#### THE FACES OF **NINLARO**® (ixazomib)



## MIKE\* IS AN ELDERLY† PATIENT WITH MULTIPLE MYELOMA AND COMORBIDITIES EXPERIENCING HIS FIRST RELAPSE

### AT THE FIRST MULTIPLE MYELOMA RELAPSE, OFFER DURABLE STRENGTH WITH THE NINLARO REGIMEN<sup>11</sup>

Learn about patients who could benefit from NINLARO at NINLAROhcp.com

The models used herein are for demonstration purposes only.

\*Hypothetical patient.

<sup>†</sup>Used herein to refer to patients aged 75 years or older.

<sup>1</sup>The NINLARO regimen includes NINLARO + lenalidomide + dexamethasone. <sup>1</sup>

#### 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 NINLARO (ixazomib) full <a href="Prescribing">Prescribing</a> Information.





MEET MIKE, AN ELDERLY
VETERAN WITH
MULTIPLE MYELOMA
AND COMORBIDITIES
EXPERIENCING HIS
FIRST RELAPSE

Mike is 76 years old. He is a veteran, is now retired, and enjoys spending time with his wife and grandchildren.

- Mike has been living with multiple myeloma (MM) for 4 years
- He received a first-line anti-CD38 antibody-based regimen, followed by maintenance therapy - Mike is not lenalidomide refractory
- Following new symptoms, a clinic visit confirmed Mike's MM had relapsed
- · Like many others with MM, Mike is an elderly patient with comorbidities

#### More about your patients like Mike

- Nearly 1 in 3 (30%) patients experiencing their first MM relapse are aged 75 years or older\*2
- Older age, and having multiple comorbidities like renal insufficiency and CVD have been associated with reduced survival in people with RRMM<sup>3,4</sup>
- In the US veteran population, smoking and obesity, together with associated comorbidities like arthritis, diabetes, skin cancer, CHD, and pulmonary disease are prevalent.<sup>5-7</sup> Their incidence tends to be higher than in the general US population,<sup>5-7</sup> potentially impacting survival outcomes and limiting veterans' inclusion in clinical trials.<sup>8</sup>

Veterans with MM who were exposed to burn pits, Agent Orange, and other toxic substances may be eligible for healthcare and benefits under the Promise to Address Comprehensive Toxics (PACT) Act<sup>9,10</sup>

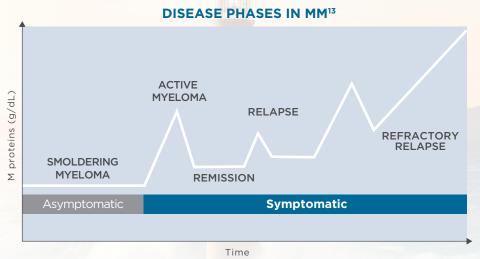
#### Mike's next treatment choice is crucial.

\*Based on chart audits, 20,277 US MM patients per year experience their first relapse; 6,054 of these patients are elderly.<sup>2</sup>

CHD=coronary heart disease; CVD=cardiovascular disease; RRMM=relapsed/refractory MM.

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

AS OUTCOMES MAY WORSEN WITH INCREASING LINES OF THERAPY, THE FIRST RELAPSE IS A CRITICAL JUNCTURE IN THE MM TREATMENT JOURNEY<sup>11,12</sup>



This figure represents a sample patient. Time to each phase differs by person.

#### MIKE'S GOALS

- Like many elderly people with cancer, Mike wants to maintain his independence<sup>14</sup>
- He wants a therapy that may allow him to maintain his lifestyle while maximizing therapeutic benefit
- An option with convenient dosing (without the need for regular travel to VA medical facility) and manageable tolerability, given his complex medical needs, is important to him

His doctor recommended a therapy that can:

- Significantly delay disease progression<sup>1</sup>
- Fit into his lifestyle with the convenience of an all-oral triplet regimen\*1,15,16
- Offer a generally tolerable safety profile<sup>1,17</sup>

After shared decision-making with his oncologist, **Mike chose the NINLARO**\* (ixazomib) triplet regimen.\*<sup>†</sup>

# WHAT ARE YOUR TREATMENT GOALS FOR AN ELDERLY PATIENT WITH MM AND COMORBIDITIES EXPERIENCING THEIR FIRST RELAPSE?

\*The NINLARO regimen includes NINLARO + lenalidomide + dexamethasone.1

†Please see pages 6-9 to review efficacy, safety, and dosing information for NINLARO. MM=multiple myeloma; VA=Veterans Affairs.

