Are You Sitting Comfortably?

Dealing with Opioid-Induced Constipation

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# TABLE OF CONTENTS

- WHAT IS OPIOID-INDUCED CONSTIPATION? .......................... 1
- HOW THE BOWEL WORKS ............................................. 2
- HEALTHY BOWEL MOVEMENTS ................................. 3
- WHAT CAUSES OPIOID-INDUCED CONSTIPATION? ............ 4
- SIGNS AND SYMPTOMS OF OPIOID-INDUCED CONSTIPATION ... 5
- WHAT INCREASES THE RISK FOR OPIOID-INDUCED CONSTIPATION? .............................................. 6
- HOW DOES OPIOID-INDUCED CONSTIPATION AFFECT EVERYDAY LIFE? .................................................. 7
- TALKING TO YOUR PROVIDER ABOUT YOUR BOWELS ......... 8
- TALKING TO YOUR PROVIDER ABOUT YOUR BOWELS .......... 9
- PATIENT TOOLS—KEEPING TRACK ................................. 10
- PATIENT TOOLS—BOWEL MOVEMENT DESCRIPTION CHART ... 11
- GET MOVING—BODY AND BOWEL ................................ 12
- GET MOVING—BODY AND BOWEL ................................ 13
- FLUID AND FIBER ....................................................... 14
- LAXATIVES ............................................................ 15
- BOWEL REGIMEN ...................................................... 16
- PRESCRIPTION MEDICATIONS FOR OPIOID-INDUCED CONSTIPATION .................................................. 17
- ADVERSE EFFECTS FROM MEDICATIONS TO TREAT OPIOID-INDUCED CONSTIPATION ...................... 18
- PATIENT RESOURCES .................................................... 19
WHAT IS OPIOID-INDUCED CONSTIPATION?

Points to Emphasize

- Opioid-induced constipation (OIC) is common in people being treated with opioids
- OIC is the most bothersome side effect of opioid therapy for many patients

Additional Information for Provider

- OIC affects 45%-90% of patients with chronic noncancer pain who take opioids\(^1\)\(^2\)
- OIC affects 60-90% of patients with cancer-related pain
- > 30% of patients with OIC do not initiate discussion with providers

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### Types of Opioid Medicines for Chronic Pain

<table>
<thead>
<tr>
<th>Opioid Medicines</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Acetaminophen (Tylenol(^5)) with codeine</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Duragesic patch, fentanyl transmucosal (Actiq, Fentora, Abstral, Onsolis)</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Acetaminophen with hydrocodone (Vicodin, Lorcet, Lortab, Norco, Zydol, others)</td>
</tr>
<tr>
<td></td>
<td>Hydromorphone with hydrocodone (Vicoprofen)</td>
</tr>
<tr>
<td></td>
<td>Hydrocodone (Zyloprim ER, Hysingla ER)</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Dilaudid, Exalgo ER</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Demerol</td>
</tr>
<tr>
<td>Methadone</td>
<td>Dolophine, Methadose</td>
</tr>
<tr>
<td>Morphine</td>
<td>Embeda, Kadian ER, MS Contin, Morphabond ER, Duramorph, Roxanol</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Acetaminophen with oxycodone (Percocet, Roxicod, others)</td>
</tr>
<tr>
<td></td>
<td>Aspirin with oxycodone (Percodan)</td>
</tr>
<tr>
<td></td>
<td>Oxycodone (OxyContin ER, Oxydo, Xtampza ER)</td>
</tr>
</tbody>
</table>

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The bowel (intestine) is a long tube that is part of the digestive tract (or gut)

The bowel has 2 parts
• The small bowel takes what your body needs from the food you eat
• The large bowel carries the food waste out of your body
• Strong muscles squeeze food waste through your bowels
• The large bowel removes water from food waste as it moves along

