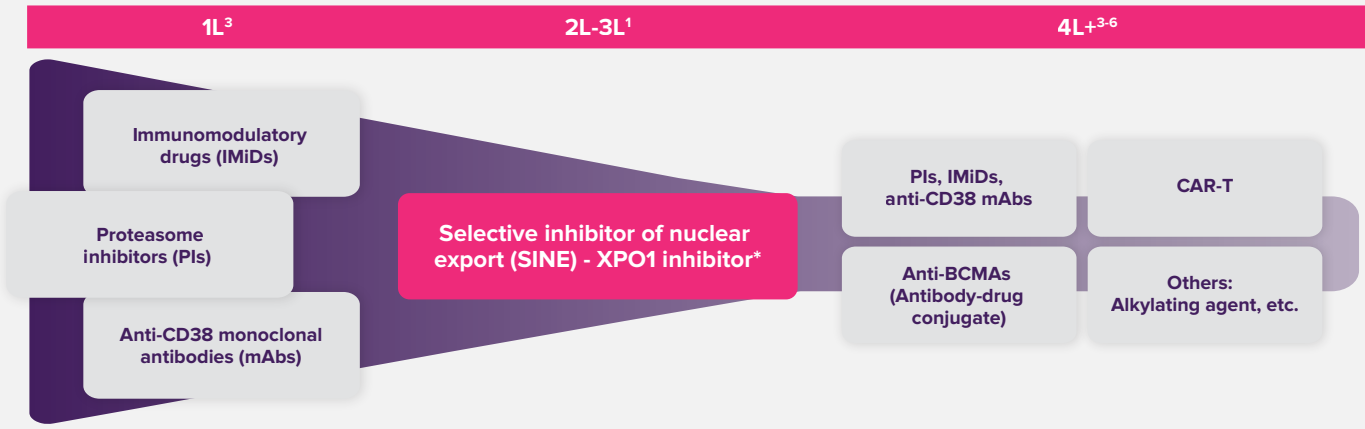
XPOVIO® (selinexor)

For patients who have progressed on commonly used combinations, including those with daratumumab,

XPOVIO provides an opportunity to introduce a different MOA[1-3]

XPOVIO demonstrated efficacy benefits in multiple myeloma (MM)[1]

Class switching across lines of therapy in MM



*XPOVIO is a prescription medicine approved in combination with bortezomib and dexamethasone (XVd) to treat adult patients with multiple myeloma who have received at least one prior therapy.
BCMA=B-cell maturation antigen; CAR-T=chimeric antigen receptor T cell; XPO1=exportin-1.

XPOVIO is the first and only FDA-approved XPO1 inhibitor that helps restore the body's own tumor suppressor pathways to fight MM after at least 1 prior therapy[1,7,8]

NCCN Category 1 Recommendation

Oral, once weekly selinexor (XPOVIO®) in combination with bortezomib and dexamethasone (XVd) is recommended by the NCCN Guidelines® as a Category 1 therapeutic option in previously treated MM[3†]

†Category 1=Based upon high-level evidence, there is uniform National Comprehensive Cancer Network® (NCCN®) consensus that the intervention is appropriate. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.3.2022. ©National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed October 28, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

INDICATION

XPOVIO® (selinexor) is a prescription medicine approved:

- in combination with bortezomib and dexamethasone (XVd) to treat adult patients with multiple myeloma who have received at least one prior therapy.

IMPORTANT SAFETY INFORMATION

Thrombocytopenia: XPOVIO can cause life-threatening thrombocytopenia, potentially leading to hemorrhage. Thrombocytopenia was reported in patients with multiple myeloma.

