



Care-Rx
HEALTH

DELIVERING PHARMACEUTICAL CARE SINCE 2008

June 2019

Editor: Tiffany Nguyen, Pharm.D.

QUICK UPDATES

NEW HOURS OF OPERATION

Home Care-Rx has extended our hours:

- Monday thru Friday 6am-2:30am
- Saturday, Sunday and Holidays 8am-12am
- On-call services available 24/7

Please note Creative Compounding hours differ:

- Monday thru Friday 9am-6pm
- Closed Saturdays, Sundays and Holidays

MEDS ON NATIONAL SHORTAGE

Hospice-related drugs currently on backorder:

- Atropine 1% ophthalmic solution
- Haloperidol tablets (0.5 mg, 1 mg, 2 mg)
- Morphine for IV infusion/CADD pump
- Nystatin 100,000 U/mL oral suspension
- Scopolamine 1 mg/3 days transdermal patch

However, our pharmacists can recommend therapeutic alternatives or compounds in order to provide our hospices with uninterrupted service, and our patients with continued care.

LOPERAMIDE: THE POOR MAN'S METHADONE

In the midst of a national opioid epidemic, overdoses of loperamide are also rising. The number of calls nationally to the poison control centers for loperamide exposures more than doubled between 2010 and 2015.

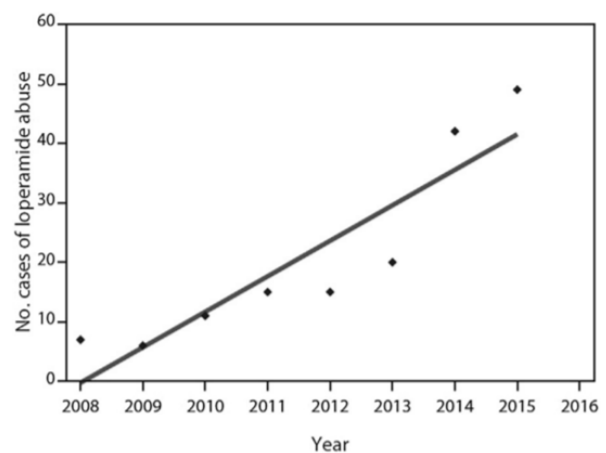


Figure 1. Number of reported cases of intentional loperamide misuse, by year—National Poison Database System, January 1, 2008-March 31, 2016.

Loperamide, better known by its brand name Imodium, is available as an over-the-counter or prescription treatment for diarrhea. It is an opioid derivative structurally related to diphenoxylate and haloperidol that works primarily on gut opioid receptors to slow down peristalsis or movement of the intestines. The U.S. Food and Drug Administration (FDA) has deemed loperamide safe when used at recommended doses, which for adults is a single 4 mg initial dose followed by 2 mg after each loose stool; the dose should not exceed 8 mg per day for over-the-counter use and 16 mg for prescription use. However, at extremely high doses—dozens or even hundreds of tablets a day—it can produce euphoria or ease withdrawal symptoms; there have been reports of people blending 400 to 500 tablets into a smoothie, and drinking it over one or two hours.

Table 1. Reported reasons for loperamide misuse

Rationale for loperamide overdose	1985-2013 (n = 21)	2014-2016 (n = 33)	1985-2016 (n = 54)
Antidiarrheal	10	3	13
Opioid alternative	0	18	18
Suicide attempt and familial conflict	3	0	3
Not reported	8	12	20

Normally, loperamide's oral bioavailability is low due to first-pass metabolism through the liver, and penetration into the brain is minimal since transporter proteins at the blood-brain barrier (BBB) actively pump the drug out of the brain. However, at extremely high doses, those pumps become saturated and overwhelmed, subsequently allowing the drug to cross the BBB and flood the brain's opioid receptors, producing a high or improving withdrawal symptoms when stronger opioids are not available.

Common adverse effects when taking therapeutic doses of loperamide can include nausea, constipation, drowsiness, and headache. However, excess consumption of any opioid can cause central nervous system (CNS) toxicities such as miosis, CNS depression (impaired thinking and/or consciousness), respiratory depression (impaired breathing)—all of which could lead to death. Its misuse is linked to another risk: abnormal heart rhythms or life-threatening cardiac arrhythmias, such as QT interval prolongation and Torsades de Pointes. The FDA has warned that excessive amounts of the drug may disrupt the electrical system in the heart that guides when and how the heart muscles squeeze. Tampering with this system can impair your heart's ability to effectively pump blood to the rest of your body. Thus, dizziness, fainting, and even cardiac arrest and death may result.

Table 2. Reported toxicities categorized by organ system

Organ system	1985-2013 (n = 21)	2014-2016 (n = 33)	Total, 1985-2016 (n = 54)
Gastrointestinal ^a	6	1	7
Cardiovascular ^b	4	15	19
Respiratory ^c	2	2	4
Neurological ^d	4	5	9
Death	10	17	27

^a Report of epigastric pain, elevated pancreatic enzymes, severe constipation, enlarged bladder, pancreatitis, peritoneal irritation, or appendicitis. Note that patients reported multiple toxicities and percentages do not equal 100%.

^b Report of syncope, chest pain, cardiac arrhythmia, cardiomegaly, tachycardia, or hypotension.

^c Report of pulmonary edema, shortness of breath, and increased respiratory rate.

^d Report of seizures, somnolence, weakness, slurred speech, withdrawal symptoms, delirium, severe motor retardation, loss of consciousness, dizziness, and cerebral edema.

According to the National Institutes of Health (NIH), an overdose can be treated by administering activated charcoal, which limits how much drug is absorbed into the body's circulation. If the patient has not vomited, gastric lavage or stomach pumping should be performed first to clean out the stomach contents before administration of activated charcoal. Gastric lavage is often used for those who have consumed large amounts of drugs, alcohol, or toxins/poisons. Naloxone is a common form of treatment for narcotic drug overdose and can be given to manage symptoms of loperamide overdose as well. As a pure opioid antagonist, naloxone competes and displaces opioids at the its receptor sites. The patient's vital signs should be monitored, and any signs and symptoms of toxicities should also be monitored for 48 hours or more since overdose symptoms may recur depending on how long loperamide remains in the patient's body or blood circulation. Since loperamide does act longer than naloxone, repeated treatments may be required.

Table 3. Loperamide Overdose Treatment Guidelines

Treatment	Notes
CPR	For opioid-associated life-threatening emergency
Gastric lavage	Stomach pumping Done first to clean out stomach contents Only if patient has not vomited
Activated charcoal	Oral, NG: Single dose: 100 grams Limits the drug concentration absorbed into body's circulation Done once patient can retain fluids
Naloxone	IV, IM, SubQ: Initial: 0.4 to 2 mg; may need to repeat every 2-3 minutes Manages overdose symptoms Monitor vital signs and for s/sxs of overdose for 48+ hours Repeated doses PRN

As indicated in January, the FDA recognizes that intentional loperamide misuse and abuse has become a growing problem and is working with manufacturers to blister pack or use other single dose packaging, and to limit the number of doses in each package. As healthcare professionals, we can help by spreading the word to our colleagues and educating patients about loperamide toxicity, many of whom may not realize that loperamide overdose is an existing and growing issue.

MANAGEMENT OF OPIOID-INDUCED CONSTIPATION

Many people suffer from constipation, which is defined as having no more than two bowel movements a week. There are many causes of constipation such as inadequate fluid or fiber intake, decreased exercise, or aggravating diseases; many medications may also result in constipation as a side effect or adverse drug reaction (see below).

Medications that can cause constipation		
<ul style="list-style-type: none"> • Aluminum (antacids, sucralfate) • Anticholinergics • Anti-Parkinsons • Antihistamines • Calcium Channel Blockers (CCBs) • Levodopa • Opiates 	<ul style="list-style-type: none"> • MAOIs • TCAs • Calcium (supplements and antacids) • Iron • Phenothiazines • Diuretics • Clonidine 	<ul style="list-style-type: none"> • Guanabenz • Guanfacine • Disopyramide • Irritant laxatives (with cathartic colon) • Vinca alkaloids • 5-HT3 antagonists • Anticonvulsants

Patients who are in hospice settings or receiving palliative treatment are often taking opioid pain medication, which commonly results in constipation. Opioid induced constipation (OIC) is due to a large number of opioid receptors found in the gastrointestinal tract, which are activated by opioids and resulting in reduced contraction in the bowels and ultimately prolongs bowel frequency. This side effect is reported in as many as 95% of patients taking opioids, and typically does not go away with use either. Consequently, this patient population is most likely on one or more medications to treat or prevent constipation.

Non-pharmacological management of OIC should be attempted first, if possible. Increasing fluid and fiber intake as well as exercise can help to produce bowel movements. Unfortunately, many patients are on fluid restrictions or are non-ambulatory—preventing them from using these non-pharmacological measures.

There are, however, several different options available for a constipated patient—many of which are offered over the counter or at low cost (see page 4). The most commonly used medications are stool softeners and stimulant laxatives. Bulk-forming laxatives on the other hand are not the best option due to causing an increase in stool bulk, which can even lead to bowel obstruction due to decreased peristalsis in OIC.

There are also a few medications for constipation that require a prescription. One of them being linaclotide (Amitza) is indicated for OIC. These medications are often very expensive so it is recommended that cheaper alternatives be tried first.

Since several of these medications are part of different drug classes and they work or affect the body through different mechanisms, multiple may be prescribed to a patient for use if one medication by itself is not adequate to relieve patient’s symptoms. Medications may be used in combination as long as they have different mechanisms of action. The most common laxative used for management of OIC is Senna-S, which is a combination of docusate (a stool softener) and Senna (a stimulant laxative).

In summary, though opioid induced constipation is a commonly seen adverse drug reaction in palliative care, there are several therapeutic options for each individual case. Preferred route or formulation, severity of constipation, desired onset, and cost are all topics to take into consideration when selecting a medication for a patient.

*Author: Tina Nguyen, Pharm.D.
Roseman College of Pharmacy c/o 2019*

MEDICAL DISCLAIMER

The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition. Never disregard professional medical advice or delay in seeking it because of something you have read on this newsletter.

HOME CARE-RX, INC.

3303 Harbor Blvd. Ste C2
Costa Mesa, CA 92626
p. 714-545-5455, f. 714-545-5694
e. orders@homecare-rx.com

We are open to any suggestions and feedback that you may have. Please email nguyen@carerxhealth.com with topics you would like to read or learn about.

Category	Medication	How they work	Onset	Formulations
Stool Softeners	Docusate	Increases incorporation of water and fat into stool allowing for stool softening	1 to 3 days	Enema Suppository Capsule Tablet Liquid
Bulk forming Laxatives	Methylcellulose (Citrucel) Polycarbophil (FiberCon) Psyllium (Metamucil) Wheat Dextrin	Absorbs water in the intestine to form a viscous liquid which promotes peristalsis and reduces transit time. Also known as fiber supplements	A few days	Powder Granules Liquid Tablet Packet Wafer
Stimulant Laxatives	Bisacodyl Senna	Stimulates peristalsis – or gut movement by directly irritating the smooth muscle of the intestine, causing the intestine to contract which this moves the stool through the intestines	6 to 10 hours	Enema Suppository Oral Liquid Capsule
Osmotic Laxatives (Sometimes known as saline laxatives)	Lactulose Magnesium Citrate Milk of Magnesia sorbitol 70% Polyethylene glycol 3350 Glycerin	Promotes peristalsis – or gut movement - by increasing osmotic pressure, drawing fluid into the colon and thus stimulating evacuation	Within 30 minutes	Enema Suppository Oral Liquid
Lubricant Laxatives	Mineral Oil (Fleet) Mineral Oil Enema)	Eases passage of stool by decreasing water absorption and lubricating the intestine; impairs colonic absorption of water	6 to 8 hours	Enema Oral Liquid
Prescription Medications	Lubiprostone (Amitiza) Linaclotide (Linzess)	Different regulations of fluid in the intestines	Within 24 hours	Oral capsule
Combination Products	Docusate/Senna (Senna S)	Combination of a stool softener and a stimulant laxative		