MEDICAL MUTUAL®

Drug Policy

Policy:	**240102**	**Initial Effective Date: 01/18/2024**
Code(s):	**HCPCS J3590, C9399**	**Annual Review Date: 01/16/2025**
SUBJECT:	**Ryzneuta® (efbemalenograstim alfa-vuxw subcutaneous)**	**Last Revised Date: 01/16/2025**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

I. Length of Authorization

Coverage will be provided for four months and may be renewed unless otherwise specified.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Ryzneuta 20 mg/mL prefilled syringe: 1 syringe per 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 20 mg per 14 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Will not be used for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation; **AND**
- Patient does not have a history of serious allergic reactions to granulocyte stimulating factor products (e.g., pegfilgrastim, filgrastim, etc.); **AND**

Prophylactic use in patients with non-myeloid malignancy † ‡ [1-7,9,10,12,13,15,17,27-29]

- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of greater than 20% **§**; **OR**
- Patient is undergoing myelosuppressive chemotherapy with an expected incidence of febrile neutropenia of 10% to 20% **§ AND** one or more of the following co-morbidities:
  - Age >65 years receiving full dose intensity chemotherapy

- Extensive prior exposure to chemotherapy
- Previous exposure of pelvis, or other areas of large amounts of bone marrow, to radiation
- Pre-existing neutropenia (ANC ≤ 1000/mm^3)
- Bone marrow involvement with tumor
- Patient has a condition that can potentially increase the risk of serious infection (i.e., HIV/AIDS with low CD4 counts)
- Recent surgery and/or open wounds
- Poor performance status
- Renal dysfunction (creatinine clearance <50 mL/min)
- Liver dysfunction (elevated bilirubin >2.0 mg/dL)
- Chronic immunosuppression in the post-transplant setting including organ transplant

  Note: Dose-dense therapy, in general, requires growth factor support to maintain dose intensity and schedule. In the palliative setting, consideration should be given to dose reduction or change in regimen.

§Febrile neutropenia is defined as: [7]
– Temperature: a single temperature ≥38.3 °C orally or ≥38.0 °C over 1 hour; **AND** – Neutropenia: <500 neutrophils/mcL or <1,000 neutrophils/mcL and a predicted decline to ≤500 neutrophils/mcL over the next 48 hours
§ Expected incidence of febrile neutropenia percentages for myelosuppressive chemotherapy regimens can be found in the NCCN Hematopoietic Growth Factors Clinical Practice Guideline at NCCN.org [7]

† FDA-Approved Indication(s); ‡ Compendium Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage may be renewed based on the following criteria:

- Patient continues to meet indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: splenic enlargement/rupture, acute respiratory distress syndrome, severe hypersensitivity reactions/anaphylaxis, severe sickle cell crises in patients with sickle cell disease, glomerulonephritis, hematologic effects (e.g., leukocytosis, thrombocytopenia), capillary leak syndrome, tumor cell mobilization, MDS/AML in patients with breast and lung cancer, aortitis, etc.

V. Dosage/Administration [1]

Indication	Dose
Prophylactic use in patients with non-myeloid malignancy	– Administer 20 mg subcutaneously once per chemotherapy cycle at least 24 hours after cytotoxic chemotherapy. Do not administer within 14 days before and <24 hours after administration of cytotoxic chemotherapy.
Note: Ryzneuta is administered subcutaneously via a single-dose prefilled syringe by a healthcare professional.	

VI. Billing Code/Availability Information

HCPCS Code:

- J3590 – Unclassified biologics

NDC:

- Ryzneuta 20 mg/mL prefilled syringe: 73491 -0627-xx

VII. References

1. Ryzneuta [package insert]. Singapore; Evive Biotech., LTD; November 2023. Accessed December 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) efbemalenograstim. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed December 2023.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hematopoietic Cell Transplantation Version 3.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed December 2023.
4. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015 Oct 1;33(28):3199-212. doi: 10.1200/JCO.2015.62.3488.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D61.81	Pancytopenia
D70.1	Agranulocytosis secondary to cancer chemotherapy
D70.9	Neutropenia, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs sequela
Z41.8	Encounter for other procedures for purposes other than remedying health state
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy
Z51.89	Encounter for other specified aftercare
Z76.89	Persons encountering health services in other specified circumstances

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J3590 and C9399

†When *Unclassified biologics* (J3590) or *unclassified drugs or biologics [hospital outpatient use]* (C9399) is determined to be Ryzenuta

Edits and Denials:

Prior approval: Prior approval is required for Nulibry **(HCPCS Codes J3490, C9399)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.