OPIOID-INDUCED CONSTIPATION MANAGEMENT GUIDELINES (Part 1 of 2)

The management of opioid-induced constipation is based on recommendations from the American Gastroenterological Association (AGA). The guideline only focuses on medical management (both prescription and over-the-counter products) and does not address the role of psychological therapy, alternative medicine approaches, surgery, or devices.

ROME IV DIAGNOSTIC CRITERIA

Opioid-induced constipation (OIC): new or worsening symptoms of constipation when initiating, changing, or increasing opioid therapy that must include ≥2 of the following (>25% of defecations):

- Straining
- Lumpy or hard stools
- Sensation of incomplete evacuation
- Sensation of anorectal obstruction or blockage
- Manual maneuvers to facilitate defecations (eg, digital evacuation, support of the pelvic floor)
- Fewer than 3 spontaneous bowel movements per week

PATIENT EVALUATION

General approach to patients with suspected OIC:

- Ensure that the indication for opioid therapy is appropriate and that the patient is taking the minimum necessary opioid dose.
- Obtain a careful history to evaluate defecation and dietary patterns, stool consistency, symptoms of dyssynergic defecation (eg, sensation of incomplete evacuation), or alarm symptoms (eg, blood in stool or accompanying weight loss).
- Obtain a medical history to assess comorbid illnesses and regular medication use.
- Explore or exclude other potential causes of constipation, such as pelvic outlet dysfunction, mechanical obstruction, metabolic abnormalities, and contributions of other diseases or medications.

MANAGEMENT

AGA recommendations:

1. Lifestyle modifications (eg, increasing fluid intake, regular moderate exercise, and toileting as soon as possible) are an appropriate first step for all patients with constipation.
2. Changing to an equianalgesic dose of an alternative, less-constipating opioid ("opioid switching") may be beneficial.
3. Once OIC is confirmed and other causes of constipation excluded, the use of laxatives as first-line agents is recommended.
4. For laxative-refractory[1] OIC, it is recommended to use PAMORAs such as naldemedine or naloxegol, and suggested to use methylnaltrexone, over no treatment.
5. No recommendations were made on the use of intestinal secretagogues (lubiprostone) and selective 5-HT agonists (prucalopride) in OIC.

PHARMACOLOGICAL TREATMENTS

Generic	Brand	Strength	Form	Adult Dose
TRADITIONAL LAXATIVES				
Osmotic				
lactulose	—	10g/15mL	oral soln	15–30mL once daily; max 60mL/day.
	Kristalose	10g, 20g	crystals for reconstitution	Dissolve 10–20g in 4oz water once daily; max 40g/day.
magnesium citrate	—	1.745g/30mL	oral soln	Take with a full 8oz glass of liquid. ≥**12yrs:** 6.5–10oz (192–296mL) once daily or in divided doses. Max 10oz/24hrs.
magnesium hydroxide	—	400mg/5mL	liquid	Take with a full 8oz glass of liquid. ≥**12yrs:** 30–60mL once daily or in divided doses.
polyethylene glycol (PEG)	**Glycolax**	17g	pwd for oral soln	Dissolve 17g in 8oz water and drink once daily for max 14 days.
	Miralax	17g	pwd for oral soln	≥**17yrs:** Dissolve 17g in 4–8oz liquid and drink once daily for max 7 days.

(continued)

OPIOID-INDUCED CONSTIPATION MANAGEMENT GUIDELINES (Part 2 of 2)

TRADITIONAL LAXATIVES *(continued)*

Stimulant				
bisacodyl	**Dulcolax**	5mg	e-c tabs	1–3 tabs daily. Results usually within 6–12hrs; reevaluate if ineffective.
		100mg	softgel	1–3 softgels daily. Results usually within 12–72hrs; reevaluate if ineffective.
		10mg	supp	1 supp rectally once daily. Retain for 15–20mins. Results usually within 15–60mins; reevaluate if ineffective.
	Fleet	5mg	tabs	1–3 tabs daily. Results usually within 6–12hrs; reevaluate if ineffective.
		10mg	supp	1 supp rectally daily. Retain for 15–20mins. Results usually within 15–60mins; reevaluate if ineffective.
		10mg/30mL	enema	1 enema rectally daily. Results usually within 5–20mins; reevaluate if ineffective.
senna	**Senokot**	8.6mg	tabs	2 tabs once daily; max 4 tabs twice daily.
	Senokot Extra Strength	17.2mg	tabs	1 tab once daily; max 2 tabs twice daily.
Detergent/surfactant stool softeners				
docusate sodium	**—**	10mg/mL	liquid	Mix in 6–8oz of milk or juice. 50–150mg once or twice daily.
	Colace	50mg, 100mg	caps	50–300mg daily.
Lubricant				
mineral oil	**Fleet Mineral Oil Enema**	100%	enema	1 enema rectally daily. Results usually within 2–15mins; reevaluate if ineffective.

PERIPHERALLY ACTING μ-OPIOID RECEPTOR ANTAGONISTS (PAMORAs)[2]

methylnaltrexone	**Relistor**[3,4]	150mg	tabs	Take on an empty stomach with water ≥30mins before first meal of day. 450mg once daily in the AM. *CrCl<60mL/min or hepatic impairment (Child-Pugh B or C):* 150mg once daily.
		8mg/0.4mL, 12mg/0.6mL	soln for SC inj	12mg SC once daily. *Advanced illness:* give once every other day as needed (max 1 dose/24hrs). <38kg or >114kg: 0.15mg/kg. 38–<62kg: 8mg. 62–114kg: 12mg. *Renal (CrCl<60mL/min) or severe hepatic impairment:* reduce dose by ½ (see full labeling).
naldemedine	**Symproic**[4]	0.2mg	tabs	0.2mg once daily.
naloxegol	**Movantik**[3,4]	12.5mg, 25mg	tabs	Take on an empty stomach. 25mg once daily in the AM; may reduce to 12.5mg once daily if not tolerated. *Renal impairment (CrCl<60mL/min):* 12.5mg once daily; may increase to 25mg once daily if tolerated.

NOTES

Key: **e-c** = enteric coated; **pwd** = powder; **soln** = solution; **supp** = suppository.

[1] Laxative-refractory OIC is defined as moderate or severe symptoms of constipation despite the use of laxatives from ≥1 laxative classes for a minimum of 4 days within a 2-week period. AGA recommends using a combination of ≥2 types of laxatives before escalating therapy, and that scheduled use of laxatives (vs "as needed" basis) is required before considering alternative treatment.

[2] Avoid in conditions that compromise the blood-brain barrier due to potential for serious withdrawal or reversal of anesthesia.

[3] Discontinue all laxative therapy prior to initiation; may use as needed if suboptimal response after 3 days.

[4] Discontinue if opioid pain therapy is also discontinued.

Not an inclusive list of medications and/or official indications. Please see drug monograph at www.eMPR.com and/or contact company for full drug labeling.

REFERENCES

Adapted from Crockett SD, Greer KB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute Guideline on the Medical Management of Opioid-Induced Constipation. *Gastroenterology*. 2018 Oct 16. pii: S0016-5085(18)34782-6. doi: 10.1053/j.gastro.2018.07.016.

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