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DRUG POLICY

Elrexfio (elranatamab-bcmm)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Elrexfio policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Elrexfio is indicated for the 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.

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review: chart notes or medical record documentation demonstrating failure of previous lines of therapy.

Criteria for Initial Approval

Multiple Myeloma

Authorization of 12 months may be granted for treatment of relapsed or refractory multiple myeloma in members who have received at least 4 prior therapies, including at least one drug from each of the following categories:

1. Anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab)
2. Proteasome inhibitor (e.g., bortezomib, ixazomib, carfilzomib)

3. Immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide)

Continuation of Therapy

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Criteria for Initial Approval when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Elrexio is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Medication	FDA-recommended dosing
Elrexio (elranatamab-bcmm) 44 mg/1.1 mL single-dose vial	Step-up Dosing • Day 1: 12 mg • Day 4: 32 mg • Day 8: 76 mg
Elrexio (elranatamab-bcmm) 76 mg/1.9 mL single-dose vial	Weekly Dosing: 76 mg through week 24 Biweekly Dosing: 76 mg week 25 and then every 2 weeks

CLINICAL RATIONALE

Multiple myeloma is a cancer resulting from abnormal and uncontrolled growth of plasma cells in the bone marrow causing damage in tissues throughout the body and including blood count abnormalities. Of the most commonly affected systems, multiple myeloma may result in: osteopenia and bone pain or fracture; anemia causing fatigue; leukopenia and diminished immunoglobulin production causing infection; thrombocytopenia leading to abnormal bleeding and bruising; nephropathy or acute kidney injury; increased risk of infection due to immunoglobulin deficiencies; and more generalized muscle weakness among other symptoms. Onset of these symptoms generally occur in adults ages 65-74 and is the second most common blood cancer resulting in an estimated 35,730 new cases in the United States in 2023.

Although advancements in the treatment of multiple myeloma (including immunomodulatory drugs, proteasome inhibitors, and anti-CD38 monoclonal antibodies) have resulted in improvements in the progression-free survival and overall survival (median 4.6 months and 12.4 months respectively), patients with disease progression represent an unmet need in relapsed or refractory multiple myeloma. Research has determined B-cell maturation antigen (BCMA) to be highly expressed on malignant plasma cells, and has been a target of various new therapies leading to multiple new approvals for the treatment of relapsed or refractory multiple myeloma in recent years.

Elranatamab-bcmm is a humanized bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the 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. Elranatamab-bcmm received accelerated approval for this indication based on the response rate and durability of response in MagnetisMM-3, an ongoing phase 2 trial assessing safety and efficacy of elranatamab in patients with relapsed or refractory multiple myeloma previously treated with multiple lines of therapy from various drug classes. Elranatamab-bcmm targets BCMA on plasma cells and CD38 on T cells inducing a T-cell response that leads to cytolysis of the BCMA-expressing myeloma cells. Elranatamab-bcmm causes a proinflammatory cytokine release resulting in cell lysis.

Trial results from MagnetisMM-3 showed a 57.7% (95% CI: 47.3%, 67.7%) overall response rate (ORR) in 97 patients enrolled in the study who were refractory to previous therapies and were BCMA-directed therapy naïve (identified as cohort A) after a median follow-up of 11.1 months among responders. Of those 97 patients, 25 (25.8%) experienced a complete response or better, 25 (25.8%) experienced a very good partial response, and 6 (6.2%) experienced a partial response. The duration of response (DOR) at 6 months was 90.4% (95% CI: 78.4%, 95.9%), and 82.3% (95% CI: 67.1%, 90.9%) at 9 months. Cohort A had a median time to first response of 1.22 months.

Patients frequently experienced cytokine release syndrome (CRS) (58% of patients), neurologic toxicity (NT) (59% of patients), and immune effector cell-associated neurotoxicity syndrome (ICANS) (3.3% of patients) in the Elranatamab-bcmm treated group resulting in a boxed warning and restricting access of Elranatamab-bcmm to the Elrexio Risk Evaluation and Mitigation Strategy (REMS). Additional side effects included; injection site reactions, diarrhea, upper respiratory tract infections, musculoskeletal pain, pneumonia, decreased appetite, rash, cough, nausea, and pyrexia. Laboratory abnormalities of Grade 3 or 4 are; decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased white blood cells, and decreased platelets. Elranatamab-bcmm may cause an increased risk of infection, neutropenia requiring complete blood cell count monitoring, hepatotoxicity requiring monitoring, and embryo-fetal toxicity requiring use of contraceptives while on therapy.

Elranatamab-bcmm continues to be studied within clinical trials. The confirmatory trial to verify clinical benefit of Elranatamab-bcmm as monotherapy as part of the accelerated approval pathway, MagnetisMM-3, is expected to yield results in 2026. MagnetisMM-5 is a clinical trial evaluating Elranatamab-bcmm plus daratumumab versus daratumumab plus pomalidomide plus dexamethasone in the double-class exposed setting for the treatment of multiple myeloma, and is expected to be completed by the end of 2024. Efficacy of Elranatamab-bcmm in newly diagnosed multiple myeloma patients after transplant is being studied in MagnetisMM-7, and the trial is looking at the medication being used as a maintenance treatment with results expected in 2029.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J1323 – Injection, elranatamab-bcmm, 1 mg (effective 4/1/24)
- C9165 – Injection, elranatamab-bcmm, 1 mg (cancelled 3/31/24)

REFERENCES

- Elrexio [package insert]. New York, NY: Pfizer Inc.; July 2025.
- American Cancer Society. Key statistics about multiple myeloma. January 12, 2023. Accessed September 29, 2023. <https://www.cancer.org/cancer/types/multiple-myeloma/about/key-statistics.html>
- Cohen AD, et al. Efficacy and safety of cilta-cel in patients with progressive multiple myeloma after exposure to other BCMA-targeting agents. *Blood*. 2023;141(3):219–230. doi:10.1182/blood.2022015526
- Van Oekelen O, et al. Interventions and outcomes of patients with multiple myeloma receiving salvage therapy after BCMA-directed CAR T therapy. *Blood*. 2023;141(7):756-765. doi:10.1182/blood.2022017848
- Leshokhin, AM, et al. Elranatamab in relapsed or refractory multiple myeloma: phase 2 MagnetisMM-3 trial results. *Nature Medicine*. 2023; V29: 2259-2267. doi:10.1038/s41591-023-02528-9.

POLICY HISTORY

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