REAL-WORLD DATA CAN HELP PROVIDE A BETTER UNDERSTANDING OF PATIENT OUTCOMES IN ROUTINE CLINICAL PRACTICE[3,6]

*The NINLARO regimen includes NINLARO+lenalidomide+dexamethasone.[1]

INDICATION AND USAGE

Indication: NINLARO is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

Limitations of Use: NINLARO is not recommended for use in the maintenance setting or in newly diagnosed multiple myeloma in combination with lenalidomide and dexamethasone outside of controlled clinical trials.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Thrombocytopenia** has been reported with NINLARO. Platelet nadirs typically occurred between Days 14-21 of each 28-day cycle and recovered to baseline by the start of the next cycle. Grade 3 thrombocytopenia was reported in 17% of patients in the NINLARO regimen and Grade 4 thrombocytopenia was reported in 13% in the NINLARO regimen. During treatment, monitor platelet counts at least monthly, and consider more frequent monitoring during the first three cycles. Manage thrombocytopenia with dose modifications and platelet transfusions as per standard medical guidelines.

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

NINLARO® (ixazomib) capsules
4mg | 3mg | 2.3mg

CLINICAL TRIAL POPULATIONS MAY NOT BE REPRESENTATIVE OF YOUR TYPICAL PATIENTS

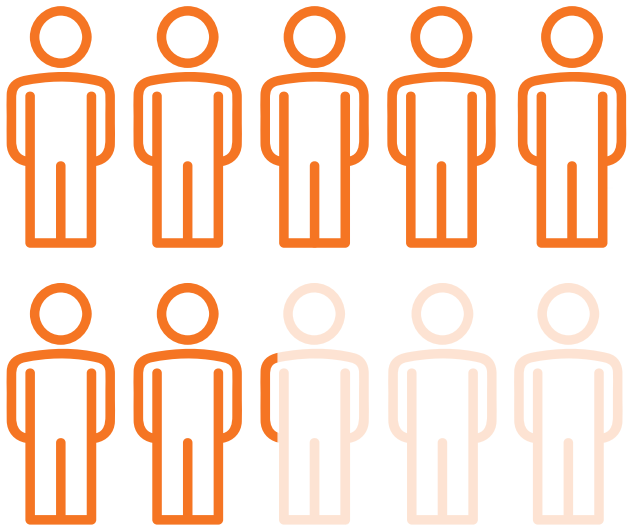
- Certain patient populations with multiple myeloma are underrepresented in clinical trials due to age, comorbidities, or poor performance status[6]

FOR THOSE WITH RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA RECEIVING ROUTINE CARE IN THE UNITED STATES

UP TO

72%

OF REAL-WORLD PATIENTS DO NOT MEET THE ELIGIBILITY CRITERIA FOR CLINICAL TRIALS[6]



Many common patient populations you see with multiple myeloma are typically underrepresented in clinical trials, including[6-8]:

- Elderly patients
- Patients from ethnic minorities or underprivileged socioeconomic backgrounds
- Patients with comorbidities or low performance status

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Gastrointestinal Toxicities,** including diarrhea, constipation, nausea and vomiting were reported with NINLARO and may occasionally require the use of antidiarrheal and antiemetic medications, and supportive care. Diarrhea resulted in the discontinuation of one or more of the three drugs in 3% of patients in the NINLARO regimen and 2% of patients in the placebo regimen. Adjust dosing for Grade 3 or 4 symptoms.
- **Peripheral Neuropathy** was reported with NINLARO. The most commonly reported reaction was peripheral sensory neuropathy (24% and 17% in the NINLARO and placebo regimens, respectively). Peripheral motor neuropathy was not commonly reported in either regimen (<1%). Peripheral neuropathy resulted in discontinuation of one or more of the three drugs in 4% of patients in the NINLARO regimen and <1% of patients in the placebo regimen. During treatment, monitor patients for symptoms of neuropathy and consider adjusting dosing for new or worsening peripheral neuropathy.
- **Peripheral Edema** was reported with NINLARO. Evaluate for underlying causes and provide supportive care, as necessary. Adjust dosing of NINLARO for Grade 3 or 4 symptoms or dexamethasone per its prescribing information.

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

WITH MANY REGIMENS IN THE RELAPSED AND/OR REFRACTORY TREATMENT SETTING, REAL-WORLD RESULTS DIFFER FROM EXPECTATIONS SET BY RANDOMIZED CLINICAL TRIALS (RCTs)

In a review of patients with relapsed and/or refractory multiple myeloma in the real world, patients who were categorized as "RCT-ineligible" had worse overall survival and higher mortality risk compared with patients with "RCT-eligible" characteristics[6]

Several factors may contribute to differences in outcomes, including[6]:

ADVERSE REACTIONS

A SIGNIFICANT DIFFERENCE IN PATIENT POPULATIONS

PATIENT ADHERENCE

CHALLENGES WITH ADMINISTRATION

BURDEN OF HAVING TO TRAVEL TO A TREATMENT CENTER

IN REAL-WORLD STUDIES, PATIENTS WITH MULTIPLE MYELOMA HAD AN INCREASED RISK OF MORTALITY AND DISEASE PROGRESSION AS COMPARED WITH PATIENTS IN CLINICAL TRIALS*[6]

*Based on a review of patients with relapsed and/or refractory multiple myeloma in the real world.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Cutaneous Reactions,** including a fatal case of Stevens-Johnson syndrome, were reported with NINLARO. If Stevens-Johnson syndrome occurs, discontinue NINLARO and manage as clinically indicated. Rash, most commonly maculo-papular and macular rash, was reported with NINLARO. Rash resulted in discontinuation of one or more of the three drugs in <1% of patients in both regimens. Manage rash with supportive care or with dose modification if Grade 2 or higher.
- **Thrombotic Microangiopathy** has been reported with NINLARO. Fatal cases of thrombotic microangiopathy, including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), have been reported in patients who received NINLARO. Monitor for signs and symptoms of TTP/HUS. If the diagnosis is suspected, stop NINLARO and evaluate. If the diagnosis of TTP/HUS is excluded, consider restarting NINLARO. The safety of reinitiating NINLARO therapy in patients previously experiencing TTP/HUS is not known.

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

NINLARO® (ixazomib) capsules
4mg | 3mg | 2.3mg

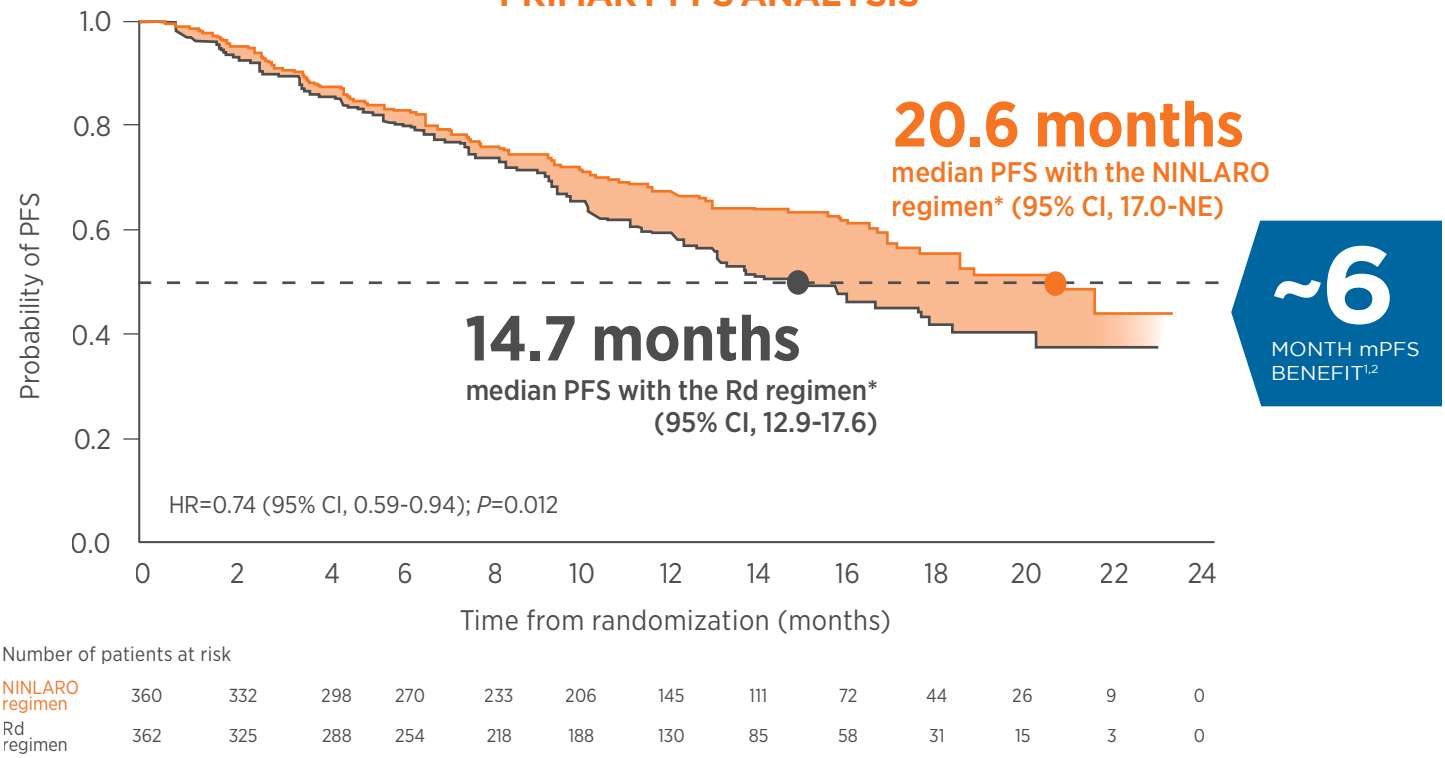
THE NINLARO® (ixazomib) REGIMEN* PROLONGED PROGRESSION-FREE SURVIVAL VS THE Rd REGIMEN*[1,2]

STUDY DESIGN[1]

TOURMALINE-MM1 was a global, phase 3, randomized (1:1), double-blind, placebo-controlled study that evaluated the safety and efficacy of the NINLARO regimen* vs the Rd regimen* until disease progression or unacceptable toxicity in 722 patients with relapsed and/or refractory multiple myeloma who received 1-3 prior therapies

- The primary endpoint of PFS, according to 2011 IMWG criteria, was assessed every 4 weeks until disease progression by a blinded IRC and was based on central laboratory results
- Key secondary endpoints included OS and OS in del(17p)[2]
- Other secondary endpoints included ORR, PFS in patients with high-risk cytogenetics,† and safety[2]
- Patients who were refractory to lenalidomide or PIs were excluded from the study

PRIMARY PFS ANALYSIS[1,2]



Number of patients at risk

NINLARO regimen	360	332	298	270	233	206	145	111	72	44	26	9	0
Rd regimen	362	325	288	254	218	188	130	85	58	31	15	3	0

Final OS Analysis[1]

- With a median follow-up of ~85 months, median OS in the ITT population was 53.6 months for patients receiving the NINLARO regimen* and 51.6 months for patients receiving the Rd regimen* (HR=0.94 [95% CI: 0.78-1.13])

*The NINLARO regimen included NINLARO+lenalidomide+dexamethasone. The Rd regimen included placebo+lenalidomide+dexamethasone.[1]
†Defined as patients with del(17p), t(4;14), and/or t(14;16).[2]
CI=confidence interval; HR=hazard ratio; IMWG=International Myeloma Working Group; IRC=independent review committee; ITT=intent-to-treat; mPFS=median PFS; NE=not evaluable; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; PI=proteasome inhibitor.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Hepatotoxicity** has been reported with NINLARO. Drug-induced liver injury, hepatocellular injury, hepatic steatosis, hepatitis cholestatic and hepatotoxicity have each been reported in <1% of patients treated with NINLARO. Hepatotoxicity has been reported (10% in the NINLARO regimen and 9% in the placebo regimen). Monitor hepatic enzymes regularly and adjust dosing for Grade 3 or 4 symptoms.

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

THE NINLARO TRIPLET REGIMEN* DEMONSTRATED A SAFETY PROFILE APPROPRIATE FOR LONG-TERM† TREATMENT[9,10]

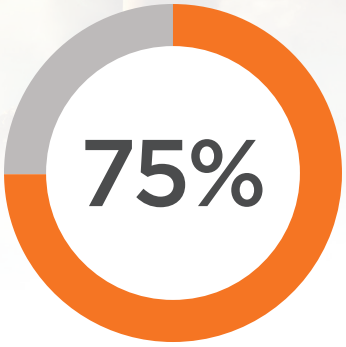
IN TOURMALINE-MM1, DISCONTINUATION RATES DUE TO ARs WERE SIMILAR ACROSS REGIMENS[9]

13% vs **11%**

with the NINLARO and Rd regimens,* respectively

Permanent discontinuation of NINLARO due to ARs occurred in 10% of patients[1]

THE MAJORITY OF PATIENTS CONTINUED AT THE STARTING DOSE OF NINLARO WITHOUT DOSE REDUCTION[9]



of patients receiving the NINLARO regimen* in TOURMALINE-MM1 continued on their starting NINLARO dose

- The median dose intensity for NINLARO and placebo was high and similar in the NINLARO and Rd regimens*: 97.8% and 100%, respectively[9]
- Relative dose intensity was calculated as 100 x (total amount of dose taken/total planned dose over treated cycles)[9]

Safety in high-risk‡ patient population

- The overall safety profiles in the high-risk and standard-risk cytogenetics patients in each group are consistent with data reported for the overall population[10]
- As seen in the overall population, in both high-risk and standard-risk cytogenetics patients, common adverse events were primarily of grade 1 or 2 severity and included diarrhea, constipation, neutropenia, and anemia[10]

*The NINLARO regimen included NINLARO+lenalidomide+dexamethasone. The Rd regimen included placebo+lenalidomide+dexamethasone.[1]
†Used herein to refer to treatment to disease progression or unacceptable toxicity.[1]
‡Defined as patients with del(17p), t(4;14), and/or t(14;16).[2]
AR=adverse reaction.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Embryo-fetal Toxicity:** NINLARO can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with NINLARO and for 90 days following the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with NINLARO and for 90 days following the last dose.
- **Increased Mortality in Patients Treated with NINLARO in the Maintenance Setting:** In two prospective randomized clinical trials in multiple myeloma in the maintenance setting, treatment with NINLARO resulted in increased deaths. Treatment of patients with NINLARO for multiple myeloma in the maintenance setting is not recommended outside of controlled trials.

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

NINLARO® (ixazomib) capsules
4mg | 3mg | 2.3mg

In TOURMALINE-MM1

THE NINLARO® (ixazomib) REGIMEN* DEMONSTRATED A SAFETY PROFILE COMPARABLE TO THE Rd REGIMEN*[1]

NONHEMATOLOGIC ARs OCCURRING IN ≥5% OF PATIENTS WITH A ≥5% DIFFERENCE BETWEEN NINLARO+Rd AND Rd IN TOURMALINE-MM1[1]

	NINLARO+Rd* (n=361)			Rd* (n=359)		
AR	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Diarrhea	52%	10%	0	43%	3%	0
Constipation	35%	<1%	0	28%	<1%	0
Peripheral neuropathies†	32%	2%	0	24%	2%	0
Nausea	32%	2%	0	23%	0	0
Peripheral edema	27%	2%	0	21%	1%	0
Back pain‡	27%	<1%	0	24%	3%	0
Rash†	27%	3%	0	16%	2%	0
Upper respiratory tract infection‡	27%	1%	0	23%	1%	0
Vomiting	26%	1%	0	13%	<1%	0
Bronchitis	22%	2%	0	17%	2%	<1%

- Serious ARs reported in ≥2% of patients in the NINLARO regimen included diarrhea (3%), thrombocytopenia (2%), and bronchitis (2%)[1]
- Incidence of thrombocytopenia in patients in the NINLARO and Rd regimens,* respectively: any grade, 85% vs 67%; grades 3-4, 30% vs 14%[1]
- Incidence of neutropenia in the NINLARO and Rd regimens,* respectively: any grade, 74% vs 70%; grades 3-4, 34% vs 37%[1]

*The NINLARO regimen included NINLARO+lenalidomide+dexamethasone. The Rd regimen included placebo+lenalidomide+dexamethasone.[1]

†Represents a pooling of preferred terms.[1]

‡At the time of the final analysis, these adverse reactions no longer met the criterion for a ≥5% difference between the NINLARO regimen and the placebo regimen.[1]

AR=adverse reaction.

THE NINLARO TRIPLET REGIMEN MAY OFFER DURABLE EFFICACY WITH SAFETY THAT IS SIMILAR TO A DOUBLET TO PATIENTS WITH RELAPSED MULTIPLE MYELOMA[1,2,5]

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

NINLARO® (ixazomib) capsules
4mg | 3mg | 2.3mg

Takeda Oncology Here2Assist

We're here to help your patients with their coverage, financial, and educational resource needs

From helping patients understand coverage options to identifying available financial assistance, Takeda Oncology Here2Assist™ is committed to offering your patients comprehensive support.

Takeda Oncology Here2Assist™

- Works with your patients' insurance company to help get your patient started on their medication
- Identifies available financial assistance that may be right for your patients
- May help eligible patients get started on treatment in the event of an insurance delay
- Identifies specialty pharmacies to help fill and ship your patients' prescriptions appropriately
- Conducts regular follow-up calls to patients
- Sends text message status updates and reminders to patients*

*Patients will need to enroll in the texting program to receive text messages.

FOR MORE INFORMATION ABOUT ACCESS SUPPORT AND FINANCIAL ASSISTANCE THAT YOUR PATIENTS MAY QUALIFY FOR, CALL TAKEDA ONCOLOGY HERE2ASSIST AT 1-844-817-6468, OPTION 2. **LET'S TALK.** WE'RE AVAILABLE MONDAY-FRIDAY, 8AM-8PM ET, OR VISIT US AT **WWW.HERE2ASSIST.COM** TO LEARN MORE.

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

PATIENTS INCLUDED IN REAL-WORLD STUDIES REFLECTED THOSE SEEN IN CLINICAL PRACTICE

REAL-WORLD STUDY LIMITATIONS

Real-world analyses are often nonrandomized, observational, retrospective studies that may have unobserved treatment-selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data.[4]

REAL-WORLD EVIDENCE STUDY DESIGNS

	TERPOS ET AL, 2020[3]	HÁJEK ET AL, 2021[4]	MINARIK ET AL, 2021[5]
	Multicenter, retrospective study	*Retrospective study*	*Prospective study*
Study group /duration	12 clinical centers between December 2015 and October 2017	Pooled analysis of data from 2 discrete sources or registries*: July 2016–September 2019 (15 countries) and May 2007–February 2020	Comparative study of patients treated with NINLARO regimen vs Rd regimen between 2016 and 2018
Patient population	• 155 patients† • Relapsed/refractory multiple myeloma • Median of 1 prior line of therapy • Some patients would not have been eligible for TOURMALINE-MM1	• 263 patients† • Relapsed/refractory multiple myeloma • Median of 2 prior lines of therapy • Some patients would not have been eligible for TOURMALINE-MM1	• 344 patients† • Relapsed/refractory multiple myeloma • Median of 1 prior line of therapy • Some patients would not have been eligible for TOURMALINE-MM1
Treatment regimen	NINLARO regimen‡ through early access program	NINLARO regimen‡ used in INSIGHT MM (n=132) and Czech RMG (n=131)	NINLARO regimen‡ (n=127) vs Rd regimen‡ (n=217) as part of Named Patient Program
Key study endpoints	• ORR • CBR • DCR • Safety	• Best response to therapy • DOT • TTNT • PFS • OS	• PFS • Response rates • OS

*Many of the patients included in the analysis were treated at academic centers; therefore, these results may not be representative of the community practice setting.[4]

†Key exclusion criteria for Minarik et al included: active 1L therapy; patients with missing data for primary endpoints; patients in clinical trials; patients who switched combination regimens. In Hájek et al, patients from INSIGHT MM were excluded if they had missing or incomplete data or had signed the study informed consent form more than 3 months after starting the NINLARO regimen. This analysis also excluded patients from RMG with missing or incomplete data. In Terpos et al, no exclusion criteria were identified.[3-5]

‡The NINLARO regimen included NINLARO+lenalidomide+dexamethasone. The Rd regimen included placebo+lenalidomide+dexamethasone.[1]

IMPORTANT SAFETY INFORMATION (cont'd)

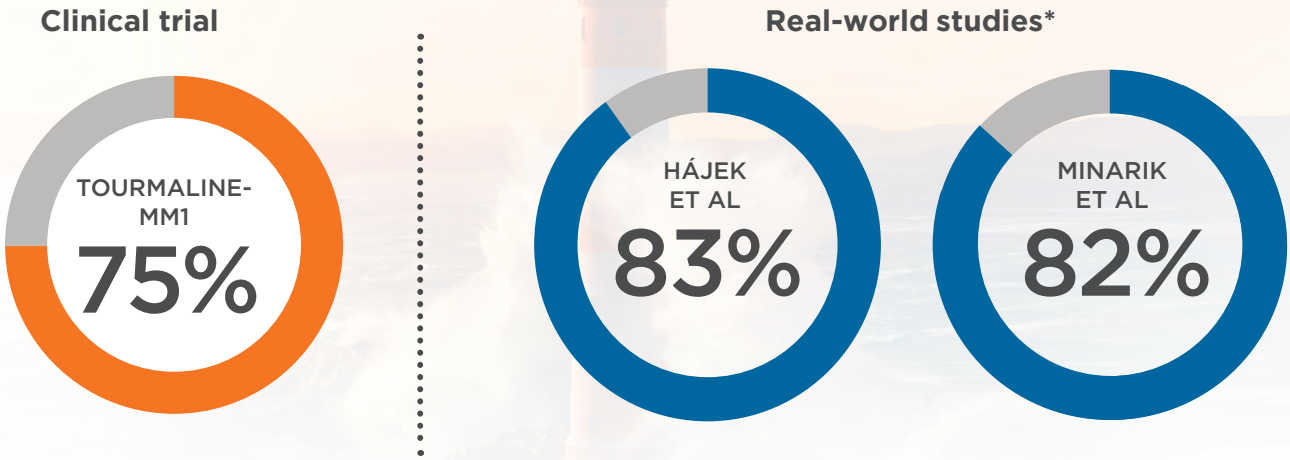
ADVERSE REACTIONS

The most common adverse reactions (≥ 20%) in the NINLARO regimen compared to placebo in combination with lenalidomide plus dexamethasone, respectively were thrombocytopenia (85%, 67%; pooled from adverse event and laboratory data), neutropenia (74%, 70%; pooled from adverse event and laboratory data), diarrhea (52%, 43%), constipation (35%, 28%), peripheral neuropathy (32%, 24%), nausea (32%, 23%), edema peripheral (27%, 21%), rash (27%, 16%), vomiting (26%, 13%), and bronchitis (22%, 17%). Serious adverse reactions reported in ≥ 2% of patients in the NINLARO regimen included diarrhea (3%), thrombocytopenia (2%), and bronchitis (2%).

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

ADVERSE REACTIONS SEEN IN REAL-WORLD SETTINGS WERE CONSISTENT WITH THE KNOWN SAFETY PROFILE[4,5,9,11]

THE MAJORITY OF PATIENTS IN THE CLINICAL TRIAL AND CLINICAL PRACTICE REMAINED ON THERAPY AT THEIR STARTING DOSE[4,5,9]



Unadjusted, indirect comparison for illustration only; clinical significance is not implied. Cross-trial comparisons are potentially confounded by differences in trial design and study population.

Observational, retrospective analyses are not intended for direct comparison with clinical trials.

In real-world studies, the NINLARO regimen demonstrated a tolerability profile comparable to the NINLARO arm in TOURMALINE-MM1[1-5]

Terpos et al (N=155)[3]

Occurrence rates of specific safety aspects of clinical interest: PN (35% vs 27%), PN grade >2 (3% vs 2%), thromboembolism (5% vs 8%), herpes zoster (5% vs 5%), hypertension (4% vs 6%) as reported in the combined study vs MM1, respectively.

Hájek et al (N=263)[11]

The most common ARs leading to NINLARO discontinuations included: infection (19%), neutropenia (6%), thrombocytopenia (6%), diarrhea (3%), rash (3%), nausea (3%), fatigue (2%), other† (32%).

Minarik et al (N=127)[5]

Grade ≥3 AEs reported in ≥10% of patients with the NINLARO regimen‡ vs Rd regimen,‡ respectively, included anemia (12% vs 26%), neutropenia (28% vs 23%), thrombocytopenia (21% vs 23%), infection (21% vs 23%), exanthema/rash (25%§ vs 0%), and other (19% vs 32%).

*Dose reduction data not available for Terpos et al.
†More than 1 AE could be assigned to 1 patient; each AE was counted only once for each patient.[4]
‡The NINLARO regimen included NINLARO+lenalidomide+dexamethasone. The Rd regimen included placebo+lenalidomide+dexamethasone.[1]
§Grade ≥3 exanthema/rash was reported in 1 patient receiving the NINLARO regimen (n=1/4).[5]
AE=adverse event; AR=adverse reaction; PN=peripheral neuropathy.

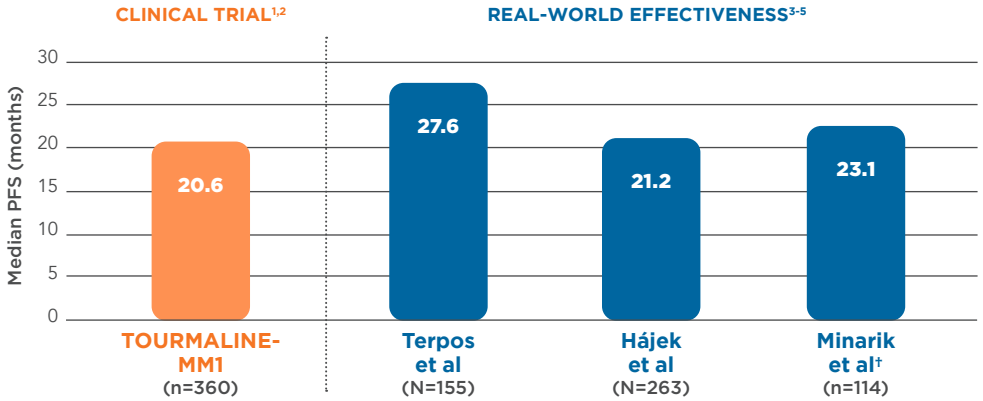
IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS: Avoid concomitant administration of NINLARO with strong CYP3A inducers.

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

NINLARO® (ixazomib) capsules
4mg | 3mg | 2.3mg

CONSISTENT PFS WAS SEEN WITH THE NINLARO® (ixazomib) REGIMEN* IN THE REAL WORLD[1-3,5]

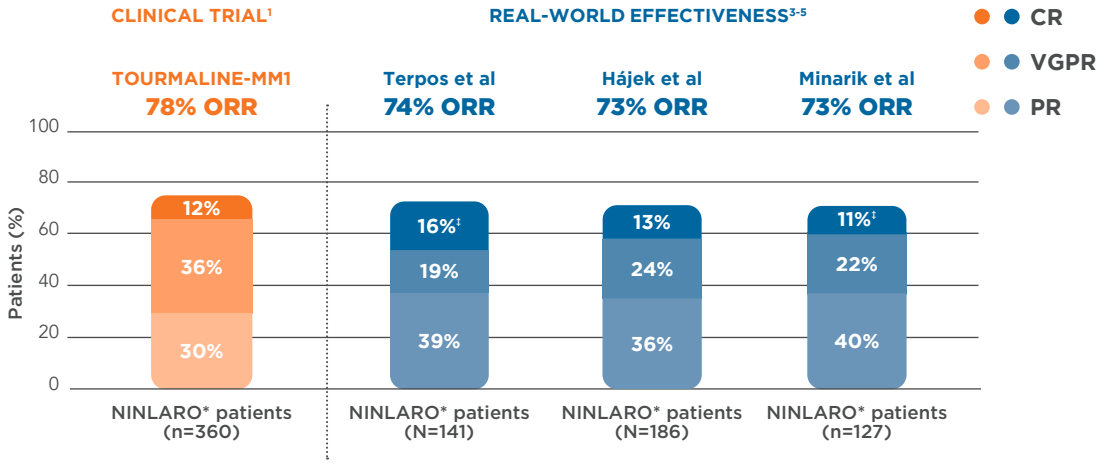


- Real-world analyses are often nonrandomized, observational, retrospective studies that may have unobserved confounding and treatment-selection biases as well as other limitations that should be considered when comparing results with clinical trials. Outcomes should be interpreted with caution because of small sample size, limited follow-up, and limited maturity of data[4]
- There is an unknown overlap in study populations across the RWE studies due to inclusion of patients from the same registries[3-5]
- These RWE studies included patients ineligible for TOURMALINE-MM1 based on refractory status to lenalidomide and/or proteasome inhibitors, comorbidities, performance status, and median lines of previous therapy. These RWE studies lack adequate controls to establish safety and efficacy in these subgroups[3-5]
- These RWE studies included analyses of PFS across select patient subgroups. In certain subgroups, the median PFS observed was not consistent with the overall PFS observed. However, these studies were not powered to show significance in PFS across these subgroups[3-5,11]
- Observational, retrospective analyses are not intended for direct comparison with clinical trials
- Unadjusted, indirect comparison for illustration only; clinical significance is not implied. Cross-trial comparisons are potentially confounded by differences in trial design and study population

1L=first line; CBR=clinical benefit rate; DOT=duration of therapy; DCR=disease control rate; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; RMG=Registry of Monoclonal Gammopathies; RWE=real-world evidence; TTNT=time to next therapy.

*The NINLARO regimen included NINLARO+lenalidomide+dexamethasone.[1]
†Treatment lines 2-4.[5]
‡Includes CR and stringent CR.
CR=complete response; ORR=overall response rate; PFS=progression-free survival; PR=partial response; VGPR=very good partial response.

CONSISTENT RESPONSE RATES WERE SEEN IN THE REAL WORLD[1,3-5]



Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS

- **Lactation:** Advise women not to breastfeed during treatment with NINLARO and for 90 days after the last dose.
- **Hepatic Impairment:** Reduce the NINLARO starting dose to 3 mg in patients with moderate or severe hepatic impairment.
- **Renal Impairment:** Reduce the NINLARO starting dose to 3 mg in patients with severe renal impairment or end-stage renal disease requiring dialysis. NINLARO is not dialyzable.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda Pharmaceuticals at 1-844-617-6468 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

WARNINGS AND PRECAUTIONS

- **Thrombocytopenia** has been reported with NINLARO. Platelet nadirs typically occurred between Days 14-21 of each 28-day cycle and recovered to baseline by the start of the next cycle. Grade 3 thrombocytopenia was reported in 17% of patients in the NINLARO regimen and Grade 4 thrombocytopenia was reported in 13% in the NINLARO regimen. During treatment, monitor platelet counts at least monthly, and consider more frequent monitoring during the first three cycles. Manage thrombocytopenia with dose modifications and platelet transfusions as per standard medical guidelines.

THE NINLARO® (ixazomib) REGIMEN* DEMONSTRATED

CONSISTENT EFFICACY AND TOLERABILITY WAS SEEN WITH THE NINLARO REGIMEN* IN THE REAL WORLD[3,6]

Real-world studies include a broader range of patients who tend to have worse outcomes vs patients in clinical trial settings[3,6]

TOURMALINE-MM1 Clinical trial[1,9]	Terpos et al Real-world study[3]	Hájek et al Real-world study[4]	Minarik et al Real-world study[5]
20.6 months mPFS	**27.6 months mPFS**	**21.2 months mPFS**	**23.1 months mPFS**
78% ORR	**74% ORR**	**73% ORR**	**73% ORR**
75% of patients continued at the starting dose of NINLARO without dose reduction	**Not evaluated**	**83% of patients** continued at the starting dose of NINLARO without dose reduction	**82% of patients** continued at the starting dose of NINLARO without dose reduction

Unadjusted, indirect comparison for illustration only; clinical significance is not implied. Cross-trial comparisons are potentially confounded by differences in trial design and study population.

SAFETY PROFILE

- In TOURMALINE-MM1, the NINLARO regimen* demonstrated a similar discontinuation rate to that of the Rd regimen* (13% vs 11%, respectively).[9] Serious ARs reported in ≥2% of patients included diarrhea (3%), thrombocytopenia (2%) and bronchitis (2%).[1]

*The NINLARO regimen included NINLARO+lenalidomide+dexamethasone. The Rd regimen included placebo+lenalidomide+dexamethasone.
AR=adverse reaction; mPFS=median progression-free survival; ORR=overall response rate.

IMPORTANT SAFETY INFORMATION (cont'd)

SUMMARY OF WARNINGS AND PRECAUTIONS

Warnings and Precautions for NINLARO include thrombocytopenia, gastrointestinal toxicities, peripheral neuropathy, peripheral edema, cutaneous reactions, including a fatal case of Stevens-Johnson syndrome, thrombotic microangiopathy, including fatal cases, hepatotoxicity, embryo-fetal toxicity, and increased mortality in patients treated with NINLARO in the maintenance setting.

ADVERSE REACTIONS

The most common adverse reactions (≥ 20%) in the NINLARO regimen compared to placebo in combination with lenalidomide plus dexamethasone, respectively were thrombocytopenia (85%, 67%; pooled from adverse event and laboratory data), neutropenia (74%, 70%; pooled from adverse event and laboratory data), diarrhea (52%, 43%), constipation (35%, 28%), peripheral neuropathy (32%, 24%), nausea (32%, 23%), edema peripheral (27%, 21%), rash (27%, 16%), vomiting (26%, 13%), and bronchitis (22%, 17%). Serious adverse reactions reported in ≥ 2% of patients in the NINLARO regimen included diarrhea (3%), thrombocytopenia (2%), and bronchitis (2%).

Please see additional Important Safety Information throughout and accompanying NINLARO (ixazomib) full Prescribing Information.

REFERENCES: 1. NINLARO. Prescribing information. Takeda Pharmaceuticals America, Inc.; 04/2022. **2.** Moreau P, Masszi T, Grzasko N, et al; for TOURMALINE-MM1 Study Group. Oral ixazomib, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*. 2016;374(17):1621-1634. **3.** Terpos E, Ramasamy K, Maouche N, et al. Real-world effectiveness and safety of ixazomib-lenalidomide-dexamethasone in relapsed/refractory multiple myeloma. *Ann Hematol*. 2020;99(5):1049-1061. **4.** Hájek R, Mina ík J, Straub J, et al. Ixazomib-lenalidomide-dexamethasone in routine clinical practice: effectiveness in relapsed/refractory multiple myeloma. *Future Oncol*. 2021;374(17):1621-1634. **5.** Minarik J, Pika T, Radocha J, et al. Survival benefit of ixazomib, lenalidomide and dexamethasone (IRD) over lenalidomide and dexamethasone (Rd) in relapsed and refractory multiple myeloma patients in routine clinical practice. *BMC Cancer*. 2021;21(1):73. **6.** Chari A, Romanus D, Palumbo A, et al. Randomized clinical trial representativeness and outcomes in real-world patients: comparison of 6 hallmark randomized clinical trials of relapsed/refractory multiple myeloma. *Clin Lymphoma Myeloma Leuk*. 2020;20(1):8-17.e16. **7.** Richardson PG, San Miguel JF, Moreau P, et al. Interpreting clinical trial data in multiple myeloma: translating findings to the real-world setting. *Blood Cancer J*. 2018;8(11):109. **8.** Yong K, Delforge M, Driessen C, et al. Multiple myeloma: patient outcomes in real-world practice. *Br J Haematol*. 2016;175(2):252-264. **9.** Data on File. Takeda Pharmaceuticals America, Inc.; 2022. **10.** Avet-Loiseau H, Bahlis NJ, Chng W-J, et al. Ixazomib significantly prolongs progression-free survival in high-risk relapsed/refractory myeloma patients. *Blood*. 2017;130(24):2610-2618. **11.** Hájek R, Mina ík J, Straub J, et al. Ixazomib-lenalidomide-dexamethasone in routine clinical practice: effectiveness in relapsed/refractory multiple myeloma. *Future Oncol*, Supplemental material. Published online March 26, 2021. Accessed April 19, 2021. https://www.futuremedicine.com/doi/suppl/10.2217/fon-2020-1225.

NINLARO® (ixazomib) capsules
4mg | 3mg | 2.3mg