Original Effective Date: 12/14/2024
Current Effective Date: 03/13/2026
Last P&T Approval/Version: 01/28/2026
Next Review Due By: 01/2027
Policy Number: C28720-A

Rytelo (imetelstat)

PRODUCTS AFFECTED

Rytelo (imetelstat)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Anemia in myelodysplastic syndromes

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

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A. ANEMIA:
1. Documented diagnosis of myelodysplastic syndrome (MDS)
   AND
2. Member has documented lower risk disease defined as one of the following: (i) Revised International Prognostic Scoring System (IPSS-R): Very Low, Low, Intermediate (Score 0 to ≤ 4.5); (ii) IPSS: Low/Intermediate-1 (Score 0 to 1), OR (iii) WHO-Based Prognostic Scoring System (WPSS): Very Low, Low, Intermediate (Score 0 to 2)
   AND
3. Documentation of ONE of the following:
   a. Serum erythropoietin > 500 mU/mL
   b. Serum erythropoietin ≤ 500 mU/mL AND Member has had an inadequate response to prior treatment with an erythropoiesis stimulating agent (i.e., epoetin alpha >40,000 units/week for at least 8 doses or darbepoetin alpha >500 mcg every 3 weeks for at least 4 doses) OR Member has a documented contraindication or agent serious side effects to the use of an erythropoiesis-stimulating
   AND
4. Documentation member is requiring 4 or more red blood cell (RBC) units over 8 weeks

CONTINUATION OF THERAPY:

A. ANEMIA:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by the member achieving transfusion independence (no longer requires pRBC transfusions) or decreased RBC transfusion burden compared to pre-treatment
   NOTE: Discontinue Rytelo if a patient does not experience a decrease in red blood cell (RBC) transfusion burden after 24 weeks of treatment (administration of 6 doses)

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified hematologist/oncologist, or other specialist with expertise in the diagnosis and management of myelodysplastic syndromes [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 ears of age and older

QUANTITY:

7.1 mg/kg every 4 weeks

PLACE OF ADMINISTRATION:

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The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Oligonucleotide Telomerase Inhibitor

FDA-APPROVED USES:
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 units over 8 weeks who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents (ESA).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Low-risk myelodysplastic syndrome (MDS) refers to a subgroup of MDS characterized by relatively slow disease progression and lower likelihood of transformation to acute myeloid leukemia (AML). Patients with low-risk MDS typically have a low International Prognostic Scoring System (IPSS) score (≤1) and often present with cytopenias, particularly anemia, but retain generally stable bone marrow function. Management often focuses on supportive care, including transfusions and erythropoiesis-stimulating agents, with some patients benefiting from lenalidomide or low-dose hypomethylating agents.

Rytelo (imetelstat) is an oligonucleotide telomerase inhibitor indicated for treatment of adult patients with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia requiring 4 or more red blood cell units over 8 weeks who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents (ESA). It binds to the template region of the RNA component of human telomerase (hTR), inhibits telomerase enzymatic activity and prevents telomere binding. Increased telomerase activity and human telomerase reverse transcriptase RNA expression have been reported in MDS and malignant stem and progenitor cells. Nonclinical studies showed imetelstat treatment led to reduction of telomere length, reduction of malignant stem and progenitor cell proliferation, and induction of apoptotic cell death.

The efficacy of Rytelo was evaluated in a randomized, double-blind, placebo-controlled, multicenter trial (IMerge; NCT02598661) in 178 patients enrolled with International Prognostic Scoring System

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(IPSS) low- or intermediate-1 risk MDS who were transfusion-dependent (requiring ≥ 4 red blood cell (RBC) units over an 8-week period during the 16 weeks prior to randomization). Eligible patients were required to have failed to respond or have lost response or be ineligible for erythropoiesis-

stimulating agents (ESAs); and had an absolute neutrophil count of 1.5 x 109 /L or greater and platelets 75 x 109 /L or greater.

Efficacy was established based upon the proportion of patients who achieved ≥ 8-week and ≥ 24-week RBC-TI, defined as the absence of RBC transfusion(s) during any consecutive 8 weeks (56 days) period, and during any consecutive 24 weeks (168 days) period, respectively, from randomization until the start of subsequent anti-cancer therapy (if any). At 8 weeks and 24 weeks, Rytelo had statistically significant effect over placebo (24.8% and 24.6%, respectively).

The NCCN guidelines for Myelodysplastic Syndromes includes imetelstat as first line when serum EPO is > 500 mU/mL and patient is ineligible for ESA treatment.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Rytelo (imetelstat) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Rytelo (imetelstat) include: No labeled contraindications.

Exclusions/Discontinuation:

Discontinue Rytelo if a patient does not experience a decrease in red blood cell (RBC) transfusion burden after 24 weeks of treatment (administration of 6 doses).

Based on findings in animal studies, Rytelo can cause embryo-fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus.

Because of the potential for adverse reactions in the breastfed child, advise women not to breastfeed during treatment with Rytelo and for 1 week after the last dose.

Rytelo was not studied in patients with deletion 5q (del 5q).

Do not use concurrently with luspatercept or erythropoiesis stimulating agents.

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all- inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry- standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS	DESCRIPTION

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CODE	
J0870	Injection, imetelstat, 1 mg

AVAILABLE DOSAGE FORMS:
Rytelo SOLR 47MG
Rytelo SOLR 188MG

REFERENCES

1. Rytelo (imetelstat) for injection, for intravenous use [prescribing information]. Foster City, CA: Geron Corporation; June 2024.
2. National Comprehensive Cancer Network. 2024. Myelodysplastic Syndromes (Version 3.2024). [online] Available at: < https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf> [Accessed 11 October 2024].
3. National Comprehensive Cancer Network. 2025. Myelodysplastic Syndromes (Version 1.2025). [online] Available at: < mds.pdf) > [Accessed 7 January 2025].
4. National Comprehensive Cancer Network. 2026. Myelodysplastic Syndromes (Version 2.2026). [online] Available at: < mds.pdf) > [Accessed 29 December 2025].

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Duration of Approval Contraindications/Exclusions/Discontinuation References	Q1 2026
REVISION- Notable revisions: Required Medical Information Coding/Billing Information References	Q1 2025
NEW CRITERIA CREATION	Q4 2024

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