#### **IMPORTANT SAFETY INFORMATION**

#### 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 threedrugs in 3% of patients in the NINLARO regimenand 2% of patients in the placebo regimen. Adjust dosing for Grade 3 or 4 symptoms.





## NEXT TIME YOU SEE A PATIENT LIKE MIKE, CONSIDER THE ALL-ORAL NINLARO TRIPLET REGIMEN\*

#### **ABOUT MIKE**

#### Reason for clinic visit

• Patient had been experiencing new-onset back pain and generalized fatigue

#### **Diagnosis**

- Diagnosed with MM 4 years ago;
   R-ISS stage II
- Patient has a history of CVD/type 2 diabetes/CKD

#### Treatment history

- Initially treated with an anti-CD38 antibody + immunomodulator + steroid
- Treated for 25 months; achieved best response of CR

- Treatment was continued with an immunomodulator as maintenance therapy
- He is not lenalidomide refractory

## Diagnostic workup at current presentation

- ECOG PS: 1
- Atrial fibrillation: Now controlled 90 bpm. Tachycardia at 124 bpm
- Blood pressure: 155/90 mmHg
- Hemoglobin: 10.3 mg/dL
- Serum creatinine: 1.1 mg/dL
- Serum calcium: 11.7 mg/dL
- Serum M protein: 1.2 g/dL
- **Skeletal imaging:** One new lytic lesion
- Cytogenetics/FISH: Negative for high-risk features

Please see additional Important Safety Information throughout and NINLARO (ixazomib) full <u>Prescribing Information</u>.

<sup>\*</sup>The NINLARO regimen includes NINLARO + lenalidomide + dexamethasone.¹

CKD=chronic kidney disease; CR=complete response; CVD=cardiovascular disease;

ECOG PS=Eastern Cooperative Oncology Group performance status; FISH=fluorescence in situ hybridization;

R-ISS=revised International Staging System.

#### MIKE'S TREATMENT JOURNEY

**48% of elderly patients with MM receive doublet regimens.**<sup>2</sup> With the NINLARO triplet regimen,\* you can offer extended PFS, tolerability, and convenient dosing.<sup>1</sup>



"It's very convenient. I'm happy that I'm taking oral medication and I can take it anywhere."

-A real patient similar to Mike

CR=complete response; MM=multiple myeloma; PFS=progression-free survival; R-ISS=revised International Staging System.

#### IMPORTANT SAFETY INFORMATION

#### WARNINGS AND PRECAUTIONS (cont'd)

• **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.



<sup>\*</sup>The NINLARO regimen includes NINLARO + lenalidomide + dexamethasone.1

<sup>†</sup>Please see pages 6-9 to review efficacy, safety, and dosing information for NINLARO.

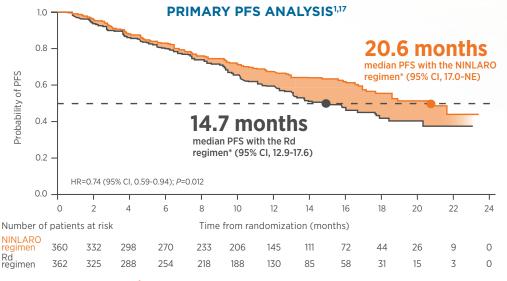
Next time you see an elderly patient with MM and comorbidities experiencing their first relapse

## THE NINLARO REGIMEN\* PROLONGED PROGRESSION-FREE SURVIVAL VS THE Rd REGIMEN<sup>1,17</sup>

#### STUDY DESIGN

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\* in 722 patients with relapsed and/or refractory multiple myeloma who received 1-3 prior therapies.<sup>1,17,18</sup>

- 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<sup>1</sup>
- Key secondary endpoints included OS and OS in del(17p)<sup>17</sup>
- Other select secondary endpoints included ORR, PFS in patients with high-risk cytogenetics,<sup>†</sup> and safety<sup>17</sup>
- Patients who were refractory to lenalidomide or Pls were excluded from the study<sup>1</sup>



#### FINAL OS ANALYSIS<sup>1</sup>

 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])

CI=confidence interval; HR=hazard ratio; IMWG=International Myeloma Working Group; IRC=independent review committee; ITT=intent-to-treat; NE=not evaluable; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; PI=proteasome inhibitor.

#### IMPORTANT SAFETY INFORMATION

#### WARNINGS AND PRECAUTIONS (cont'd)

• **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 NINLARO (ixazomib) full <a href="Prescribing Information">Prescribing Information</a>.

 $<sup>^*</sup>$ The NINLARO regimen included NINLARO + lenalidomide + dexamethasone. The Rd regimen included placebo + lenalidomide + dexamethasone.  $^1$ 

<sup>†</sup>Defined as patients with del(17p), t(4;14), and/or t(14;16).17

#### In TOURMALINE-MM1

## THE NINLARO 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<sup>1</sup>

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

#### Safety in high-risk<sup>§</sup> 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<sup>19</sup>
- 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<sup>19</sup>

 $^{1}$ At the time of the final analysis, these ARs no longer met the criterion for a  $\geq$ 5% difference between the NINLARO regimen and the placebo regimen. $^{1}$ 

 $^{\rm s}$ Defined as patients with del(17p), t(4;14), and/or t(14;16). AR=adverse reaction.

#### IMPORTANT SAFETY INFORMATION

#### WARNINGS AND PRECAUTIONS (cont'd)

• Cutaneous Reactions. Stevens-Johnson syndrome and toxic epidermal necrolysis, including fatal cases, have been reported with NINLARO. If Stevens-Johnson syndrome or toxic epidermal necrolysis occurs, discontinue NINLARO and manage as clinically indicated. Rash, most commonly maculo-papular and macular rash, was reported with NINLARO. Rash resulted in

4mg | 3mg | 2.3mg

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.

<sup>\*</sup>The NINLARO regimen included NINLARO + lenalidomide + dexamethasone. The Rd regimen included placebo + lenalidomide + dexamethasone.

<sup>†</sup>Represents a pooling of preferred terms.1

# THE NINLARO TRIPLET REGIMEN\* DEMONSTRATED A SAFETY PROFILE APPROPRIATE FOR LONG-TERM\* TREATMENT

#### AT FINAL SAFETY ANALYSIS<sup>‡1</sup>

THE MAJORITY OF PATIENTS DID NOT EXPERIENCE PERMANENT DISCONTINUATION OF NINLARO DUE TO ARS<sup>1</sup>

10%

After a median follow-up of ~85 months, permanent discontinuation of NINLARO due to an AR occurred in 10% of patients<sup>1,20</sup>

### THE MAJORITY OF PATIENTS CONTINUED AT THE STARTING DOSE OF NINLARO WITHOUT DOSE REDUCTION<sup>20</sup>

75%

of patients (n=269/361) receiving NINLARO + Rd in TOURMALINE-MM1 continued on their starting NINLARO dose<sup>\$20</sup>

- The median relative dose intensity for NINLARO + Rd and placebo + Rd was high and similar between both arms: 97.8% and 100%, respectively<sup>20</sup>
- Relative dose intensity was calculated as: 100 x (total amount of dose taken)
   ÷ (total prescribed dose of treated cycles)
- Serious ARs reported in ≥2% of patients in the NINLARO regimen included diarrhea (3%), thrombocytopenia (2%), and bronchitis (2%),¹

# THE NINLARO TRIPLET REGIMEN\* MAY OFFER PATIENTS LIKE MIKE EXTENDED EFFICACY WITH SAFETY THAT IS SIMILAR TO A DOUBLET\*1,17

#### IMPORTANT SAFETY INFORMATION

#### WARNINGS AND PRECAUTIONS (cont'd)

• 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 NINLARO (ixazomib) full <u>Prescribing Information</u>.

<sup>\*</sup>The NINLARO regimen includes NINLARO + lenalidomide + dexamethasone.1

<sup>†</sup>Used herein to refer to treatment until disease progression or unacceptable toxicity.1

<sup>&</sup>lt;sup>1</sup>Data cut-off for the final analysis: 28 September 2020.<sup>20</sup>

<sup>&</sup>lt;sup>§</sup> Median duration of exposure to NINLARO was 457 days (range: 1-2768 days).<sup>21</sup>

<sup>&</sup>lt;sup>4</sup>Total prescribed doses equals (dose prescribed at enrolment x number of prescribed doses per cycle x the number of treated cycles).<sup>20</sup> AR=adverse reaction: RCT=randomized controlled trial: Rd=lenalidomide + dexamethasone.

#### DOSING: CONSIDER AN ALL-ORAL PI-BASED REGIMEN YOUR PATIENTS CAN TAKE AT HOME 1,15,16

#### **DOSING SCHEDULE**<sup>1</sup>

| WEEK | DAY 1          | DAY 2                         | DAY 3    | DAY 4               | DAY 5         | DAY 6         | DAY 7      |
|------|----------------|-------------------------------|----------|---------------------|---------------|---------------|------------|
| 1    |                |                               |          |                     |               |               |            |
| WEEK | DAY 8          | DAY 9                         | DAY 10   | DAY 11              | DAY 12        | DAY 13        | DAY 14     |
| 2    |                | <b>d</b>                      | <b>d</b> | <b>d</b>            |               |               |            |
| WEEK | DAY 15         | DAY 16                        | DAY 17   | DAY 18              | DAY 19        | DAY 20        | DAY 21     |
| 3    |                |                               |          |                     |               | •             | <b>4</b> D |
| WEEK | DAY 22         | DAY 23                        | DAY 24   | DAY 25              | DAY 26        | DAY 27        | DAY 28     |
| 4    | •              | NO DOSE                       | NO DOSE  | NO DOSE             | NO DOSE       | NO DOSE       | NO DOSE    |
|      | NINLA<br>(4 mg | <b>ARO</b><br>y, 3 mg, 2.3 mg |          | nalidomide<br>5 mg) | Dexame (40 mg | ethasone<br>) |            |

As the graphic shows,

NINLARO is administered orally on days 1, 8, and 15 of a 28-day cycle.1 Lenalidomide is administered orally on days 1-21 of a 28-day cycle.<sup>1,15</sup>

Dexamethasone is administered orally on days 1, 8, 15, and 22 of a 28-day cycle.<sup>1,16</sup> Please note that there is **NO DOSING** on days 23-28.

- Advise patients to take NINLARO once a week on the same day and at approximately the same time for the first 3 weeks of a 4-week cycle. The importance of carefully following all dosage instructions should be discussed with patients starting treatment. Instruct patients to take the recommended dosage as directed because overdosage has led to deaths1
- The recommended starting dose of NINLARO is 4 mg (one capsule) in combination with lenalidomide and dexamethasone<sup>1</sup>
- A 3 mg starting dose is recommended for patients with moderate or severe hepatic impairment and patients with severe renal impairment or end-stage renal disease requiring dialysis. A 2.3-mg dose is also available for subsequent dose reductions due to ARs1

AR=adverse reaction; PI=proteasome inhibitor.

Grade 3 or 4 symptoms.

#### IMPORTANT SAFETY INFORMATION

#### 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

4mg | 3mg | 2.3mg

#### INDICATION AND USAGE

**Indication:** NINLARO\* (ixazomib) 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.
- 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.
- Cutaneous Reactions. Stevens-Johnson syndrome and toxic epidermal necrolysis, including fatal cases, have been reported with NINLARO. If Stevens-Johnson syndrome or toxic epidermal necrolysis 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 NINLARO (ixazomib) full Prescribing Information.

#### **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.
- 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.

#### **ADVERSE REACTIONS**

The most common adverse reactions ( $\geq$  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  $\geq$  2% of patients in the NINLARO regimen included diarrhea (3%), thrombocytopenia (2%), and bronchitis (2%).

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

#### **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.

Please see NINLARO (ixazomib) full Prescribing Information.



#### THE NINLARO REGIMEN\* OFFERS LONG-TERM† PROTEASOME INHIBITION UNTIL PROGRESSION 1,177



#### **EFFICACY**

In TOURMALINE-MM1, mPFS was extended by ~6 months (20.6 months with the NINLARO triplet regimen\* compared with 14.7 months with the Rd regimen\*).117



#### **TOLERABILITY**

- In TOURMALINE-MM1, permanent discontinuation of NINLARO due to an AR occurred in 10% of patients 1,20
- 75% of patients receiving the NINLARO regimen\* in TOURMALINE-MM1 continued on their starting dose of NINLARO<sup>\$20</sup>
- Serious ARs reported in ≥2% of patients included diarrhea (3%). thrombocytopenia (2%), and bronchitis (2%)<sup>1</sup>



#### **CONVENIENT DOSING**

The NINLARO triplet regimen\* is the first and only PI-based therapy with the convenience of all-oral administration. 1,15,16

#### OFFER THE NINLARO REGIMEN\* TO YOUR ELDERLY PATIENT WITH MM AND COMORBIDITIES EXPERIENCING THEIR FIRST RELAPSE

- \*The NINLARO regimen includes NINLARO + lenalidomide + dexamethasone.1
- <sup>†</sup>Used herein to refer to treatment to disease progression or unacceptable toxicity.<sup>1</sup>
- <sup>1</sup>After a medial follow-up of ~85 months; data cut-off for the final analysis: 28 September 2020.<sup>20</sup>
- Median duration of exposure to NINLARO was 457 days (range: 1-2768 days).21
- AR=adverse reaction; mPFS=median progression-free survival; PI=proteasome inhibitor.

#### IMPORTANT SAFETY INFORMATION

#### SUMMARY OF WARNINGS AND PRECAUTIONS

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

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.

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

References: 1. NINLARO. Prescribing information. Takeda Pharmaceuticals America, Inc.; 04/2024. 2. Data on File. Takeda Pharmaceuticals U.S.A., Inc., 2022. 3. Hari P, Romanus D, Luptakova K, et al. The impact of age and comorbidities on practice patterns and outcomes in patients with relapsed/refractory multiple myeloma in the era of novel therapies. J Geriatr Oncol. 2018;9(2):138-144. 9:138-144; 4. Touzeau C, Quignot N, Meng J, et al. Survival and treatment patterns of patients with relapsed or refractory multiple myeloma in France - a cohort study using the French National Healthcare database (SNDS). *Ann Hematol.* 2021;100(7):1825-1836. **5.** Mshigeni S, Moore C, Arkadie N, et al. The prevalence rate of smoking among Veterans: A forgotten epidemic. *J Mil Veteran Fam Health.* 2021;7(2): 16-25. **6.** Betancourt J, Stigler Granados P, Pacheco G, et al. Obesity and morbidity risk in the U.S. Veteran. Healthcare (Basel). 2020;8(3):191. 7. Betancourt J, Granados P, Pacheco G, et al. Exploring health outcomes for U.S. Veterans compared to Non-Veterans from 2003 to 2019. Healthcare (Basel). 2021;9(5):604. 8. Fillmore N, DuMontier C, Yildirim C, et al. Defining multimorbidity and its impact in older United States Veterans newly treated for multiple myeloma. J Natl Cancer Inst. 2021;113(8):1084-1093. 9. U.S. Department of Veteran Affairs. The PACT Act and your VA benefits. Available at: https://www.va.gov/resources/the-pact-act-and-your-va-benefits/.

Accessed: April 2024. 10. U.S. Department of Veteran Affairs. VA benefits for multiple myeloma. Available at: https://www.publichealth.va.gov/exposures/agentorange/conditions/multiple\_myeloma.asp#::text=VA%20benefits%20for%20multiple%20myeloma,disability%20compensation%20and%20health%20care. Accessed: April 2024. 11. Borrello I. Can we change the disease biology of multiple myeloma? Leuk Res. 2012;36 Suppl 1(0 1):S3-S12. 12. Sonneveld P. Management of multiple myeloma in the relapsed/refractory patient. Hematology Am Soc Hematol Educ Program. 2017;2017(1):508-517.

13. Durie BGM. Concise Review of the Disease and Treatment Options: Multiple Myeloma: Cancer of the Bone Marrow.

2011/2012 ed. International Myeloma Foundation; 2011. 14. Mina R, Bringhen S, Wildes TM, et al. Approach to the older Adult with multiple myeloma. Am Soc Clin Oncol Educ Book. 2019;39:500-518. 15. Revlimid. Prescribing information. Celgene Corporation; 03/2023; 16. Hemady. Prescribing information. Acrotech Biopharma LLC; 06/2021. 17. 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. 18. 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 [supplemental appendix]. 19. 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. 20. Data on File. Takeda Pharmaceuticals U.S.A., Inc.; 2023. 21. Data on



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