DRUG NAME: Plerixafor

SYNONYM(S): AMD3100[1]

COMMON TRADE NAME(S): MOZOBIL®

CLASSIFICATION: molecular targeted therapy

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Plerixafor is a selective chemokine receptor (CXCR4) antagonist used in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation. Plerixafor reversibly binds and blocks CXCR4 on stem cells to inhibit interaction with stroma-cell-derived factor-1α ligand in the bone marrow. The CXCR4/SDF-1α binding interruption releases hematopoietic stem cells from the bone marrow into peripheral blood.[1,2]

PHARMACOKINETICS:

Absorption	rapid; peak concentration 30-60 minutes	
Distribution	widely distributed; high/sustained levels in liver, kidney, spleen, injection site, epiphyseal plate, and cartilage[3]	
	cross blood brain barrier?	yes; low levels detected in pituitary, cerebrum, olfactory lobe, and spinal fluid[3]
	volume of distribution	0.3 L/kg
	plasma protein binding	≤58%
Metabolism	not metabolized *in vitro* by human liver microsomes[4]	
	active metabolite(s)	none
	inactive metabolite(s)	three cupric ion complexes identified (insignificant amounts)[3]
Excretion	major route of elimination is urinary; reduced with renal impairment	
	urine	70% as unchanged drug in 24 hours
	feces	no information found
	terminal half life	3-5 hours
	clearance	4380 mL/h

Adapted from standard reference[5] unless specified otherwise.

USES:

Primary uses:
*Hematopoietic stem cell mobilization

Other uses:

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Caution:
- moderate to severe ***renal impairment*** requires starting dose adjustment; use caution with drugs that reduce renal function or compete for active tubular secretion[6]

Carcinogenicity: no information found

Mutagenicity: Not mutagenic in Ames test. Plerixafor is not clastogenic in mammalian *in vitro* and *in vivo* chromosome tests.[5]

Fertility: In animal studies, spermatogenesis was normal, drug did not accumulate in the testes, and there were no histopathological changes in male or female reproductive organs.[5]

Pregnancy: In animal studies, plerixafor exposure resulted in increased resorptions, post-implantation loss, and fetal abnormalities, as well as decreased fetal weight, delayed skeletal development, and fetal death at doses ten times the expected human dose. Women of childbearing potential should use effective contraception during treatment.[2,5]

Breastfeeding is not recommended due to the potential secretion into breast milk.[5]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.[7,8] **Incidence data in the Side Effects table is based on combination therapy with granulocyte colony stimulating factor (G-CSF).**

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
blood and lymphatic system/ febrile neutropenia	leukocytosis (severe 7%)
	thrombocytopenia (<5%)[4]
cardiac	myocardial infarction (<1%)
gastrointestinal	*emetogenic potential:* low[8,9]
	abdominal distention, discomfort, pain (1-5%)
	constipation (1-5%)
	diarrhea (37%, severe <1%)
	dyspepsia (1-5%)
	nausea (34%, severe 1%)
	oral hypoesthesia (1-5%)
	vomiting (10%, severe <1%)
general disorders and administration site conditions	*extravasation hazard:* none[10]
	injection site reaction (34%); including erythema, swelling, pruritus, rash, and urticaria
	malaise (1-5%)
immune system	***allergic reaction*** (<1%); see paragraph following **Side Effects** table

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
	anaphylaxis, including anaphylactic shock (<1%); see paragraph following **Side Effects** table
musculoskeletal and connective tissue	myalgia (1-5%)
nervous system	dizziness (11%)
	vasovagal reaction (<1%); usually occurs within one hour of administration
psychiatric	insomnia (1%)
	nightmares, abnormal dreams, anxiety (<1%)
skin	hyperhidrosis (1-5%)

Adapted from standard reference[5] unless specified otherwise.

Allergic reactions and ***anaphylactic shock*** have been rarely reported. Symptoms usually develop within thirty minutes of administration and include urticaria, periorbital swelling, dyspnea, and/or hypoxia. Symptoms may resolve spontaneously and usually resolve with supportive treatment (e.g., antihistamines, corticosteroids, hydration, or supplemental oxygen). All patients should be observed during administration of plerixafor and for at least thirty minutes after administration or until clinically stable.[4]

INTERACTIONS: no information found

SUPPLY AND STORAGE:

***Injection*:** sanofi-aventis Canada Inc. supplies plerixafor as 24 mg single-use (preservative free) vials in a concentration of 20 mg/mL. Store at room temperature.[5]

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in ***bold***, ***italics***

Subcutaneous	***into the abdomen***[5]
Intramuscular	no information found
Direct intravenous	no information found
Intermittent infusion	has been used[11]
Continuous infusion	no information found
Intraperitoneal	no information found

BCCA administration guideline noted in ***bold***, ***italics***

Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response, and concomitant therapy.

***Adults*:**

BCCA usual dose noted in ***bold, italics***

Subcutaneous: ***0.24 mg/kg SC once daily*** for up to 4 consecutive days
max = 40 mg/day[5,8,12-14]

Concurrent radiation: no information found

Dosage in renal failure[5,8,12]:

Creatinine clearance (mL/min)	Dose
>50	0.24 mg/kg (max = 40 mg/day)
20-50	0.16 mg/kg (max = 27 mg/day)
< 20	no information found

calculated creatinine clearance = $\frac{N^* \times (140 - Age) \times \text{weight in kg}}{\text{serum creatinine in micromol/L}}$

* For males N=1.23; for females N=1.04

Dosage in hepatic failure: no information found

Dosage in dialysis: no information found; however, physicochemical properties suggest significant drug removal is likely during high permeability dialysis[15]

Children: safety and effectiveness is not established in children

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