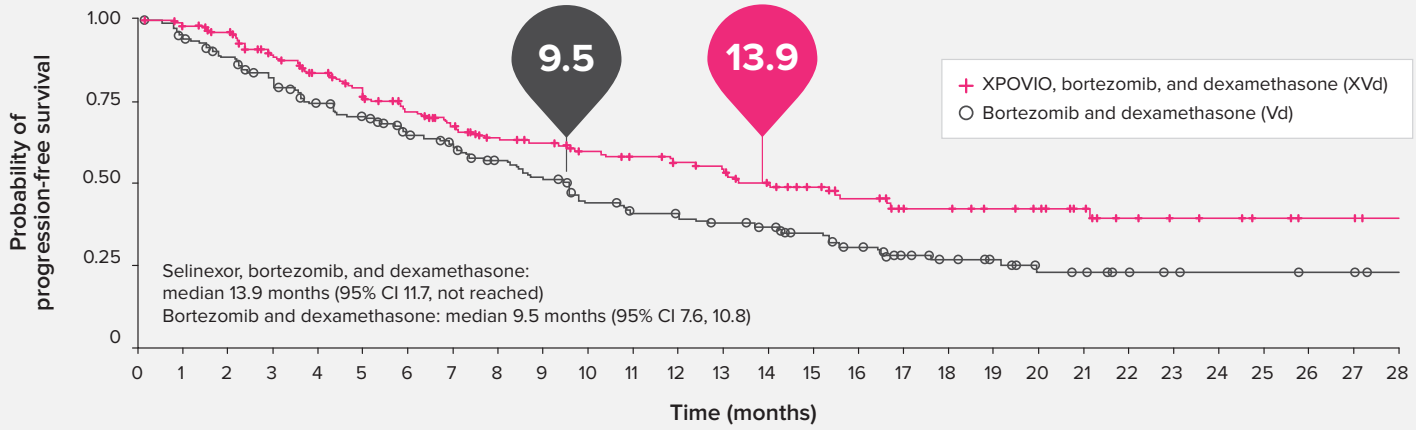
Thrombocytopenia is the leading cause of dosage modifications. Monitor platelet counts at baseline and throughout treatment. Monitor more frequently during the first 3 months of treatment. Monitor patients for signs and symptoms of bleeding. Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

Please see Important Safety Information and full Prescribing Information.

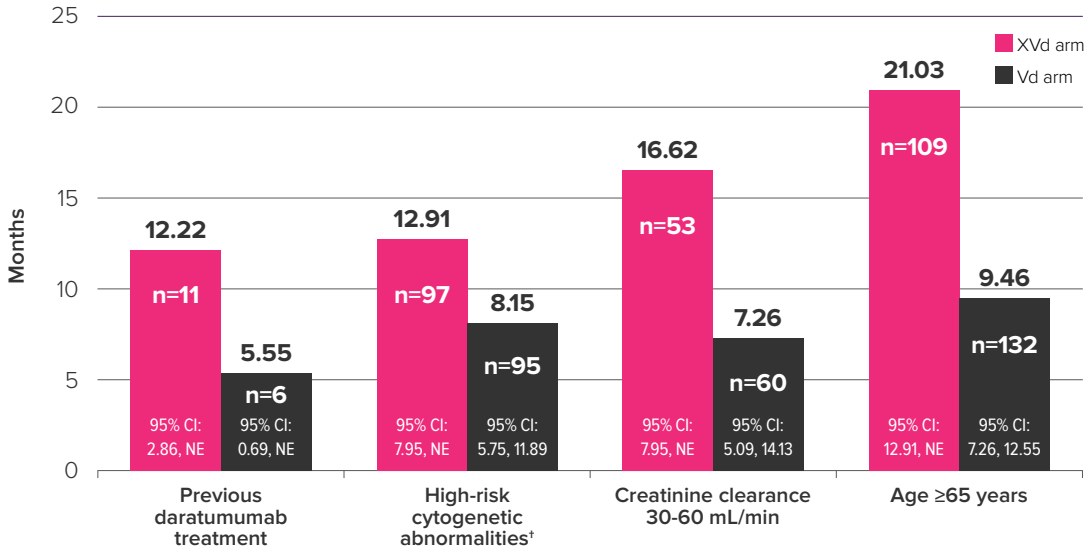
In the XVd trial, XPOVIO + Vd demonstrated an early and sustained progression-free survival (PFS) benefit vs Vd[1]

