



## ACTIVITY DESCRIPTION

---

**Target Audience**  
 This continuing pharmacy education activity is planned to meet the needs of pharmacists in a variety of practice settings, including large and small health systems, outpatient clinics, managed-care organizations, long-term care facilities, community, and academia. This activity would be especially beneficial for pharmacists, clinical specialists, managers, leaders, and educators who are interested in pain management, new drug therapies, and improving the care of patients with chronic pain.

**Learning Objectives**  
 Upon completing this activity, participants will be able to:

- Describe current and emerging abuse-deterrent technologies utilized in opioid medications
- Evaluate the role of abuse-deterrent formulations of opioid medications when making pain management decisions
- Discuss the impact of opioid-induced constipation (OIC) on a patient's quality of life and overall well-being
- Evaluate the use of peripherally-acting mu-opioid receptor antagonists (PAMORAs) in the prevention and management of OIC



## FACULTY

---

**Gregory L. Holmquist, PharmD, CPE**  
 Certified Pain Educator  
 Pain Management / Palliative Care Pharmacist Specialist  
 Hospice / Palliative Care Consultant  
 Chronic Non-cancer Pain Consultant  
 LTC Elderly Pain Consultant  
 Private Pain Management Consultant  
 Palliative Care Strategies  
 Everett, WA

Gregory Holmquist, PharmD has relevant financial relationships with the following commercial interests:  
 Speakers Bureau: Bausch Health and Daiichi-Sankyo  
*Dr. Holmquist does not intend to discuss off-label uses of any products.*

No (other) speakers, authors, planners or content reviewers have any relevant financial relationships to disclose. No (other) speakers or authors will discuss off-label use of a product. Content review confirmed that the content was developed in a fair, balanced manner free from commercial bias. Disclosure of a relationship is not intended to suggest or condone commercial bias in any presentation, but it is made to provide participants with information that might be of potential importance to their evaluation of a presentation.



## Considerations with Opioids

---

- Risk for overdose
- Driving and work safety
- Long-term safety
- **Risk for misuse, abuse, diversion**
- Dependency, addiction, hyperalgesia
- Dose escalation
- Side effects – constipation being the most common

Chou R, et al. *J Pain.* 2009;10:113-130.  
 Becker G, et al. *Lancet.* 2009;373:1198-1206.



## Quick Facts

---

- Opioids are powerful painkillers that can be highly addictive.
- Opioid dependence affects nearly 5 million people in the United States.
- According to the CDC, rates of overdose deaths jumped from 7.9 per 100,000 in 2013 to 9.0 per 100,000 in 2014, a 14% increase.
- 2015: 33,091 deaths (15.6% increase from 2014)
  - Much of increase due to:
    - Heroin deaths, increased by 20.6%
    - Synthetic opioids deaths, other than methadone (e.g. tramadol, fentanyl) increased by 72.2%
    - Fentanyl mixed with heroin and cocaine
    - Carfentanil – 100x more potent than fentanyl, approved only for veterinary use

Dart RC, et al. *N Engl J Med.* 2015;372:241-8.  
 Brauser D. Prescription opioid abuse warning. Available at: <http://www.Medscape.com/viewarticle/338538>  
 Rudd RA, et al. *Morb Mortal Wkly Rep.* 2016;64:1378-82  
 Rudd RA et al. *Morb Mort Wkly Rep.* 2016;65(50-51):1445-52.  
 Centers for Disease Control and Prevention. Fentanyl. Available at: <https://www.cdc.gov/drugoverdose/opioids/fentanyl.html>.  
 Ludden J. An even deadlier opioid, carfentanil, is hitting the streets. Sept. 2, 2016. Available at: <http://www.npr.org/sections/health-shots/2016/09/02/492106992/in-even-deadlier-opioid-carfentanil-is-hitting-the-streets>.



