UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – Bispecific – BCMA-Directed) – Elrexfio Utilization Management Medical Policy
- Elrexfio™ (elranatamab-bcmm subcutaneous injection – Pfizer)

REVIEW DATE: 09/10/2025

OVERVIEW

Elrexfio, a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager, is indicated for the treatment of relapsed or refractory **multiple myeloma** in adults who have received at least four prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.[1]

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).

Dosing Information

Elrexfio is administered by subcutaneous injection.[1] Dosing begins with step-up doses of 12 mg on Day 1 and 32 mg on Day 4, followed by the first full treatment dose of 76 mg on Day 8. Treatment with the 76 mg dose is continued once weekly through Week 24. Beginning at Week 25, patients with at least a partial response to therapy who have maintained this response for at least 2 months can transition to a once every 2 week dosing regimen through Week 48. At Week 49, patients who have maintained the response following 24 weeks of treatment at the biweekly dosing schedule can extend the dosing interval to every 4 weeks. Treatment can continue until disease progression or unacceptable adverse events.

Guidelines

The National Comprehensive Cancer Network clinical practice guidelines for multiple myeloma (version 2.2026 – July 16, 2025) recommend Elrexfio as a "Preferred Regimen" for the treatment of relapsed or refractory multiple myeloma in patients who have received at least four prior lines of therapy including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent (category 2A).[2,3]

Safety

Elrexfio has a Boxed Warning for cytokine release syndrome (CRS) and neurologic toxicity including immune effector cell-associated neurotoxicity syndrome (ICANS).[1] In addition, Elrexfio was approved with a Risk Evaluation and Mitigation Strategy (REMS) program due to the risk of CRS and neurologic toxicity, including ICANS.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Elrexfio. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Elrexfio as well as the monitoring required

for adverse events and long-term efficacy, approval requires Elrexfio to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Elrexfio is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. Multiple Myeloma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has tried at least four systemic regimens; AND
- **C)** Among the previous regimens tried, the patient has received at least one drug from each of the following classes (i, ii, and iii):
  - **i.** Proteasome inhibitor; AND
    Note: Examples include bortezomib, Kyprolis (carfilzomib intravenous infusion), and Ninlaro (ixazomib capsules).
  - **ii.** Immunomodulatory drug; AND
    Note: Examples include lenalidomide, Pomalyst (pomalidomide capsules), and Thalomid (thalidomide capsules).
  - **iii.** Anti-CD38 monoclonal antibody; AND
    Note: Examples include Darzalex (daratumumab intravenous infusion), Darzalex Faspro (daratumumab and hyaluronidase-fihj subcutaneous injection), and Sarclisa (isatuximab-irfc intravenous infusion).
- **D)** The medication will be prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimens (A and B):
- **A)** Step-up dosing (i, ii, and iii):
  - **i.** Dose 1: Approve 12 mg given by subcutaneous injection on Day 1; AND
  - **ii.** Dose 2: Approve 32 mg given by subcutaneous injection, 2 to 14 days after Dose 1; AND
  - **iii.** Dose 3: Approve 76 mg given by subcutaneous injection, 3 to 14 days after Dose 2; AND
- **B)** Approve 76 mg given by subcutaneous injection no more frequently than once weekly.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Elrexfio is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Elrexfio™ subcutaneous injection [prescribing information]. New York, NY: Pfizer; July 2025.
2. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 8, 2025. Search term: elranatamab.
3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 2.2026 – July 16, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on September 8, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	08/23/2023
Annual Revision	No criteria changes.	09/11/2024
Update	04/08/2025: The policy name was changed from "Oncology (Injectable) – Elrexfio UM Medical Policy" to "Oncology (Injectable – Bispecific – BCMA-Directed) – Elrexfio UM Medical Policy".	N/A
Annual Revision	No criteria changes.	09/10/2025