

Drug Policy:

Rytelo™ (imetelstat)

POLICY NUMBER UM ONC_1506	SUBJECT Rytelo™ (imetelstat)		DEPT/PROGRAM UM Dept	PAGE 1 OF 3
DATES COMMITTEE REVIEWED 08/14/24	APPROVAL DATE August 14, 2024	EFFECTIVE DATE August 30, 2024	COMMITTEE APPROVAL DATES 08/14/24	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Rytelo (imetelstat) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The member has not experienced disease progression on the requested medication **AND**
2. The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Myelodysplastic Syndrome (MDS)

1. Rytelo (imetelstat) may be used in adult members with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia requiring four 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 (ESAs).

REVISED INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS-R)

Prognostic variable	Score Value						
	0	0.5	1	1.5	2	3	4
Cytogenetic ^e	Very good	—	Good	—	Intermediate	Poor	Very poor
Marrow blasts (%)	≤2	—	>2–<5	—	5–10	>10	—
Hemoglobin	≥10	—	8–<10	<8	—	—	—
Platelets	≥100	50–<100	<50	—	—	—	—
ANC	≥0.8	<0.8	—	—	—	—	—

PROGNOSIS ACCORDING TO IPSS-R RISK SCORE²

IPSS-R Risk Category (% IPSS-R pop.)	Overall Score	Median Survival (y) in the Absence of Therapy	25% AML Progression (y) in the Absence of Therapy
VERY LOW (19)	≤1.5	8.8	Not reached
LOW (38)	>1.5–≤3.0	5.3	10.8
INT ³ (20)	>3.0–≤4.5	3	3.2
HIGH (13)	>4.5–≤6.0	1.6	1.4
VERY HIGH (10)	>6.0	0.8	0.7

Cytogenetic risks: Very good = -Y, del(11q); Good = normal, del(5q), del(12p), del(20q), double including del(5q); Intermediate = del(7q), +8, +19, i(17q), any other single or double independent clones; Poor = -7, inv(3)/t(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities; Very poor = complex: >3 abnormalities.

III. EXCLUSION CRITERIA

- A. Disease progression while taking Rytelo (imetelstat).
- B. Concurrent use with other anticancer therapies.
- C. Dosing exceeds single dose limit of 7.1 mg/kg.
- D. Treatment exceeds the maximum limit of 6 doses.
- E. Investigational use of Rytelo (imetelstat) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
 1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
 2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
 3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
 4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).

5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

- A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

- A. Rytelo prescribing information Geron Corporation, Foster City, CA 94404, 2024
- B. Platzbecker U, 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):249-260. doi: 10.1016/S0140-6736(23)01724-5
- C. Clinical Pharmacology Elsevier Gold Standard 2024.
- D. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2024.
- E. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.
- F. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
- G. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.