## Opioids as a “Friend” of Pain Management

---

- As sole entities, no risk of GI bleeds, renal toxicity, hepatotoxicity
- Strongest of analgesics
- Quick onset
- Ability to dose-titrate upwards rapidly with many opioids
- Ability to provide analgesia in a variety of pain syndromes



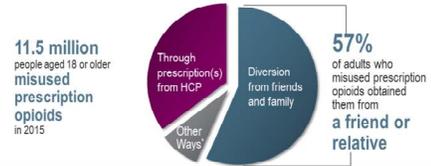
## Opioids as a “Foe” of Pain Management

- Sedation, constipation
- Risk of dependency, addiction
- Lack of anti-inflammatory effect
- Tolerance, neuroadaptation, hyperalgesia
- Potential of misuse, abuse and diversion



## Diversion of Prescription Opioids

Source where prescription opioids were obtained for most recent misuse among adults reporting misuse without use disorder in past 12 months



Han B, et al. *Ann Intern Med.* 2017;167:293-301.



## Opioid Abuse is Complex

### Is there a role for Abuse-Deterrent Formulations (ADFs)?

- Not every extended-release opioid product is formulated with abuse deterrence components.
  - Products with and those without abuse deterrence components may have dramatic cost differences, leading insurance companies to not cover ADFs.
- Wide variety of how ADFs are formulated.
- ADFs may still be abused.
- Limited number of immediate-release (IR) opioids with abuse deterrence components.
- There is limited real-world evidence demonstrating the impact of ADFs on opioid abuse. This is partly due to confounding factors, including limited market share of ADFs.

1. US DSHS, Center for Drug Evaluation and Research. Abuse-deterrent opioids – evaluation and labeling. Available at: <https://www.fda.gov/downloads/Drugs/Guidance/UCM334743.pdf>.
2. Coplan PM, et al. *Clin Pharmacol Ther.* 2016;100:275-286.
3. Severtson SG, et al. *Drug Alcohol Depend.* 2016;168:219-229.
4. Institute for Clinical and Economic Review. Abuse-deterrent formulations of opioids: effectiveness and value. Available at: [https://www.icer-review.org/wp-content/uploads/2016/03/NECEFRAC\\_ADF\\_Final\\_Report\\_08\\_08\\_17.pdf](https://www.icer-review.org/wp-content/uploads/2016/03/NECEFRAC_ADF_Final_Report_08_08_17.pdf).



## Definitions

- **Misuse**
  - Using an opioid for purposes other than intended
    - Depression, sleep, anxiety, constipation pain, euphoria, “party time”
- **Abuse**
  - Manipulating an opioid delivery system, or using an opioid at a higher than prescribed dose to attempt to obtain a faster onset, or greater euphoria
  - FDA definition: “Intentional, non-therapeutic use of a drug product or substance, even once, to achieve a desirable psychological or physiological effect”
- **Diversion**
  - Selling/giving/buying a portion of a prescription to/from another person
  - Stealing medication from a friend/relative/stranger



## Risk Assessment Tool to Help Stratify Risk of Abuse Among Pain Patients

Example of screening tools<sup>1</sup>

<p><b>Patient-reported questionnaires to assess risk of aberrant drug-related behaviors</b></p> <ul style="list-style-type: none"> <li>• Screener and Opioid Assessment for Patients with Pain (SOAPP) Version 1</li> <li>• Revised SOAPP (SOAPP-R)</li> <li>• Opioid Risk Tool (ORT)</li> </ul>	<p><b>Clinician-administered questionnaire to assess potential efficacy as well as harms</b></p> <ul style="list-style-type: none"> <li>• Diagnosis, Intractability, Risk, Efficacy (DIRE) instrument</li> </ul>
--	--

<sup>1</sup>Note that although standardized risk assessment tools have been recommended, none are foolproof.<sup>2</sup>

- However, there are currently no validated tools to assess patients’ environment and risk of prescription diversion.
- **87% of individuals** who obtained prescription opioids from a friend or relative reported that the friend or relative received opioids from a physician.<sup>3</sup>

1. Chou R, et al. *J Pain.* 2009;10:113-30.; 2. Manworren RCB, et al. *Am J Nursing.* 2015;115:34-40.; 3. Han B, et al. *Ann Intern Med.* 2017;167:293-301.



