Rizmoic ▼(naldemedine) Prescribing Information
Please refer to the Summary of Product Characteristics (SPC) before prescribing.
Presentation: Each film coated tablet contains 200 micrograms naldemedine (as tosylate) for oral administration.
Indication: Rizmoic is indicated for the treatment of opioid-induced constipation (OIC) in adult patients who have previously been treated with a laxative.
Dosage and Method of Use: The recommended dose is 200 micrograms (one tablet) daily. Rizmoic may be used with or without laxative(s) and can be taken with or without food. It may be taken at any time of the day but it is recommended to be taken at the same time every day. Alteration of the analgesic dosing regimen prior to initiating Rizmoic is not required. Rizmoic must be discontinued if treatment with the opioid is discontinued. Special populations *Elderly patients (> 65 years of age):* No dose adjustment required, initiate in caution in those ≥ 75 years. *Renal impairment:* No dose adjustment required. Patients with severe renal impairment should be clinically monitored during initiation. *Hepatic impairment:* No dose adjustment required in mild or moderate hepatic impairment, not recommended in severe hepatic impairment. *Opioid pain medicinal products:* Limited experience in patients treated with daily doses > 400 mg equivalent of morphine. No experience in patients treated for constipation induced by partial opioid mu-agonists (e.g. buprenorphine). *Paediatric population (<18 years of age):* The safety and efficacy have not yet been established. No data are available.
Contraindications: Hypersensitivity to the active substance or to any of the excipients; patients with known or suspected gastrointestinal obstruction or perforation or patients at increased risk of recurrent obstruction, due to the potential for gastrointestinal perforation.
Warnings and Precautions: Gastrointestinal perforation**:** Cases of gastrointestinal perforation have been reported in the post-marketing setting, including fatal cases, when naldemedine was used in patients who were at an increased risk of gastrointestinal (GI) perforation. Naldemedine must not be used in patients with known or suspected GI obstruction or in patients at increased risk of recurrent obstruction. Caution should be exercised in patients with any conditions which might result in impaired integrity of the GI tract wall. The overall benefit risk for each patient should be taken into account. Patients should be monitored for the development of severe, persistent or worsening abdominal pain. If obstruction or perforation are suspected, naldemedine must be discontinued. Gastrointestinal adverse reactions: Abdominal adverse reactions have been reported. Patients should be advised to report severe, persistent or worsening symptoms to their physician. In cases of severe diarrhoea or abdominal pain, the patient should be monitored and treated for dehydration using rehydration and appropriate treatment as needed. Opioid withdrawal syndrome: Caution should be exercised with regards to opioid withdrawal. Patients should be advised to discontinue naldemedine and to contact their physician if opioid withdrawal occurs. Cases of possible opioid withdrawal syndrome have been reported. Patients having disruptions to the blood-brain barrier may be at increased risk of opioid withdrawal or reduced analgesia, and the overall benefit-risk should be considered with close monitoring for symptoms of opioid withdrawal. Patients with cardiovascular conditions: Naldemedine was not studied in the clinical trial programme in patients who had a recent history of myocardial infarction, stroke or transient ischaemic attack within 3 months of screening. These patients should be clinically monitored when taking Rizmoic. Severe hepatic impairment: Naldemedine has not been studied in patients with severe hepatic impairment, not recommended in these patients. Concomitant use with strong CYP3A inhibitors and inducers: Concomitant use with strong CYP3A inhibitors leads to an increase in naldemedine exposure, may increase the risk of adverse reactions and should be avoided. Concomitant use of naldemedine with strong CYP3A inducers leads to a decrease in naldemedine exposure and may reduce the efficacy of naldemedine. Concomitant use with strong CYP3A inducers is not recommended, use in caution with moderate CYP3A inducers.
Interactions: Naldemedine is primarily metabolised by CYP3A with some contribution from UGT1A3 and is a substrate of P-glycoprotein (P-gp). *Interactions with CYP3A inhibitors*: Concomitant use with strong CYP3A inhibitors should be avoided. If use is unavoidable, monitor for adverse reactions. Concomitant use of moderate CYP3A inhibitors may increase the plasma concentration. If used, monitor for adverse reactions. There is no risk of interaction with concomitant use of mild CYP3A inhibitors. *Interaction with strong and moderate CYP3A inducers*: Concomitant use of strong CYP3A inducers is not recommended. Concomitant use of naldemedine with moderate inducers has not been established, and patients should be monitored. *Interaction with strong P-gp inhibitors:* Concomitant use may increase plasma concentrations of naldemedine. If used with strong P-gp inhibitors, monitor for adverse reactions.
Pregnancy, Breast-feeding and Fertility: Pregnancy: Should not be used during pregnancy unless the clinical condition of the woman requires treatment with naldemedine. Breast-feeding: Should not be used during breast-feeding. Fertility: No human data are available. Studies in rats found to have no clinically relevant adverse effects on fertility or reproductive performance.
Effects on Ability to Drive and Use Machines: No or negligible influence on the ability to drive and use machines.
Undesirable Effects: In patients with non-cancer pain: The most commonly reported adverse reactions were abdominal pain, diarrhoea, nausea, and vomiting. The majority of these were of mild to moderate severity and resolved without discontinuation. One serious case of abdominal pain and one serious case of nausea were reported. Common (≥ 1/100 to < 1/10) adverse events: diarrhoea, abdominal pain, nausea, vomiting. Adverse events less frequently reported: opioid withdrawal syndrome, hypersensitivity, gastrointestinal perforation. In patients with cancer pain: The most commonly reported adverse reactions were diarrhoea and abdominal pain. The majority of these were of mild to moderate severity and resolved with treatment. Two serious cases of diarrhoea were reported. Very common (≥ 1/10) adverse events: diarrhoea, common (≥ 1/100 to < 1/10): abdominal pain, less commonly reported adverse events: opioid withdrawal syndrome and gastrointestinal perforation. Prescribers should consult the SPC in relation to other adverse reactions.
Legal Category: POM. **Basic NHS List Price**: £41.72 per pack of 28 tablets. **Marketing Authorisation (MA) Number**: EU/1/18/1291/002. **MA Holder:** Shionogi B.V., Kingsfordweg, 151 1043GR Amsterdam, The Netherlands. **Local Representative:** Sandoz UK Limited, Park View, Riverside Way, Watchmoor Park, Camberley, Surrey, GU15 3YL, UK.
Last Date of Revision: January 2020**.** UK/MKT/RZM/19-0002(1).

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Sandoz Ltd at: uk.patientsafety@novartis.com.