NEW ZEALAND DATASHEET

1 NAME OF THE MEDICINE

Plerixafor Eugia, 24 mg/1.2 mL (20 mg/mL), solution for subcutaneous injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single-use vial contains 24 mg plerixafor in 1.2 mL solution, equivalent to 20 mg/mL.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Solution for injection

Plerixafor Eugia is supplied as a clear, colourless to pale yellow solution, essentially free from visible particles in a clear glass (Type-I) vial, with rubber stopper and sealed with aluminium seals having polypropylene disc.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Plerixafor Eugia is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilise haematopoietic stem cells (HSCs) to the peripheral blood for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma (MM).

4.2 DOSE AND METHOD OF ADMINISTRATION

Plerixafor Eugia therapy should be initiated and supervised by a physician experienced in oncology and/or haematology. Plerixafor Eugia therapy should be administered by a nurse, physician, or other health care professional.

Begin treatment with Plerixafor Eugia after the patient has received G-CSF once daily for 4 days. The recommended dose of Plerixafor Eugia is 0.24 mg/kg body weight by subcutaneous injection. Plerixafor Eugia should be administered 6 to 11 hours prior to initiation of apheresis. In clinical trials, subcutaneous administration to the abdomen was recommended; however, some patients received SC injections in the extremities. G-CSF should be continued each morning prior to apheresis.

Plerixafor has been commonly used for 2 to 4 consecutive days. It has been used for up to 7 consecutive days in a clinical setting.

The patient's actual body weight will be used to calculate the volume of Plerixafor Eugia to be administered. Each vial delivers 1.2 mL of 20 mg/mL solution, and the volume to be administered to patients will be calculated from the following equation:

0.012 X patient's actual body weight (in kg) = dose to be administered (in mL)

In clinical studies, plerixafor dose has been calculated based on actual body weight in patients up to 175% of ideal body weight. Plerixafor dose and treatment of patients weighing more than 175% of ideal body weight have not been investigated.

The weight used to calculate the volume of Plerixafor Eugia should be obtained within 1 week of the first dose of Plerixafor Eugia.

Recommended Concomitant Medications

In pivotal clinical studies supporting the use of plerixafor, all patients received daily morning doses of G-CSF 10 mcg/kg for 4 days prior to the first dose of plerixafor and on each morning prior to apheresis. (See Section 5.1 PHARMACODYNAMIC PROPERTIES-Clinical Efficacy and Safety)

Dose Modification Guidelines

Patients with moderate and severe renal insufficiency (CrCl 20-50 mL/min based on Cockroft Gault formula) should have their dose of Plerixafor Eugia reduced by one-third to 0.16 mg/kg. Similar systemic exposure is expected if the dose is reduced by one-third in patients with moderate and severe renal impairment compared with subjects with normal renal function.Clinical data with this dose adjustment in patients with renal impairment are limited.

There is insufficient information to make dosage recommendations in patients on haemodialysis or those with creatinine clearance < 20 mL/min.

4.3 CONTRAINDICATIONS

General

Hypersensitivity to the active substance or to any of the excipients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Potential for tumour cell mobilisation in patients with lymphoma and multiple myeloma

When Plerixafor Eugia is used in conjunction with G-CSF for haematopoietic stem cell mobilisation in patients with lymphoma or multiple myeloma, tumour cells may be released from the marrow and subsequently collected in the leukapheresis product. The effect of potential re-infusion of tumour cells has not been well-studied. In clinical studies of patients with non-Hodgkin's lymphoma and multiple myeloma, mobilisation of tumour cells has not been observed with plerixafor.

Tumour cell mobilisation in leukaemia patients

In a compassionate use programme, plerixafor and G-CSF have been administered to patients with acute myelogenous leukaemia and plasma cell leukaemia. In some instances, these patients experienced an increase in the number of circulating leukaemia cells. For the purpose of haematopoietic stem cell mobilisation, Plerixafor Eugia may cause mobilisation of leukaemic cells and subsequent contamination of the apheresis product. Therefore, Plerixafor Eugia is not recommended for haematopoietic stem cell mobilisation and harvest in patients with leukaemia.

Haematological effects

Leukocytosis

Administration of Plerixafor Eugia in conjunction with G-CSF increases circulating leukocytes as well as haematopoietic stem cell populations. White blood cell counts should be monitored during Plerixafor Eugia therapy. Clinical judgment should be exercised when administering Plerixafor Eugia to patients with peripheral blood neutrophil counts above 50 X 10^9 cells/L.

Thrombocytopenia

Thrombocytopenia is a known complication of apheresis and has been observed in patients receiving plerixafor. Platelet counts should be monitored in all patients receiving Plerixafor Eugia and undergoing apheresis.

Allergic reactions

Mild to moderate allergic reactions were observed in less than 1% of patients approximately 30 min after plerixafor administration, including one or more of the following: urticaria (n = 2), periorbital swelling (n =2), dyspnoea (n =1) or hypoxia (n =1). Symptoms generally responded to treatments (e.g. antihistamines, corticosteroids, hydration or supplemental oxygen) or resolved spontaneously. Cases of anaphylactic reactions, including anaphylactic shock, have been reported from world-wide post-marketing experience. Patients should be monitored for these adverse reactions following Plerixafor Eugia injection.

Vasovagal reactions

In plerixafor oncology and healthy volunteer clinical studies, less than 1% of subjects experienced vasovagal reactions (orthostatic hypotension and/or syncope) following subcutaneous administration of plerixafor doses ≤ 0.24 mg/kg. The majority of these events occurred within 1 hour of plerixafor administration.

Potential effect on spleen

In nonclinical studies, higher absolute and relative spleen weights were observed following prolonged (2 to 4 weeks) daily plerixafor subcutaneous administration in rats at doses approximately 5 fold higher than the recommended human dose (based on AUC values).

The effect of plerixafor on spleen size in patients has not been specifically evaluated in clinical studies. Cases of splenic enlargement and/or rupture have been reported following the administration of plerixafor in conjunction with growth factor G-CSF. Individuals receiving Plerixafor Eugia in conjunction with G-CSF who report left upper abdominal pain and/or scapular or shoulder pain should be evaluated for splenic integrity.

Use in renal Impairment

Plerixafor Eugia should be used with caution in patients with moderate and severe renal dysfunction.

Use in the elderly

In the two placebo-controlled clinical studies of plerixafor, 24% of patients were ≥ 65 years old. No notable differences in the incidence of adverse reactions were observed in elderly and younger patients.

Paediatric use

The safety and efficacy of plerixafor in paediatric patients have not been established in controlled clinical studies.

Effect on laboratory tests

Plerixafor Eugia has not been shown to interfere with any routine clinical laboratory tests.

White blood cell and platelet counts should be monitored during Plerixafor Eugia use and apheresis.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No interaction studies have been performed.

Drug interactions have not been observed in clinical trials with plerixafor. Plerixafor did not act as a substrate or inhibitor of P-glycoprotein in an in vitro study. It is therefore unlikely that there would be pharmacokinetic interactions between plerixafor and drugs that are inhibitors or substrates of P-glycoprotein.

In clinical studies of patients with non-Hodgkin's lymphoma, the addition of rituximab to a mobilisation regimen of plerixafor and G-CSF did not impact patient safety or CD34+ cell yield.

Drug/Food Interactions

Plerixafor Eugia is administered parenterally, and interactions with food and drink are considered unlikely.

Drug/Laboratory Test Incompatibilities

Plerixafor has not been shown to interfere with any routine clinical laboratory tests.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

The potential effects of plerixafor on male and female fertility have not been evaluated in non-clinical studies. In studies conducted to measure the distribution of 14C-plerixafor, there was no evidence of accumulation in testes. The staging of spermatogenesis measured in a 28-day repeat-dose toxicity study in rats revealed no abnormalities considered to be related to plerixafor at doses 36-fold higher than the recommended human dose, based on AUC values. No histopathological evidence of toxicity to male or female reproductive organs was observed in repeated dose toxicity studies.

Use in pregnancy – Pregnancy Category D

Medicines which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human foetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to the fetus.

SDF-1α and CXCR4 play major roles in embryo-foetal development. Animal models indicated modulation of foetal haematopoiesis, vascularisation, and cerebellar development by SDF 1α and CXCR4. Plerixafor was teratogenic in animals; it caused increased resorptions, decreased foetal weights, retarded skeletal development, and increased foetal abnormalities in rats and/or rabbits. The no-observed effect levels (NOEL) of plerixafor in rats was less than clinical exposure at the recommended human dose of 0.24 mg/kg/day based on AUC values. There are no adequate and well-controlled clinical studies in pregnant women. Females should not become pregnant during treatment with Plerixafor Eugia. Women of childbearing potential treated with Plerixafor Eugia should use effective contraception during treatment and for one week after cessation of treatment.

Men treated with Plerixafor Eugia should use effective contraception during treatment and for one week after cessation of treatment.

Use in Lactation

The potential effects of plerixafor on post-natal development have not been evaluated in non-clinical studies. It is not known whether plerixafor is excreted in human milk. Because many drugs are excreted in human milk, and exposure of breastfed infants to plerixafor may cause serious adverse reactions, plerixafor should not be administered to a breast-feeding woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects of plerixafor on the ability to drive and use machines have been performed. Plerixafor Eugia may influence the ability to drive and use machines. Some patients have experienced dizziness, fatigue or vasovagal reactions; therefore caution is advised when driving or operating machinery.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The following CIOMS frequency rating is used, when applicable:

Very common ≥10%; Common ≥1 and <10%; Uncommon ≥0.1 and <1; Rare ≥0.01 and< 0.1; Very rare <0.01. Not known (cannot be estimated from available data).

Clinical Trial Experience

Safety data for plerixafor in conjunction with G-CSF in oncology patients were obtained from two placebo-controlled Phase 3 studies and 10 uncontrolled Phase 2 studies in 543 patients. Patients were primarily treated with daily doses of 0.24 mg/kg plerixafor by SC injection. The exposure to plerixafor in these studies ranged from 1 to 7 consecutive days (median = 2 days).

In the two Phase 3 studies in patients with NHL and MM (AMD3100-3101 and AMD3100-3102, respectively), a total of 301 patients received daily doses of plerixafor 0.24 mg/kg SC and 292 patients received placebo. All patients received daily morning doses of G-CSF 10 mcg/kg for 4 days prior to the first dose of plerixafor or placebo and on each morning prior to apheresis.

The adverse reactions that occurred in ≥ 5% of the patients who received plerixafor regardless of causality and were more frequent with plerixafor than placebo during HSC mobilisation and apheresis are shown in Table 1.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice dosage and administration.

Table 1 - Adverse Reactions in ≥ 5% of Non-Hodgkin's Lymphoma and Multiple Myeloma Patients Receiving Plerixafor and More Frequent than Placebo During HSC Mobilisation and Apheresis in Phase 3 Studies

	Percent of Patients (%)					
	Plerixafor and G-CSF (n = 301)			Placebo and G-CSF (n = 292)		
	All Grades[a]	Grade 3	Grade 4	All Grades	Grade 3	Grade 4
Gastrointestinal disorders						
Diarrhoea	37	< 1	0	17	0	0
Nausea	34	1	0	22	0	0
Vomiting	10	< 1	0	6	0	0
Flatulence	7	0	0	3	0	0
General disorders and administration site conditions						
Injection site reactions	34	0	0	10	0	0
Fatigue	27	0	0	25	0	0
Musculoskeletal and connective tissue disorders						
Arthralgia	13	0	0	12	0	0
Nervous system disorders						
Headache	22	< 1	0	21	1	0
Dizziness	11	0	0	6	0	0
Psychiatric disorders						
Insomnia	7	0	0	5	0	0

[a] Grades based on criteria from the World Health Organisation (WHO)

Other adverse reactions that occurred in < 5% of patients but were reported as related to plerixafor during HSC mobilisation and apheresis included abdominal pain, injection site irritation, hyperhidrosis, injection site reaction, abdominal distention, dry mouth, erythema, stomach discomfort, malaise, hypoaesthesia oral, constipation, dyspepsia and injection site rash.

The adverse reactions reported in oncology patients who received plerixafor in the controlled Phase 3 studies and uncontrolled studies, including a Phase 2 study of plerixafor as monotherapy for HSC mobilisation, are similar. No notable differences in the incidence of adverse reactions were observed for oncology patients by disease, age or sex.

Myocardial Infarction

In clinical studies, seven of 679 oncology patients experienced myocardial infarctions after HSC mobilisation with plerixafor and G-CSF. All events occurred at least 14 days after last plerixafor administration. Additionally, two female oncology patients in the compassionate use program experienced myocardial infarctions following HSC mobilisation with plerixafor and G-CSF. One of these events occurred 4 days after last plerixafor administration. Lack of temporal relationship in 8 of 9 patients coupled with risk profile of patients with myocardial infarction does not suggest plerixafor confers an independent risk for myocardial infarction in patients who also receive G CSF.

Allergic Reactions

Plerixafor has been associated with potential systemic reactions related to SC injection. (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Gastrointestinal Disorders

In plerixafor clinical studies of oncology patients, there have been rare reports of severe gastrointestinal events, including diarrhoea, nausea, vomiting and abdominal pain.

Paresthesias

Paresthesias are commonly observed in oncology patients undergoing autologous transplantation following multiple disease interventions. In the placebo-controlled Phase 3 studies, the incidence of paraesthesias was 20.6% and 21.2% in the plerixafor and placebo groups, respectively.

Post-marketing experience

In addition to adverse reactions reported from clinical trials, the following adverse reactions have been reported from worldwide post-marketing experience with plerixafor. As these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relation to drug exposure.

Blood and lymphatic system disorder: Splenomegaly and splenic rupture (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE)

Immune system disorders: Anaphylactic reactions, including anaphylactic shock (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Psychiatric disorders: Abnormal dreams and nightmares (from post-marketing experience and phase III studies).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at https://pophealth.my.site.com/carmreportnz/s/ (New Zealand).

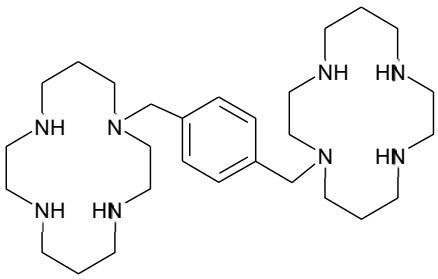
4.9 OVERDOSE

In clinical trials of plerixafor in oncology patients, patients received up to 0.32 mg/kg SC for HSC mobilisation. Some patients have received plerixafor at a dose of ≥ 0.48 mg/kg SC for HSC mobilisation. Adverse events reported in these patients were similar to those reported in patients who received the recommended dose of 0.24 mg/kg SC.

For information on the management of overdose, contact the the National Poisons Centre on 0800 POISON or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

CHEMICAL STRUCTURE



Molecular Weight: 502.79 g/mol

Chemical Name: l, 1'-[1,4-phenylenebis (methylene)]-bis-1,4,8,11- tetraazacyclotetradecane

CAS Number

110078-46-1

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Plerixafor is a reversible antagonist of the CXCR4 chemokine receptor and blocks binding of its cognate ligand, stromal cell-derived factor-1α (SDF-1 α), also known as CXCL12. SDF-1α and CXCR4 are involved in the trafficking and homing of human haematopoetic stem cells (HSCs) to the marrow compartment. Stem cells express CXCR4 and migrate to the bone marrow through a chemoattractant effect of SDF-1α that is produced locally by bone marrow stromal cells. Once in the marrow, it is postulated that stem cell CXCR4 can act to help "anchor" these cells to the marrow matrix, either directly via SDF-1α or through the induction of other adhesion molecules. Plerixafor-induced leukocytosis and elevations in circulating haematopoietic progenitor cell levels are thought to result from a disruption of CXCR4 binding to its cognate ligand, resulting in the appearance of both mature and pluripotent cells in the systemic circulation.

CD34+ cells mobilised by plerixafor were capable of engraftment with long-term repopulating capacity in dog and monkey transplantation models.

Data on the fold increase in peripheral blood CD34+ cell count (cells/mcL) by apheresis day were collected in two placebo-controlled clinical studies in patients with non-Hodgkin's lymphoma and multiple myeloma (MM) (AMD3100-3101 and AMD3100-3102, respectively). The fold increase in CD34+ cell count (cells/mcL) over the 24-hour period starting from the day prior to the first apheresis and ending the next morning to just before the first apheresis is summarised in Table 2. During that 24-hour period, the first dose of plerixafor 0.24 mg/kg or placebo was administered 10-11 hours prior to apheresis.

Table 2 - Fold Increase in Peripheral Blood CD34+ Cell Count Following Plerixafor Administration

Study	Plerixafor and G-CSF		Placebo and G-CSF	
	Median	Mean (SD)	Median	Mean (SD)
AMD3100-3101	5.0	6.2 (5.4)	1.4	1.9 (1.5)
AMD3100-3102	4.8	6.4 (6.8)	1.7	2.4 (7.3)

In pharmacodynamic studies of plerixafor in healthy volunteers, peak mobilisation of CD34+ cells was observed between 6 and 9 hours after administration. In pharmacodynamic studies of plerixafor in conjunction with granulocyte-colony stimulating factor (G-CSF) in healthy volunteers, a sustained elevation in the peripheral blood CD34+ count was observed from 4 to 18 hours after plerixafor administration with peak response between 10 and 14 hours.

Clinical trials

Clinical efficacy and safety

The efficacy and safety of plerixafor in conjunction with G-CSF in lymphoma and MM were evaluated in two placebo-controlled Phase 3 studies (Studies AMD3100-3101 and AMD3100-3102). Patients were randomised to receive either plerixafor 0.24 mg/kg or placebo on each evening prior to apheresis. Patients received daily morning doses of G-CSF 10 mcg/kg for 4 days prior to the first dose of plerixafor or placebo and on each morning prior to apheresis. The primary endpoint was collection of a target number of CD34+ cells/kg within a given number of apheresis days. Two hundred and ninety-eight (298) NHL patients were included in the primary efficacy analyses for AMD3100-3101. The mean age was 55.1 years (29-75) and 57.5 years (22-75) in the plerixafor and placebo groups, respectively, and 93% of subjects were Caucasian. Three hundred and two (302) MM patients were included in the primary efficacy analyses for AMD3100-3102. The mean age was 58.2 years (28-75) and 58.5 years (28-75) in the plerixafor and placebo groups, respectively, and 81% of subjects were Caucasian.

In study AMD3100-3101, 59.3% of non-Hodgkin's lymphoma patients who were mobilised with plerixafor and G-CSF achieved the primary endpoint of collection of ≥ 5 x 10^6 CD34+cells/kg from the peripheral blood in four or fewer apheresis sessions, compared with 19.6% of patients who were mobilised with placebo and G-CSF ($p < 0.001$). Secondary CD34+ cell mobilisation outcomes were consistent with the primary endpoint (**Table 3**).

Table 3 - Study AMD3100-3101 Efficacy Results - CD34+ Cell Mobilisation in Non-Hodgkins Lymphoma Patients

Efficacy Endpoint	Plerixafor and G-CSF (n = 150)	Placebo and G-CSF (n = 148)	p-value[a]
Patients achieving ≥ 5 X 10^6 cells/kg in ≤ 4 apheresis days	89 (59.3%)	29 (19.6%)	< 0.001
Patients achieving ≥ 2 X 10^6 cells/kg in ≤ 4 apheresis days	130 (86.7%)	70 (47.3%)	< 0.001

[a]p-value calculated using Pearson's Chi-Squared test

The median number of days to reach the primary endpoint of ≥ 5 x 10^6 CD34+ cells/kg was 3 days for the plerixafor group and not evaluable for the placebo group. Table 4 presents the proportion of patients who achieved ≥ 5 x 10^6 CD34+ cells/kg by apheresis day.

Table 4 - Study AMD3100-3101 Efficacy Results – Proportion of Patients Who Achieved ≥ 5 x 10^6 CD34+ cells/kg by Apheresis Day in NHL Patients

Days	Proportion[a] in Plerixafor and G-CSF (n=147[b])	Proportion[a] in Placebo and G-CSF (n=142[b])
1	27.9%	4.2%
2	49.1%	14.2%
3	57.7%	21.6%
4	65.6%	24.2%

[a] Percents determined by Kaplan Meier method
[b] n includes all patients who received at least one day of apheresis

In AMD3100-3102, 71.6% of MM patients who were mobilised with Plerixafor and G-CSF achieved the primary endpoint of collection of ≥ 6 X 10^6 CD34+ cells/kg from the peripheral blood in two or fewer apheresis sessions, compared with 34.4% of patients who were mobilised with placebo and G-CSF ($p < 0.001$). Secondary CD34+ cell mobilisation outcomes were consistent with the primary endpoint (**Table 5**)

Table 5 - Study AMD3100-3102 Efficacy Results – CD34+ Cell Mobilisation in Multiple Myeloma Patients

Efficacy Endpoint	Plerixafor and G-CSF (n = 148)	Placebo and G-CSF (n = 154)	p-value[a]
Patients achieving $\geq 6 \times 10^6$ cells/kg in ≤ 2 apheresis days	106 (71.6%)	53 (34.4%)	< 0.001
Patients achieving $\geq 6 \times 10^6$ cells/kg in ≤ 4 apheresis days	112 (75.7%)	79 (51.3%)	< 0.001
Patients achieving $\geq 2 \times 10^6$ cells/kg in ≤ 4 apheresis days	141 (95.3%)	136 (88.3%)	0.031

[a]p-value calculated using Cochran-Mantel-Haenszel statistic blocked by baseline platelet count

The median number of days to reach the primary endpoint of $\geq 6 \times 10^6$ CD34+ cells/kg was 1 day for the plerixafor group and 4 days for the placebo group. **Table 6** presents the proportion of patients who achieved $\geq 6 \times 10^6$ CD34+ cells/kg by apheresis day.

Table 6 - Study AMD3100-3102 – Proportion of Patients Who Achieved $\geq 6 \times 10^6$ CD34+ cells/kg by Apheresis Day in MM Patients

Days	Proportion[a] in Plerixafor and G-CSF (n=144[b])	Proportion[a] in Placebo and G-CSF (n=150[b])
1	54.2%	17.3%
2	77.9%	35.3%
3	86.8%	48.9%
4	86.8%	55.9%

[a] Percents determined by Kaplan Meier method
[b] n includes all patients who received at least one day of apheresis

For transplanted patients in the Phase 3 studies, time to neutrophil and platelet engraftment and graft durability up to 12 months post-transplantation were similar across the treatment groups. The median time to neutrophil engraftment was 10 days in AMD3100-3101 and 11 days in AMD3100-3102 (p = 0.330 and 0.690, respectively) and to platelet engraftment was 20 days in AMD3100-3101 and 18 days in AMD3100-3102 (p = 0.630 and 0.180, respectively). No difference in graft durability was observed across treatment groups in AMD3100-3101 or AMD3100-3102.

The efficacy and safety of plerixafor in conjunction with G-CSF in lymphoma and MM were also evaluated in two supportive Phase 2 studies (Studies AMD3100-2101 and AMD3100-2106). In these studies, patients with NHL, Hodgkin's disease, or MM received plerixafor 0.24 mg/kg on the evening or morning prior to apheresis. Patients received daily morning doses of G-CSF 10 mcg/kg for 4 days prior to the first dose of plerixafor and on each morning prior to apheresis. Mobilisation and engraftment data for these studies were similar to those data for the Phase 3 studies.

5.2 PHARMACOKINETIC PROPERTIES

The pharmacokinetics of plerixafor have been evaluated in patients with lymphoma and MM at the clinical dose level of 0.24 mg/kg following pre-treatment with G-CSF (10 mcg/kg once daily for 4 consecutive days).

Absorption

Plerixafor is rapidly absorbed following subcutaneous (SC) injection with peak concentrations reached in approximately 30-60 minutes. Following subcutaneous administration of plerixafor the absolute bioavailability is at least 70%.

Distribution

Plerixafor is moderately bound to human plasma proteins (37-58%). The apparent volume of distribution of plerixafor in humans is 0.3 L/kg demonstrating that plerixafor is largely confined to, but not limited to, the extravascular fluid space.

Metabolism

Plerixafor was not metabolised *in vitro* using human liver microsomes or human primary hepatocytes and did not exhibit inhibitory activity *in vitro* towards the major drug metabolising CYP450 enzymes (1A2, 2C9, 2C19, 2D6, and 3A4/5). In *in vitro* studies with human hepatocytes, plerixafor does not induce CYP1A2, CYP2B6, or CYP3A4 enzymes. These findings indicate that plerixafor has a low potential for involvement in P450-dependent drug-drug interactions.

Excretion

The major route of elimination of plerixafor is urinary. Following a 0.24 mg/kg dose in healthy volunteers with normal renal function, approximately 70% of the dose was excreted in the urine as the parent drug during the first 24 hours following administration. The half-life in plasma is 3-5 hours.

Special Populations

Elderly

In the two placebo-controlled clinical studies of plerixafor, 24% of patients were ≥ 65 years old. No notable differences in the incidence of adverse reactions were observed in elderly and younger patients.

Paediatric Patients

The safety and efficacy of plerixafor in paediatric patients have not been established in controlled clinical studies.

Renal Impairment

Following a single 0.24 mg/kg dose of plerixafor, plerixafor clearance was reduced in subjects with varying degrees of renal dysfunction and was positively correlated with creatinine clearance (CrCl). The mean AUC0-24 of plerixafor in subjects with mild (CrCl 51-80 mL/min), moderate (CrCl 31-50 mL/min), and severe (CrCl < 31 mL/min) renal impairment was 7%, 32%, and 39% higher than healthy subjects with normal renal function, respectively. Renal impairment had no effect on C_{max}. (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION)

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Plerixafor was not genotoxic in an in vitro bacterial mutation assay (Ames test in Salmonella), an in vitro chromosomal aberration test using Chinese hamster ovary cells, and an in vivo rat bone marrow micronucleus test.

Carcinogenicity

Carcinogenicity studies with plerixafor have not been conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

5.9 mg sodium chloride

Water for Injection,

adjusted to a pH of 6.0-7.5 with hydrochloric acid and with sodium hydroxide, if required.

6.2 INCOMPATIBILITIES

Incompatibilities were either nor assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25ºC.

DO NOT USE Plerixafor Eugia after the expiration date indicated on the vial. Each vial of Plerixafor Eugia is intended for single use only. Any unused drug remaining after injection must be discarded.

Plerixafor Eugia is supplied as a ready-to-use formulation. The contents of the vial must be transferred to a suitable syringe for SC administration. Vials should be inspected visually for particulate matter and discolouration prior to administration and should not be used if there is particulate matter or if the solution is discoloured.

6.5 NATURE AND CONTENTS OF CONTAINER Plerixafor Eugia is supplied in 2 mL Type-I tubular clear glass vials with 13 mm grey chlorobutyl rubber stoppers and sealed with aluminium seals having polypropylene disc and the pack size is 1 vial.

Product is for single use in one patient only. Discard any residue.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Any unused medicine or waste materials should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription Only Medicine

8 SPONSOR

CARSL Consulting
24 Side Road, Parkhill Farm, RD10
P O Box 766
Hastings 4156, New Zealand
Telephone: 027 5086002
www.carsl.co.nz
carsl@xtra.co.nz

DISTRIBUTED BY

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9 DATE OF FIRST APPROVAL

19 December 2025

10 DATE OF REVISION OF THE TEXT

9 August 2025

Summary of changes

Section changed	Summary of changes
N/A	