Important Safety Information

WARNINGS AND PRECAUTIONS

Cases of GI perforation have been reported with use of another peripherally acting opioid antagonist in patients with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the GI tract. Monitor for the development of severe, persistent, or worsening abdominal pain; discontinue if this symptom develops.

Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, increased lacrimation, hot flush/flushing, pyrexia, sneezing, feeling cold, abdominal pain, diarrhea, nausea, and vomiting have occurred in patients treated with SYMPROIC®.

Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal or reduced analgesia. Take into account the overall risk-benefit profile when using SYMPROIC® in such patients. Monitor for symptoms of opioid withdrawal in such patients.

DRUG INTERACTIONS

Avoid use with strong CYP3A inducers (e.g., rifampin) because they may reduce the efficacy of SYMPROIC®.

Use with moderate (e.g., fluconazole) and strong (e.g., itraconazole) CYP3A inhibitors and P-glycoprotein inhibitors (e.g., cyclosporine) may increase SYMPROIC® concentrations. Monitor for potential adverse reactions.

Avoid use of SYMPROIC® with another opioid antagonist due to the potential for additive effect and increased risk of opioid withdrawal.

USE IN SPECIFIC POPULATIONS

Naldemedine crosses the placenta and may precipitate opioid withdrawal in a fetus due to the immature fetal blood-brain barrier. SYMPROIC® should be used during pregnancy only if the potential benefit justifies the potential risk. Because of the potential for serious adverse reactions, including opioid withdrawal in breastfed infants, a decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother.

Avoid use in patients with severe hepatic impairment. No dose adjustment of SYMPROIC® is required in patients with mild or moderate hepatic impairment.

Please see Prescribing Information in this brochure.
Please see full Prescribing Information at SYMPROIC.com.

Important Safety Information

ADVERSE REACTIONS

The most common adverse reactions with SYMPROIC® compared to placebo in two pooled 12-week studies were: abdominal pain (8% vs 2%), diarrhea (7% vs 2%), nausea (4% vs 2%), and gastroenteritis (2% vs 1%).

The incidence of adverse reactions of opioid withdrawal in two pooled 12-week studies was 1% (8/542) for SYMPROIC® and 1% (3/546) for placebo. In a 52-week study, the incidence was 3% (20/621) for SYMPROIC® and 1% (9/619) for placebo.

To report SUSPECTED ADVERSE REACTIONS, contact BioDelivery Sciences International, Inc. at 1-800-469-0261 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

References: 1. SYMPROIC [package insert]. Raleigh, NC: BioDelivery Sciences International, Inc.; 2019. **2.** MOVANTIK [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2014. **3.** RELISTOR [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North American LLC; 2016. **4.** AMITIZA [package insert]. Bedminster, NJ: Sucampo Pharma Americas, LLC; 2018.

Please see Prescribing Information in this brochure.
Please see full Prescribing Information at SYMPROIC.com.

Symproic® (naldemedine) tablets 0.2 mg

biodelivery SCIENCES

Dosing and Administration of Oral Products for Opioid-Induced Constipation

In chronic non-cancer pain

Symproic® (naldemedine) tablets 0.2 mg

INDICATION

SYMPROIC® (naldemedine) is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

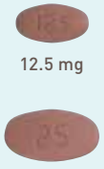
Important Safety Information

CONTRAINDICATIONS

- Patients with known or suspected gastrointestinal (GI) obstruction and patients at increased risk of recurrent obstruction, due to the potential for GI perforation.
- Patients with a history of a hypersensitivity reaction to naldemedine. Reactions have included bronchospasm and rash.

Please see Prescribing Information in this brochure.
Please see full Prescribing Information at SYMPROIC.com.

Oral Products Indicated for the Treatment of Opioid-Induced Constipation in Adults With Chronic Non-Cancer Pain[1-4]

	Products*	Strength	Dosing and Administration	
PAMORA	Symproic® (naldemedine) tablets 0.2 mg	 0.2 mg *(actual size)*	• 0.2 mg once daily, any time of day • With or without food • With or without laxatives	• No alteration of analgesic dose before initiation • Patients taking opioids for less than 4 weeks may be less responsive • Discontinue Symproic if treatment with the opioid pain medication is discontinued
PAMORA	movantik® (naloxegol) 25 mg tablets	 12.5 mg 25 mg *(actual sizes)*	• 25 mg once daily in the morning — Start at 12.5 mg dose for renally impaired — If patients are not able to tolerate Movantik, reduce to 12.5 mg once daily • Take on an empty stomach at least 1 hour before first meal of the day or 2 hours after • For patients who are unable to swallow the tablet whole, the tablet can be crushed to a powder mixed with 4 oz of water and consumed immediately • Can be administered via a nasogastric tube; please see full Prescribing Information for details	• Alteration in analgesic dosing regimen before initiating Movantik is not required • Patients receiving opioids for less than 4 weeks may be less responsive to Movantik • Discontinue Movantik if treatment with the opioid pain medication is also discontinued • Discontinue all maintenance laxative therapy before initiation of Movantik. Laxative(s) can be used as needed if there is a suboptimal response to Movantik after 3 days • Avoid consumption of grapefruit or grapefruit juice during treatment with Movantik
PAMORA	RELISTOR® methylnaltrexone bromide Tablets	 150 mg *(actual sizes)*	• Oral: 450 mg (or 3 x 150 mg tablets) once daily in the morning — 150 mg once daily in the morning in patients with moderate and severe renal and hepatic impairment • Take with water on an empty stomach at least 30 minutes before the first meal of the day • Be in close proximity to toilet facilities once administered	• Patients receiving opioids for less than 4 weeks may be less responsive to Relistor • Discontinue Relistor if treatment with the opioid pain medication is discontinued • Discontinue all maintenance laxative therapy before initiation. Laxative(s) can be used as needed if there is a suboptimal response after 3 days • Re-evaluate the continued need for Relistor when opioid regimen is changed to avoid adverse reactions
SECRETAGOGUE	amitiza® lubiprostone	 8 mcg 24 mcg *(actual sizes)*	• 24 mcg twice daily • Take orally with food and water • Swallow capsules whole and do not break apart or chew	• Assess periodically the need for continued therapy • See the full Prescribing Information for dose adjustment in patients with moderately or severely impaired hepatic function

No head-to-head clinical trials have been conducted.

Please see Prescribing Information in this brochure.
Please see full Prescribing Information at SYMPROIC.com.

PAMORA=peripherally acting mu-opioid receptor antagonist.

*Products listed are indicated for opioid-induced constipation in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer who do not require frequent (eg, weekly) opioid dosage escalation. Some products may have additional indications and/or formulations.