Medication Management for Chronic Pain:

The Pharmacist's Perspective

Claire Nolan, PharmD

Program Manager, Mi-CCSI

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Objectives

At the conclusion of this presentation, the participant will be able to:

1. Develop an opioid tapering plan for an individual patient.
2. Implement side effect mitigation and response strategies through an opioid taper.
3. Identify polypharmacy and opportunities to deprescribe to increase patient safety.
4. Prescribe or recommend naloxone for harm reduction.
5. Describe opportunities to optimize the expertise of the pharmacist as a member of the care team.

Safe Opioid Tapering

Why Taper?

- Reduce risk
- Neutral impact on pain
- Patient request
- Intolerable side effects
- Payer requirements

*Patient taking > 100 MME for chronic pain are **7x more likely to die** than those taking < 20 MME*

MME = morphine milligram equivalents

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Quick MME Refresher

90 MME/Day Equals:

- 90 mg hydrocodone (9 tablets of hydrocodone 10/APAP 325 mg)
- 60 mg of oxycodone (~2 tablets of oxycodone 30 mg sustained release
- ~20 mg of methadone (4 tablets of methadone 5 mg)

Sample Prescription

Norco (Hydrocodone/APAP) 10/325 mg
Take 1-2 tablets every 4-6 hours as needed

When taken around the clock, per prescribed directions = 120 MME/day

YIKES!

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Calculating total daily dose of opioids for safer dosage. Centers for Disease Control and Prevention. Available from: https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf. Accessed February 1, 2021.

When to Taper

- > 90 MME/day for chronic non-cancer pain
- Risks > benefits
  - Functional goals of therapy not met
  - Intolerable side effects
  - Signs of opioid use disorder (OUD)
- Painful condition has resolved

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Calculating total daily dose of opioids for safer dosage. Centers for Disease Control and Prevention. Available from: https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf. Accessed February 1, 2021.

Opioid Taper - General Principals

1. Shared decision making
2. Go slow
3. Provide support
4. Don't go backwards

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Prior to Initiating Taper

- Screen for comorbidities that may complicate pain management and/or the taper itself
  - Mental health conditions, OUD, etc.
- Establish goals in collaboration with the patient
  - Define success
- **Offer naloxone** and communicate increased risk of overdose

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Patient communication

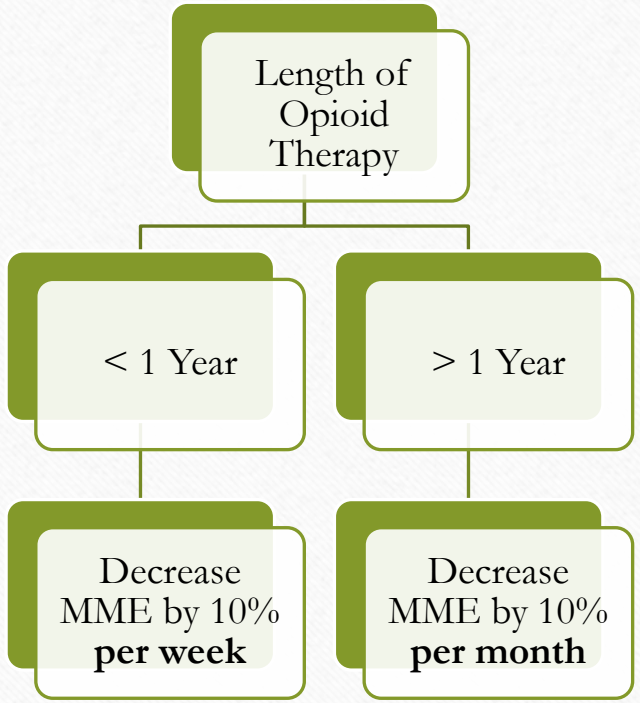
- Acknowledge patient fear, anxiety, and other emotions
- Explore motivations and goals
- Emphasize safety
- Clarify logistics
- Include in decision making
- Engage family member(s), caregiver(s), and support person(s) as appropriate

