STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Elrexfio (elranatamab-bcmm)
PAM–077

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	01/01/2024
Revision Number:	1	**Last Rev Date:**	07/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	07/18/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	07/19/2024

Overview

Medication:[1]	elranatamab-bcmm
Brand Name:	Elrexfio™
Pharmacologic Category:	Antineoplastic; bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager
FDA-Approved Indication(s):	Treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. ➢ This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial(s).
How Supplied:	Single-dose vial containing either 76 mg/1.9 mL or 44 mg/1.1 mL
Dosage and Administration:	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.

Dosing Schedule	**Day**	**ELREXFIO Dose**	
Step-up Dosing Schedule	Day 1	Step-up dose 1	12 mg
	Day 4	Step-up dose 2	32 mg
	Day 8	First treatment dose	76 mg
Weekly Dosing Schedule	One week after first treatment dose and weekly thereafter **through week 24**	Subsequent treatment doses	76 mg
Biweekly (Every 2 Weeks) Dosing Schedule*	Week 25 and every 2 weeks thereafter	Subsequent treatment doses	76 mg

* Responders only, week 25 onward

Benefit Category:	Medical

BOXED WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- Cytokine Release Syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving Elrexfio™. Initiate treatment with Elrexfio™ step-up dosing schedule to reduce the risk of CRS. Withhold Elrexfio™ until CRS resolves or permanently discontinue based on severity.
- Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), and serious and life-threatening reactions, can occur in patients receiving Elrexfio™. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS, during treatment. Withhold Elrexfio™ until the neurologic toxicity resolves or permanently discontinue based on severity.
- Because of the risk of CRS and neurologic toxicity, including ICANS, Elrexfio™ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called ELREXFIO REMS.

Descriptive Narrative

Multiple myeloma (MM) is a malignant hematological disorder characterized by the clonal proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow and can result in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathologic fractures. Most patients with MM present with signs or symptoms related to the infiltration of plasma cells into the bone or other organs or to kidney damage from immunoglobulin deposition. While the clinical presentation is usually subacute, a small percentage of patients present acutely with findings that require rapid attention and intervention (e.g., spinal cord compression, kidney failure, hyperviscosity).

The acronym "CRAB" is sometimes used to remember myeloma-defining events that are used in the diagnosis of MM: **c**alcium elevation; **r**enal insufficiency (kidney impairment); **a**nemia; and **b**one disease. It is important to distinguish MM both from other causes of the clinical presentations above and from other plasma cell dyscrasias for the purposes of prognosis and treatment.

MM primarily affects older individuals, the median age at diagnosis is 65 to 74 years. It is slightly more frequent in men than in women (approximately 1.4:1), and while MM occurs in all races and all geographic locations, the incidence varies by ethnicity. The incidence in African Americans and Black populations is two to three times that in White populations in studies from the United States and United Kingdom. In contrast, the risk is lower in the Japanese and Mexican populations.[2]

Data from the US Surveillance, Epidemiology, and End Results (SEER) registry estimates 35,780 new cases of MM and 12,540 deaths from MM in the United States in 2024 (representing 1.8 percent of all new cancer cases and 2.0 percent of all cancer deaths). This correlates with an annual incidence of approximately 7 per 100,000 men and women per year. [3]

Treatment alleviates symptoms, reverses cytopenias, and decreases end-organ damage, and it aims to achieve a sustained response, improve quality of life, and prolong overall survival (OS). While most patients with multiple myeloma will have an initial response to treatment, conventional therapy is not curative, and MM will ultimately relapse. In addition, a minority will have primary refractory disease that does not respond to initial treatment.[4]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[5]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for Multiple Myeloma (Version 4.2024 – April 26, 2024)[6]

NCCN Guidelines® recommendation(s) for Elrexfio™ in previously treated multiple myeloma [a, b]
(1) Relapsed/refractory disease after 3 prior therapies A. After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD i. Elrexfio (elranatamab-bcmm): Category 2A, preferred PI = proteosome inhibitor IMiD = immunomodulatory drug [a] Regimens included under 1–3 prior therapies can also be used later in the disease course. Attempt should be made to use drugs/drug classes the patients have not been exposed to or exposed to >1 line prior. [b] Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale[7]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.
5	Dead.

Criteria

Prior authorization is required.

Elrexfio™ is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of multiple myeloma (MM); **AND**
2. Member has relapsed or refractory disease after **four** or more prior therapies, which include **AT LEAST ONE OF EACH** of the following categories:
    a. An anti-CD38 monoclonal antibody (e.g., daratumumab, daratumumab and hyaluronidase, or isatuximab); **AND**
    b. An immunomodulatory agent (e.g., lenalidomide, pomalidomide, or thalidomide); **AND**
    c. A proteasome inhibitor (e.g., bortezomib, carfilzomib, or ixazomib); **AND**
3. Member is 18 years of age or older; **AND**
4. Member has an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0, 1, or 2; **AND**
5. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
6. Member will receive treatment with Elrexfio™ at a facility that is certified under the Elrexfio™ Risk Evaluation and Mitigation Strategy (REMS) program; **AND**
7. Request for Elrexfio™ meets one of the following (a or b):
    a. Prescribed as monotherapy and does not exceed 76 mg once weekly (after initial step-up dosing schedule); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Elrexfio™ is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
4. Member will receive treatment with Elrexfio™ at a facility that is certified under the Elrexfio™ Risk Evaluation and Mitigation Strategy (REMS) program; **AND**
5. Request for Elrexfio™ meets one of the following (a or b):
    a. Prescribed as monotherapy and does not exceed one of the following (i or ii):
        i. Up to week 24 of therapy: 76 mg once weekly; or
        ii. Week 25 of therapy and beyond: 76 mg every 2 weeks; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	76 mg once weekly (after completion of step-up dosing schedule)	• 76 mg once weekly (through week 24) • 76 mg once every 2 weeks (responders only, week 25 and onward)

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
~~C9165~~	~~Injection, elranatamab-bcmm, 1 mg~~ *(effective 1/1/2024 to 3/31/2024)*
J1323	Injection, elranatamab-bcmm, 1 mg *(effective 4/1/2024)*

ICD-10	Description
C90.0	Multiple myeloma
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma in relapse

NDC (strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
00069-4494-02 (76 mg/1.9 mL)	Pfizer Inc. (00069)	1 mg	1	EA	76
00069-2522-02 (44 mg/1.2 mL)	Pfizer Inc. (00069)	1 mg	1	EA	44

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Elrexfio™ prescribing information (08/2023). Pfizer Inc.: New York, NY. Available online at: elrexfio.pfizerpro.com. Accessed May 24, 2024.

[2] Laubach JP. Multiple myeloma: Clinical features, laboratory manifestations, and diagnosis. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 3, 2024.

[3] SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD. Available online at seer.cancer.gov/statfacts/html/mulmy.html. Accessed June 3, 2024.

[4] Laubach JP. Multiple myeloma: Overview of management. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 3, 2024.

[5] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[6] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma (v.4.2024 – April 26, 2024). Accessed June 1, 2024. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

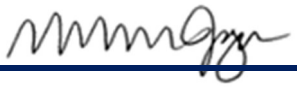
[7] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
07/19/2024	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee