NEW ZEALAND DATA SHEET

1 NAME OF THE MEDICINAL PRODUCT

MOZOBIL® Plerixafor, Injection, solution for subcutaneous use

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single-use vial contains 24 mg plerixafor.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Plerixafor is a white to off-white crystalline solid. Mozobil is supplied as a clear, colourless to pale yellow, sterile, preservative-free, isotonic solution in a 2.0 mL clear glass (Type I) vial, sealed with a rubber stopper and aluminium seal with a plastic flip-off cap.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Mozobil 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

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

Begin treatment with Mozobil after the patient has received G-CSF once daily for 4 days. The recommended dose of Mozobil is 0.24 mg/kg body weight by subcutaneous injection. Mozobil 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.

Mozobil 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 Mozobil 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, Mozobil dose has been calculated based on actual body weight in patients up to 175% of ideal body weight. Mozobil 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 Mozobil should be obtained within 1 week of the first dose of Mozobil.

Recommended Concomitant Medications

In pivotal clinical studies supporting the use of Mozobil, all patients received daily morning doses of G-CSF 10 mcg/kg for 4 days prior to the first dose of Mozobil 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 Mozobil 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 Mozobil 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 Mozobil.

Tumour cell mobilisation in leukaemia patients

In a compassionate use programme, Mozobil 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, Mozobil may cause mobilisation of leukaemic cells and subsequent contamination of the apheresis product. Therefore, Mozobil is not recommended for haematopoietic stem cell mobilisation and harvest in patients with leukaemia.

Haematological effects

Leukocytosis

Administration of Mozobil in conjunction with G-CSF increases circulating leukocytes as well as haematopoietic stem cell populations. White blood cell counts should be monitored during Mozobil therapy. Clinical judgment should be exercised when administering Mozobil to patients with peripheral blood neutrophil counts above 50 X 109 cells/L.

Thrombocytopenia

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

Allergic reactions

Mild to moderate allergic reactions were observed in less than 1% of patients approximately 30 min after Mozobil 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 Mozobil injection.

Vasovagal reactions

In Mozobil 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 Mozobil 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 Mozobil on spleen size in patients has not been specifically evaluated in clinical studies. Cases of splenic enlargement and/or rupture have been reported following theadministration of Mozobil in conjunction with growth factor G-CSF. Individuals receiving Mozobil 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

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

Paediatric use

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

Use in the elderly

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

Effect on laboratory tests

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

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No interaction studies have been performed.

Drug interactions have not been observed in clinical trials with Mozobil. 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 Mozobil and G-CSF did not impact patient safety or CD34+ cell yield.

Drug/Food Interactions

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

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 (Category D)

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. Mozobil should not be used during pregnancy unless the potential benefit justifies the potential risk to the foetus. 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. Advise women of childbearing potential to use effective contraception during 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 Mozobil on the ability to drive and use machines have been performed. Mozobil 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 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 Mozobil 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 Mozobil 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 Mozobil 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 Mozobil or placebo and on each morning prior to apheresis.

The adverse reactions that occurred in ≥ 5% of the patients who received Mozobil regardless of causality and were more frequent with Mozobil 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 MOZOBIL and More Frequent than Placebo During HSC Mobilisation and Apheresis in Phase 3 Studies

	Percent of Patients (%)					
	Mozobil 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 Mozobil 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 Mozobil in the controlled Phase 3 studies and uncontrolled studies, including a Phase 2 study of Mozobil 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 Mozobil and G-CSF. All events occurred at least 14 days after last Mozobil administration. Additionally, two female oncology patients in the compassionate use program experienced myocardial infarctions following HSC mobilisation with Mozobil and G-CSF. One of these events occurred 4 days after last Mozobil administration. Lack of temporal relationship in 8 of 9 patients coupled with risk profile of patients with myocardial infarction does not suggest Mozobil confers an independent risk for myocardial infarction in patients who also receive G CSF.