Tapering can be scary!!
acknowledge this truth

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Taper Strategy

- Approach guided by length of opioid therapy (LOT)
- Other patient-specific factors to consider:
  - Preferences
  - Safety
  - Ongoing response
- Keep moving in the right direction



Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Tapering Logistics

- Do not switch drug or formulation
- Taper and discontinue long-acting opioid therapy first
- Monthly (or more frequent) visits throughout the taper
- Optimize side effect management throughout
- Consider buprenorphine when appropriate

Reduce dose to smallest pill increment

Reduce frequency

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Clinical Pearls

- For a patient who is not ready or willing (and no immediate safety concerns) – reassess quarterly
- PRN (e.g., as needed) opioids
  - Formal tapering plan not necessary
- Continuously monitor and modify the plan as needed

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Example 1

- Morphine ER 30 mg three times daily
- Morphine IR 15 mg every 6 hours
- LOT = 2 years
- Baseline MME = 150

Getting started:

1. Reduce MME by 10% per **month** based on LOT
2. Focus on decreasing the dose of the ER product first (dose and THEN frequency)

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Opioid Dose Calculator. Agency Medical Directors' Group. Available from: http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm. Last Updated: 2015. Accessed September 24, 2020.

Example 1: Taper Schedule

Month	Morphine Extended-Release Dose (mg)	Morphine Immediate-Release Dose (mg)	MME Per Day	Percent Reduction
Baseline	30-30-30	15-15-15-15	150	--
1	15-30-30	15-15-15-15	135	10%
2	15-15-30	15-15-15-15	120	11%
3	15-15-15	15-15-15-15	105	13%
4	15-15	15-15-15-15	90	14%
5	15	15-15-15-15	75	17%
6	None	15-15-15	45	20%
7	None	15-15	30	33%
8	None	15	15	50%
9	None	None	0	100%

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Opioid Dose Calculator. Agency Medical Directors' Group. Available from: http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm. Last Updated: 2015. Accessed September 24, 2020.

Example 2

- Norco (hydrocodone/acetaminophen) 5/325 mg 1-2 tablets by mouth every 4-6 hours as needed for pain (max 12 tablets per day)
  - Patient takes 12 tablets per day
- LOT = 5 years
- Baseline MME = 60

Getting started:

1. Reduce MME by 10% per **month** based on LOT

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Opioid Dose Calculator. Agency Medical Directors' Group. Available from: http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm. Last Updated: 2015. Accessed September 24, 2020.
Hydrocodone and acetaminophen. In: Lexicomp Online Database. Hudson (OH): Lexicomp Inc.: 2020.

Example 2: Taper Schedule

Month	Hydrocodone/ Acetaminophen 5/325 mg (tablets)	MME Per Day	Percent Reduction
Baseline	12	60	--
1	11	55	8%
2	10	50	9%
3	9	45	10%
4	8	40	11%

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Opioid Dose Calculator. Agency Medical Directors' Group. Available from: http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm. Last Updated: 2015. Accessed September 24, 2020.
Hydrocodone and acetaminophen. In: Lexicomp Online Database. Hudson (OH): Lexicomp Inc.: 2020.

Side Effect Mitigation and Response

Withdrawal Symptoms

- Patient-specific onset, order, and severity
- Slow and gradual approach to tapering reduces the risk
- Do not reverse the taper if symptoms occur
- Management will be similar to treatment under other circumstances

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Image available from: https://elitetrack.com/slow-down-to-speed-up/. Accessed February 1, 2021.