The XVd trial was a phase 3, global, randomized, open-label study of patients with MM who had received 1-3 prior therapies. The primary efficacy endpoint was median PFS (mPFS). In the trial, 402 patients were randomized into 2 study arms[1,9]:

- 195 patients were treated with once-weekly XPOVIO + bortezomib and twice-weekly dexamethasone (XVd)[1]
- 207 patients were treated with twice-weekly bortezomib and four-times-weekly dexamethasone (Vd)[1*]



Efficacy was observed in select subgroups, including in patients previously treated with daratumumab-containing regimens[2,9]



Limitations of subgroup analyses:

- **These subgroup analyses were exploratory in nature, not included in the study objectives, and do not control for type 1 error**
- **These subgroup analyses were not powered or adjusted for multiplicity to assess PFS across these prespecified subgroups**

*Randomization was stratified based on prior proteasome inhibitor exposure, number of prior regimens, stage, and region.
†Includes any of del(17p)/p53, t(14;16), t(4;14), 1q21.
CI=confidence interval; NE=not evaluable.

IMPORTANT SAFETY INFORMATION

Neutropenia: XPOVIO can cause life-threatening neutropenia, potentially increasing the risk of infection.

Monitor more frequently during the first 3 months of treatment. Consider supportive measures, including antimicrobials and growth factors (e.g., G-CSF). Interrupt, reduce dose, or permanently discontinue based on severity of adverse reaction.

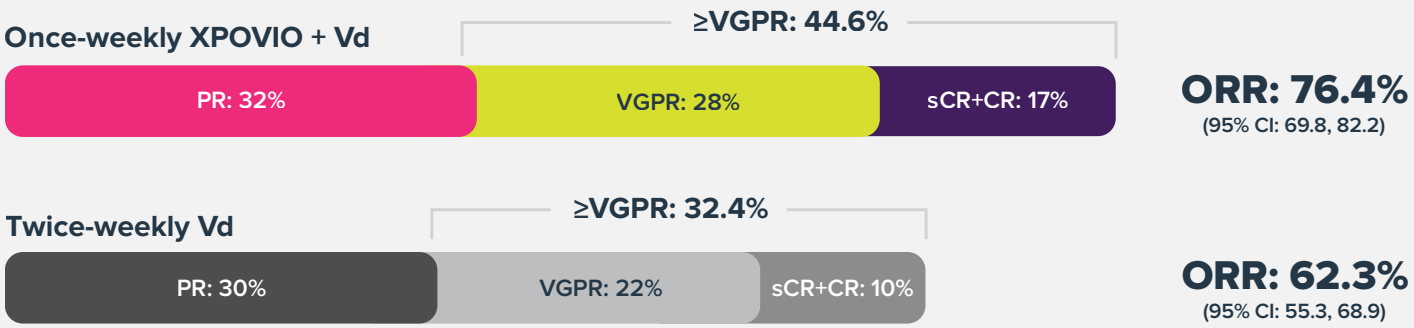
Gastrointestinal Toxicity: XPOVIO can cause severe gastrointestinal toxicities in patients.

Please see Important Safety Information and full Prescribing Information.