3 Main Areas of Bowel Control

<table>
<thead>
<tr>
<th>Small intestine</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mixes bowel contents with help from increased gastric, pancreatic, biliary secretions</td>
</tr>
<tr>
<td>• Transit is usually 2-4 hours</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Propels digested contents through body via peristalsis</td>
</tr>
<tr>
<td>• Mixes ileal fluids, recovers carbohydrate residues, dehydrates the remainder to form stool</td>
</tr>
<tr>
<td>• Mixing occurs about 6 times/day, triggered by food/meal ingestion</td>
</tr>
<tr>
<td>• Stool is transported for evacuation with the help of neurotransmitters and colonic reflexes</td>
</tr>
<tr>
<td>• Contents remain in colon for 2-3 days on average</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Defecation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Involves coordinated interaction between involuntary internal anal sphincter and voluntary external anal sphincter</td>
</tr>
<tr>
<td>• Feces distend the rectum and initiate expulsion</td>
</tr>
<tr>
<td>• Longitudinal rectal and abdominal muscles contract and when the voluntary external sphincter relaxes, defecation occurs</td>
</tr>
</tbody>
</table>

Additional Information for Provider

• Enteric nervous system (one of the main divisions of the autonomic nervous system) is also involved in moving bowel contents through GI tract
  — Smooth muscles communicate with the CNS to regulate transit time
  — GI tract and brain interact via neurotransmitters and signaling molecules
  — These and other neural and hormonal pathways mediate gut sensitivity and motility in response to stress
• Normal bowel function involves secretion, absorption, transport and storage
HEALTHY BOWEL MOVEMENTS

Points to Emphasize
• Many factors promote healthy bowel functioning
• It is important to optimize fluid intake (in patients not on fluid restriction)
• Dietary fiber is important to trigger peristalsis and form adequate stool size and consistency
• Physical activity promotes regular bowel movements
• Changes in usual daily routine, food or fluid intake can affect bowel movements
• Emotional disturbances can affect gut motility and increase or reduce peristalsis

Additional Information for Provider
• The colon absorbs large quantities of water and electrolytes
• The GI tract typically handles 9-10 liters/day of secretions and ingested fluids
  — 9 liters of fluid are reduced to 1.5L by the time contents reach the ascending colon
• The end volume for waste is 150mL

WHAT CAUSES OPIOID-INDUCED CONSTIPATION?

Additional Information for Provider

• Exogenous opioids bind to receptors in the central and peripheral nervous systems
• Mu-receptors in the GI tract mediate the role of endogenous and exogenous opioids
• Activated mu-opioid receptors trigger an intracellular signaling pathway
  — Decreases neurotransmitter release from enteric nerves
  — Reduces peristalsis by binding to specific receptors in GI tract and CNS
  — Slows down GI transit time
  — Increases water and electrolyte reabsorption from feces
  — Inhibits relaxation of the pyloric and internal rectal sphincters

SIGNS AND SYMPTOMS OF OPIOID-INDUCED CONSTIPATION

The most common symptoms of Opioid-Induced Constipation are:
- Fewer than 3 bowel movements in a week
- Hard, lumpy, dry stools
- Straining to pass bowel movements
- A sensation that the colon is not empty after a bowel movement
- Bloating
- Passing gas

If you have more severe opioid-induced constipation, you might also feel:
- Pain
- Bowel cramping
- Abdominal swelling

Additional symptoms may include:
- Lack of appetite
- Nausea
- Vomiting
- Heartburn (gastric reflux)
- Fatigue
- Insomnia

Points to Emphasize
- Constipation can refer to a broad range of signs and symptoms, including:8-9
  - Hard, dry, or infrequent stools that are difficult to evacuate
  - Having <3 bowel movements (BM) per week
  - Straining required to pass stool
  - Pain with evacuation
  - Abdominal bloating
  - Feeling of incomplete evacuation
- OIC refers to specific changes in bowel habits caused by treatment with opioids
  - OIC can develop after a single dose or within days or weeks of opioid initiation

Additional Information for Provider
- A proposed definition for OIC is “a change from baseline bowel habits after starting opioids that is characterized by any of the following symptoms recorded over ≥7 days”10:
  - Reduced BM frequency
  - Development or worsening of straining to pass stool
  - Harder stool consistency
  - Sense of incomplete evacuation

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WHAT INCREASES THE RISK FOR OPIOID-INDUCED CONSTIPATION?