Withdrawal Symptoms

- Gastrointestinal Distress
- Flu-Like Symptoms
- Sympathetic and CNS Arousal
- Other

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Withdrawal Symptoms – General Approach

- Open communication with patient (prior to taper and throughout)
- Avoid pre-treatment
- Slow or pause the taper (do not reverse) and consider medication therapy if symptoms occur
- Refer to a specialist for a patient unable to tolerate a taper

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Managing Withdrawal Symptoms

- Alpha-2 adrenergic agonists
  - Most effectively relieve autonomic symptoms
  - Least effective for myalgias, restlessness, insomnia, and cravings

Alpha-2 Adrenergic Agonist	Typical Dosing	Notes
Clonidine	0.1-0.2 mg every 6-8 hours	• Most widely used • Monitor BP and hold if BP < 90/60
Lofexidine	0.54 mg 4 times daily (every 5 to 6 hours)	• Approved in 2018 • Equal in efficacy to clonidine • Trend towards reduced likelihood of hypotension
Tizanidine	2-4 mg every 6-8 hours as needed	• Used primarily to relieve muscle spasms during withdrawal

Lofexidine. In: Lexicomp Online Database. Hudson (OH): Lexicomp Inc.: 2020.
Pain Management Opioid Taper Decision Tool. A VA Clinician's Guide. U.S. Department of Veterans Affairs. Available from: https://www.pbm.va.gov/AcademicDetailingService/Documents/Pain_Opioid_Taper_Tool_IB_10_939_P96820.pdf. Last Updated: October 2016. Last Accessed September 28, 2020.
Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Severino KA. Medically supervised opioid withdrawal during treatment for addiction. . In: UpToDate, Saxon AJ (Ed), UpToDate, Waltham, MA, 2020.

Targeted Symptom Relief – GI Distress

Abdominal Cramps	• Dicyclomine 10-20 mg every 6-8 hours as needed (max: 160 mg/day)
Diarrhea	• Bismuth 524 mg every 30-60 minutes as needed (max: 4200 mg/day) • Loperamide 4 mg followed by 2 mg after each loose stool (max: 16 mg/day)
Nausea and Vomiting	• Ondansetron 4-8 mg every 12 hours as needed (max 16 mg/day) • Alternatives: prochlorperazine or promethazine

Sevarino KA. Medically supervised opioid withdrawal during treatment for addiction. . In: UpToDate, Saxon AJ (Ed), UpToDate, Waltham, MA, 2020.

Targeted Symptom Relief – Insomnia

- Trazodone 25-100 mg at bedtime
  - Can be titrated to 300 mg at bedtime, if needed
- Alternatives (dose at bedtime)
  - Doxepin 6-50 mg
  - Mirtazapine 7.5-15 mg
  - Quetiapine 50-100 mg
  - Zolpidem 5-10 mg (max 5 mg for female patients)

Sevarino KA. Medically supervised opioid withdrawal during treatment for addiction. . In: UpToDate, Saxon AJ (Ed), UpToDate, Waltham, MA, 2020.

Targeted Symptom Relief – Muscle Aches

- Ibuprofen 400 mg every 4-6 hours as needed (max 2400 mg/day)
- Alternatives
  - Acetaminophen
  - Ketorolac
  - Naproxen

Sevarino KA. Medically supervised opioid withdrawal during treatment for addiction. . In: UpToDate, Saxon AJ (Ed), UpToDate, Waltham, MA, 2020.

Targeted Symptom Relief – Anxiety/Restlessness

- Diphenhydramine 50-100 mg every 4-6 hours as needed (max 300 mg/day)
- Alternatives
  - Hydroxyzine
  - Clonazepam
  - Lorazepam
  - Oxazepam

Exercise caution with benzodiazepine therapy
- Avoid if possible
- Short term use only

Sevarino KA. Medically supervised opioid withdrawal during treatment for addiction. . In: UpToDate, Saxon AJ (Ed), UpToDate, Waltham, MA, 2020.

Polypharmacy

Polypharmacy

- Use of multiple medications concurrently and the use of additional medications to correct adverse effects
- "Inappropriate polypharmacy" can lead to adverse outcomes
  - Risk increases with # of medications

Masnoon N, et al. What is polypharmacy? A systematic review of definitions. BMC Geriatrics. 2017;17:230.
Rochon PA. Drug prescribing for older adults. In: UpToDate, Givens J (Ed), UpToDate, Waltham, MA, 2020.

Polypharmacy and Opioids

- Opioids + benzodiazepines = increased risk of respiratory depression, overdose, and **death**
- Opioids + gabapentin or pregabalin = increased risk of opioid-related mortality
- Compounded risk with agents that may increase sedation

Tauben D and Stacey B. Pharmacologic management of chronic non-cancer pain in adults. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.
Rosenquist R. Use of opioids in the management of chronic non-cancer pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Polypharmacy and Opioids

- Opioid metabolism mainly involves CYP 3A4 and CYP 2D6
- Exercise caution when co-prescribing medications that may result in drug-drug interactions
- Consult a drug interaction tool or your pharmacist for review of patient-specific scenarios

Rosenquist R. Use of opioids in the management of chronic non-cancer pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Concomitant Opioids + Benzodiazepines

- Taper sequentially – **opioids first**
- Tapering benzodiazepines
  - Similar principals
  - Reduction of ~25% every two weeks
    - ~12.5% dose reduction every two weeks near the end of the taper
  - Withdrawal symptoms may occur

Taper Opioid Therapy FIRST

THEN Taper Benzodiazepine Therapy

Steinman M and Reeve E. Deprescribing. In: UpToDate, Schmader KE (Ed), UpToDate, Waltham, MA, 2020.
Interagency Guideline on Prescribing Opioids for Pain. Washington State Agency Meical Directors' Group. Available from: http://www.agencymeddirectors.wa.gov/files/2015amdgopioidguideline.pdf. Last Updated: June 2015. Accessed: September 24, 2020.

Naloxone for Harm Reduction

Naloxone for Harm Reduction

- Tolerance to opioid therapy can be lost very rapidly during an opioid taper
  - **As little as seven days**
- Increased risk of overdose if the patient returns to their previously prescribed dose of opioid therapy or takes illicit opioids during a taper
- Naloxone and relevant education should be prescribed for **all patients** undergoing an opioid taper

Pisansky AJB, et al. Opioid tapering for patients with chronic pain. In: UpToDate, Crowley M (Ed), UpToDate, Waltham, MA, 2020.

Naloxone Pharmacology

- Pure opioid antagonist – competes and displaces opioids at opioid receptor sites
- Onset of action depends on route of administration
- Repeat doses are usually necessary
  - Due to short half-life of naloxone

Naloxone. In: Lexicomp Online Database. Hudson (OH): Lexicomp Inc.: 2020.

Naloxone Side Effects

- Abrupt reversal of opioid effects
  - Nausea and vomiting
  - Tachycardia
  - Elevated BP
  - Tremulousness

Typically, transient in patients without underlying cardiovascular or pulmonary disease

- Rare serious side effects

Coffin P. Prevention of lethal opioid overdose in the community. In: UpToDate, Friedman M (Ed), UpToDate, Waltham, MA, 2020.

Product Availability

Dosage Form	Strength	How Supplied	Instructions for Use	Relative Cost
Injectable (and intranasal) prefilled syringes	2 mg/ 2mL	2 mucosal atomizer devices and necessary syringes	• Spray 1 ml (1/2 of syringe) into each nostril. • Repeat after 2-3 minutes if no or minimal response.	$
Nasal Spray	4 mg/0.1 mL	2-pack of 4 mg/0.1 mL intranasal devices	• Spray 0.1 mL into one nostril. • Repeat with second device into other nostril after 2-3 minutes if no or minimal response.	$$
Injectable vials	0.4 mg/mL 4 mg/10 mL	0.4 mg/mL or 4 mg/10 mL vial with necessary syringes and needles	• