When an adequate trial of traditional laxatives results in suboptimal symptom control of opioid-induced constipation (OIC), the

American Gastroenterological Association (AGA) recommends the use of MOVANTIK as one of the prescription treatment options for the management of OIC[1]

"Because OIC results from the specific effects of opioids, it differs mechanistically from other forms of constipation, and therefore, medical management of this disorder deserves dedicated attention."[1]

INDICATION

MOVANTIK® (naloxegol) 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 (eg, weekly) opioid dosage escalation.

IMPORTANT SAFETY INFORMATION ABOUT MOVANTIK

- MOVANTIK is contraindicated in:
  - — Patients with known or suspected gastrointestinal (GI) obstruction and patients at increased risk of recurrent obstruction, due to the potential for GI perforation
  - — Patients receiving strong CYP3A4 inhibitors (eg, clarithromycin, ketoconazole) because these medications can significantly increase exposure to naloxegol which may precipitate opioid withdrawal symptoms
  - — Patients with a known serious or severe hypersensitivity reaction to MOVANTIK or any of its excipients

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movantik® (naloxegol) 25 mg tablets

Summary of AGA Recommendations[1]

Recommendations	Strength of recommendation	Quality of evidence
1. Traditional laxatives a. In patients with OIC, the AGA recommends use of laxatives as first-line agents	Strong	Moderate
2. PAMORAs a. In patients with laxative-refractory OIC, the AGA recommends Symproic® (naldemedine) over no treatment*	Strong	High
b. In patients with laxative-refractory OIC, the AGA recommends MOVANTIK® (naloxegol) over no treatment	Strong	Moderate
c. In patients with laxative-refractory OIC, the AGA recommends Relistor® (methylnaltrexone bromide) over no treatment†	Conditional	Low
3. Intestinal secretagogues a. In patients with OIC, the AGA makes no recommendation for the use of Amitiza® (lubiprostone)‡	No recommendation	Evidence gap
4. Selective 5-HT agonists a. In patients with OIC, the AGA makes no recommendation for the use of Motegrity™ (prucalopride)§	No recommendation	Evidence gap

GRADE Definitions on Strength of Recommendation and Guide to Interpretation[1]

Strength of recommendation	Wording in the guideline	For the patient	For the clinician
Strong	"The AGA recommends..."	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	Most individuals should receive the recommended course of action. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.
Conditional	"The AGA suggests..."	The majority of individuals in this situation would want the suggested course of action, but many would not.	Different choices will be appropriate for different patients. Decision aids may be useful in helping individuals in making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision.
No recommendation	"The AGA makes no recommendation..."		The confidence in the effect estimate is so low that any recommendation is speculative at this time.

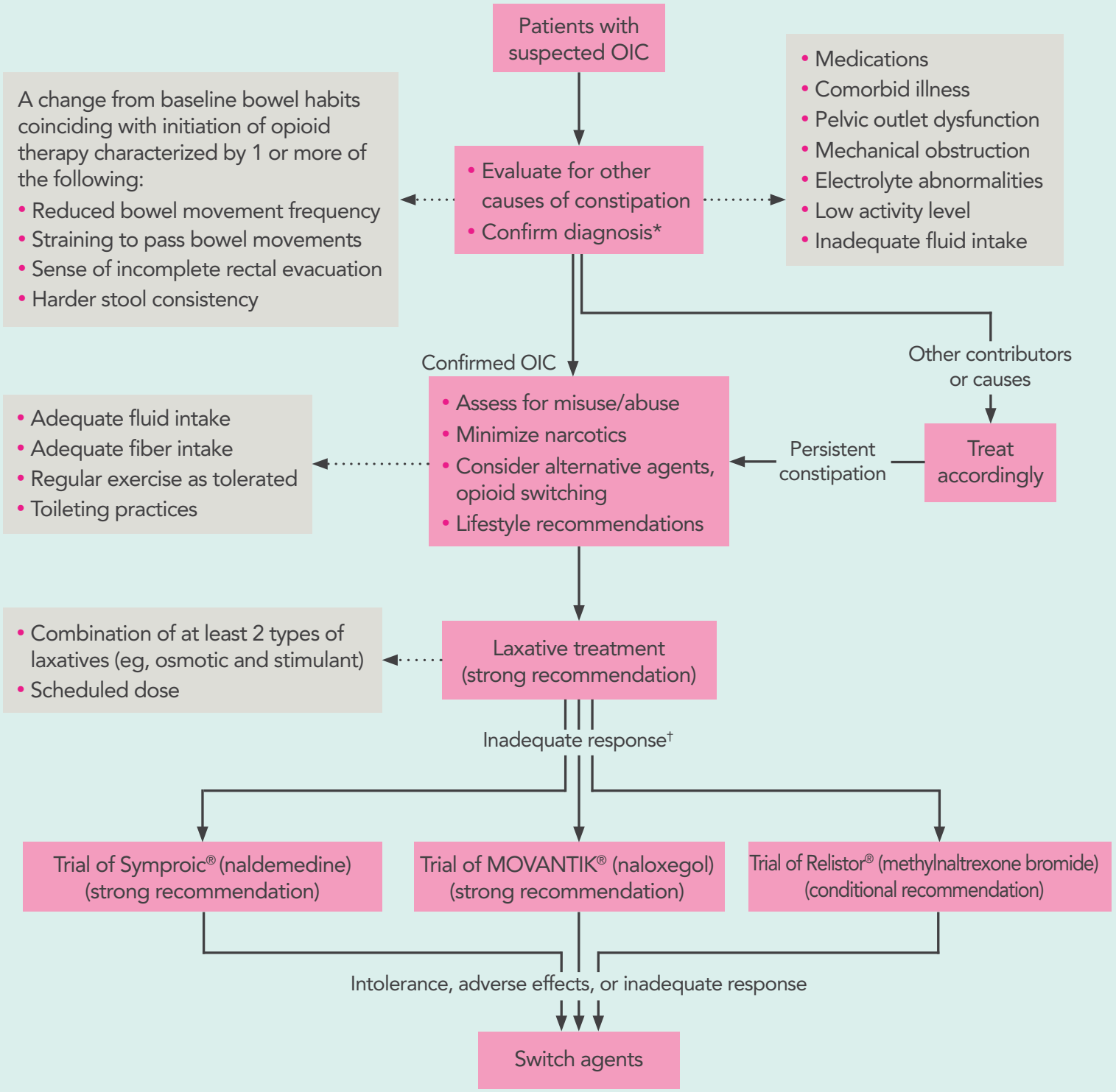
GRADE Definitions of Quality and Certainty of the Evidence[1]