## What are some Common Methods of Abuse?

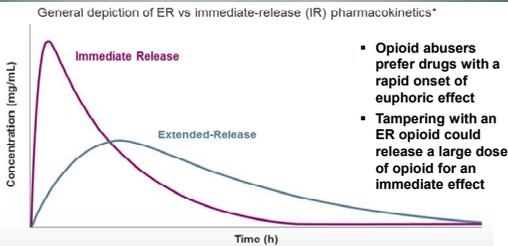
<p><b>Primary routes of opioid abuse<sup>1</sup></b></p>	<ul style="list-style-type: none"> <li>• Oral (chewing, swallowing additional pills)</li> <li>• Inhaling (e.g., snorting, vaporization)</li> <li>• Parenteral (IV, IM, SC)</li> <li>• Smoking</li> </ul>
<p><b>Primary forms of opioid manipulation<sup>2</sup></b></p>	<ul style="list-style-type: none"> <li>• Crushing or grinding into small particles or powder</li> <li>• Dissolving in a solvent (eg, alcohol, acetone)</li> <li>• Extraction by exposure to hot or cold temperatures (microwaving, freezing)</li> </ul>

IV = intravenous; IM = intramuscular; SC = subcutaneous

1. Schaeffer T. *J Med Toxicol.* 2012;8(4):400-407.  
2. U.S. Food and Drug Administration. Guidance for Industry: Abuse Deterrent Opioids – Evaluation and Labeling. April 2015. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM334743.pdf>.



## Defeating Extended-Release (ER) Opioids



\*Graph shown is a theoretical representation of typical ER and IR pharmacokinetics, and is for illustrative purposes only.

## Majority of Abusers Desire to Spend <10 Minutes Manipulating Opioids

- Goal of abuse-deterrent formulations (ADF) is to curb abuse for majority of abusers
- Many ADFs can be defeated with time and effort
- Knowing most common abuse methods allows appropriate evaluation of abuse deterrent potential

Sellers EM, et al. *J Psychopharmacol.* 2013;27:808-16.  
Perrino PJ. Presented at PAINWeek. Sept. 4-7, 2013, Las Vegas, NV.

## Defeating ADF...

(Fudin J. *Pharmacy Times*. January 26, 2015)

"None of the ADFs can address one lingering concern: all medications can be misused and abused if the user ingests medications that are not prescribed to them or ingests more tablets than prescribed, regardless of the technology."

"Furthermore, there are ways to circumvent some of these ADFs. Google "methods to crush OxyContin." There are several blogs and YouTube videos that offer techniques to crush the new formulation of OxyContin. A blog called [BlueLight](#) suggests that OxyContin users can place the drug into their mouths for roughly 1 to 2 minutes to dissolve the coating, and then allow it to dissolve in acidic beverages such as lemon juice or root beer. Once in the beverage, the tablets expand and start to break apart (in as little as 2 to 4 hours) and are easy to consume."

Fudin J. *Pharm Times*. Jan 26, 2015. Available at: <https://www.pharmacytimes.com/contributor/jeffrey-fudin/2015/01/abuse-deterrent-opioid-formulations-purpose-practically-and-garadigms>.

