PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrELREXFIO®

elranatamab injection

44 mg/1.1 mL (40 mg/mL) solution for subcutaneous injection

76 mg/1.9 mL (40 mg/mL) solution for subcutaneous injection

Professional Standard

Antineoplastic, monoclonal antibody

ATC code: L01FXXX

"Elrexfio (elranatamab solution for injection), indicated for:

- the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy

has been issued market authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for Elrexfio please refer to Health Canada's Notice of Compliance with conditions - drug products web site: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/notice-compliance/conditions.html"

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Pfizer Canada licensee

What is a Notice of Compliance with Conditions (NOC/c)?

An NOC/c is a form of market approval granted to a product on the basis of promising evidence of clinical effectiveness following review of the submission by Health Canada.

Products authorized under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.

RECENT MAJOR LABEL CHANGES

4 DOSAGE AND ADMINISTRATION, 4.2 Recommended Dose and Dosage Adjustment	09/2025

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Elrexfio (elranatamab injection) is a B-cell maturation antigen (BCMA)-directed and CD3-directed bispecific antibody indicated as monotherapy for:

- the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy

1.1 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use (see 7.1.3 Pediatrics).

1.2 Geriatrics

Geriatrics (≥ 65 years of age): Of the 183 patients with relapsed or refractory multiple myeloma treated with Elrexfio in a clinical trial at the recommended dosage, 62% were 65 years of age or older, and 19% were 75 years of age or older. Evidence from clinical studies does not suggest that use in the geriatric population is associated with differences in safety or effectiveness (see 7.1.4 Geriatrics).

2 CONTRAINDICATIONS

- Elrexfio is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- 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. Monitor patients for signs or symptoms of CRS. Withhold Elrexfio until CRS resolves. Provide supportive care and treatment as needed or permanently discontinue based on severity (see 4 DOSAGE AND ADMINISTRATION and 7 WARNINGS AND PRECAUTIONS).
- Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious and life-threatening reactions, can occur with Elrexfio. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS, during treatment. The onset of ICANS may be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Withhold Elrexfio until the neurologic toxicity resolves or permanently discontinue based on severity (see 4 DOSAGE AND ADMINISTRATION and 7 WARNINGS AND PRECAUTIONS).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Premedication prior to the first three doses of Elrexfio is recommended (see 4.4 Administration, Pre-treatment Medications).
- Elrexfio should be administered by a healthcare professional with appropriate medical support to manage severe reactions, including cytokine release syndrome (CRS) and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS) (see 7 WARNINGS AND PRECAUTIONS).
- Pregnancy status for females of child-bearing potential should be verified prior to starting treatment with Elrexfio.
- Do not initiate treatment with Elrexfio in patients with active infection.
- Prior to initiating treatment with Elrexfio, prophylactic antimicrobials (eg., prevention of pneumocystis jirovecii pneumonia) and anti-virals (eg., prevention of herpes zoster reactivation) should be considered per local institutional guidelines.
- Administer Elrexfio subcutaneously according to the step-up dosing schedule to reduce the incidence and severity of CRS and ICANS (see 4.2 Recommended Dose and Dosage Adjustment, Table 1).

4.2 Recommended Dose and Dosage Adjustment

Recommended Dose

The recommended dosing schedule for Elrexfio is provided in Table 1. The recommended doses of Elrexfio subcutaneous (SC) injection are step-up doses of 12 mg on Day 1 and 32 mg on Day 4 of week 1, 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 and have achieved a response (i.e., a partial response or better that has been maintained for at least 2 months), the dose interval should transition to an every two-week schedule. For patients who have received at least 24 weeks of treatment with Elrexfio at the every two-weeks dosing schedule and have maintained the response, the dose interval should transition to an every four-weeks schedule (see Table 1).

Continue treatment with Elrexfio until disease progression or unacceptable toxicity.

Administer Elrexfio subcutaneously according to the step-up dosing schedule in Table 1. The step-up regimen is intended to reduce the risk and/or severity of CRS and/or ICANS. Failure to follow the recommended dosing schedule for initiation or re-initiation of therapy may increase the risk and/or severity of adverse events such as CRS.

Table 1 – Elrexfio Dosing Schedule

Dosing Schedule	Week / Day	Dose	
Step-up Dosing[a], [b]	Week 1: Day 1	Step-up dose 1	12 mg SC
	Week 1: Day 4	Step-up dose 2	32 mg SC
Weekly Dosing[a], [c, d]	Week 2-24: Day 1	Treatment dose	76 mg SC once weekly
Every 2 Weeks Dosing[d], [e]	Week 25-48: Day 1	Treatment dose	76 mg SC once every two weeks
Every 4 weeks Dosing[d], [f, g]	Week 49 onward: Day 1	Treatment dose	76 mg SC once every four weeks

Abbreviations: SC = subcutaneous

a. Administer pre-treatment medications prior to the first three doses of Elrexfio (see 4.4 Administration, Pre-treatment Medications).
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 full treatment (76 mg) dose.
d. Maintain a minimum of 6 days between treatment doses.
e. For patients who have achieved and maintained a partial response or better for 2 months.
f. For patients who have received at least 24 weeks of treatment at the every two-week schedule.
g. For patients who maintained the response.

Note: See Table 2 for recommendations on restarting Elrexfio after dose delays.

Restarting Elrexfio After Dosage Delay

If a dose of Elrexfio is delayed, restart therapy based on the recommendations listed in Table 2 and resume the dosing schedule accordingly (see 4.2 Recommended Dose and Dosage Adjustment). Administer pre-treatment medications prior to step-up dose 1 and step-up dose 2. Monitor patients accordingly.

Table 2 – Recommendations for Restarting Therapy with Elrexfio After Dosage Delay

Last administered dose	Duration of delay from the last administered dose	Action
Step-up dose 1 (12 mg)	2 weeks or less (≤14 days)	Restart Elrexfio at step-up dose 2 (32 mg).[a] If tolerated, increase to 76 mg 4 days later.
	Greater than 2 weeks (>14 days)	Restart Elrexfio step-up dosing schedule at step-up dose 1 (12 mg).[a]
Step-up dose 2 (32 mg)	2 weeks or less (≤14 days)	Restart Elrexfio at 76 mg.
	Greater than 2 weeks to less than or equal to 4 weeks (15 days and ≤28 days)	Restart Elrexfio at step-up dose 2 (32 mg).[a] If tolerated, increase to 76 mg 1 week later.

	Greater than 4 weeks (>28 days)	Restart Elrexfio step-up dosing schedule at step-up dose 1 (12 mg).[a]
Any full treatment dose (76 mg)	6 weeks or less (≤42 days)	Restart Elrexfio at 76 mg.
	Greater than 6 weeks to less or equal to 12 weeks (43 days to ≤84 days)	Restart Elrexfio at step up dose 2 (32 mg)[a]. If tolerated, increase to 76 mg 1 week later.
	Greater than 12 weeks (>84 days)	Restart Elrexfio step-up dosing schedule at step-up dose 1 (12 mg).[a]

a. Administer pre-treatment medications prior to the Elrexfio dose.

If a dose of Elrexfio is missed, administer the dose as soon as possible, and adjust the dosing schedule as needed to maintain the dosing interval (see 4.5 Missed Dose).

Dosage Modifications for Elrexfio

Dosage reductions of Elrexfio are not recommended.

Dose delays may be required to manage toxicities related to Elrexfio (see 7 WARNINGS AND PRECAUTIONS). Recommendations on restarting Elrexfio after a dose delay are provided in Table 2.

See Tables 3 and 4 for recommended actions for adverse reactions of CRS and ICANS, respectively. See Table 5 for recommended actions for other adverse reactions following administration of Elrexfio. Consider further management per current practice guidelines.

Management of Cytokine Release Syndrome (CRS)

Identify CRS based on clinical presentation (see 7 WARNINGS AND PRECAUTIONS). Evaluate and treat other causes of fever, hypoxia, and hypotension.