Responses with once-weekly XVd were deep and durable[1]

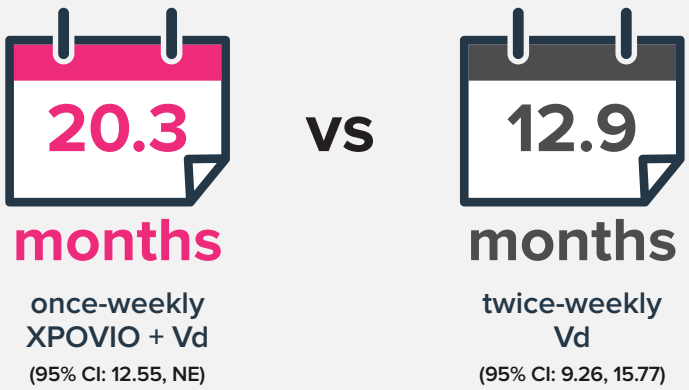
3 out of 4 patients experienced a response to XVd[1]

Overall response rates (ORRs) demonstrated in the XVd trial[1]
***P*=0.0012**



Of the XVd patients who responded, half kept responding for >20 months[1]

Median duration of response (DOR) demonstrated in the XVd trial[1,2]
***P*=0.1364**



IMPORTANT SAFETY INFORMATION

Nausea/Vomiting/Diarrhea: Provide prophylactic antiemetics or treatment as needed.

Anorexia/Weight Loss: Monitor weight, nutritional status, and volume status at baseline and throughout treatment and provide nutritional support, fluids, and electrolyte repletion as clinically indicated.

Hyponatremia: XPOVIO can cause severe or life-threatening hyponatremia.

Monitor sodium level at baseline and throughout treatment.

Please see Important Safety Information and full Prescribing Information.

Oral, once-weekly XPOVIO dosing allows flexibility to help mitigate potential adverse reactions[1]

DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
XPOVIO 100 mg + bortezomib 1.3 mg/m² + dexamethasone 20 mg	dexamethasone 20 mg	**No dose**	**No dose**	**No dose**	**No dose**	**No dose**

= 50 mg

65% of patients in the XVd arm of the XVd trial had an XPOVIO dose reduction (126/195 patients)[2]

The median dosage of XPOVIO in the XVd arm was 80 mg (range: 30-137 mg) taken once weekly[1]

Dose reduction steps for ARs[1]

Indication starting dose	100 mg
DOSE REDUCTION	
First reduction	80 mg
Second reduction	60 mg
Third reduction	40 mg
Fourth reduction	PERMANENTLY DISCONTINUE

Please see full Prescribing Information for specific dose modification guidelines as they pertain to individual ARs.

IMPORTANT SAFETY INFORMATION

Serious Infection: XPOVIO can cause serious and fatal infections. Atypical infections reported after taking XPOVIO include, but are not limited to, fungal pneumonia and herpesvirus infection.

Neurological Toxicity: XPOVIO can cause life-threatening neurological toxicities.

Coadministration of XPOVIO with other products that cause dizziness or mental status changes may increase the risk of neurological toxicity.

Advise patients to refrain from driving and engaging in hazardous occupations or activities until the neurological toxicity fully resolves. Institute fall precautions as appropriate.

Please see Important Safety Information and full Prescribing Information.

XPOVIO dosing was adjusted without compromising efficacy[1,2]

XPOVIO dose was reduced to help manage side effects[1]

XVd trial (XVd arm)

	ITT Patient Population[1,2]	Patients With Dose Modification[2]
Patient population	N=195	n=126
% of ITT population	100	65
mPFS, mo	13.9 (95% CI: 11.7, NE)	16.6 (95% CI: 12.9, NE)
ORR, %*	76.4	81.7
≥VGPR, %	44.6	51.6
mDOR, mo	20.3 months (95% CI: 12.6, NE)	Not evaluable (95% CI: 13.8, NE)

*The above table presents data from a post hoc subgroup analysis and is not intended to suggest efficacy comparisons between treatment groups.