## Ideal Characteristics of Abuse-Deterrent Formulations

- Minimize impact of abuse/misuse by retaining ER properties following manipulation
- Target known or expected routes of abuse by majority of abusers
- Deter intentional abuse, make less attractive to abusers
- Protect patients from rapid release of opioid from either innocent/unintentional or from intentional product manipulation
- Protect patients from dose-dumping with alcohol

## Currently Available Extended-Release ADF Opioids

Product Name	Opioid used	Description of technology (in descending order of date of FDA product approval)
Embeda®	Morphine	Addition of sequestered naltrexone – designed to release antagonist if crushed, and then snorted, or crushed, dissolved and then injected intravenously
OxyContin®	Oxycodone	INTAC polyethylene oxide matrix – designed to render tablet highly resistant to crushing; when exposed to water forms a gel leading to difficulty drawing into a syringe.
Opana®	Oxymorphone	INTAC polyethylene oxide matrix – designed to render tablet highly resistant to crushing; when exposed to water forms a gel leading to difficulty drawing into a syringe.
Nucynta®	Tapentadol	Polyethylene oxide matrix – designed to render tablet highly resistant to crushing or extraction of active drug (not FDA approved as being an ADF)
Exalgo®	Hydromorphone	OROS technology - osmotically active bilayer core enclosed in a semipermeable tablet shell membrane – designed to minimize crushing and active drug extraction
Targiniq®	Oxycodone	Addition of naloxone – designed to block the euphoric effect if it's crushed and then snorted, or crushed, dissolved and then injected intravenously.

## Currently Available Extended-Release ADF Opioids (continued)

Product Name	Opioid used	Description of technology (in descending order of date of FDA product approval)
Hysingla®	Hydrocodone	Resistec polymer matrix – designed to be plastic-like, hard to break, becomes gel in water, thus difficult to use in a syringe
Zohydro®	Hydrocodone	BeadTek formulation – designed to make it hard to crush and snort. Not FDA approved as having ADF technology
Xtampza®	Oxycodone	DETERx microspheres technology – manipulation resistant, has no FDA warnings regarding crushing, chewing or breaking
Troxyca®	Oxycodone	Addition of sequestered naltrexone – designed to release antagonist if crushed, and then snorted, or crushed, dissolved and then injected intravenously
Ventrela®	Hydrocodone	CIMA technology combines three physical and chemical barriers (gelling, barrier and matrix) as a deterrent against the main forms of abuse: Crushing for snorting, IV extraction and dose dumping in alcohol.
MorphoBond®	Morphine	SentryBond technology using multiple overlapping abuse-deterrent barriers

## Currently Available Immediate-Release ADF Opioids

Product Name	Opioid used	Description of technology (in descending order of date of FDA product approval)
Oxaydo®	Oxycodone	According to the FDA, product is not a true ADF, more of an irritant. Nasal inhalation leads to burning, discouraging nasal abuse.
RoxyBond®	Oxycodone	First and only immediate-release opioid classified by the FDA as abuse deterrent.  Formulated with inactive ingredients that make the tablet more difficult to manipulate for misuse and abuse even if the tablet is subjected to physical manipulation and/or attempts at chemical extraction.  Laboratory test data have shown that, compared oxycodone immediate-release tablets, product has increased resistance to cutting, crushing, grinding, or breaking using selected tools.  Both intact and manipulated product resisted extraction in selected household and laboratory solvents under various conditions, including selected pretreatments.  Compared with oxycodone immediate-release tablets, the product forms a viscous material that resists passage through a needle; it is also more difficult to prepare solutions suitable for intravenous injection.

## Emerging: Prodrug Technology for Abuse-Deterrent Opioids

- Prodrugs are chemically-modified versions of pharmacological agents that must undergo transformation in the body to release the active drug.
- FOR ADF:
  - Prodrug itself would be inactive at opioid receptors.
  - Only through oral administration would the prodrug become activated as the enzymes necessary to release the active drug are only present in the GI tract.
  - Intravenous and intranasal administration would yield little or no active drug.
  - Overdose protection may be possible if the activating enzyme system is saturable.



