disordered development of blood cells within the bone marrow. The World Health Organization (WHO) has classified six types of MDS based on how many early cell types show dysplasia, the type of cytopenias a patient is experiencing, the portion of ring sideroblasts, the portion of blasts in the blood or bone marrow, and the type of genetic mutations in the bone marrow cells. Rytelo was only studied in patients without a del 5q cytogenetic abnormality. The classification system for MDS automatically classifies patients with the del 5q mutation as a separate unique subtype.

- One in three patients with MDS will progress to acute myeloid leukemia (AML). Risk of disease progression to AML and risk of mortality are assessed using the International Prognostic Scoring System (IPSS) or Revised International Prognostic Scoring System (IPSS-R). Both the IPSS and IPSS-R risk stratify patients with newly diagnosed MDS into risk categories based on blast percentage, number of cytopenias, and cytogenetic profile. The IPSS-R categorizes patients into 1 of 5 groups, from very low risk to very high risk using the patient's disease presentation including cytogenic groups, percentage of medullary blasts, hemoglobin, platelets, and absolute neutrophil count. Very low, low, or intermediate risk on the IPSS-R are conventionally defined as a risk score in the low or intermediate-1 range on the IPSS scale. Rytelo was only studied in patients classified as low or intermediate-1 risk disease using the IPSS.

- Safety and efficacy of Rytelo were evaluated in the IMerge trial, a randomized, double-blind, placebo-controlled, phase III study of 178 patients with low- to intermediate-1 risk MDS. Subjects were enrolled in the trial if they met the following criteria: RBC transfusion-dependent, defined as requiring at least 4 RBC units transfused over an 8 week period during the 16 weeks prior to randomization; pre-transfusion hemoglobin (Hgb) less than or equal to 9.0 g/dL; relapsed or refractory to ESA treatment or have an erythropoietin level greater than 500 mU/mL; an absolute neutrophil count (ANC) greater than or equal to 1.5 x 10^9/L independent of growth factor support; and platelets greater than or equal to 75 x 10^9/L independent of platelet transfusion. Refractory to ESAs was defined as at least one of the following: non-response or response that is no longer maintained to a prior ESA-containing regimen of either recombinant human erythropoietin > 40,000 IU/week for at least 8 doses or equivalent OR darbepoetin alpha > 500 µg every 3 weeks for at least 4 doses or equivalent. Patients were ineligible if they had del(5q) cytogenetic abnormality. The primary endpoint was 8 week and 24 week RBC transfusion independence (RBC-TI) defined as the proportion of subjects without any RBC transfusion during any consecutive 8 weeks or 24 weeks starting from study day 1 until subsequent anti-cancer therapy, if any. Median follow-up was 19.5 months (range: 12.0, 23.4) in the Rytelo group and 17.5 months (range: 12.1, 22.7) in the placebo group. Rytelo demonstrated significantly higher rates of RBC-TI versus placebo for at least eight consecutive weeks (Rytelo 39.8% [95% CI: 30.9, 49.3]; placebo 15.0% [95% CI: 7.1, 26.6]; p-value < 0.001) and for at least 24 weeks (Rytelo 28.0% [95% CI: 20.1, 37.0]; placebo 3.3% [95% CI: 0.4, 11.5]; p-value < 0.001). RBC-TI was durable and sustained in the Rytelo treated population, with a median RBC-TI duration for 8-week responders and 24-week responders of approximately 1 year and 1.5 years, respectively.

- The current NCCN guidelines recommend ESAs as the preferred treatment in all patients and Reblozyl® as an alternative unless their serum erythropoietin is greater than 500 mU/mL in those with ring sideroblasts less than 15% or ring sideroblasts less than 5% with an SF3B1 mutation. Reblozyl is recommended first-line in instances where a

patient presents with an erythropoietin greater than 500 mU/mL or a patient has ring sideroblasts greater than or equal to15% or ring sideroblasts greater than or equal to 5% with an SF3B1 mutation.

References:

1. Rytelo [prescribing information]. Foster City, CA: Geron Corporation; June 2024.
2. Clinicaltrials.gov. Study to evaluate imetelstat (GRN163L) in subjects with international prognostic scoring system (IPSS) low or intermediate-1 risk myelodysplastic syndrome (MDS) (NCT02598661). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT02598661. Accessed on April 9, 2024.
3. Platzbecker U, Santini V, Fenaux P, et al. Imetelstat in patients with lower-risk myelodysplastic syndromes who have relapsed or are refractory to erythropoiesis-stimulating agents (IMerge): a multinational, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2024 Jan 20; 403 (10423): 249 – 60.
4. American Cancer Society. What are myelodysplastic syndromes. 2018 Jan 22. Available at: https://www.cancer.org/cancer/myelodysplastic-syndrome/about/what-is-mds.html. Accessed on June 9, 2024.
5. Leukemia and Lymphoma Society. Myelodysplastic syndromes. Available at: https://www.lls.org/search?search=myelodysplastic+syndromes. Accessed on June 9, 2024.
6. Greenberg P, Cox C, LeBeau MM, et al. International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood. 1997; 89: 2079 – 88.
7. Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood. 2012; 120: 2454 – 65.
8. National Comprehensive Cancer Network. Myelodysplastic syndromes (Version 2.2025). 2025 Jan 17. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed on June 12, 2025.

Policy History		
#	Date	Change Description
1.0	Initial Effective Date: 01/01/2026	New policy

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*