CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hematology – Rytelo Utilization Management Medical Policy
- Rytelo® (imetelstat intravenous infusion – Geron)

REVIEW DATE: 01/28/2026

OVERVIEW

Rytelo, an oligonucleotide telomerase inhibitor, is indicated for the treatment of **transfusion-dependent anemia** in adults with **low- to intermediate-1 risk myelodysplastic syndrome (MDS)** requiring ≥ 4 red blood cell units over 8 weeks who have not responded to, have lost response to, or are ineligible for erythropoiesis-stimulating agents (ESAs).[1]

Discontinue if a patient does not experience a decrease in red blood cell transfusion burden after 24 weeks of treatment (administration of 6 doses) or if unacceptable toxicity occurs at any time.[1]

Dosing Information

The recommended dosage of Rytelo is 7.1 mg/kg given by a healthcare provider via intravenous infusion over 2 hours once every 4 weeks.[1]

Guidelines

The National Comprehensive Cancer Network guidelines for MDS (version 3.2026 – January 12, 2026) are extensive.[2] Rytelo is recommended for lower risk disease associated with symptomatic anemia with no del(5q) mutation with or without other cytogenetic abnormalities in certain scenarios. A patient is considered ring sideroblast positive (RS+) if ring sideroblasts are ≥ 15% (or ring sideroblasts ≥ 5% with an *SF3B1* mutation). A patient is considered ring sideroblast negative (RS-) if ring sideroblasts < 15% (or ring sideroblasts < 5% with an SF3B1 mutation). The guidelines categorize patients without the del(5q) abnormality on the basis of ring sideroblasts and serum erythropoietin level without specifying red blood cell transfusion burden.

- For patients who are RS- and have a serum erythropoietin ≤ 500 mU/mL, Rytelo is recommended as a Preferred agent following no response to ESAs (specifically epoetin alfa products or Aranesp) or Reblozyl® (luspatercept-aamt subcutaneous injection) [category 1]. For patients who are RS- and have a serum erythropoietin level > 500 mU/mL, Rytelo is listed as a "Preferred" agent (category 2A) for patients with a poor probability to respond to immunosuppressive therapy.
- For patients who are RS+, Rytelo is recommended as an "Other Recommended Regimen" (category 2A) if serum erythropoietin levels are > 500 mU/mL [ineligible for ESAs]. Following no response or relapse to Rytelo, Reblozyl, or other therapies, Rytelo is a cited as a "Preferred" agent (category 1) and if serum erythropoietin levels are ≤ 500 mU/mL or Preferred (category 2A) if serum erythropoietin levels are > 500 mU/mL.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Rytelo. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is

authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Rytelo as well as the monitoring required for adverse events and long-term efficacy, approval requires Rytelo to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rytelo is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Myelodysplastic Syndrome.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** According to the prescriber, patient has very low- to intermediate-risk myelodysplastic syndrome (MDS); AND
       Note: MDS risk category is determined using the International Prognostic Scoring System (IPSS).
     - **iii.** Patient does not have a confirmed mutation with deletion 5q [del(5q)]; AND
     - **iv.** According to the prescriber, the patient has symptomatic anemia; AND
     - **v.** Rytelo will not be used in combination with an erythropoiesis stimulating agent; AND
     - **vi.** The medication is being prescribed by or in consultation with an oncologist or hematologist; OR
   - **B)** Patient is Currently Receiving Rytelo. Approve for 1 year if, according to the prescriber, the patient has experienced a clinically meaningful decrease in transfusion burden.
     Note: For a patient who has not received 6 months (24 weeks) of therapy or who is restarting therapy, refer to Initial Therapy criteria above.

   Dosing. Approve up to 7.1 mg/kg by intravenous infusion administered not more frequently than once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Rytelo is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Rytelo® intravenous infusion [prescribing information]. Foster City, CA: Geron; June 2024.
2. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 3.2026 – January 12, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 26, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	06/12/2024

Update	**08/02/2024:** Overview section updated with National Comprehensive Cancer Network guidelines version 3.2024 – July 25, 2024 which includes recommendations for Rytelo.	--
Annual Revision	No criteria changes.	06/11/2025
Early Annual Revision	**Myelodysplastic Syndrome:** Regarding the diagnosis of myelodysplastic syndrome, the qualifier of "very" was added to "low" and "intermediate-1" was changed to "intermediate". Also, removed the requirement that the patient does not have deletion 5q [del{5q)] cytogenic abnormality. In the requirement that the patient has responded, lost response, or is ineligible for erythropoiesis-stimulating agents, a Note was added that a patient with a serum erythropoietin level > 500 mU/mL is considered ineligible for erythropoiesis-stimulating agents.	10/08/2025
Early Annual Revision	**Myelodysplastic Syndrome:** For initial, therapy the following requirements were removed: patient has transfusion-dependent anemia, defined as requiring transfusion of ≥ 4 red blood cell units over an 8-week period, and according to the prescriber, patient has not responded, lost response to, or is ineligible for erythropoiesis-stimulating agents along with the note of examples of erythropoiesis-stimulating agents. The following requirements were added: Patient does not have a confirmed mutation with deletion 5q [del(5q)], and according to the prescriber, the patient has symptomatic anemia.	01/28/2026