## Mythology of ADF Technology

- **MYTH:** ADF prevents all abuse/misuse/diversion
- Pearls:
  - The right ADF can be an important extra tool to assist providers in preventing misuse/abuse
  - ADF does not prevent the swallowing of supratherapeutic doses of non-manipulated product
  - ADF does not prevent improper prescribing
    - PRN use of extended-release opioids
    - Prescriptions for "half-tablets"



## Mythology of ADF Technology

- **MYTH:** All ADF technologies are fail-safe
- Pearls:
  - Many FDA-approved ADF products have been proven to NOT resist all extraction methods
  - But some currently available ER opioids with ADF have proven very resistant to both standard tools and solvents as well as advanced extraction techniques



## Mythology of ADF Technology

- **MYTH:** ADF technology alone will ensure that my patients will not misuse, abuse or divert their opioids
- Pearls:
  - Universal precautions are still part of "best practices"



## Common Universal Precautions

- Comprehensive pain assessment including opioid misuse risk assessment
- Formulation of pain diagnosis(es)
- Opioid prescriptions should be considered a test or trial; continued or discontinued based on assessment and reassessment of risks and benefits
- Regular face-to-face visits
- Clear documentation

Federation of State Medical Boards. Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain. July 2013. Available at: [http://www.painpolicy.wisc.edu/files/ModelPolicyontheUseofOpioidAnalgesicsintheTreatmentofChronicPain\\_Policy\\_July2013.pdf](http://www.painpolicy.wisc.edu/files/ModelPolicyontheUseofOpioidAnalgesicsintheTreatmentofChronicPain_Policy_July2013.pdf)  
Gourlay DL, et al. *Pain Med.* 2005;6(2):107-12.  
Chou R, et al. *J Pain.* 2009;10:147-69.  
Franklin OM. *Neurology.* 2014;93:1277-84.



## Common Universal Precautions

- Patient Prescriber Agreements (PPA)
- Informed Consent (goals and risks)
- Plan of Care
- Efficacy not well established but no evidence of a negative impact on patient outcomes
- Monitoring for adherence, misuse, and diversion
  - Urine drug testing
  - Pill counts
  - Prescription Drug Monitoring Program (PDMP) data

FSMB Model Policy 2013. Available at: [http://www.painpolicy.wisc.edu/sites/default/files/files/www.painpolicy.wisc.edu/files/pain\\_policy\\_july2013.pdf](http://www.painpolicy.wisc.edu/sites/default/files/files/www.painpolicy.wisc.edu/files/pain_policy_july2013.pdf)  
Gourlay DL, et al. *Pain Med*. 2009;8:107-12.; Chou R, et al. *J Pain*. 2009;10:147-59.; Chesite MD, Savage SR. *J Pain Symptom Manage*. 2012;44:105-16.  
Fishman SM, Kreis PG. *Clin J Pain*. 2002;18(4 Suppl):S70-S.; Arnold RM, et al. *Am J Med*. 2006;119:292-6.; Starrels J, et al. *Ann Intern Med*. 2010;152:712-20.  
Franklin GM. *Neurology*. 2014;83:1277-84.



## Mythology of ADF Technology

- **MYTH:** ADF technology has been proven to decrease addiction, abuse, over-dosages, misuse, diversion, etc.
  - Pearls:
    - Category 4 studies have not been completed with any FDA-approved product demonstrating a reduction in these areas.



## Mythology of ADF Technology

- **MYTH:** All ADF technology is the same
  - Pearls:
    - Some ADF use one physical barrier, others use multiple layers of barriers
    - Some ADF use antagonists
      - Could lead to acute withdrawal reactions if manipulated
    - ADF may or may not prevent alcohol dose-dumping, each product needs to be evaluated on the results of their testing.



## Mythology of ADF Technology

- **MYTH:** ADF technology ensures that the product will have the best pharmacokinetics in its opioid delivery system.
  - Pearls:
    - This is a separate evaluation that every pharmacist should perform.
      - Will an extended-release product maintain its delivery system in fed and fasted states?
      - Will the product hold to a 12-hour, or 24-hour duration of adequate serum levels of the opioid?



