Go with Confidence
Go with Symproic®

Symproic® (naldemedine) tablets 0.2 mg

Help your patients Go with Symproic

Proven efficacy for OIC

- In two 12-week, placebo-controlled studies, responder rates were significantly higher with Symproic than with placebo (48% vs 35% [*P*=0.0020] and 53% vs 34%, respectively [*P*<0.0001])[1,2]*

Demonstrated long-term safety and tolerability

- Once-daily naldemedine (Symproic) was generally well-tolerated over 52 weeks (abdominal pain‡ 8.2% vs 3.1%, diarrhea 11.0% vs 5.3%, nausea 7.9% vs 5.7%, and vomiting 6.0% vs 3.1% for Symproic and placebo, respectively)[1,3]
- In a 52-week study, Symproic showed a significant and sustained increase in bowel movements from baseline vs placebo (*P*≤0.0001)[1,3§]

	OIC treatment	Once-daily dosing?	Can be taken any time of day?	Can be taken with or without food?	Can keep taking laxatives when starting therapy?
PAMORA	Symproic® (naldemedine) tablets 0.2 mg	✓ YES[1]	✓ YES[1]	✓ YES[1]	✓ YES[1]
PAMORA	movantik® (naloxegol) 25 mg tablets	✓ YES[4]	✗ NO[4]	✗ NO[4]	✗ NO[4]
PAMORA	RELISTOR® methylnaltrexone bromide Tablets	✓ YES[5]	✗ NO[5]	✗ NO[5]	✗ NO[5]

No head-to-head clinical trials of Symproic have been conducted comparing the safety or efficacy between Symproic and the other PAMORAs mentioned.[1]

Administering Symproic[1]

- Alteration of analgesic dosing regimen prior to initiating Symproic is not required
- Patients receiving opioids for less than 4 weeks may be less responsive to Symproic
- Discontinue Symproic if treatment with the opioid pain medication is discontinued

Symproic is an AGA-RECOMMENDED OIC therapy**

Symproic (naldemedine) is the **only PAMORA with both a strong recommendation and high quality of evidence** from the American Gastroenterological Association (AGA)[6]

OIC=opioid-induced constipation; PAMORA=peripherally acting mu-opioid receptor antagonist.
*Symproic was studied in two 12-week, randomized, double blind, placebo-controlled trials (Study 1: N=547, Study 2: N=553). The primary endpoint was responder rate. To be a responder, patients had to achieve ≥3 spontaneous bowel movements (SBM) per week and a change from baseline of ≥1 SBM per week, for at least 9 of 12 weeks, including 3 of the last 4 weeks.[1,2]
†Adverse reactions occurring in ≥2% of patients receiving Symproic and at an incidence greater than placebo.
‡Abdominal pain includes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper.
§Randomized, double-blind, placebo-controlled 52-week safety study. Patients were allowed to maintain their current laxative therapy throughout study duration.
**For laxative refractory OIC

Please see Important Safety Information and full Prescribing Information accompanying this piece, or at symproic.com/PI.

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.

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.

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.

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To report SUSPECTED ADVERSE REACTIONS, contact Collegium Pharmaceutical, Inc. at 1-855-331-5615 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

References: 1. SYMPROIC [package insert]. Stoughton, MA: Collegium Pharmaceutical, Inc.; 2020. **2.** Hale M, Wild J, Reddy J, Yamada T, Arjona Ferreira JC. Naldemedine versus placebo for opioid-induced constipation (COMPOSE-1 and COMPOSE-2): two multicentre, phase 3, double-blind, randomised, parallel-group trials. *Lancet Gastroenterol Hepatol*. 2017;2(8):555-564. **3.** Webster LR, Nalamachu S, Morlion B, et al. Long-term use of naldemedine in the treatment of opioid-induced constipation in patients with chronic noncancer pain: a randomized, double-blind, placebo-controlled phase 3 study. *Pain*. 2018;159(5):987-994. **4.** MOVANTIK [package insert]. Raleigh, NC: RedHill Biopharma Inc.; 2020. **5.** RELISTOR [package insert]. Bridgewater, NJ: Salix Pharmaceuticals, Inc.; 2020. **6.** Crockett SD, Greer KB, Heidelbaugh JJ, Falck-Ytter Y, Hanson BJ, Sultan S, American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute guideline on the medical management of opioid induced constipation *Gastroenterology*. 2019;156(1):218-222.

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