If CRS is suspected, withhold Elrexfio until CRS resolves. Manage CRS according to the recommendations in Table 3 and consider further management per current practice guidelines. Administer supportive therapy for CRS, which may include intensive care for severe or life-threatening CRS and also, but not limited to, the use of anti-pyretic agents, intravenous fluid support, vasopressors, anti-IL-6 or anti-IL-6 receptor medications, corticosteroids or supplemental oxygen. Consider laboratory testing to monitor for disseminated intravascular coagulation (DIC), hematology parameters, as well as pulmonary, cardiac, renal, and hepatic function.

Table 3 – Recommendations for Management of CRS

Grade[a]	Presenting Symptoms	Actions
Grade 1	Temperature ≥38°C[b]	• Withhold Elrexfio until CRS resolves.[c]
Grade 2	Temperature ≥38°C with either: • Hypotension responsive to fluid and not requiring vasopressors, and/or • Oxygen requirement of low-flow nasal cannula[d] or blow-by	• Withhold Elrexfio until CRS resolves.[c] • Monitor patient daily for 48 hours following the next dose of Elrexfio. Instruct patients to remain within proximity of a healthcare facility.
Grade 3 (First occurrence)	Temperature ≥38°C with either: • Hypotension requiring one vasopressor with or without vasopressin, and/or • Oxygen requirement of high-flow nasal cannula[d], facemask, non-rebreather mask, or Venturi mask	• Withhold Elrexfio until CRS resolves.[c] • Provide supportive therapy, which may include intensive care. • Monitor patient daily for 48 hours following the next dose of Elrexfio. Instruct patients to remain within proximity of a healthcare facility. • Administer pretreatment medications prior to next dose of Elrexfio
Grade 3 (Recurrent)	Temperature ≥38 °C with either: • Hypotension requiring one vasopressor with or without vasopressin, and/or • Oxygen requirement of high-flow nasal cannula[d], facemask, non-rebreather mask, or Venturi mask.	• Permanently discontinue therapy with Elrexfio. • Provide supportive therapy, which may include intensive care.
Grade 4	Temperature ≥38°C with either: • Hypotension requiring multiple vasopressors (excluding vasopressin), and/or • Oxygen requirement of positive pressure (e.g., continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, and mechanical ventilation)	• Permanently discontinue therapy with Elrexfio. • Provide supportive therapy, which may include intensive care.

a. Based on American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for CRS.
b. Attributed to CRS. Fever may not always be present concurrently with hypotension or hypoxia as it may be masked by interventions such as antipyretics or anti-cytokine therapy.
c. See Table 2 for recommendations on restarting Elrexfio after dose delays.
d. Low-flow nasal cannula is ≤6 L/min, and high-flow nasal cannula is >6 L/min.

Management of Neurologic Toxicity Including ICANS

At the first sign of neurologic toxicity, including ICANS, withhold Elrexfio and consider neurology evaluation. Rule out other causes of neurologic symptoms. Provide supportive therapy, which may include intensive care, for severe or life-threatening neurologic toxicities, including ICANS (see

7 WARNINGS AND PRECAUTIONS). Manage ICANS according to the recommendations in Table 4 and consider further management per current practice guidelines.

Table 4 – Recommendations for Management ICANS

Grade[a]	Presenting Symptoms[b]	Actions
Grade 1	ICE score 7-9[c] or depressed level of consciousness[d]: awakens spontaneously.	• Withhold Elrexfio until ICANS resolves[e]. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis.
Grade 2	ICE score 3-6[c] or depressed level of consciousness[d]: awakens to voice.	• Withhold Elrexfio until ICANS resolves[e]. • Administer dexamethasone[f] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis. • Monitor patient daily for 48 hours following the next dose of Elrexfio[e]. Instruct patients to remain within proximity of a healthcare facility.

Grade[a]	Presenting Symptoms[b]	Actions
Grade 3 (First occurrence)	ICE score 0-2[c] or depressed level of consciousness[d]: awakens only to tactile stimulus, or seizures[d], either: • any clinical seizure, focal or generalized, that resolves rapidly, or • non-convulsive seizures on electroencephalogram (EEG) that resolve with intervention, or raised intracranial pressure: focal/local edema on neuroimaging[d]	• Withhold Elrexfio until ICANS resolves[e]. • Administer dexamethasone[f] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis. • Provide supportive therapy, which may include intensive care. • Monitor patient daily for 48 hours following the next dose of Elrexfio[e]. Instruct patients to remain within proximity of a healthcare facility.
Grade 3 (recurrent)	ICE score 0-2[c] or depressed level of consciousness[d]: awakens only to tactile stimulus, or seizures[d], either: • any clinical seizure, focal or generalized, that resolves rapidly, or • non-convulsive seizures on electroencephalogram (EEG) that resolve with intervention, or raised intracranial pressure: focal/local edema on neuroimaging[d]	• Permanently discontinue Elrexfio • Administer dexamethasone[f] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis. • Provide supportive therapy, which may include intensive care.

Grade[a]	Presenting Symptoms[b]	Actions
Grade 4	ICE score 0[c] or depressed level of consciousness[d] either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, or seizures[d], either: • life-threatening prolonged seizure (>5 minutes), or • repetitive clinical or electrical seizures without return to baseline in between, or motor findings[d]: • deep focal motor weakness such as hemiparesis or paraparesis, or raised intracranial pressure / cerebral oedema[d], with signs/symptoms such as: • diffuse cerebral oedema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilledema, or • Cushing's triad	• Permanently discontinue Elrexfio • Administer dexamethasone[f] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Alternatively, consider administration of methylprednisolone 1,000 mg per day intravenously for 3 days. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicinal products (e.g., levetiracetam) for seizure prophylaxis. • Provide supportive therapy, which may include intensive care.

a. Based on American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for ICANS.
b. Management is determined by the most severe event, not attributable to any other cause.
c. If patient is arousable and able to perform Immune Effector Cell-Associated Encephalopathy (ICE) Assessment, assess: Orientation (oriented to year, month, city, hospital = 4 points); Naming (name 3 objects, e.g., point to clock, pen, button = 3 points); Following Commands (e.g., "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); Writing (ability to write a standard sentence = 1 point; and Attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.
d. Not attributable to any other cause.
e. See Table 2 for recommendations on restarting Elrexfio after dose delays.
f. All references to dexamethasone administration are dexamethasone or equivalent.

Table 5 – Recommended Dosage Modifications for Other Adverse Reactions

Adverse Reactions	Severity	Actions
Hematologic Adverse Reactions (see 8 ADVERSE REACTIONS)	Absolute neutrophil count less than 0.5 X 10^9/L	• Withhold Elrexfio until absolute neutrophil count is 0.5 X 10^9/L or higher.[b]
	Febrile neutropenia	• Withhold Elrexfio until absolute neutrophil count is 1 x 10^9/L or higher and fever resolves.[b]
	Hemoglobin less than 8 g/dL	• Withhold Elrexfio until hemoglobin is 8 g/dL or higher.[b]
	Platelet count less than 25,000/mcL Platelet count between 25,000/mcL and 50,000/mcL with bleeding	• Withhold Elrexfio until platelet count is 25,000/mcL or higher and no evidence of bleeding.[b]
Infections and other Non-hematologic Adverse Reactions[a] (see 8 ADVERSE REACTIONS)	Grade 3	• Withhold Elrexfio until recovery to ≤Grade 1 or baseline.[b]
	Grade 4	• Consider permanent discontinuation of Elrexfio • If Elrexfio is not permanently discontinued, withhold subsequent treatment doses of Elrexfio (e.g., doses administered after Elrexfio step-up dosing schedule) until adverse reaction improves to Grade 1 or less.

a. Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), Version 5.0.
b. See Table 2 for recommendations on restarting Elrexfio after dose delays.

Special Populations

Elderly (65 years of age and older)

No dose adjustment is necessary (see 10.2 Pharmacodynamics and 10.3 Pharmacokinetics).

Renal impairment

No dose adjustment is recommended in patients with mild to moderate renal impairment. Elrexfio has not been studied in patients with severe renal impairment (see 10.3 Pharmacokinetics).

Hepatic impairment

No dose adjustments are required for mild hepatic impairment. The effects of moderate to severe hepatic impairment on the pharmacokinetics of elranatamab have not been studied (see 10.3 Pharmacokinetics).

Pediatric population

Health Canada has not authorized an indication for pediatric use (see 7.1.3 Pediatrics).