## Counseling Tips for All Patients on Extended-Release Opioids

- **NEVER.....**
  - Drink alcohol while on opioids
  - Crush, chew, snort, smoke, pulverize, inject, etc. ER opioid products
  - Use an external heat source on transdermal opioids
  - Cut, tear, rip open transdermal opioid patches
  - Share with a friend or relative any of your opioid products
  - Take more medication than your physician has prescribed
  - Take illicit drugs while on opioid medications
  - Brag to neighbors, friends, relatives about being on opioids (extended-release or immediate-release formulations)



## Counseling Tips for All Patients on Extended-Release Opioids

- **ALWAYS....**
  - Store medication in a safe (preferably locked) place
  - Keep opioids away from children, teens
  - Adhere to the instructions listed on the prescription
  - Adhere to your medication agreement
  - Ask your pharmacist or physician FIRST if you are planning to take any OTC medication or herbal/vitamin product while on LA/ER/IR opioids
  - Call 911 if you experience shortness of breath or have difficulty breathing while on LA/ER/IR opioids



## Considerations with Opioids

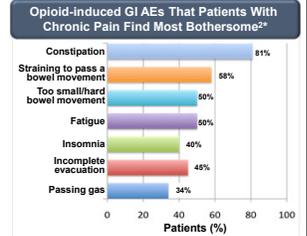
- Risk for overdose
- Driving and work safety
- Long-term safety
- Risk for misuse, abuse, diversion
- Dependency, addiction, hyperalgesia
- Dose Escalation
- Side effects – constipation being the most common

Chou R, et al. *J Pain*. 2009;10:113-130.  
Becker G, et al. *Lancet*. 2009;373:1198-1206.

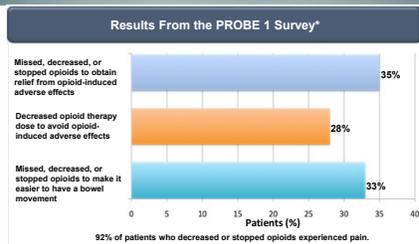


## Opioid-Induced Constipation (OIC)

- Opioid-induced constipation (OIC) is one of the most common and troublesome adverse events (AEs) with opioid therapies<sup>1,2</sup>
  - Reported in 95% of patients with cancer pain and up to 80% of patients with nonmalignant pain<sup>1,2</sup>
- Tolerance to OIC rarely develops<sup>2,3</sup>
- Prevalence of constipation increased with duration of opioid treatment in patients with chronic, non-cancer pain<sup>4</sup>



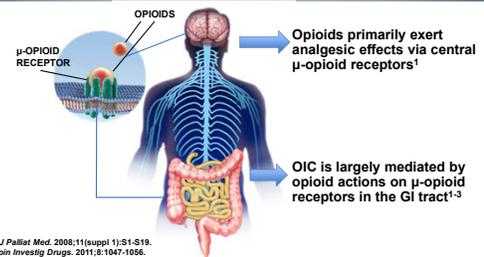
## OIC Can Compromise Pain Management in Patients with Chronic, Non-cancer Pain



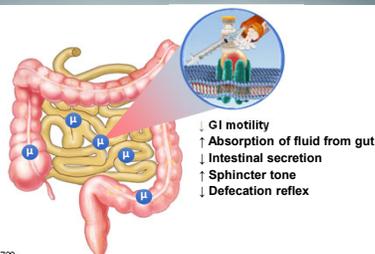
Bell TJ, et al. *Pain Med*. 2009;10:35-42.