Limitations of post hoc analysis:

- This post hoc analysis is exploratory in nature and was not a study objective. This analysis was not powered to evaluate efficacy outcomes within this subgroup
- This post hoc analysis was underpowered to detect clinically meaningful differences in treatment effect

XVd offers a generally manageable adverse reaction (AR) profile[1]

Most common adverse reactions in the safety population[9]

	XVd group (n=195)		Vd group (n=204)*	
	Any grade†	Grade 3-4	Any grade‡	Grade 3-4
Hematological adverse events				
Thrombocytopenia	117 (60%)	77 (39%)	55 (27%)	35 (17%)
Anemia	71 (36%)	21 (16%)	47 (23%)	20 (10%)
Neutropenia	29 (15%)	17 (9%)	12 (6%)	7 (3%)
Non-hematological adverse events				
Fatigue	82 (42%)	26 (13%)	37 (18%)	2 (1%)
Nausea	98 (50%)	15 (8%)	20 (10%)	0
Diarrhea	63 (32%)	12 (6%)	51 (25%)	1 (<1%)
Peripheral neuropathy§	63 (32%)	9 (5%)	96 (47%)	18 (9%)
Decreased appetite	69 (35%)	7 (4%)	11 (5%)	0
Weight loss	51 (26%)	4 (2%)	25 (12%)	2 (1%)
Asthenia	48 (25%)	16 (8%)	27 (13%)	9 (4%)
Constipation	33 (17%)	0	35 (17%)	3 (1%)
Cough	35 (18%)	1 (1%)	30 (15%)	0
Insomnia	31 (16%)	2 (1%)	32 (16%)	4 (2%)
Back pain	30 (15%)	1 (1%)	29 (14%)	2 (1%)
Pneumonia¶	35 (18%)	24 (12%)	34 (17%)	21 (10%)
Pyrexia	30 (15%)	3 (2%)	22 (11%)	2 (1%)
Cataract	42 (22%)	17 (9%)	13 (6%)	3 (1%)
Vomiting	40 (21%)	8 (4%)	9 (4%)	0
Peripheral edema	23 (12%)	1 (1%)	26 (13%)	0
Dyspnea	18 (9%)	1 (1%)	27 (13%)	5 (2%)
Bronchitis	24 (12%)	3 (2%)	20 (10%)	1 (<1%)
Upper respiratory tract infection	35 (18%)	5 (3%)	30 (15%)	1 (<1%)

Data are n (%). Events that occurred in <10% of patients are not shown. Events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03).

*Three patients from Vd group who did not receive any doses of study drug were excluded from the safety population.

†Includes four grade 5 events: three (2%) cases of pneumonia and one (1%) case of bronchitis.

‡Includes four grade 5 events: three (1%) cases of pneumonia and one (<1%) case of anemia.

§Includes high-level MedDRA term "peripheral neuropathies NEC".

¶Includes pneumonia, lung infection, haemophilus infection, pulmonary sepsis, and pneumonia respiratory syncytial viral, pneumonia pneumococcal, pneumonia influenza viral, pneumonia parainfluenza viral, pneumonia bacterial, and pneumonia fungal infections.

XVd was not associated with major organ, cardiac, pulmonary, renal, or liver toxicities.[2]

