NINLARO® ▼ (ixazomib) PRESCRIBING INFORMATION

Refer to Summary of Product Characteristics (SmPC) before prescribing

Presentation: Ixazomib 2.3 mg, 3 mg and 4 mg hard capsules. **Indication:** NINLARO in combination with lenalidomide and dexamethasone is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. **Dosage and administration:** Treatment must be initiated and monitored under the supervision of a physician experienced in the management of multiple myeloma. As NINLARO is administered in combination with lenalidomide and dexamethasone, refer to their SmPCs for further information. Recommended starting doses: NINLARO 4 mg (one capsule) administered orally once a week on Days 1, 8, and 15 of a 28-day treatment cycle at least 1 hour before or at least 2 hours after food; lenalidomide 25 mg administered daily on Days 1 to 21 of a 28-day treatment cycle; dexamethasone 40 mg administered on Days 1, 8, 15, and 22 of a 28-day treatment cycle. Prior to initiating a new cycle of therapy, absolute neutrophil count should be ≥ 1,000/mm^3, platelet count should be ≥ 75,000/mm^3, non-haematologic toxicities should, at the physician's discretion, generally be recovered to patient's baseline condition or ≤ Grade 1. Treatment should be continued until disease progression or unacceptable toxicity. Treatment with NINLARO in combination with lenalidomide and dexamethasone for longer than 24 cycles should be based on an individual benefit risk assessment, as the data on the tolerability and toxicity beyond 24 cycles are limited. Antiviral prophylaxis should be considered in patients being treated with NINLARO to decrease the risk of herpes zoster reactivation. Thromboprophylaxis is recommended in patients being treated with NINLARO in combination with lenalidomide and dexamethasone, and should be based on an assessment of the patient's underlying risks and clinical status. Elderly: No dose adjustment is necessary in patients over 65 years of age. Renal impairment: Mild or moderate renal impairment, no dose adjustment is necessary. Reduced 3 mg starting dose recommended in severe renal impairment or end-stage renal disease requiring dialysis. Hepatic impairment: Mild hepatic impairment, no dose adjustment is necessary. Reduced 3 mg starting dose recommended in moderate or severe hepatic impairment. Paediatric population: No data are available. **Contraindications:** Hypersensitivity to the active substance or to its excipients. **Warnings and precautions:** Thrombocytopenia: Thrombocytopenia has been reported with NINLARO with platelet nadirs typically occurring between Days 14-21 of each 28-day cycle and recovery to baseline by the start of the next cycle. Thrombocytopenia did not result in an increase in haemorrhagic events or platelet transfusions. Platelet counts should be monitored at least monthly during NINLARO treatment. Thrombocytopenia can be managed with dose modifications and platelet transfusions as per standard medical guidelines. Gastrointestinal toxicities: Diarrhoea, constipation, nausea and vomiting have been reported with NINLARO, occasionally requiring use of antiemetic and antidiarrhoeal medicinal products and supportive care. The dose should be adjusted for severe (Grade 3–4) symptoms. Peripheral neuropathy: Peripheral neuropathy has been reported with NINLARO. Patients should be monitored for symptoms of peripheral neuropathy. Patients experiencing new or worsening peripheral neuropathy may require dose modification. Peripheral oedema: Peripheral oedema has been reported with NINLARO. Patients should be evaluated for underlying causes and provided supportive care, as necessary. The dose of dexamethasone should be adjusted per its SmPC or NINLARO for Grade 3 or 4 symptoms. Cutaneous reactions: Rash has been reported with NINLARO. Rash should be managed with supportive care or with dose modification if Grade 2 or higher. Thrombotic microangiopathy (TMA): Cases of TMA, including thrombocytopenic purpura have been reported in patients who received NINLARO. Some of these have been fatal. Signs and symptoms of TMA should be monitored for and NINLARO stopped if diagnosis is suspected. Hepatotoxicity: Drug-induced liver injury, hepatocellular injury, hepatic steatosis, hepatitis cholestatic and hepatotoxicity have been uncommonly reported with NINLARO. Hepatic enzymes should be monitored regularly and dose should be adjusted for Grade 3 or 4 symptoms. Pregnancy: Women should avoid becoming pregnant while being treated with NINLARO. Posterior reversible encephalopathy syndrome (PRES): PRES has occurred in patients receiving NINLARO. In patients developing PRES, discontinue NINLARO. **Interactions:** Strong cytochrome P450 (CYP) 3A inducers: Co-administration of strong CYP3A inducers with NINLARO is not recommended. Strong CYP3A inhibitors: No dose modification is required for NINLARO with co-administration of strong CYP3A inhibitors. Strong CYP1A2 inhibitors: No dose modification is required for NINLARO with co-administration of strong CYP1A2 inhibitors. **Fertility, pregnancy and lactation:** As NINLARO is administered in combination with lenalidomide and dexamethasone, refer to their SmPCs for further information on fertility, pregnancy and lactation. Women should avoid becoming pregnant while being treated with NINLARO. Male and female patients of childbearing potential must use effective contraceptive measures during and for 90 days following treatment. Women using oral hormonal contraceptives should additionally use a barrier method of contraception. No data from use in pregnant women. Not recommended during pregnancy. Unknown whether NINLARO or its metabolites are excreted in human milk, a risk to newborns/infants cannot be excluded; therefore, breast feeding should be discontinued. No human fertility studies have been conducted. **Undesirable effects:** Very common (≥1/10) (all grades): Upper respiratory tract infection, thrombocytopenia, neutropenia, peripheral neuropathies, diarrhoea, nausea, vomiting, constipation, rash, back pain, oedema peripheral, eye disorders and hypokalaemia. Common (≥1/100 to <1/10) (all grades): Herpes zoster Other serious undesirable effects: Outside of the Phase 3 study, the following serious adverse reactions were rarely (≥ 1/10,000 to < 1/1,000) reported; acute febrile neutrophilic dermatosis (Sweet's syndrome), Stevens-Johnson syndrome, transverse myelitis, posterior reversible encephalopathy syndrome, tumour lysis syndrome and thrombotic microangiopathy. **Refer to the SmPC for details on full side effect profile and interactions. Pharmaceutical Precautions:** Do not store above 30°C. Do not freeze. Store in the original package in order to protect from moisture. **UK Basic NHS Price:** £6336 for 3 capsules. **Legal classification:** POM.

Marketing authorization (MA): EU/1/16/1094/001, EU/1/16/1094/002, EU/1/16/1094/003. **Business sale and supply: United Kingdom (UK):** Takeda UK Ltd, 1 Kingdom

Street, London, W2 6BD. **Ireland:** 5 River Walk, Citywest Business Campus, Dublin 24, D24 TW13. **Additional information is available on request from:** Takeda UK Ltd, 1 Kingdom Street, London, W2 6BD, UK. **PI approval code:** pi-00965. **Date of preparation:** September 2020.

NINLARO has received a conditional marketing authorisation in Europe. A conditional marketing authorisation is granted to a medicinal product that fulfils an unmet medical need when the benefit to public health of immediate availability outweighs the risk inherent in the fact additional data are still required. The European regulatory agency will review new information on NINLARO at least every year and the summary of product characteristics will be updated as necessary.

UK: Adverse events should be reported to the Medicines and Healthcare products Regulatory Agency. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Takeda UK Ltd DSO-UK@takeda.com

Ireland: Adverse Events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority (medsafety@hpra.ie). Information about Adverse Event reporting can be found on the HPRA website (www.hpra.ie).
Adverse events should also be reported to Takeda UK Ltd DSO-UK@takeda.com