## Pathophysiology of OIC



## Opioid Effects on the Gastrointestinal Tract



1. Leppert W. *Adv Ther*. 2010;27:714-730.  
2. Kurz A, Sessler DI. *Drugs*. 2003;63:949-951.

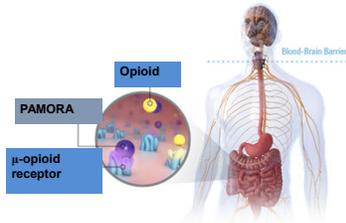


## PAMORAs – A Newer Approach to Treating OIC

- Peripherally Acting Mu Opioid Receptor Antagonists
- Three FDA-approved products in the U.S. market
  - Methylnaltrexone (Relistor<sup>®</sup>)
  - Naloxegol (Movantik<sup>®</sup>)
  - Naldemedine (Symproic<sup>®</sup>)
- Contraindicated for patients with bowel obstruction or at risk for obstruction



## PAMORAs: Overall Mechanism of Action



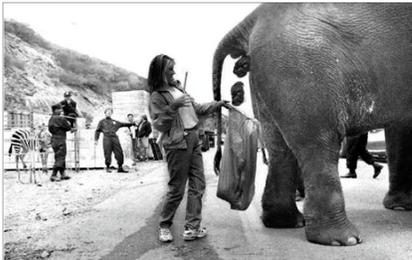
## What do Patients Think about OTC Laxatives?

>50% of patients who use OTC laxatives are dissatisfied with treatment due to lack of efficacy (range: 58% for stimulant laxatives to 84% for osmotic laxatives)\*

\*Prospective longitudinal study conducted in the United States, Canada, Germany, and the United Kingdom assessed the burden of OIC in 489 patients with non-cancer pain

LoCasale RJ, et al. *J Manag Care Spec Pharm.* 2016;22:246-253.

## Goal for OIC....RELIEF!



## PAMORA Comparison

Name (trade)	Indications	Dosing	Drug interactions
Methylnaltrexone (Relistor®)	SQ – OIC in palliative care, advanced illness, cancer and non-cancer pain patients Oral – OIC in non-cancer and in cancer patients with chronic pain	SQ – either weight-based at 0.15 mg/kg daily or 12 mg daily, reduce by 50% in moderate-to-severe renal insufficiency. Oral – 450 mg daily, reduce dose to 150 mg for moderate-to-severe renal/hepatic insufficiency.	None of clinical significance
Naloxegol (Movantik®)	Oral – OIC in non-cancer and in cancer patients with chronic pain	Oral – 25 mg daily, reduce dose to 12.5 mg for moderate-to-severe renal insufficiency, and moderate 3A4 drug interactions	Contraindicated with strong 3A4 inhibitors Reduce dose with moderate 3A4 inhibitors
Naldemedine (Symproic®)	Oral – OIC in non-cancer and in cancer patients with chronic pain	Oral – 0.2 mg daily, no dose adjustments needed in renal insufficiency or in mild-to-moderate liver impairment.	Strong CYP3A inducers (e.g., rifampin): avoid concomitant use. Moderate CYP3A4 inhibitors: monitor for adverse reactions; P-gp inhibitors (e.g., cyclosporine): Monitor for adverse reactions

Relistor® [package insert]. Raleigh, NC: Salix Pharmaceuticals, Inc.; 2017.  
Movantik® [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; 2016.  
Symproic® [package insert]. Florham Hills NJ: Shionogi Inc. 2017.

## Practice Case 1: OIC in a Patient with Chronic, Non-cancer Pain

- A 62-year-old female patient recently seen by her PCP for chronic unremitting joint pain.
- Patient has suffered with chronic OA for over 10 years, utilizing acetaminophen, NSAIDS, and a variety of both regularly scheduled and PRN opioid medications.
- Patient presents prescriptions for hydrocodone ER 40 mg daily and hydrocodone/acetaminophen 5/325 mg PRN.

## OIC Counseling Pearls

- Patients are reluctant to discuss constipation with their physician.
  - Fear of pain medication being reduced
  - Accept OIC as an unmanageable side effect
  - Already tried (and failed) multiple laxatives
- The pharmacist is often the last chance to provide a proactive recommendation for treating OIC.