Points to Emphasize
- All patients exposed to opioids are at risk for OIC
  - OIC affects some people much more than others, even at low opioid doses
- Other risk factors for OIC
  - Immobility
  - More common in females
  - Advancing age, >70 years
  - Other conditions that can cause or exacerbate constipation (Box 1)
- Assess for non-opioid medications that may cause constipation (Box 2)

Other Conditions that Raise Opioid-Induced Constipation Risk
- Hypothyroidism
- Diabetes mellitus
- Depression
- Taking certain medicines

Box 1. Risk Factors for OIC

<table>
<thead>
<tr>
<th>Concurrent disease</th>
<th>Functional bowel conditions</th>
<th>Malignancy-Associated Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Denervated bowel (e.g., spinal cord injury, neurogenic bowel)</td>
<td>Anorexia</td>
</tr>
<tr>
<td>Metabolic conditions (e.g., diabetes, hypothyroidism)</td>
<td>Tumor-related bowel obstruction</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Neurologic conditions (e.g., Parkinson’s disease, multiple sclerosis)</td>
<td>Underlying rectal problems—anal fissures, chronic hemorrhoids, anal rectal scarring s/p radiation therapy (e.g., prostate seed implants)</td>
<td>Hypercalcemia</td>
</tr>
<tr>
<td></td>
<td>Irritable bowel syndrome constipation predominant</td>
<td>Hypokalemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spinal cord compression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Colon cancer</td>
</tr>
</tbody>
</table>

Box 2. Other drugs classes commonly known to cause constipation

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum antacids</td>
<td>Calcium carbonate (e.g., Maalox, Mylanta, Gaviscon)</td>
</tr>
<tr>
<td>Antiemetics</td>
<td>5-HT3 serotonin receptor antagonists (e.g., ondansetron)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Tricyclic (e.g., amitriptyline, doxepin), serotonin and norepinephrine reuptake inhibitors (e.g., duloxetine), selective serotonin reuptake inhibitors (e.g., paroxetine)</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>amantadine</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>Calcium channel blockers (e.g., verapamil)</td>
</tr>
<tr>
<td>Iron supplements</td>
<td>Ferrous sulfate</td>
</tr>
<tr>
<td>Phenothiazines</td>
<td>prochlorperazine (e.g., Compazine)</td>
</tr>
<tr>
<td>Vinca alkaloid chemotherapy</td>
<td>vincristine</td>
</tr>
</tbody>
</table>

Additional Information for Provider

HOW DOES OPIOID-INDUCED CONSTIPATION AFFECT EVERYDAY LIFE?

Points to Emphasize

- OIC can cause significant social and psychological distress for patients and caregivers
- The additional effects of OIC are significant
  - Patients with chronic pain already experience a high symptom burden
  - Patients may skip, decrease, or stop opioids because of OIC symptoms
- It may be difficult for patients with OIC to talk about their symptoms
  - Due to embarrassment or not wanting to take provider’s time
  - May feel that nothing can be done
  - Concerned that they may need to reduce pain medication

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Physical | Psychological | Practical Issues
---|---|---
• Problems with sitting, walking or tiredness | • Anxiety, fear, distress | • Time lost from work
• Difficulty performing usual activities | • Anticipatory worry about having a BM | • Diminished work productivity
• Low self-esteem | • Social isolation | • Higher health care costs

Here’s what other people with opioid-induced constipation say about the effect it has on their lives.

PAIN AND STRAIN
When my bowel movement is over I am hot and tired, and I just want to rest.

DIFFICULT TO SIT
Leakage and intense pain have me in tears.

INTENSE PAIN
Leaves me feeling unable to walk.

SORE RECTUM AND LOWER BACK
Sometimes I can barely move.

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TALKING TO YOUR PROVIDER ABOUT YOUR BOWELS

Your provider may ask you questions about your bowel patterns, like:

- Did you have constipation before you started using opioid pain medicines?
- How often do you have a bowel movement?
- Do you have to push hard when having a bowel movement?
- Do you have pain in your abdomen before or during a bowel movement?
- Do you need to use your fingers to get stool out?

Points to Emphasize

- OIC is diagnosed on the basis of a change in bowel patterns after starting opioid therapy
  - Assessment is based on clinical history and physical examination
  - Ask when constipation started relative to taking opioids

Additional Information for Provider

- Constipation that starts or worsens in patients taking opioids is likely to be opioid-induced, but it is important to exclude other reasons for constipation
- Adopt a straightforward approach to OIC assessment to relieve patient embarrassment
- Obtain thorough history
  - Symptom analysis
  - Baseline elimination pattern before starting opioids
  - Medication review for drugs that may exacerbate OIC
  - Current and prior use of laxatives

Questions to ask patients

- In addition to the above questions: ask your patients:
  - When did you last have a bowel movement?
  - When was the bowel movement before that?
  - Do you feel like your bowels do not completely empty?
- Ask patient if they are manually disimpacting themselves

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TALKING TO YOUR PROVIDER ABOUT YOUR BOWELS

Points to Emphasize

- Physical examination: inspect body habitus, nutritional status (i.e., signs of deficiency), abdomen
  - Bowel sounds, tenderness, distension, tympany, palpation of stool mass in LLQs
  - Abdominal examination is often normal even with significant constipation
  - If necessary, consider anorectal examination to exclude masses or fecal impaction

- Diagnostic tests
  - If clinically indicated could include complete blood count, metabolic panel, thyroid stimulating hormone
  - Plain x-ray to identify air/fluid levels which may indicate fecal impaction or obstruction

Additional Information for Provider

- Alarm features may warrant additional testing
  - Rectal bleeding (hematochezia or melena)
  - Unintentional weight loss is defined as >5% over 6 months
  - Personal or family history of colon cancer

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**PATIENT TOOLS—KEEPING TRACK**

**Points to Emphasize**
- Instruct patients how to complete the bowel diary for one week
- Offer patients a take-home sheet with bowel diary

**Bowel Diary**
- Explain the bowel diary will help patients track the following:
  - Time of BM
  - Stool description (using Bowel movement description chart)
  - Straining
  - Fluid intake
  - Physical Activity
  - Laxatives
  - Did they fully evacuate their bowels
PATIENT TOOLS—Bowel Movement Description Chart

This chart can help you describe your bowel movements to your provider.

### Bowel Movement Description

<table>
<thead>
<tr>
<th>Constipation</th>
<th>A</th>
<th>Small hard pellets, difficult to have bowel movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>B</td>
<td>Hard stool with lumps and cracks</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>Formed and soft; easy to have a bowel movement with no pain</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>D</td>
<td>Loose or watery bowel movement (mushy)</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>Liquid stool</td>
</tr>
</tbody>
</table>

**Points to Emphasize**

- Patients might not recall their bowel patterns
  - Assessment tools can help patients taking opioids
- Offer patients an info sheet with the Bowel Movement Description chart and bowel diary

**Bowel Movement Description Chart**

- Start by asking patients:
  - To describe their stool consistency and normal BM pattern using the Bowel Movement Description chart
  - This scale categorizes stool forms into 5 groups ranging from small hard pellets (category A) to liquid stool (category E)
GET MOVING—BODY AND BOWEL

Points to Emphasize

• Physical activity stimulates peristalsis, increases intestinal gas clearance and reduces bloating
  — Activity also improves mood
• Even small changes in physical activity and fluid intake can make a difference to patients with OIC
• Gradually increase activity
  — Start with walking 10-15 minutes three times a week, and build up to 30 minutes daily, if able

Additional Information for Provider

• The effect of lifestyle changes on OIC population has not been specifically studied
  — Benefits of these strategies on patients with OIC is extrapolated from studies on those with chronic constipation
• Increases in spontaneous BM frequency has been associated with consistent improvements in patient-reported outcomes

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13 Webster LR. Opioid-Induced Constipation. Pain Medicine. 2015;16(S16-21).
GET MOVING—BODY AND BOWEL

Points to Emphasize

- Reset bowel function
  - Respond promptly to the urge to defecate
- Create dedicated time, get comfortable and establish privacy before defecation
- Consider use of a foot stool to help relax the pelvic floor muscle

Additional Information for Provider

- A small percentage of persons may need counseling to address issues in childhood that impact successful stooling
  - e.g., people who suffered adverse childhood experiences, such as trauma or sexual abuse