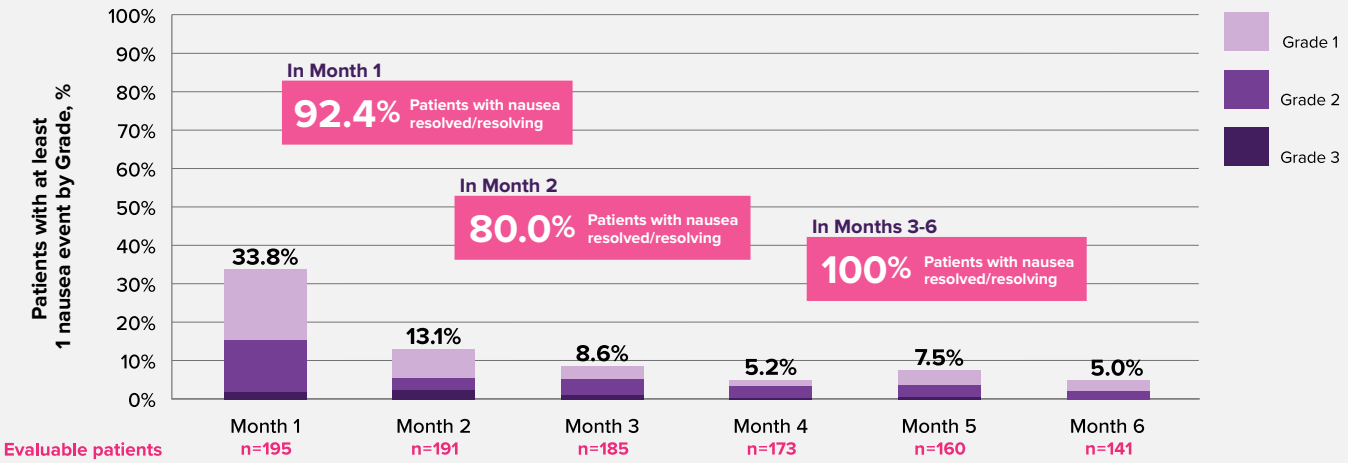
- **Fatal ARs occurred in 6% of patients within 30 days of last treatment, including pneumonia (n=3) and sepsis (n=3)[1]**
- **Serious ARs occurred in 52% of patients. Treatment discontinuation rate due to ARs was 19%. The most frequent ARs requiring permanent discontinuation in >2% of patients included fatigue, nausea, thrombocytopenia, decreased appetite, peripheral neuropathy and vomiting[1]**

Treatment-related nausea associated with XVd was generally manageable and transient[1,2]

In the XVd trial, over **92%** of nausea cases were resolved in the first month[2]

Nausea events were observed in 50% of patients (8% Grade 3).[1]

Percentage of patients experiencing nausea events per month in the XVd arm of XVd trial[2]



The XVd trial protocol required a prophylactic 5-HT3 antagonist to address nausea but allowed for other interventions as required.[2]

Before starting therapy with XPOVIO, provide 2 prophylactic antiemetics[1]

Ondansetron
8 mg PO[10] 30 to 60 minutes prior to each dose and continued for every 8 hours for 2 days following dosing

+

Olanzapine
2.5 mg–5.0 mg PO qhs[2]

OR

Aprepitant
125 mg PO QAM day 1 and 80 mg for 2 days each week[10-12]

OR

Rolapitant
180 mg PO 2 hours before XPOVIO Q2W[10,13]

Alternatively, once weekly oral dose of Akynzeo (netupitant 300 mg + palonosetron 0.5 mg)[14,15]

A 5-HT3 receptor antagonist and other antinausea agents should be provided prior to and during treatment with XPOVIO.[1] Specific antiemetics listed above are for reference purposes only. All treatment decisions must be individualized and made solely at the discretion of the healthcare professional.

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

The most common adverse reactions (ARs) (≥20%) in patients with multiple myeloma who received XVd were fatigue, nausea, decreased appetite, diarrhea, peripheral neuropathy, upper respiratory tract infection, decreased weight, cataract, and vomiting.

Grade 3-4 laboratory abnormalities (≥10%) were thrombocytopenia, lymphopenia, hypophosphatemia, anemia, hyponatremia and neutropenia.

Please see Important Safety Information and full Prescribing Information.