## OIC Counseling Pearls

- Even low-to-moderate doses of opioid pain medications can lead to opioid-induced constipation.
- Better to prevent constipation than to react to it after the patient has become impacted with stool.
- Constipation from opioids can be easily treated and does not have to affect patient's life or pain regimen.
- High-fiber diet alone will not be helpful and may be harmful.



## OIC Counseling Pearls

- Watch for early signs of constipation becoming worse:
  - Infrequent stools (1–2 small BM per week)
  - Feeling bloated or full
  - Not feeling that bowels completely empty
  - Straining
- Consider other causes of constipation
- Consider targeted medication options for constipation caused by opioid pain medications



## Practice Case 2: OIC in a Patient with Chronic, Non-cancer Pain

- A 45-year-old male with severe low back pain has been taking methadone every 8 hours on a chronic basis for several months.
  - Additionally, using PRN oxycodone, of which in the last month, usage appears to have doubled.
- He was initially prescribed docusate and senna to manage constipation.
- Despite treatment with these laxatives and increasing the dose to TID, the patient continues to experience infrequent stools that are hard and difficult to pass.
- He also complains that he spends excessive time on the toilet and frequently feels that he has failed to completely evacuate his stools.



## OIC Counseling Pearls

- All opioids can be constipating.
  - Mu receptor activity leads to constipation.
- Patients do not build up a tolerance to the constipating effects of opioids.
- Straining to have a bowel movement can exacerbate low back pain, leading to an increased use of PRN opioids.
- OIC itself can often cause significant abdominal pain leading to increased dosing of PRN pain medications by the patient.
  - Not best practice to use opioids for the management of abdominal pain caused by constipation.



## OIC Counseling Pearls

- Constipation is often a constellation and progression of symptoms.  
**PREVENTION IS KEY TO PREVENTING SEVERE COMPLICATIONS.**
- Higher dosages of ineffective traditional laxatives typically do not improve the overall management of OIC.
- Consider newer FDA-approved alternatives for OIC.



## Practice Case 3: OIC in a Cancer Patient

- A 53-year-old male with advanced lung cancer with bone metastases receiving palliative care has been an inpatient for over a week.
- He has been receiving morphine and fentanyl for severe pain.
- The patient now complains of abdominal pain and the medical chart indicates no bowel movement for several days.
- Malignant causes for the pain and bowel obstruction have been ruled out.
- The medical team determines the patient has OIC.



## OIC Counseling Pearls

- Constipation in cancer and palliative care patients is a serious health issue and can lead to serious morbidity if not dealt with rapidly.
- OIC is often resistant to regimens that include only traditional laxatives and an alternative approach should be explored.
- Inappropriate strategies for OIC may contribute to extending the length of hospital stay for patients.



## OIC Counseling Pearls

- Enemas and disimpaction are time-consuming, humiliating, painful and costly; and will most likely not improve the patient in the short- or long-term.
- Consider a PAMORA to rapidly treat OIC in hospitalized patients or patients in the ED setting.
  - SQ may be a preferred route initially in hospitalized patients
- Upon discharge, continue the outpatient use of the PAMORA as long as the patient continues on opioid therapy.
  - Patients with OIC may be effectively treated in the hospital with a PAMORA, then discharged on a traditional (and ineffective) laxative that may lead to a costly re-admission for OIC to the ED or the hospital



## Balancing Medication Use in Patients

### Non-pharmacological strategies

- ✓ Pain control
- ✓ Comfort level



- ✓ Improve overall function
- ✓ Minimize side effects
- ✓ Maximize safety
- ✓ Minimize misuse, abuse and diversion

- ✓ Medical/legal guidelines for opioid use
- ✓ Be pro-active in treating side effects (e.g., constipation)
- ✓ Use all available tools, including abuse-deterrent technology to diminish risks



## Learning By Sharing: Q & A

