Elrexfio™ (elranatamab-bcmm)
(Subcutaneous)

Document Number: IC-0724

Last Review Date: 03/05/2024
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Dates Reviewed: 09/2023, 03/2024

I. Length of Authorization

Following initial hospital administration of 2 doses (step-up dose 1, step-up dose 2), coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

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

- Elrexfio 76 mg/1.9 mL solution for injection in a single-dose vial: 1 vial on day 1 and 4 then 1 vial weekly through week 24 then 1 vial every two weeks thereafter
- Elrexfio 44 mg/1.1 mL solution for injection in a single-dose vial: 1 vial on day 1 and 4 then 1 vial weekly through week 24 then 1 vial every two weeks thereafter

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

- Titration: 44 billable units (44 mg) on day 1, 44 billable units (44 mg) on day 4 and 76 billable units (76 mg) on day 8
- Maintenance: 76 billable units (76 mg) weekly through week 24 then 76 billable units (76 mg) every two weeks thereafter

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Used as continuation therapy following inpatient administration of step-up dose 1 and step-up dose 2; **AND**
- Patient had an absence of unacceptable toxicity while on inpatient administration of step-up doses; **AND**

Universal Criteria [1]

- Prescribers are enrolled in and meet the conditions of the ELREXFIO REMS® program; **AND**
- Patient does not have an active infection, including clinically important localized infections; **AND**
- Patient will be administered prophylaxis for infection according to local guidelines; **AND**

- Patient has not had an allogenic or an autologous stem cell transplant within the previous 12 weeks; **AND**
- Used as single agent treatment; **AND**

Multiple Myeloma † ‡ Φ [1-3]

- Patient has relapsed or refractory disease; **AND**
- Patient has received at least four (4) prior therapies, including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib etc.), an immunomodulatory agent (e.g., lenalidomide, thalidomide, pomalidomide, etc.) and an anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab, etc.)

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

IV. Renewal Criteria [1]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infections, neutropenia/febrile neutropenia, severe hepatotoxicity, neurologic toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), cytokine release syndrome (CRS), etc.

V. Dosage/Administration [1]

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Multiple Myeloma</td><td>The recommended dosages of Elrexfio subcutaneous injection are: step-up dose 1 of 12 mg on Day 1, step-up dose 2 of 32 mg on Day 4, followed by the first treatment dose of 76 mg on Day 8, and then 76 mg weekly thereafter through week 24.

For patients who have received at least 24 weeks of treatment with Elrexfio and have achieved a response [partial response (PR) or better] and maintained this response for at least 2 months, the dose interval should transition to an every two-week schedule.

Continue treatment with Elrexfio until disease progression or unacceptable toxicity.
<table>
<tr><th>Dosing schedule</th><th>Day</th><th colspan="2">Dose</th></tr>
<tr><td rowspan="2">Step-up dosing schedule</td><td>Day 1 [a]</td><td>Step-up dose 1</td><td>12 mg</td></tr>
<tr><td>Day 4 [a,b]</td><td>Step-up dose 2</td><td>32 mg</td></tr>
</table>
</td></tr>
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		Day 8 [a,c]	First treatment dose	76 mg
	Weekly dosing schedule	One week after first treatment dose and weekly thereafter [d] through week 24	Subsequent treatment doses	76 mg
	Biweekly (Every 2 Weeks) Dosing Schedule ***Responders only week 25 onward***	Week 25 and every 2 weeks thereafter [d]	Subsequent treatment doses	76 mg
	– **a.** Administer pre-treatment medications prior to each dose in the Elrexfio step-up dosing schedule, which includes step-up dose 1, step-up dose 2, and the first treatment dose. – **b.** A minimum of 2 days should be maintained between step-up dose 1 (12 mg) and step-up dose 2 (32 mg). – **c.** A minimum of 3 days should be maintained between step-up dose 2 (32 mg) and the first treatment (76 mg) dose. – **d.** A minimum of 6 days should be maintained between treatment doses. Note: See the PI for recommendations on restarting Elrexfio after dose delays.			
Note: Elrexfio is intended for subcutaneous use by a healthcare provider only. Administer Elrexfio subcutaneously according to the step-up dosing schedule to reduce the incidence and severity of cytokine release syndrome (CRS). Due to the risk of CRS, patients should be hospitalized for 48 hours after administration of the first step-up dose, and for 24 hours after administration of the second step-up dose.				

VI. Billing Code/Availability Information

HCPCS Code(s):

- J9999 – Not otherwise classified, antineoplastic drugs *(Discontinue use on 04/01/2024)*
- C9165 – Injection, elranatamab-bcmm, 1 mg; 1 billable unit = 1 mg *(Discontinue use on 04/01/2024)*
- J1323 – Injection, elranatamab-bcmm, 1 mg; 1 billable unit = 1 mg *(Effective 04/01/2024)*

NDC(s):

- Elrexfio 76 mg/1.9 mL solution for injection in a single-dose vial: 00069-4494-xx
- Elrexfio 44 mg/1.1 mL solution for injection in a single-dose vial: 00069-2522-xx

VII. References

1. Elrexfio [package insert]. New York, NY; Pfizer, Inc.; August 2023. Accessed February 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for elranatamab. National Comprehensive Cancer Network, 2024. 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 February 2024.

3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma Version 2.2024. National Comprehensive Cancer Network, 2024. 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 February 2024.
4. BGM Durie, J-L Harousseau, J S Miguel, et al on behalf of the International Myeloma Working Group. International uniform response criteria for multiple myeloma. Leukemia. Sep; 20(9):1467-73.
5. Lesokhin AM, Arnulf B, Niesvizky R, et al. Initial safety results for MagnetisMM-3: A phase 2 trial of elranatamab, a B-cell maturation antigen (BCMA)-CD3 bispecific antibody, in patients (pts) with relapsed/refractory (R/R) multiple myeloma (MM). Journal of Clinical Oncology 2022 40:16_suppl, 8006-8006.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

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/LCD/LCA): 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.
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