## Prescription Medications for Treatment of Opioid-Induced Constipation (OIC)

Medication Name <sup>1,2</sup> (Brand Name)	FDA- Approval Date	FDA-Labeled Indication	Mechanism of Action	Typical Starting Dose in Adult Patients	Dosing Pearls	Time to Bowel Movement	Common and <i>Serious</i> Adverse Effects
Linaclotide (Linzess®)	August 2012	No	Increases ion secretion into the GI tract	72 mcg PO once daily	No dose adjustments for renal or hepatic dysfunction	Within 1 week of consistent use	Diarrhea, headache, fatigue, dehydration, abdominal pain, flatulence, vomiting
Lubiprostone (Amitiza®)	January 2006	Yes	Increases ion secretion into the GI tract	24 mcg PO twice daily	No dose adjustments for renal dysfunction; Dose adjust in moderate-severe hepatic dysfunction	24-48 hr	Nausea, diarrhea, headache, abdominal pain, flatulence, vomiting, dyspnea, syncope
<b>Methlynaltrexone</b> <sup>3</sup> (Relistor®)	April 2008 (SQ); July 2016 (PO)	Yes	Peripherally- acting µ opioid receptor antagonist	12 mg SQ once daily 450 mg PO once daily	Dose in the morning; No more than 1 dose in a 24-hour period; Dose adjust for CrCL < 60 mL/min; Avoid in moderate to severe hepatic dysfunction	30-60 min	Abdominal pain, flatulence, nausea, diarrhea, hyperhidrosis, vomiting, GI perforation, opioid withdrawal
Naldemedine (Symproic®) Schedule II	March 2017	Yes	Peripherally- acting μ, δ, and κ opioid receptor antagonist	0.2 mg PO once daily	No dose adjustments for renal dysfunction; Avoid use in severe hepatic dysfunction	Unknown	Abdominal pain, diarrhea, nausea, vomiting, gastroenteritis, GI perforation, opioid withdrawal
Naloxegol (Movantik®)	September 2014	Yes	Peripherally- acting µ opioid receptor antagonist	25 mg PO once daily	Dose in the morning; Dose adjust for CrCL < 60 mL/min; Avoid use in severe hepatic dysfunction	6-12 hr	Abdominal pain, flatulence, nausea, diarrhea, hyperhidrosis, vomiting, headache, GI perforation, opioid withdrawal

Abbreviations: mg, milligram; PO, by mouth; PR, by rectum; hr, hour; min, minute; g, gram; mL, milliliter; mcg, microgram; SQ, subcutaneous; CrCL, creatinine clearance; min, minute; GI, gastrointestinal

## References

- Argoff CE, Brennan MJ, Camilleri M, et al. Consensus recommendations on initiating prescription therapies for opioid-induced constipation. Pain Med. 2015;16:2324-2337.
- ANDA 208592: Methylnaltrexone ANDA Tentative Approval [Internet]. Silver Spring (MD): U.S. Food and Drug Administration. [cited 2017 Dec 13]. Available from: https://www.accessdata.fda.gov/drugsatfda\_docs/appletter/2017/208592Orig1s000TAltr.pdf.
- Camilleri M, Drossman DA, Becker G, Webster LR, Davies AN, Mawe GM. Emerging treatments in neurogastroenterology: a multidisciplinary working group consensus statement on opioid-induced constipation. Neurogastroenterol Motil. 2014;26(10):1386-1395.
- Camilleri M, Lembo A, Katzka DA. Opioids in gastroenterology: treating adverse effects and creating therapeutic benefits. Clin Gastroenterol Hepatol. 2017;15(9):1338-1349.
- Drugs@FDA: FDA Approved Drug Products [Internet]. Silver Spring (MD): U.S. Food and Drug Administration. [cited 2017 Dec 13]. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
- Lexi-Drugs® [Internet]. Hudson (OH): Lexi-Comp, Inc. [cited 2017 Sep 13]. Available from: <a href="http://online.lexi.com/lco/action/home">http://online.lexi.com/lco/action/home</a>.
- Lexi-Drugs® [Internet]. Laxatives, Classification and Properties. Hudson (OH): Lexi-Comp, Inc. [cited 2017 Sep 13]. Available from: http://online.lexi.com/lco/action/home.
- Micromedex® 2.0 [Internet]. Greenwood Village (CO): Truven Health Analytics. [cited 2017 Sep 20]. Available from: http://www.micromedexsolutions.com/.

<sup>&</sup>lt;sup>1</sup> All medications are currently available only as branded products.

<sup>&</sup>lt;sup>2</sup>Alvimopan (Entereg®) used off label in an inpatient setting is not included in this table.

<sup>&</sup>lt;sup>3</sup> Mylan Labs Ltd has received tentative approval for a generic form of subcutaneous methylnaltrexone.