



THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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Palliative Care
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If you have a topic you
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TODAY'S TOPIC:

Requested Topic: Opioid-Induced Constipation Treatment Review

Background:

Opioids bind to mu receptors in the GI tract and can precipitate reduced GI motility, increased fluid absorption, and lead to opioid-induced constipation (OIC). OIC's definition is variable among provider groups; Rome IV definition of OIC is "new/worsening constipation when initiating, changing, or increasing opioid therapy that must include 2 or more of the following: (1) straining during more than one-fourth (25%) of defecations; (2) lumpy or hard stools more than one-fourth (25%) of defecations; (3) sensation of incomplete evacuation more than one-fourth (25%) of defecations; (4) sensation of anorectal obstruction/blockage more than one-fourth (25%) of defecations; (5) manual maneuvers to facilitate more than one-fourth (25%) of defecations (eg, digital evacuation, support of the pelvic floor); or (6) fewer than 3 spontaneous bowel movements per week." First-line agents for treatment of OIC include: senna, bisacodyl, polyethylene glycol, lactulose, sorbitol, magnesium citrate, or magnesium hydroxide. If patients have inadequate response to appropriate trial of laxatives (ie. use of 2 types of scheduled laxatives), it may be necessary to escalate treatment. Peripherally acting mu-opioid receptor antagonists (PAMORAs) are effective for treating OIC. Other classes of medications such as intestinal secretagogues and selective 5-HT agonists are lacking data to support use in OIC.

Importance:

OIC is common in our palliative care population. It is important for palliative care clinicians to be aware of the guidelines for treating OIC to treat our patients and educate others about appropriate pharmacologic management.

OIC Agent Review:

| Class | Medications | Mechanism of Action |
|--|---|--|
| Osmotic laxative | PEG, lactulose, magnesium citrate, magnesium hydroxide | Draw water into intestine, hydrating and softening stool |
| Stimulant laxative | Bisacodyl, senna, sodium picosulfate | Irritate sensory nerve endings to stimulate colonic motility and reduce colonic water absorption |
| Lubricant Laxative | Mineral oil | Lubricate lining of gut |
| Peripheral acting mu opioid receptor antagonists (PAMORAs) | Naldemedine (Symproic) Naloxegol (Movantik) Methylnaltrexone (Relistor)** | Block mu opioid receptors in the gut, restoring function of enteric nervous system |
| Intestinal secretagogues | Lubiprostone (Amitiza) | Act on chloride channels to stimulate fluid secretion into intestinal lumen |

Alvimopan (Entereg), Linactolide (Linzess), Prucalopride (Motegrity) are not addressed as they are not FDA-approved for OIC

**Methylnaltrexone is the only PAMORA with an FDA-approved indication for OIC in patients with advanced illness or pain caused by active cancer requiring dosage escalation. Others are approved for patients with OIC in chronic noncancer pain

The Guidelines:

American Gastroenterological Association OIC Guidelines: [AGA OIC Guidelines 2019](#)

| Recommendations | Strength of Recommendation | Quality of Evidence |
|--|--|----------------------------------|
| First line: Traditional laxatives* | Strong | Moderate |
| Second Line: PAMORAs 1. Naldemedine 2. Naloxegol 3. Methylnaltrexone | 1. Strong 2. Strong 3. Conditional | 1. High 2. Moderate 3. Low |
| Intestinal Secretagogues | No recommendation | Evidence Gap |

*recommend use of combination of at least 2 types of laxatives before escalating therapy to PAMORA

| Medication | Dosing Regimen | Monitoring |
|-----------------------------|---|--|
| Naldemedine (Symproic) | 0.2mg PO daily | Avoid use in patients with severe hepatic impairment Do not use in case of obstruction |
| Naloxegol (Movantik) | 25mg PO daily, can dose-reduce to 12.5mg | Requires dose adjustment for renal impairment, avoid in severe hepatic impairment Do not use in case of obstruction |
| Methylnaltrexone (Relistor) | Chronic non-cancer pain: 450mg PO daily or 12mg SubQ daily Advanced illness: weight based dose SubQ every other day as needed | Requires dose adjustment for renal and hepatic impairment Do not use in case of obstruction |
| Lubiprostone (Amitiza) | 24mcg PO BID | Requires dose adjustment for liver impairment Do not use in case of obstruction |

Bottom Line:

- It is important to keep in mind that UPMC has a formulary for OIC:
 - UPMC Formulary: OIC 2019**
 - Preferred, formulary agent: 1st line: Naloxegol (Movantik®)
 - Formulary-restricted agents (restricted to: Pain Service, Oncology, Critical Care, GI, Palliative Care): 2nd line: Naldemedine (Symproic®) 3rd line: Methylnaltrexone (Relistor®)
- Some agents are not specifically approved for OIC; therefore would not recommend their use for OIC
- No head-to-head trials of these OIC agents exist

Stay tuned in 2 weeks for a review of the evidence behind some of these recommendations...

CLINICAL PEARL: After an adequate trial of traditional laxatives, PAMORAs are first line for treating OIC.