XPOVIO® (selinexor)

XPOVIO is approved as early as first relapse in MM[1]

- XPOVIO provides an opportunity to introduce a different MOA for patients with MM who have progressed on commonly used therapy combinations, including those with daratumumab[1-3]
- XVd demonstrated an early and sustained PFS benefit over Vd, with deep and durable responses[1]
- Oral, once-weekly XPOVIO provides dosing flexibility without compromising efficacy[1,2]

KaryFORWARD®
PATIENT SUPPORT BY KARYOPHARM

KaryForward is a patient support program dedicated to providing assistance and resources to patients and their caregivers for XPOVIO treatment

ENROLL YOUR PATIENTS OR LEARN MORE:

CALL
1-877-KARY4WD (1-877-527-9493)
Monday through Friday, 8 AM to 8 PM ET

VISIT
KaryForward.com/hcp

References: 1. XPOVIO (selinexor) [prescribing information]. Newton, MA: Karyopharm Therapeutics Inc.; August 2021. **2.** Data on File. Karyopharm Therapeutics Inc. 2021. **3.** National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma V.3.2022. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed October 28, 2021. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **4.** FDA website. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-granted-accelerated-approval-belantamab-mafodotin-blmf-multiple-myeloma. Accessed October 26, 2021. **5.** FDA website. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-melphalan-flufenamide-relapsed-or-refractory-multiple-myeloma. Accessed October 26, 2021. **6.** FDA website. https://www.fda.gov/news-events/press-announcements/fda-approves-first-cell-based-gene-therapy-adult-patients-multiple-myeloma. Accessed October 26, 2021. **7.** Benkova K, Mihalyova J, Hajek R, Jelinek T. Selinexor, selective inhibitor of nuclear export: unselective bullet for blood cancers. *Blood Rev*. 2021;46:100758. **8.** Azmi AS, Uddin MH, Mohammad RM. The nuclear export protein XPO1 - from biology to targeted therapy. *Nat Rev Clin Oncol*. 2021;18(3):152-169. **9.** Grosicki S, Simonova M, Spicka I, et al. Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. *Lancet*. 2020;396(10262):1563-1573. **10.** Gavriatopoulou M, Chari A, Chen C, et al. Integrated safety profile of selinexor in multiple myeloma: experience from 437 patients enrolled in clinical trials. *Leukemia*. 2020;34(9):2430-2440. **11.** Mikhael J, Noonan KR, Faiman B, et al. Consensus recommendations for the clinical management of patients with multiple myeloma treated with selinexor. *Clin Lymphoma Myeloma Leuk*. 2020;20(6):351-357. **12.** EMEND (aprepitant) [prescribing information]. Whitehouse Station, NJ: Merck & Co, Inc; 2021. **13.** VARUBI (rolapitant) [prescribing information]. Deerfield, IL: TerSera Therapeutics LLC; 2020. **14.** AKYNZEO (netupitant and palonosetron) [prescribing information]. Lugano, Switzerland: Helsinn Healthcare SA; 2021. **15.** Magen H, Geva M, Volchik Y, Avigdor A, Nagler A. Selinexor, bortezomib, and dexamethasone for heavily pretreated multiple myeloma: a case series. *Clin Lymphoma Myeloma Leuk*. 2020;20(12):e947-e955.

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS (cont'd)

Fatal ARs occurred in 6% of patients within 30 days of last treatment. Serious ARs occurred in 52% of patients. Treatment discontinuation rate due to ARs was 19%. The most frequent ARs requiring permanent discontinuation in >2% of patients included fatigue, nausea, thrombocytopenia, decreased appetite, peripheral neuropathy and vomiting. Adverse reactions led to XPOVIO dose interruption in 83% of patients and dose reduction in 64% of patients.

USE IN SPECIFIC POPULATIONS

No overall difference in effectiveness of XPOVIO was observed in patients >65 years old when compared with younger patients. Patients ≥65 years old had a higher incidence of discontinuation due to an adverse reaction (AR) and a higher incidence of serious ARs than younger patients. The effect of end-stage renal disease (CL_{CR} <15 mL/min) or hemodialysis on XPOVIO pharmacokinetics is unknown.

Please see Important Safety Information and full Prescribing Information.

To report SUSPECTED ADVERSE REACTIONS, contact Karyopharm Therapeutics Inc. at 1-888-209-9326 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Karyopharm® Therapeutics