Quality grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.
Evidence gap	Available evidence insufficient to determine true effect.

GRADE=Grading of Recommendations Assessment, Development, and Evaluation.
PAMORA=peripherally acting mu-opioid receptor antagonist.

*Symproic is a registered trademark of Shionogi & Co., Ltd.[2]
†Relistor is a trademark of Salix Pharmaceuticals or its affiliates.[3]
‡Amitiza is a trademark of Mallinckrodt Pharmaceuticals, registered with the U.S. Patent and Trademark Office and used under license by Takeda Pharmaceuticals America, Inc.[4]
§Motegrity is a trademark or registered trademark of Shire LLC, a wholly-owned, indirect subsidiary of Shire plc.[5]

Opioid-Induced Constipation Clinical Decision Support Tool[6]



*OIC definition from Camilleri et al. *Neurogastroenterol Motil*. 2014.[6]
†Laxative-refractory OIC defined as persistent constipation (eg, Bowel Function Index score ≥30) despite scheduled use of at least 2 classes of laxatives for at least 2 weeks.[6]

IMPORTANT SAFETY INFORMATION ABOUT MOVANTIK (CONT'D)

- Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, irritability, and yawning, occurred in patients treated with MOVANTIK. Patients receiving methadone as therapy for their pain condition were observed in the clinical trials to have a higher frequency of GI adverse reactions that may have been related to opioid withdrawal than patients receiving other opioids. Patients with disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal or reduced analgesia. These patients (eg, multiple sclerosis, recent brain injury, Alzheimer's disease, and uncontrolled epilepsy) were not enrolled in the clinical studies. Take into account the overall risk-benefit profile when using MOVANTIK in such patients. Monitor for symptoms of opioid withdrawal when using MOVANTIK in such patients
- Severe abdominal pain and/or diarrhea have been reported, generally within a few days of initiation of MOVANTIK. Monitor and discontinue if severe symptoms occur. Consider restarting MOVANTIK at 12.5 mg once daily
- Cases of GI perforation have been reported with the 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 severe, persistent, or worsening abdominal pain; discontinue if this symptom develops
- Avoid concomitant use of moderate CYP3A4 inhibitors (eg, diltiazem, erythromycin, verapamil) because they may increase the risk of adverse reactions. Use of strong CYP3A4 inducers (eg, rifampin, carbamazepine, St. John's Wort) is not recommended because they may decrease the efficacy of MOVANTIK. Avoid concomitant use of MOVANTIK with another opioid antagonist due to the increased risk of opioid withdrawal
- The use of MOVANTIK during pregnancy may precipitate opioid withdrawal in the pregnant woman and the fetus. Because of the potential for adverse reactions, including opioid withdrawal in breastfed infants, advise women that breastfeeding is not recommended during treatment with MOVANTIK
- The most common adverse reactions with MOVANTIK as compared to placebo in clinical trials were: abdominal pain (21% vs 7%), diarrhea (9% vs 5%), nausea (8% vs 5%), flatulence (6% vs 3%), vomiting (5% vs 4%), headache (4% vs 3%), and hyperhidrosis (3% vs <1%)

References: 1. Crockett SD, Greer KB, Heidelbaugh JJ, Falck-Ytter Y, Hanson BJ, Sultan S; American Gastroenterological Association Institute Clinical Guidelines Committee. *Gastroenterology*. 2019;156:218-226. **2.** Symproic Prescribing Information. Florham Park, NJ: Shionogi Inc.; 2018. **3.** Relistor Prescribing Information. Bridgewater, NJ: Salix Pharmaceuticals; 2017. **4.** Amitiza Prescribing Information. Bedminster, NJ: Sucampo Pharma Americas, LLC; 2018. **5.** Motegrity Prescribing Information. Lexington, MA. Shire US Inc.; 2018. **6.** Modified from American Gastroenterological Association, Opioid-Induced Constipation (OIC) Clinical Decision Support Tool, *Gastroenterology*. 2019;156:218-226.

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