4.4 Administration

Elrexfio should be administered by a healthcare professional with access to appropriate medical support to manage severe reactions, including CRS and neurologic toxicity, including ICANS (see 7 WARNINGS AND PRECAUTIONS).

Elrexfio is intended for subcutaneous use by a healthcare provider only. Do not administer Elrexfio intravenously.

Pre-Treatment Medications

Administer the following pre-treatment medications approximately 1 hour before the first three doses of Elrexfio in the dosing schedule, which includes step-up dose 1, step-up dose 2, and the first full treatment dose (76 mg) as described in Table 1 to reduce the risk of CRS (see 7 WARNINGS AND PRECAUTIONS):

- acetaminophen (or equivalent) 650 mg orally
- dexamethasone (or equivalent) 20 mg orally or intravenously
- diphenhydramine (or equivalent) 25 mg orally

Preparation of Elrexfio

Elrexfio 76 mg/1.9 mL (40 mg/mL) vial and 44 mg/1.1 mL (40 mg/mL) vial are supplied as ready-to-use solutions that do not need dilution prior to administration.

Elrexfio is a clear to slightly opalescent, and colourless to pale brown liquid solution. Inspect Elrexfio visually for particulate matter and discolouration prior to administration, whenever solution and container permit. Do not administer if solution is discoloured or contains particulate matter.

Use aseptic technique to prepare and administer Elrexfio.

Elrexfio vials are single-use and do not contain any preservatives.

Prepare Elrexfio following the instructions below (see Table 6) depending on the required dose. It is suggested to use a 44 mg/1.1 mL (40 mg/mL) single-use vial for step-up dose 1 or step-up dose 2.

Table 6 - Preparation Instructions for Elrexfio

Required Dose	Dose Volume
76 mg (Full treatment dose)	1.9 mL
32 mg (Step-up dose 2)	0.8 mL
12 mg (Step-up dose 1)	0.3 mL

Remove the appropriate strength Elrexfio vial from refrigerated storage (2 °C to 8 °C). Once removed from refrigerated storage, equilibrate Elrexfio to ambient temperature (15 °C to 30 °C). Do not warm ELREXFIO in any other way.

Withdraw the required injection volume of Elrexfio from the vial into an appropriately sized syringe with stainless steel injection needles (30G or wider) and polypropylene or polycarbonate syringe material. Discard unused portion.

Once punctured, use vial and dosing syringe immediately. If the prepared dosing syringe is not used immediately, store syringe between 2°C to 30°C for a maximum of 4 hours. Discard any solution remaining in the vial after single withdrawal (see 11 STORAGE, STABILITY AND DISPOSAL).

Administration

Inject Elrexfio into the subcutaneous tissue of the abdomen (preferred injection site). Alternatively, Elrexfio may be injected into the subcutaneous tissue at other sites (e.g., thigh). Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard or not intact.

Monitoring

- Instruct the patient to remain within proximity of a healthcare facility for 48 hours after each step-up dose.
- Monitor daily for 48 hours for signs and symptoms of CRS after administration of step-up dose 1 or step-up dose 2 (See Table 1).
- Alternatively, consider monitoring the patient in hospital for 48 hours after each step-up dose (see Table 1) (see 4 DOSAGE AND ADMINISTRATION and 7 WARNINGS AND PRECAUTIONS).

4.5 Missed Dose

If a dose of Elrexfio is missed, administer the dose as soon as possible, and adjust the dosing schedule to maintain the dosing interval (see Table 1).

5 OVERDOSAGE

There has been minimal experience of overdose in clinical studies. The maximum tolerated dose of elranatamab has not been determined. In clinical studies, doses up to 76 mg once weekly have been administered.

Treatment

In the event of an overdose, the patient should be monitored for any signs or symptoms of adverse reactions and appropriate supportive treatment should be instituted immediately.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, health professionals should record the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the administered product.

Table 7 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous	Solution for injection, 40 mg/mL 44 mg/1.1 mL and 76 mg/1.9 mL single-use vials	edetate disodium dihydrate, L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sucrose, water for injection

Elrexfio is a sterile, preservative-free, clear to slightly opalescent and colourless to pale brown liquid solution supplied as:

- 76 mg/1.9 mL (40 mg/mL) in a single-use vial
- 44 mg/1.1 mL (40 mg/mL) in a single-use vial

Elrexfio is supplied in a single-use glass vial sealed with a chlorobutyl rubber stopper (rubber serum stopper) and an aluminum seal with a flip-off cap. Each Elrexfio carton contains 1 glass vial.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

Driving and Operating Machinery

Elrexfio may impair one's ability to drive and use machines.

Due to the potential for neurologic toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), patients receiving Elrexfio are at risk of depressed level of consciousness (see 8 ADVERSE REACTIONS). Advise patients not to drive or operate heavy or potentially dangerous machinery during the Elrexfio step-up dosing schedule and for 48 hours after completing each of the 2 step-up doses within the Elrexfio and in the event of new onset of neurologic toxicity until resolution of any neurological symptoms.

Hematologic

Neutropenia

Elrexfio can cause neutropenia and febrile neutropenia. In patients who received Elrexfio at the recommended dose in the clinical trial, decreased neutrophils occurred in 61.7%, with Grade 3 or 4 neutrophil decrease in 50.8%. Febrile neutropenia occurred in 2.2% of patients (see 8 ADVERSE REACTIONS).

Monitor complete blood cell counts at baseline and periodically during treatment. Provide supportive care according to current practice guidelines. Monitor patients with neutropenia for signs of infection. Withhold Elrexfio based on severity (see 4.2 Recommended Dose and Dosage Adjustment, Dosage Modifications for Elrexfio).

Hepatic

Elrexfio can cause hepatotoxicity. In the clinical trial, elevated ALT occurred in 36% of patients, with Grade 3 or 4 ALT elevation occurring in 3.8%; elevated AST occurred in 40% of patients, with Grade 3 or 4 AST elevation occurring in 6%. Grade 3 or 4 total bilirubin elevations occurred in 0.5% of patients. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold Elrexfio or consider permanent discontinuation of Elrexfio based on severity.

Immune

Concomitant use of Live Viral Vaccines

The safety of immunization with live viral vaccines during or following Elrexfio treatment has not been studied. Vaccination with live virus vaccines is not recommended within 4 weeks of the first dose of Elrexfio and during treatment with Elrexfio.

Cytokine Release Syndrome (CRS)

Elrexfio can cause CRS, including life-threatening or fatal reactions (see 8 ADVERSE REACTIONS).

In the clinical trial, CRS occurred in 57.9% of patients who received Elrexfio at the recommended dosing schedule (see 4.2 Recommended Dose and Dosage Adjustment), with Grade 1 CRS in 43.7% of patients, Grade 2 CRS in 13.7% of patients, and Grade 3 CRS in 0.5% of patients. Recurrent CRS occurred in 13.1% of patients. CRS was most common after the first step-up dose (43.2% of patients) or the second step-up dose (19.1% of patients), with 7.1% of patients having CRS after the first treatment dose (76 mg) and 1.6% of patients after a subsequent dose. The median time to onset of CRS was 2 (range: 1 to 9) days after the most recent dose, with a median duration of 2 (range: 1 to 19) days.

Clinical signs and symptoms of CRS may include, but are not limited to, fever, hypoxia, chills, hypotension, tachycardia, headache, and elevated liver enzymes. Among patients who received Elrexfio according to the recommended dosing schedule, 19.1% received tocilizumab (or siltuximab) and 8.7% received corticosteroids for treatment of CRS.

Initiate therapy according to Elrexfio step-up dosing schedule to reduce risk of CRS. Administer pre-treatment medications prior to the first three doses of Elrexfio to reduce risk of CRS and monitor patients following administration of Elrexfio accordingly (see 4.2 Recommended Dose and Dosage Adjustment).