Allergic Reactions

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

Gastrointestinal Disorders

In Mozobil 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 Mozobil 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 Mozobil. 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 of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

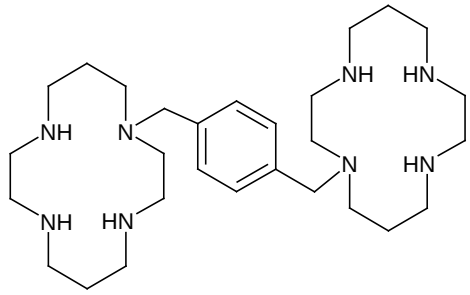
4.9 OVERDOSE

In clinical trials of Mozobil in oncology patients, patients received up to 0.32 mg/kg SC for HSC mobilisation. Some patients have received Mozobil 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.

Contact the New Zealand National Poisons Information Centre (telephone 0800 POISON or 0800 764 766) for advice on management.

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 Mozobil 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 Mozobil Administration

Study	Mozobil 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 Mozobil in healthy volunteers, peak mobilisation of CD34+ cells was observed between 6 and 9 hours after administration. In pharmacodynamic studies of Mozobil 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 Mozobil administration with peak response between 10 and 14 hours.

Clinical efficacy and safety

The efficacy and safety of Mozobil 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 Mozobil 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 Mozobil 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 Mozobil 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 Mozobil 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 Mozobil and G-CSF achieved the primary endpoint of collection of ≥ 5 x 106 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-Hodgkin's Lymphoma Patients

Efficacy Endpoint	Mozobil 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 106 CD34+ cells/kg was 3 days for the Mozobil group and not evaluable for the placebo group. **Table 4** presents the proportion of patients who achieved ≥ 5 x 106 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 Mozobil and G-CSF (n=147b)	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 Mozobil and G-CSF achieved the primary endpoint of collection of ≥ 6 X 106 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	Mozobil and G-CSF (n = 148)	Placebo and G-CSF (n = 154)	p-value[a]
Patients achieving ≥ 6 X 10^6 cells/kg in ≤ 2 apheresis days	106 (71.6%)	53 (34.4%)	< 0.001
Patients achieving ≥ 6 X 10^6 cells/kg in ≤ 4 apheresis days	112 (75.7%)	79 (51.3%)	< 0.001

Patients achieving ≥ 2 X 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 ≥ 6 x 10^6 CD34+ cells/kg was 1 day for the Mozobil group and 4 days for the placebo group. **Table 6** presents the proportion of patients who achieved ≥ 6 x 10^6 CD34+ cells/kg by apheresis day.

Table 6 - Study AMD3100-3102 – Proportion of Patients Who Achieved ≥ 6 x 106 CD34+ cells/kg by Apheresis Day in MM Patients

Days	Proportion[a] in Mozobil 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 Mozobil 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 Mozobil 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 Mozobil 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 Mozobil, 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 Mozobil in paediatric patients have not been established in controlled clinical studies.

Renal Impairment

Following a single 0.24 mg/kg dose of Mozobil, 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 Cmax. (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

Sodium chloride

Water for Injections,

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

6.2 INCOMPATIBILITIES

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

6.3 SHELF LIFE

36 months from date of manufacture.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store Mozobil at 25ºC (77ºF); excursions permitted to 15ºC-30ºC (59ºF-86ºF).

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

Mozobil 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

Mozobil is supplied as a sterile, preservative-free, clear, colourless to pale yellow, pH neutral, isotonic solution in a single-use 2.0 mL clear glass (Type I) vial, sealed with a rubber stopper and aluminium seal with a plastic flip-off cap. Each vial contains 24 mg plerixafor in 1.2 mL solution.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

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

7 MEDICINE SCHEDULE

Schedule 4 (Prescription Only Medicine)

8 SPONSOR

Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics
PO Box 62027
Sylvia Park Auckland 1644
Freecall: 0800 283 684
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

18 May 2010

10 DATE OF REVISION OF THE TEXT

20 June 2022

Summary of changes

Section changed	Summary of new information
8	Change of sponsor