Drug Coverage Policy

Effective Date.....1/1/2025
Coverage Policy Number.....IP0693
Policy Title.....Rytelo

Hematology – Rytelo

- Rytelo® (imetelstat intravenous infusion – Geron)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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]

Rytelo was not studied in patients with deletion 5q [del(5q)] cytogenetic abnormality.[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.

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 3.2024 – July 25, 2024) are extensive.[2] The following NCCN recommendations for Rytelo for the treatment of MDS in lower-risk disease associated with symptomatic anemia are for patients without del(5q) with or without other cytogenic abnormalities. 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 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 > 500 mU/mL, Rytelo is listed as an "Other Recommended Regimen" to the preferred (azacitidine injection) [category 2A] for patients with a poor probability to respond to immunosuppressive therapy and/or following no response or an intolerance to immunosuppressive therapy.
- For patients who are RS+, Rytelo is recommended following no response to Reblozyl if serum erythropoietin ≤ 500 mU/mL (**category 1**) and if serum erythropoietin > 500 mU/mL (category 2A). For patients who are RS+ and have serum erythropoietin > 500 mU/mL, Rytelo is recommended as initial treatment as well as recommended following no response to Reblozyl (both category 2A).

Medical Necessity Criteria

Rytelo is considered medically necessary when the following is met:

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, vi, vii and viii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** According to the prescriber, patient has low- to intermediate-1 risk myelodysplastic syndrome (MDS); AND
       Note: MDS risk category is determined using the International Prognostic Scoring System (IPSS).
     - **iii.** Patient has transfusion-dependent anemia, defined as requiring transfusion of ≥ 4 red blood cell units over an 8-week period; AND
     - **iv.** According to the prescriber, patient has not responded, lost response to, or is ineligible for erythropoiesis-stimulating agents; AND
       Note: Examples of erythropoiesis-stimulating agents include an epoetin alfa product (e.g., Epogen, Procrit, or Retacrit), a darbepoetin alfa product (e.g., Aranesp), or a methoxy polyethylene glycol-epoetin beta product (e.g., Mircera).
     - **v.** Patient does NOT have deletion 5q [del(5q)] cytogenic abnormalities; AND
     - **vi.** Rytelo will NOT be used in combination with an erythropoiesis stimulating agent; AND
     - **vii.** The medication is being prescribed by or in consultation with an oncologist or hematologist; AND
     - **viii.** Preferred product criteria is met for the product(s) as listed in the below table(s) 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.

Employer Plans:

Product	Criteria
Rytelo (imetelstat intravenous infusion)	ONE of the following (1, 2 or 3): 1. Patient has tried Reblozyl (luspatercept) 2. Patient meets ALL of the following (A, B, and C): A. Patient does NOT have a deletion 5q [del(5q)]; AND B. Patient has ring sideroblasts < 15% (or ring sideroblasts < 5% with an SF3B1 pathogenic variant); AND C. Patient has tried or has a poor probability to respond to immunosuppressive therapy 3. Patient has already been started on therapy with Rytelo

Individual and Family Plans:

Product	Criteria
Rytelo (imetelstat intravenous infusion)	ONE of the following (1, 2 or 3): 1. Patient has tried Reblozyl (luspatercept) 2. Patient meets ALL of the following (A, B, and C): A. Patient does NOT have a deletion 5q [del(5q)]; AND B. Patient has ring sideroblasts < 15% (or ring sideroblasts < 5% with an SF3B1 pathogenic variant); AND C. Patient has tried or has a poor probability to respond to immunosuppressive therapy 3. Patient has already been started on therapy with Rytelo

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding Information

Note: 1) This list of codes may not be all-inclusive.

2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0870	Injection, imetelstat, 1 mg (Code effective 1/1/2025)
C9399	Unclassified drugs or biologicals (Code effective until 12/31/2024)
J3490	Unclassified drugs (Code effective until 12/31/2024)
J9999	Not otherwise classified, antineoplastic drugs (Code effective until 12/31/2024)

References

1. Rytelo® intravenous infusion [prescribing information]. Foster City, CA: Geron; June 2024.
2. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 2.2024 – May 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 7, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	10/1/2024
Selected Revision	**Preferred Product Table:** **Added** a prerequisite step through Reblozyl prior to coverage of Rytelo, for both Employer and Individual and Family Plans.	11/1/2024
Selected Revision	**Updated Coding:** **Added:** J9399, J3490, J9999 (Codes effective until 12/31/2024) **Added:** J0870 (Code effective 1/1/2025)	1/1/2025

The policy effective date is in force until updated or retired.