Counsel patients to seek medical attention should signs or symptoms of CRS occur. At the first sign of CRS, immediately evaluate the patient's need for hospitalization. Manage CRS according to the

recommendations in Table 3 and consider further management per current practice guidelines. Supportive therapy for CRS (including but not limited to anti-pyretic agents, intravenous fluid support, vasopressors, corticosteroids, anti-IL-6 or anti-IL-6 receptor medications, supplemental oxygen) should be administered as appropriate. Laboratory testing to monitor for disseminated intravascular coagulation (DIC), hematology parameters, as well as pulmonary, cardiac, renal and hepatic function should be considered. Withhold or permanently discontinue Elrexfio based on severity (see 4.2 Recommended Dose and Dosage Adjustment, Dosage Modifications for Elrexfio).

Hypogammaglobulinemia

Hypogammaglobulinemia was reported as an adverse reaction in 13.1% of patients receiving Elrexfio at the recommended dosage in the clinical trial (see 8 ADVERSE REACTIONS).

Monitor immunoglobulin levels during treatment with Elrexfio. Consider subcutaneous or intravenous immunoglobulin therapy if IgG levels fall below 400 mg/dL and treat patients according to current practice guidelines, including infection precautions and antimicrobial prophylaxis.

Infections

Elrexfio can cause severe, life-threatening, or fatal infections. In the clinical trial, in patients who received Elrexfio according to the recommended dosing schedule, serious infections, including opportunistic infections, occurred in 41.5% of patients, with Grade 3 or 4 infections in 31.1%, and fatal infections in 6.6% (see 8 ADVERSE REACTIONS). Opportunistic infections included cytomegalovirus infection reactivation, pneumocystis jirovecii pneumonia, adenovirus infection, and hepatitis B reactivation. Progressive multifocal leukoencephalopathy (PML) has also occurred in therapy with Elrexfio.

Do not initiate treatment with Elrexfio in patients with active infections. Monitor patients for signs and symptoms of infection prior to and during treatment with Elrexfio and treat appropriately. Withhold Elrexfio based on severity (see 4.2 Recommended Dose and Dosage Adjustment, Dosage Modifications for Elrexfio). Administer prophylactic antimicrobials and anti-virals according to current practice guidelines. Consider treatment with subcutaneous or intravenous immunoglobulin (IVIG) as appropriate (see 7 WARNINGS AND PRECAUTIONS, Immune, Hypogammaglobulinemia).

Hepatitis B Virus reactivation

Hepatitis B virus reactivation has been reported in patients treated with drugs directed against B cells, and in some cases, may result in fulminant hepatitis, hepatic failure, and death.
Patients with evidence of positive HBV serology should be monitored for clinical and laboratory signs of HBV reactivation while receiving Elrexfio, and for at least six months following the end of treatment.

In patients who develop reactivation of HBV while on Elrexfio, withhold treatment with Elrexfio as indicated in Table 5 and manage per local institutional guidelines (see 4 DOSAGE AND ADMINISTRATION).

Neurologic

Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

Elrexfio can cause serious or life-threatening neurologic toxicity, including ICANS.

In the clinical trial, neurologic toxicity occurred in 59% of patients who received Elrexfio at the recommended dosing schedule (see 4.2 Recommended Dose and Dosage Adjustment), with Grade 3 neurologic toxicity occurring in 7.1% of patients. Neurologic toxicities included headache (18%),

encephalopathy (14%), sensory neuropathy (13%), motor dysfunction (14%) and Guillain-Barre Syndrome (0.5%).

In the clinical trial, ICANS occurred in 3.3% of patients who received Elrexfio at the recommended dosing schedule (see 4.2 Recommended Dose and Dosage Adjustment). Most patients had ICANS after the first step-up dose (2.7%), 1 (0.5%) patient had ICANS after the second step-up dose and 1 (0.5%) patient had ICANS after subsequent dose(s). Recurrent ICANS occurred in 1.1% of patients. The median time to onset was 3 (range: 1 to 4) days after the most recent dose, with a median duration of 2 (range: 1 to 18) days. The most frequent clinical manifestations of ICANS included a depressed level of consciousness and Grade 1 or Grade 2 Immune Effector Cell-Associated Encephalopathy (ICE) scores. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Among patients who received Elrexfio at the recommended dosing schedule, 2.2% received corticosteroids, 1.1% received tocilizumab (or siltuximab), and 0.5% received anakinra for treatment of ICANS.

Counsel patients to seek medical attention should signs or symptoms of neurologic toxicity occur. Monitor patients for signs and symptoms of neurologic toxicities during treatment with Elrexfio. At the first sign of neurologic toxicity, including ICANS, evaluate and treat patients immediately based on severity. Withhold or permanently discontinue Elrexfio based on severity per recommendations in Table 4 and consider further management per current practice guidelines.

Reproductive Health: Female and Male Potential

Elrexfio may cause fetal harm when administered to a pregnant woman (see 7.1.1 Pregnant women).

Pregnancy Testing

Verify the pregnancy status of females of reproductive potential prior to initiating treatment with Elrexfio.

Contraception

Advise women of reproductive potential to use effective contraception during treatment and for 5 months after the last dose.

Fertility

There are no data on the effect of Elrexfio on human fertility. Effects of elranatamab on male and female fertility have not been evaluated in animal studies.

7.1 Special Populations

7.1.1 Pregnant Women

There are no human or animal data to assess the risk of elranatamab use during pregnancy. Human immunoglobulin (IgG) is known to cross the placenta after the first trimester of pregnancy. Based on the mechanism of action, elranatamab may cause fetal harm when administered to a pregnant woman and therefore Elrexfio is not recommended for use during pregnancy (see 10.1 Mechanism of Action).

Elrexfio is associated with hypogammaglobulinemia, therefore, assessment of immunoglobulin levels in newborns of mothers treated with Elrexfio should be considered.

7.1.2 Breast-feeding

It is not known whether elranatamab is excreted in human or animal milk, affects breastfed infants or affects milk production. Human IgGs are known to be excreted in breast milk.

A risk to the breastfed child cannot be excluded and therefore breast-feeding is not recommended during treatment with Elrexfio and for 5 months after the last dose.

7.1.3 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics

Geriatrics (≥ 65 years of age): Of the 183 patients with relapsed or refractory multiple myeloma treated with Elrexfio in study C1071003 at the recommended dosage, 62.0% were 65 years of age or older, and 19.3% were 75 years of age or older. No overall differences in safety or effectiveness were observed between patients ≥65 and ≥75 years of age compared to younger patients.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The following adverse reactions associated with Elrexfio are discussed in detail under 7 WARNINGS AND PRECAUTIONS. Appropriate management and dosing considerations regarding these adverse events are outlined under 4 DOSAGE AND ADMINISTRATION, Dosage modifications for Elrexfio.

- Cytokine release syndrome
- Neurologic toxicity, including ICANS
- Infections
- Hypogammaglobulinemia
- Neutropenia

The most frequent adverse reactions of any grade in patients enrolled in study C1071003 who received the recommended dosing regimen were CRS (57.9%), anaemia (53.6%), neutropenia (44.3%), fatigue (42.6%), injection site reaction (37.2 %), diarrhea (35.5%), upper respiratory tract infection (34.4%), thrombocytopenia (35.0%), pneumonia (31.7%), lymphopenia (29.5%), decreased appetite (26.2%), rash (25.7%), arthralgia (21.9%), nausea (21.3%), hypokalemia (21.3%), and pyrexia (21.3%).

Serious adverse reactions were reported in 68.3% of patients who received Elrexfio, including pneumonia (25.1%), sepsis (13.1%), CRS (12.6%), anaemia (5.5%), upper respiratory tract infection (4.4%), urinary tract infection (3.3%), dyspnoea (2.2%), pyrexia (2.2%), and febrile neutropenia (2.2%).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Relapsed/Refractory Multiple Myeloma

The clinical trial data described in 7 WARNINGS AND PRECAUTIONS and in this section reflect exposure to Elrexfio in study C1071003 in 183 patients who received the recommended dose regimen (N=183 including 64 patients with prior BCMA-directed antibody drug conjugate [ADC] or chimeric antigen receptor [CAR] T cell therapy [supportive Cohort B]). Among patients who received Elrexfio, 42.1% were exposed for 6 months or longer and 9.3% were exposed for one year or longer. The median duration of Elrexfio treatment was 4.1 (range: 0.03 to 14.9) months.

The median age of patients who received Elrexfio was 68 years (range: 36 to 88 years); 52% were male; 61% were White, 10% were Hispanic/Latino, 9% were Asian, and 6% were Black.

Table 8 summarizes adverse reactions with ≥10% incidence.

Table 8 – Adverse Reactions (≥10%) in Patients who Received Elrexfio in Study C1071003 (MagnetisMM-3)

System Organ Class Preferred Term	Elrexfio n = 183	
	All Grades (%)	Grade 3/4 (%)
Blood and lymphatic system disorders		
Anemia[a]	53.6	42.1
Neutropenia[b]	44.3	42.6
Thrombocytopenia[c]	35.0	25.1
Lymphopenia[d]	29.5	27.3
Leucopenia[e]	15.8	10.9
Cardiac disorders		
Cardiac arrhythmia[f]	16.4	1.6
Gastrointestinal disorders		
Diarrhea	35.5	1.1
Nausea	21.3	0
Constipation	14.2	0
Vomiting	14.2	0
General disorders and site administration conditions		
Fatigue[g]	42.6	5.5
Injection site reaction[h]	37.2	0
Pyrexia	21.3	2.7
Edema[i]	18.0	1.1
Immune system disorders		
Cytokine release syndrome	57.9	0.5
Hypogammaglobulinemia[j]	13.1	2.2
Infections and infestations		
Upper respiratory tract infection[k]	34.4	4.9
Pneumonia[l]	31.7	19.1
Sepsis[m]	15.3	10.9
Urinary tract infection[n]	12.0	4.4
Injury, poisoning and procedural complications		
Fall	10.4	0.5

System Organ Class Preferred Term	Elrexfio n = 183	
	All Grades (%)	Grade 3/4 (%)
Investigations		
Transaminases increased[o]	15.8	4.9
Metabolism and nutrition disorders		
Decreased appetite	26.2	1.1
Hypokalemia	21.3	8.2
Musculoskeletal and connective tissue disorders		
Arthralgia[p]	21.9	1.1
Nervous system disorders		
Headache	18.0	0
Encephalopathy[q]	14.2	2.2
Sensory neuropathy[r]	12.6	0.5
Motor dysfunction[s]	14.2	1.1
Psychiatric disorders		
Insomnia	13.1	0
Respiratory, thoracic and mediastinal disorders		
Cough[t]	24.0	0
Dyspnea[u]	15.8	3.8
Skin and Subcutaneous Tissue disorders		
Rash[v]	25.7	0
Dry skin	13.7	0
Skin exfoliation[w]	10.4	0
Vascular disorders		
Hemorrhage[x]	12.6	1.6

a. Anemia includes anaemia, haemoglobin decreased, red blood cell count decreased, haematocrit decreased, normochromic anaemia, normocytic anaemia, normochromic normocytic anaemia, aplasia pure red cell.
b. Neutropenia includes neutropenia, neutrophil count decreased, neutrophil percentage decreased, cyclic neutropenia, agranulocytosis, granulocytopenia, granulocyte count decreased.
c. Thrombocytopenia includes thrombocytopenia, platelet count decreased.
d. Lymphopenia includes lymphopenia, lymphocyte count decreased, lymphocyte percentage decreased, CD4 lymphocytes decreased, CD4 lymphocyte percentage decreased, CD8 lymphocytes decreased, CD8 lymphocyte percentage decreased.
e. Leucopenia includes leucopenia, white blood cell count decreased.
f. Cardiac arrhythmia includes atrial fibrillation, bradycardia, sinus bradycardia, sinus tachycardia, tachycardia, ventricular extrasystoles, ventricular tachycardia.
g. Fatigue includes fatigue, asthenia, malaise.
h. Injection site reaction includes injection site reaction, injection site erythema, injection site pruritus, injection site rash, injection site induration, injection site pain, injection site urticaria, injection site dryness, injection site haemorrhage, injection site inflammation.
i. Edema includes oedema, oedema peripheral, eye oedema, fluid retention, lip oedema, localised oedema, periorbital oedema, peripheral swelling.
j. Hypogammaglobulinemia includes participants with adverse events of blood immunoglobulin G decreased, hypogammaglobulinaemia, immunoglobulins decreased.
k. Upper respiratory tract infection includes upper respiratory tract infection, sinusitis, acute sinusitis, pharyngitis, rhinitis, rhinovirus infection, viral upper respiratory tract infection, bronchitis viral, chronic

sinusitis, nasopharyngitis, sinusitis bacterial, bronchitis, respiratory tract infection viral.

l. Pneumonia includes pneumonia, COVID-19 pneumonia, bronchopulmonary aspergillosis, lower respiratory tract infection, lower respiratory tract infection viral, pneumocystis jirovecii pneumonia, pneumonia adenoviral, pneumonia bacterial, pneumonia cytomegaloviral, pneumonia fungal, pneumonia influenzal, pneumonia pseudomonal, pneumonia viral.

m. Sepsis includes sepsis, bacteraemia, device related bacteraemia, device related sepsis, escherichia bacteraemia, escherichia sepsis, klebsiella sepsis, pseudomonal sepsis, septic shock, staphylococcal bacteraemia, staphylococcal sepsis, streptococcal sepsis, urosepsis.

n. Urinary tract infection includes urinary tract infection, cystitis, urinary tract infection bacterial, escherichia urinary tract infection, urinary tract infection enterococcal.

o. Transaminases increased includes alanine aminotransferase increased and aspartate aminotransferase increased.

p. Arthralgia includes arthralgia, pain in extremity.

q. Encephalopathy includes agitation, altered state of consciousness, cognitive disorder, confusional state, delirium, depressed level of consciousness, disorientation, hallucination, lethargy, memory impairment, metabolic encephalopathy, somnolence, toxic encephalopathy.

r. Sensory neuropathy includes burning sensation, dysesthesia, hypoesthesia, neuropathy peripheral, paresthesia, parosmia, peripheral sensorimotor neuropathy, peripheral sensory neuropathy, polyneuropathy, sensory loss.

s. Motor dysfunction includes ataxia, balance disorder, gait disturbance, motor dysfunction, muscle contracture, muscle spasms, muscular weakness, peripheral motor neuropathy, peroneal nerve palsy, tremor.

t. Cough includes cough, productive cough, upper-airway cough syndrome.

u. Dyspnea includes dyspnea, dyspnea exertional, respiratory distress.

v. Rash incudes erythema, palmar-plantar erythrodysaesthesia syndrome, rash, rash erythematous, rash macular, rash maculo-papular, rash pustular, symmetrical drug-related intertriginous and flexural exanthema.

w. Skin exfoliation includes dermatitis exfoliative, dermatitis exfoliative generalised, skin exfoliation.

x. Hemorrhage includes anal haemorrhage, conjunctival haemorrhage, diarrhoea haemorrhagic, ear haemorrhage, epistaxis, haemarthrosis, haematoma, haematoma muscle, haematuria, haemorrhoidal haemorrhage, intestinal haemorrhage, rectal haemorrhage, subdural haematoma, upper gastrointestinal haemorrhage, vascular access site haemorrhage.

8.3 Less Common Clinical Trial Adverse Reactions

Clinically relevant adverse reactions in <10% of patients who received Elrexfio included the following: ICANS (3.3%) and febrile neutropenia (2.2%).

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

Table 9 summarizes laboratory abnormalities in patients who received the recommended dose regimen in study C1071003.

Table 9 – Select Laboratory Abnormalities (≥30%) That Worsened from Baseline in Patients Who Received Elrexfio in Study C1071003

Laboratory Abnormality	Elrexfio n = 183	
	All Grades (%)	Grade 3/4 (%)
Hematology		
Hemoglobin decreased	68.1	43.4
Lymphocyte count decreased	90.7	83.6
Neutrophil count decreased	61.7	50.8
Platelet count decreased	61.2	31.7
White blood cell decreased	68.9	40.4
Chemistry		
Albumin decreased	55.2	5.5
Alkaline phosphatase increased	34.4	1.1
ALT increase	35.5	3.8
AST increase	39.8	5.5
Creatinine clearance decreased	32.2	9.9
Creatinine increased	37.9	3.3
Potassium decrease	36.3	8.2

Laboratory tests were graded according to NCI CTCAE Version 5.0.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No clinical studies evaluating the drug interaction potential of elranatamab have been conducted.

Elrexfio causes release of cytokines (see 10.2 Pharmacodynamics) that may suppress activity of cytochrome P450 (CYP) enzymes, resulting in increased exposure of CYP substrates. The highest risk of drug-drug interaction is expected to occur during and up to 14 days after the step-up dosing schedule for Elrexfio (see 4 DOSAGE AND ADMINISTRATION) as well as during and up to 14 days after CRS. Monitor for toxicity or concentrations of drugs that are sensitive CYP substrates where minimal concentration changes may lead to serious adverse reactions. Adjust the dose of the concomitant CYP substrate drug as needed.

9.3 Drug-Food Interactions

No formal drug-food interaction studies have been conducted with Elrexfio.

9.4 Drug-Herb Interactions

No formal drug-herb interaction studies have been conducted with Elrexfio.

9.5 Drug-Laboratory Test Interactions

No formal drug-laboratory test interaction studies have been conducted with Elrexfio.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Elranatamab is a bispecific B-cell maturation antigen (BCMA)-directed T-cell engaging antibody that binds BCMA on plasma cells, plasmablasts, and multiple myeloma cells and CD3-epsilon on T cells leading to selective cytolysis of the BCMA expressing cells. The anticancer activity of elranatamab involves selective therapeutic targeting and activation of T cells re-directed against BCMA-expressing malignant plasma cells. Elranatamab activated T-cells, caused proinflammatory cytokine release, and resulted in multiple myeloma cell lysis.

10.2 Pharmacodynamics

Exposure-Response Relationships

Serum concentrations of cytokines (IL-2, IL-6, IL-8, IL-10, TNF-α, and IFN-γ) were measured before and after administration of step-up dose 1, step-up dose 2, and the first three full treatment doses of Elrexfio. Time of the maximum cytokine concentration generally occurred during the step-up dosing and concentrations continue to decrease over the course of the first month of treatment.

10.3 Pharmacokinetics

Pharmacokinetic parameters are presented as a geometric mean (coefficient of variation [CV]%) and are based upon subcutaneously administered unless otherwise specified.

The C_{max} and AUC_{tau} of unbound elranatamab after the first subcutaneous dose increased in an approximately dose proportional manner over the evaluated dose range via SC administration (~6 to 76 mg). The median accumulation ratios after 24 weeks of weekly dosing (steady state), relative to the first subcutaneous dose of elranatamab 76 mg, for C_{max} and AUC_{tau} were observed to be 6.6-fold and 11.2-fold, respectively. The summary of predicted unbound elranatamab pharmacokinetics parameters presented in Table 10, and the PK parameters in the text below, are based on estimates from a population pharmacokinetic (POPPK) model.

Table 10 - Geometric mean (CV%) of Predicted Elranatamab Pharmacokinetic Parameters After Dosing via SC Administration (76 mg) in Patients with Relapsed or Refractory Multiple Myeloma

Timepoint	Parameters		
	C_{avg} (mcg/mL)	C_{max} (mcg/mL)	C_{trough} (mcg/mL)
End of weekly dose (week 24)[a]	32.0 (46%)	33.0 (46%)	30.5 (48%)
Steady state (biweekly dosing)[a,b]	17.7 (53%)	19.5 (51%)	15.1 (60%)
Steady state (every 4 weeks dosing)[a,c]	8.8 (58%)	11.5 (54%)	5.9 (78%)

Abbreviations: C_{max}=maximum serum concentration; Cavg=average drug concentration during the dosing interval; C_{trough}=trough concentration.

a. In patients who have achieved a response.
b. Steady state exposure of elranatamab biweekly dose is approximated at week 48.
c. Steady state exposure of elranatamab once every 4 weeks dose is approximated at week 72.

Absorption

The predicted mean bioavailability of elranatamab was 56.2% when administered subcutaneously. The median T_{max} after the first dose of elranatamab SC administration across all SC dose levels ranged from 3 to 7 days.

Distribution

The mean (coefficient of variation [CV]%) central volume of distribution of unbound elranatamab in the population PK model was estimated to be 4.78 L (69%). The mean peripheral volume of distribution was 2.83 L.

Metabolism

Metabolism studies were not conducted with elranatamab as these are not considered necessary or relevant for biologics. Similar to other therapeutic proteins with molecular weights above the glomerular filtration cut-off, elranatamab is expected to be metabolized primarily by catabolic degradation following endocytosis by the mononuclear phagocytic system.

Elimination

The predicted half-life of unbound elranatamab from the population PK model was 22 days (64%) at the 76 mg dose. The clearance estimated from the population PK model was 0.324 L/day (100%).

Special Populations and Conditions

Age, ethnic origin, sex and Obesity: No clinically relevant differences in the pharmacokinetics of elranatamab were observed age (36 to 89 years), sex (167 male, 154 female), race (193 White, 49 Asian, 29 Black), and body weight (37 to 160 kg).

Hepatic Impairment: No formal studies of Elrexfio in patients with hepatic impairment have been conducted. Based on population pharmacokinetics covariate analysis, free elranatamab exposure in the model was not affected by mild hepatic impairment (total bilirubin >1 to 1.5 times upper limit of normal (ULN) and any aspartate aminotransferase (AST), or total bilirubin ≤ULN and AST>ULN). No data are available in patients with moderate (total bilirubin >1.5 to 3.0 x ULN and any AST) or severe (total bilirubin >3.0 x ULN and any AST) hepatic impairment.

Renal Impairment*:* No formal studies of Elrexfio in patients with renal impairment have been conducted. Based on population pharmacokinetics covariate analysis, free elranatamab exposure in the model was not affected by mild (60 mL/min/1.73 m^2 ≤estimated glomerular filtration rate (eGFR) <90 mL/min/1.73 m^2) or moderate renal impairment (30 mL/min/1.73 m^2 ≤eGFR <60 mL/min/1.73 m^2). Limited data are available in patients with severe renal impairment.

11 STORAGE, STABILITY AND DISPOSAL

Store at 2°C to 8°C in the original carton until time of use to protect from light.

Do not freeze or shake the vial or carton.

12 SPECIAL HANDLING INSTRUCTIONS

Once punctured, the vial and dosing syringe should be used immediately. If the prepared dosing syringe is not used immediately, store syringe between 2°C to 30°C for a maximum of 4 hours. The vial and any contents remaining after withdrawal of a single-use should be discarded. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

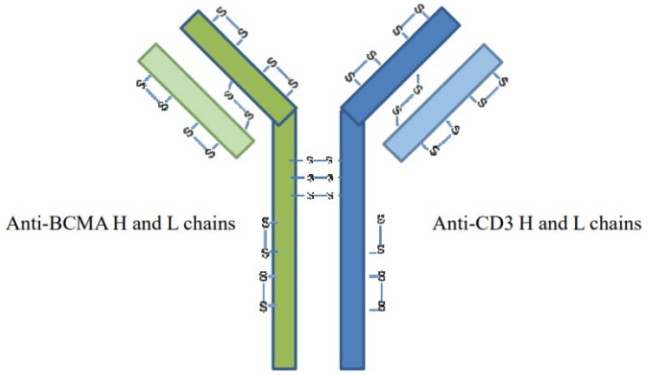
Drug Substance

Proper name: elranatamab injection

Chemical name: Not applicable. Elranatamab a recombinant humanized bispecific antibody.

Molecular formula and molecular mass: Elranatamab is a recombinant humanized bispecific antibody (immunoglobulin gamma-2 with kappa light chains, IgG2 kappa), with one heavy chain / light chain pair directed against cluster of differentiation 3 (CD3) and one heavy chain/light chain pair directed against B-cell maturation antigen (BCMA). The molecular weight of elranatamab is approximately 148.5 kDa.

Structural formula:



Physicochemical properties:

Elranatamab injection is a sterile, preservative-free, clear to slightly opalescent, and colourless to pale brown liquid solution for subcutaneous administration. The pH is 5.8.

Product Characteristics:

Elranatamab is a bispecific, humanized modified immunoglobulin 2 (IgG2) kappa antibody derived from two monoclonal antibodies (mAbs), an anti-BCMA mAb and an anti-CD3 mAb. Each of these mAbs contributes one distinct heavy (H) chain and one distinct light (L) chain to the bispecific elranatamab. The resulting 4-chain bispecific antibody is covalently linked via five inter-chain disulfide bonds.

Elranatamab is produced using two recombinant Chinese hamster ovary (CHO) cell lines, one that contains the DNA encoding the sequence for anti-BCMA monoclonal antibody (mAb) and one that contains the sequence for anti-CD3 mAb, which are grown separately in suspension culture using chemically-defined (CD), animal-derived component-free (ACF) media.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Relapsed or refractory multiple myeloma

The efficacy of Elrexfio monotherapy was evaluated in adult patients with relapsed or refractory multiple myeloma in an open-label, non-randomized, multi-center, Phase 2 study (MagnetisMM-3, C1071003). The study included patients who were refractory to at least one proteasome inhibitor (PI), one immunomodulatory agent (IMiD), and one anti-CD38 monoclonal antibody. MagnetisMM-3 included 123 patients who were naïve to prior BCMA-directed therapy (pivotal Cohort A). Patients had measurable disease by International Myeloma Working Group (IMWG) criteria at enrollment. The study included patients with an Eastern Cooperative Oncology Group (ECOG) score of ≤2, adequate baseline bone marrow (absolute neutrophil count ≥1.0 x 10^9/L, platelet count ≥25 x 10^9/L, hemoglobin level ≥8 g/dL), renal (CrCL ≥ 30 mL/min), and hepatic (AST and ALT ≤2.5 x ULN, total bilirubin ≤2 x ULN) function, and left ventricular ejection fraction ≥40%. Stem cell transplant within 12 weeks prior to enrollment; active infection; ongoing grade ≥2 peripheral sensory or motor neuropathy; and history of Guillain-Barre syndrome (GBS), GBS variants, or grade ≥ 3 peripheral motor polyneuropathy were study exclusion criteria.

Eligible patients were administered Elrexfio by subcutaneous injection at step-up doses of 12 mg on Day 1 and 32 mg on Day 4. On day 8, patients received the first treatment dose of Elrexfio (76 mg). Thereafter, patients received 76 mg once weekly. After 24 weeks, in patients who achieved an IMWG response category of partial response or better with responses persisting for at least 2 months, the dose interval was changed from 76 mg every week to 76 mg every 2 weeks, and from every 2 weeks to every 4 weeks after at least 24 weeks of 76 mg every 2 weeks dosing (see 4 DOSAGE AND ADMINISTRATION).

Table 11 - Summary of patient demographics in study C1071003 MagnetisMM-3

Study #	Study design	Dosage, route of administration and duration	Study subjects (N)	Mean age (Range)	Sex
C1071003	Phase 2, open label, multicenter, non-randomized study of elranatamab monotherapy in participants with MM who are refractory to at least one proteasome inhibitor, one immunomodulatory drug and one anti-CD38 antibody	Elranatamab monotherapy SC QW at 76 mg starting Day 8 with step-up priming doses of 12 mg on Day 1 and 32 mg on Day 4. After 24 weeks, for patients who achieved PR or better for at least 2 months, SC Q2W at 76 mg and from Q2W to Q4W after at least 24 weeks of 76 mg every Q2W dosing. Cohort A (pivotal): No prior BCMA-directed treatment	N= 123 Cohort A: 123	Cohort A: 68 (36 to 89) years	Cohort A: 68 (55.3%) Male 55 (44.7%) Female

Abbreviations: ADC = antibody drug conjugate; BCMA = B cell maturation antigen; CAR-T = chimeric antigen receptor T-cell therapy; MM = multiple myeloma; PR = Partial Response; QW = weekly; Q2W = once every two weeks; SC = subcutaneous.

Among the 123 patients treated in pivotal Cohort A, the median age was 68 (range: 36 to 89) years with 19.5% of patients ≥75 years of age. Forty-five percent were female; 58.5% were White, 13.0% were Asian, 8.9% were Hispanic/Latino, 7.3% were Black. Disease stage (R-ISS) at study entry was 22.8% in Stage I, 55.3% in Stage II, and 15.4% in Stage III. The median time since initial diagnosis of multiple myeloma to enrollment was 72.9 (range: 16 to 228) months. Patients had received a median of 5 prior lines of therapy (range: 2 to 22) with 96.0% having received ≥3 prior lines of therapy. Ninety-seven percent were triple-class refractory, and 95.9% were refractory to their last line of therapy. Sixty-eight percent received prior autologous stem cell transplantation, and 5.7% received prior allogenic stem cell transplantation. High-risk cytogenetics [t(4;14), t(14;16),or del(17p)] were present in 25.2% of patients. Thirty-two percent of patients had extramedullary disease [presence of any plasmacytoma (extramedullary and/or paramedullary) with a soft-tissue component] at baseline by Blinded Independent Central Review (BICR).

Efficacy results were based on response rate and duration of response (DOR), as assessed by BICR based on the IMWG criteria. Results from BCMA-directed therapy naïve patients (pivotal Cohort A) are shown in Table 12. The median (range) follow-up for responders was 10.9 (3.6,20.1) months.

Table 12 – Efficacy Results of MagnetisMM-3 study (pivotal Cohort A) in Relapsed or Refractory Multiple Myeloma

	Elrexfio BCMA-directed therapy naïve subjects (Cohort A) (N = 123)
Objective Response Rate (ORR: sCR+CR+VGPR+PR), n (%)(95% CI)	75 (61.0%) (51.8, 69.6)
Stringent complete response (sCR)	16 (13.0%)
Complete response (CR)	18 (14.6%)
Very good partial response (VGPR)	34 (27.6%)
Partial response (PR)	7 (5.7%)
Complete Response Rate (sCR+CR), n (%) (95% CI)	34 (27.6%) (20.0, 36.4)
Duration of Response (DOR) (months)	
Number of responders	75
Median[a] (95% CI)	NR (12.0, NE)
Probability of retaining response at 6 months[a] (95% CI)	90 (80.2, 95.1)
Probability of retaining response at 9 months[a] (95% CI)	84.4 (72.7, 91.4)

Abbreviations: CI = Confidence interval; NR = Not reached; NE = Not estimable

[a] Kaplan-Meier estimate

Among responders (n=75), the median time to first response was 1.2 months (range 0.9 – 7.4 months).

After a median (range) follow-up of 27.9 (3.6, 36.8) months for responders, the ORR was 61.0% (95% CI: 51.8, 69.6), with 16.3% of patients achieving sCR, 21.1% of patients achieving CR, 18.7% of patients achieving VGPR, and 4.9% of patients achieving a PR. The median duration of response was not estimable (95% CI: NE, NE). The probability of retaining response at 12 months was 73.4% (95% CI: 61.4, 82.1), and 66.9% (95% CI: 54.4, 76.7) at 24 months.

14.3 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies (ADA) in the studies described below with the incidence of anti-drug antibodies in other studies, including those of elranatamab or of other elranatamab products.

In the MagnetisMM-3 study, 16 out of 168 participants evaluable for immunogenicity (9.5%) treated with Elrexfio for up to 36 months at the recommended dose developed anti-elranatamab antibodies. There was no identified clinically significant effect of aDA on PK, safety or effectiveness of elranatamab.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: Pivotal 1- and 3-month toxicity studies using the subcutaneous route were conducted with Elrexfio in cynomolgus monkey. The key effects identified in these studies were increased cytokines, decreased BCMA-expressing cells (a subset of B cells and plasma cells), fluctuations in peripheral T cell and NK cell numbers, immunosuppression and secondary infection.

Carcinogenicity: Carcinogenicity studies with Elrexfio have not been conducted.

Genotoxicity: Genotoxicity studies with Elrexfio have not been conducted.

Reproductive and Developmental Toxicology: Reproductive and developmental toxicity studies with Elrexfio have not been conducted.

Due to B cell lymphocytopenia and the potential impact of CRS on pregnancy, there is a probable risk of fetal harm associated with the use of Elrexfio.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr ELREXFIO®

(elranatamab injection)

Read this carefully before you start receiving **Elrexfio** and each time you get an injection. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Elrexfio**.

Serious Warnings and Precautions

- A serious side effect called cytokine release syndrome (CRS), which can be severe or fatal, may occur. Symptoms usually include fever (38°C or higher) and chills. Other symptoms of CRS may include difficulty in breathing, dizziness or feeling light-headed, feeling the need to throw up, headache, fast heartbeat, low blood pressure, feeling tired, vomiting, muscle pain and joint pain.
- Serious or life-threatening neurologic problems may occur after taking Elrexfio. Symptoms may include headache, confusion, difficulty with memory, difficulty speaking or slow speech, difficulty understanding speech, difficulty in writing, being confused about time or surroundings, being less alert, or excessive sleepiness, and seizures (fits). Some of these may be signs of a serious immune reaction called 'immune effector cell associated neurotoxicity syndrome' (ICANS). These effects can occur days or weeks after you receive the injection, and may be subtle at first.
- Your healthcare provider will monitor for signs and symptoms of CRS and neurological problems during treatment with Elrexfio. You should call your healthcare provider right away if you develop any of the signs and symptoms of CRS or neurologic problems at any time during your treatment with Elrexfio.

What is Elrexfio used for?

- Elrexfio is a cancer medicine that contains the active substance "elranatamab" and is used to treat adults with a type of cancer of the bone marrow called multiple myeloma.
- It is used for patients who have had at least three different treatments that have not worked or have stopped working.

"For the following indication(s) Elrexfio has been approved with conditions (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional."

- the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How does Elrexfio work?

Elrexfio is an antibody, a type of protein which has been designed to recognize and attach to specific targets in your body. Elrexfio targets B cell maturation antigen (BCMA), which is found on multiple myeloma cancer cells, and cluster of differentiation 3 (CD3), which is found on T cells of your immune system. This medicine works by attaching to these cells and bringing them together, so that your immune system can kill the multiple myeloma cancer cells.

What are the ingredients in Elrexfio?

Medicinal ingredients: elranatamab

Non-medicinal ingredients: edetate disodium dihydrate, L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sucrose, water for injection.

Elrexfio comes in the following dosage forms:

- Solution for injection, 44 mg/1.1 mL (40 mg/mL)
- Solution for injection, 76 mg/1.9 mL (40 mg/mL)

Do not use Elrexfio if:

- you are allergic to elranatamab or any of the other ingredients of this medicine. If you are not sure if you are allergic, talk to your doctor or nurse before you are given Elrexfio.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Elrexfio. Talk about any health conditions or problems you may have, including if you:

- had any infection within the last 4 weeks. Before you are given Elrexfio, your doctor will check your blood counts for signs of infection. If you have any infection, it will be treated before you start Elrexfio.
- are pregnant or plan to become pregnant. Elrexfio may harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Elrexfio passes into your breast milk. You must not breastfeed during treatment and for 5 months after stopping treatment with Elrexfio.
- could become pregnant. You must use effective contraception during treatment and for 5 months after stopping treatment with Elrexfio.
- had a recent vaccination or are going to have a vaccination. You should not receive live vaccines from four weeks before until four weeks after you are treated with Elrexfio.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Other warnings you should know about:

- Do not drive, use tools, operate heavy or potential dangerous machinery, or do things that could pose a danger to yourself until at least 48 hours after each of your 2 step-up doses, or as instructed by your healthcare provider. Some people may feel tired, dizzy, or confused while receiving Elrexfio.

How you will receive Elrexfio:

- Your healthcare provider will give you Elrexfio through an injection under your skin ("subcutaneous" injection). It is given in the stomach area (abdomen) or thigh.

Usual dose:

- The dose of Elrexfio solution for subcutaneous injection is 76 mg, but the first two doses will be lower. Elrexfio is given as follows:
  - You will receive a "Step-up dose 1" of 12 mg on Week 1: Day 1
  - You will then receive a "Step-up dose 2" of 32 mg on Week 1: Day 4
  - You will then receive a 'Treatment dose' of 76 mg on Week 2: Day 1.
  - You will then continue receiving a 'Treatment dose' once a week from Week 3 to Week 24, as long as you are getting benefit from Elrexfio.
  - You will then continue receiving a 'Treatment dose' once every other week from Week 25 to Week 48, as long as you are getting benefit from Elrexfio.
  - You will then continue receiving a 'treatment dose' once every four weeks from Week 49 onwards, as long as you are getting benefit from Elrexfio.
- You will be given other medicines 1 hour before each of your first three doses of Elrexfio, which help lower the chance of side effects, such as cytokine release syndrome. These may include:
  - Medicine to reduce the risk of fever (such as acetaminophen)
  - Medicine to reduce the risk of inflammation (corticosteroids)
  - Medicine to reduce the risk of an allergic reaction (antihistamines such as diphenhydramine)
- You may also be given these medicines for later doses of Elrexfio based on any symptoms you have.
- You may also be given additional medicines based on any symptoms you experience or your medical history.
- Your doctor will monitor you for side effects for 48 hours after each of your first two doses (step-up doses). You should stay close to a healthcare facility for 48 hours after the first two doses in case you have side effects. Your doctor may recommend that you stay in the hospital after the first two doses.
- Your doctor will regularly check your blood counts, as the number of blood cells and other blood components may decrease.

Overdose:

This medicine will be given by your doctor or nurse. In the unlikely event that you are given too much, your doctor will monitor you for side effects.

If you think you, or a person you are caring for, have taken too much Elrexfio, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

It is very important to go to all your appointments to make sure your treatment works.
If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment. It is important for you to be monitored closely for side effects during treatment with Elrexfio.

What are possible side effects from using Elrexfio?

These are not all the possible side effects you may have when taking Elrexfio. If you experience any side effects not listed here, tell your healthcare professional.

Very common (may affect more than 1 in 10 people):

- Low levels of red blood cells (anemia)
- Feeling tired or weak
- Edema (excess fluid in body tissue, causing swelling of the hands and feet)
- Diarrhea, feeling sick (nausea), constipation, vomiting
- Low levels of blood platelets (cells that help blood to clot, thrombocytopenia)
- Nose and throat infection (upper respiratory tract infection)
- Lung infection (pneumonia)
- Low levels of types of white blood cells (lymphopenia, leucopenia)
- Decreased appetite
- Pain in your joints
- Fever
- Skin reactions at or near the injection site, including redness of the skin, itching, swelling, pain, bruising, rash, or bleeding
- Low level of “potassium” in the blood (hypokalemia)
- Dry skin
- Skin rash
- Increased level of liver enzymes “transaminases” in the blood
- Cough
- Being short of breath (dyspnea)
- Bladder infection (urinary tract infection)

Common (may affect up to 1 in 10 people):

- Low level of “phosphate” in the blood (hypophosphatemia)
- Low number of a type of white blood cell with a fever (febrile neutropenia)

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Cytokine Release Syndrome (CRS) (serious immune reaction): fever (38°C or higher), chills, nausea, headache, fast heartbeat, feeling dizzy or lightheadedness, confusion or restlessness, and difficulty breathing		√	√
Hypogammaglobulinemia: low levels of antibodies called "immunoglobulins" in the blood which may make infections more likely		√	
Neutropenia: low levels of a type of white blood cells, fever, general weakness, tendency to develop infections		√	
Infection: fever, chills, shivering, cough, shortness of breath, rapid breathing, and rapid pulse		√	√
COMMON			
Neurologic problems, including Immune effector cell associated neurotoxicity syndrome (ICANS) (effects on the nervous system): headache, agitation, trouble staying awake, feeling confused, feeling less alert, having difficulty writing, having trouble speaking, tremors, problems walking, muscle weakness, numbness and tingling		√	√
UNCOMMON **Liver problems (increased liver enzymes in your blood):** tiredness, loss of appetite, pain in your right upper stomach-area (abdomen), dark urine, yellowing of your skin or the white part of your eyes		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Elrexfio will be stored at the hospital or clinic by your doctor.

Keep out of reach and sight of children.

Store in a refrigerator (2°C to 8°C). Do not freeze. Do not shake.

Store in the original carton in order to protect from light.

If you want more information about Elrexfio:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website https://www.pfizer.ca, or by calling 1-800-463-6001.

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