Motixafortide (APHEXDA)
National Drug Monograph
August 2024

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Motixafortide inhibits CXCR4, which prevents anchoring of cells to the marrow matrix, resulting in an increase in circulating hematopoietic stem and progenitor cells
Indication Under Review[1]	In combination with filgrastim to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with multiple myeloma
Dosage Regimen	1.25 mg/kg (actual wgt) via slow subcutaneous injection 10-14 hours prior to initiation of first apheresis. A second dose can be given 10-14 hours prior to a third apheresis.
Dosage Forms Under Review	62 mg lyophilized powder in a SDV for reconstitution

EFFICACY CONSIDERATIONS

Trial	**GENESIS (NCT 03246529)**
Design	Randomized 2:1, DB, PC study
Population	N=122 patients with multiple myeloma
Demographic	mAge 63 yrs (34-75); male 65%; Caucasian 86%; African American 8%; Asian 2%
Intervention	Motixafortide 1.25 mg/kg SQ (n=80) x1
Comparator	Vs. Placebo (n=42) x1
	All rec'd filgrastim 10-15 mg/kg daily, Days 1-4 + Days 5-8, if apheresis continues due to inadequate collection Motixafortide or placebo given Day 4 (10-14 hrs prior to 1st apheresis) Day 5 = 1st apheresis; Day 6 = 2nd apheresis; Day 7 = 3rd apheresis; Day 8 = 4th apheresis
Results	Primary endpoint/collection goal: $\geq$ 6 x10^6 CD34+ cells/kg in up to 2 apheresis procedures Secondary goal: $\geq$ 6 x10^6 CD34+ cells/kg in 1 apheresis procedure

Cell collection goal	Motixafortide and filgrastim	Placebo and filgrastim	P value
$\geq$ 6 x10^6 CD34+ cells/kg ($\leq$ 2 apheresis)	67.5%	9.5%	<0.0001
$\geq$ 6 x10^6 CD34+ cells/kg (1 apheresis)	63.8%	2.4%	<0.0001
$\geq$ 2 x10^6 CD34+ cells/kg (1 apheresis)	87.5%	38.1%	<0.0001

Cell collection goal was achieved in up to 2 apheresis procedures in significantly more patients who received motixafortide with filgrastim than those receiving placebo with filgrastim.

SAFETY CONSIDERATIONS

Boxed Warnings	n/a
Contraindications	History of hypersensitivity to motixafortide
Other Warnings	Anaphylactic shock and HS reactions. Premedicate with H1-, H2-blocker and leukotriene inhibitor; administer drug in staffed and equipped setting where immediate treatment can be provided. Injection site reactions. Premedication with acetaminophen is recommended. Leukocytosis. Monitor WBC counts. Potential for tumor cell mobilization. Effect of reinfusion of tumor cells is unknown. Embryo-fetal toxicity. Can cause fetal harm. Advise of potential risk to fetus; Use effective contraception.
Top 5 AEs	Injection site reaction, site pain, site erythema, site pruritus, pruritus
Drug Interactions	Low potential for metabolism- and transporter-mediated drug interactions

	DRUG/VANF status/CFU?	FDA LABEL	DOSING	EFFICACY
ALTERNATIVE THERAPY	Motixafortide TBD CFU TBD	HSC mobilization for autologous HSCT in MM	Subcutaneous injection; Dose 1.25 mg/kg* given 10-14 hrs prior to 1st apheresis 2nd dose may be given 10-14 hrs prior to 3rd apheresis, if needed	Efficacy in MM Study: Pop'n mAge 63 years; 70% rec'd lenalidomide induction **Motixafortide + filgrastim vs. placebo + filgrastim** # patients achieving ≥ 6x 10^6 cells/kg in ≤ 2 apheresis days: 67.5 vs. 9.5%; p<0.0001 # patients achieving ≥ 6x 10^6 cells/kg in 1 aphereses: 63.8 vs. 2.4%; p<0.0001 # patients achieving ≥ 2x 10^6 cells/kg in 1 aphereses: 87.5 vs. 38.1%; p<0.0001
	Plerixafor Non-formulary No CFU	HSC mobilization for autologous HSCT in NHL and MM	Subcutaneous injection; *Dose per FDA label:* ≤ 83 kg: 20mg fixed dose once daily up to 4 consecutive days > 83 kg: 0.24mg/kg once daily for up to 4 consecutive days; max 40 mg/day *Dose per risk-adapted mobilization strategy:* Filgrastim 10mcg/kg daily x 4, if day 4 CD34 count < 10/mcL, then plerixafor dose given 11 hrs prior to collection day 5.	Efficacy in MM study from 2009, given per FDA label: Pop'n 58 years; 5.9% rec'd lenalidomide induction **Plerixafor + filgrastim vs. placebo + filgrastim** # patients achieving ≥ 6x 10^6 cells/kg in ≤ 2 apheresis days: 72 vs. 34%; p<0.001 # patients achieving ≥ 6x 10^6 cells/kg in ≤ 4 apheresis days: 76 vs. 51%; p<0.001 # patients achieving ≥ 2x 10^6 cells/kg in ≤ 4 apheresis days: 95 vs. 88%; p=0.028

VHA PLACE IN THERAPY	**Potential Use in VHA**	1. Motixafortide has been compared to placebo, as has plerixafor. Both drugs appear to help mobilize PBSC in anticipation of autologous transplant. It is difficult to determine if one drug is more effective than the other; although similar patient populations, standard induction regimens have changed, as evidenced by the populations who received prior lenalidomide in the plerixafor and motixafortide trials. By comparing clinical trials that led to approval, it does not consider alternative plerixafor dosing strategies, such as the risk-adapted mobilization strategy. 2. Stem cell mobilizers have the potential to reduce apheresis procedures and optimize cell collections; they should be available to HSCT settings in anticipation of inadequate PBSC collections. 3. Motixafortide may be useful in patients with hypersensitivity or allergy to plerixafor and those with insufficient cell mobilization utilizing filgrastim and plerixafor.

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References

1 Motixafortide (APHEXDA) formulation [prescribing information online]. Modi'in, Israel: BioLineRx LTD 9/2023. Available at: 217159s000lbl.pdf (fda.gov) Accessed June 28, 2024.

2 Micallef INM, Sinha S, Gastineau DA, et al. Cost-Effectiveness Analysis of a Risk-Adapted Algorithm of Plerixafor Use for Autologous Peripheral Blood Stem Cell Mobilization. Biol Blood Marrow Transplant 2013; 19: 87-93.

3 Crees ZD, Rettig MP, Jayasinghe RG, et al. Motixafortide and G-CSF to mobilize hematopoietic stem cells for autologous transplantation in multiple myeloma: a randomized phase 3 trial. Nat Med 2023; 29: 869-879.