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FLUID AND FIBER

Points to Emphasize

• Patient should drink at least 2 liters of water/fluid per day (64 ounces, unless on fluid restriction)
• The Western diet is low in fiber
• Insoluble fiber is found in skins of fruits and vegetables, seeds, nuts and whole grains, and supplements (e.g., corn fiber, wheat bran)
  — Pushes food waste through your body
  — Increases stool bulk
  — Does not dissolve in water
• Soluble fiber is found in barley, flax, oats, certain fruits and vegetables
  — Better tolerated and more effective than insoluble fiber
• Soluble fiber is also found in supplements (i.e. psyllium, methylcellulose, polycarbophil)
  — Supplements lack the variety of fibers, vitamins, or minerals found in food naturally
  — Contraindicated in patients who are on fluid restrictions (e.g., heart failure, kidney failure, advanced disease)

• Increasing fiber too quickly can cause bloating or flatulence
  — Advise patient to increase fiber gradually over 2-3 weeks to 25-34 g/day
• Fiber absorbs liquid in the bowel
  — It is important to increase fluids with fiber
  — This goal might not be possible in older, more debilitated patients

LAXATIVES

Laxatives can provide symptom relief from opioid-induced constipation

<table>
<thead>
<tr>
<th>TYPES OF LAXATIVES</th>
<th>HOW TO TAKE LAXATIVES</th>
<th>POSSIBLE ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool Softeners</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docusate</td>
<td>• Once or twice a day</td>
<td>• Irritation of the anus</td>
</tr>
<tr>
<td></td>
<td>• Can be taken with other laxatives</td>
<td>• Leaking from rectum</td>
</tr>
<tr>
<td>Stimulants that increase gut movement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senna</td>
<td>• Tablets once or twice a day</td>
<td>• Abdominal cramps, pain</td>
</tr>
<tr>
<td>Bisacodyl</td>
<td>• Tablets once or twice a day</td>
<td></td>
</tr>
<tr>
<td>Sugars that are not absorbed—Increase fluid in the colon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyethylene glycol (PEG)</td>
<td>• 1 heaping tablespoon in 8 ounces of fluid once daily</td>
<td></td>
</tr>
<tr>
<td>Lactulose (available by prescription)</td>
<td>Can be added to hot tea or hot water to reduce sweet taste</td>
<td>• Abdominal cramping, pain, gas</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>Add to water</td>
<td></td>
</tr>
<tr>
<td>Magnesium oxide magnesium hydroxide</td>
<td>Comes in tablet or liquid form</td>
<td></td>
</tr>
<tr>
<td>Bulk-forming—increases stool size and helps stool move through the colon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylcellulose</td>
<td>• Sprinkled over food</td>
<td>• Fluid overload</td>
</tr>
<tr>
<td></td>
<td>• Tablet</td>
<td>• Flatulence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Bloating</td>
</tr>
<tr>
<td>Psyllium</td>
<td>• Sprinkled over food</td>
<td>Avoid bulk-forming laxatives if you have fluid restrictions or cannot drink 64 ounces of fluid per day</td>
</tr>
<tr>
<td></td>
<td>• Tablet</td>
<td></td>
</tr>
<tr>
<td>Polycarbophil</td>
<td>• Tablet</td>
<td></td>
</tr>
</tbody>
</table>

LAXATIVE TYPES | DOSAGE AND ADMINISTRATION*

<table>
<thead>
<tr>
<th>Stool Softeners</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Docusate</td>
<td>Starting dose 100 mg once or twice daily</td>
<td>Max 300 mg daily</td>
</tr>
<tr>
<td>Stimulants—increase intestinal motility/secretion and peristalsis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senna (available as single agent or in combination with docusate 50mg)</td>
<td>Starting dose 8.6 mg once daily</td>
<td>Max 8 tablets daily</td>
</tr>
<tr>
<td>Bisacodyl</td>
<td>Starting dose Oral 5 mg once daily</td>
<td>Rectal 10 mg</td>
</tr>
<tr>
<td>Osmotic Agents—non-absorbable sugars that increase fluid secretions in the small intestine by retaining fluid in the bowel lumen12,22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyethylene glycol (PEG)</td>
<td>Starting dose 17g mixed with fluid</td>
<td>Maximum daily dose 68g</td>
</tr>
<tr>
<td>Lactulose (prescription only)</td>
<td>Starting dose 15 ml every other day</td>
<td>Maximum daily dose 60 ml daily in divided doses</td>
</tr>
<tr>
<td>Magnesium oxide magnesium hydroxide</td>
<td>Tablets</td>
<td>Liquid</td>
</tr>
<tr>
<td>Bulk-Forming Laxatives—natural or synthetic polysaccharides or cellulose derivatives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylcellulose</td>
<td>Starting dose 1 tablespoon in 8 ounces fluid 1-3 times daily</td>
<td></td>
</tr>
<tr>
<td>Psyllium</td>
<td>Starting dose 1 tablespoon in 8 ounces fluid 1-3 times per day</td>
<td></td>
</tr>
<tr>
<td>Polycarbophil</td>
<td>Starting dose 625 mg up to 1-4 times per day</td>
<td></td>
</tr>
</tbody>
</table>

Additional Information for Provider*

*Consult prescribing guidelines for medication (see page 18 for potential adverse effects)

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**BOWEL REGIMEN**

### Points to Emphasize

- Fluid, fiber and activity may not be enough to prevent OIC - The majority of patients treated with opioids need a daily bowel maintenance regimen

### Additional Information for Provider

- Laxatives are associated with a range of GI effects including bloating, flatulence, abdominal fullness (which are also symptoms of constipation)
- If vigorous measures are used to prevent and manage constipation, more invasive therapies can be avoided
- Manual disimpaction, suppositories, or enemas are often uncomfortable and embarrassing for patients — Risks include bleeding, fluid and electrolyte imbalance, and vasovagal reaction
- Patients with OIC may require additional prescription therapies beyond OTC laxatives

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**Example Bowel Regimen**

- Most bowel regimens require a combination of an osmotic laxative (or softener) added to a stimulant, for example:
  - Osmotic laxatives (e.g., polyethylene glycol) — "GUSH" effect
  - Stimulants (e.g., senna, bisacodyl) — "PUSH" effect
  - Stool softeners (e.g., docusate) — "MUSH" effect
- Counsel patients to consider either of these regimens:
  - Gush + Push
  - Mush + Push

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PRESCRIPTION MEDICATIONS FOR OPIOID-INDUCED CONSTIPATION

Points to Emphasize

• Consider prescription medications if OTC options and lifestyle changes do not result in adequate relief.

• Opioid receptor antagonists only block opioid receptors in the bowels.
  — These drugs DO NOT reduce opioid analgesia.

Additional Information for Provider

• Peripherally-acting mu-opioid receptor antagonist (PAMORAs)

• Locally-acting Chloride channel-2 activator (CC2)
  — Are an evidence-based treatment option for OIC
  — Selectively block GI-receptors
  — Do not cross the blood-brain barrier or affect the centrally-mediated analgesic effects of opioids
  — Do not induce central opioid withdrawal.

Reassess patient in 2-6 weeks after starting a prescription for OIC

| FDA-Approved Medications for OIC in Patients with Chronic Noncancer Pain |
|-----------------------------|------------------|-----------------------------|
| **Peripherally-acting mu-opioid receptor antagonist (PAMORAs)** |
| **Drug** | **Clinical Information** | **Dose/Administration** |
| Methylnaltrexone† | • Subcutaneous | • 12 mg daily |
| | • Oral†† | • 450 mg orally once daily in morning |
| Naloxegol* | • Increased BM from 1>3 per week | • 12.5 mg to 25 mg orally once daily in morning |
| Naldemedine* | • Increased in >1 BM per week†† over baseline for ~50% patients within 1 week of taking medication | • 0.2 mg once daily with or without food |
| **Locally-acting chloride channel-2 activator (CC2)** |
| **Drug** | **Clinical Information** | **Dose/Administration** |
| Lubiprostone~ | • Increased in BM frequency for most patients within 1 week of drug administration | • 24 g twice per day |

†Stop all other laxatives when starting a PAMORA
††Also approved for OIC in patients with advanced illness receiving palliative care—weight-based dosing
*Can be used off-label for patients with cancer and OIC
*Also approved for patients with chronic pain related to prior cancer or its treatment who do not require frequent opioid dose escalation

Current as of the printing of this tool May 2018

References:

39 All drug information from prescribing information www.accessdata.fda.gov
ADVERSE EFFECTS FROM MEDICATIONS TO TREAT OPIOID-INDUCED CONSTIPATION

Points to Emphasize

• Patients should report side effects while taking medications to treat OIC
• Reassure patients that there are effective ways to manage side effects

Additional Information for Provider

Contraindications of prescription PAMORAs medications

• Known or suspected gastrointestinal obstruction
• Risk of recurrent obstruction

Monitoring of prescription PAMORAs and CC2 medications

• Symptoms of GI obstruction
  — Severe, persistent, or worsening abdominal pain
• Symptoms of opioid withdrawal
  — Chills, diaphoresis, anxiety, irritability, changes in blood pressure or heart rate

• Discontinue OIC medication if opioid therapy is stopped
• Action
  — Stop drug immediately if GI symptoms worsen

<table>
<thead>
<tr>
<th>Medication</th>
<th>Side Effects</th>
<th>Consideration</th>
</tr>
</thead>
</table>
| Methylnaltrexone (PAMORA) | • Nausea, diarrhea, vomiting, and cramping  
 • Response to the initial dose may be abrupt | • Advise patient that response to the first dose may be abrupt, with cramping and diarrhea  
 — Tell patient to stay near a toilet for at least 2 hours after injection of first dose  
 — If traveling, carry towels and clean underwear. |
| Naloxegol (PAMORA) | • Nausea, diarrhea, vomiting, and cramping  
 • Response to the initial dose may be abrupt | • Discontinue maintenance laxatives prior to initiation  
 • Take on an empty stomach prior to first meal of day or 2 hours after meal |
| Naldemedine (PAMORA) | • Abdominal pain, diarrhea, nausea, vomiting, gastroenteritis | • Avoid concomitant use with CYP3A4 inducers (e.g., clarithromycin, carbamazepine) |
| Lubiprostone (CC2)  | • Nausea, diarrhea, abdominal distension  
 • Headache, edema, chest discomfort/pain, dizziness, fatigue | • Take drug with food to avoid nausea |
## PROVIDER RESOURCES

For general information and resources on OIC, see American College of Gastroenterology

www.acg.gi.org

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### CLINICAL ASSESSMENT TOOLS FOR BOWEL FUNCTION

<table>
<thead>
<tr>
<th>TOOL</th>
<th>PURPOSE</th>
<th>ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel Function Diary</td>
<td>3-item questionnaire to assess ease or severity of defecation, feeling of incomplete bowel evacuation, patient judgment of constipation on a scale of 0-100</td>
<td>Patient self-administered. 11 items are independently assessed, no method for calculating total score</td>
</tr>
<tr>
<td>Patient Assessment of Constipation Symptoms (PAC-SYM)</td>
<td>12-item, 3-domain measures of stool, rectal, abdominal symptoms but not BM frequency</td>
<td>Patient self-administered</td>
</tr>
<tr>
<td>Patient Assessment of Constipation Quality of Life</td>
<td>28-item, 4-domain scales assesses feeling of incomplete bowel evacuation and BM frequency, patient dissatisfaction, physical and psychosocial discomfort, worries and concerns</td>
<td>Patient self-administered</td>
</tr>
<tr>
<td>Bowel Function Index</td>
<td>Focus on ease of defecation and patient assessment of OIC (e.g., bloating, pain)</td>
<td>Clinician administered, shortest of the 5 tools. Clinicians can assess OIC severity by calculating the total BFI score using the average score of its 3 items. A score of ≥30 is a threshold for considering prescription medications.</td>
</tr>
<tr>
<td>Stool Symptom Screener</td>
<td>A shorter version of PAC-SYM that can be used to initiate communication</td>
<td>Clinician administered, no information on score calculation</td>
</tr>
</tbody>
</table>


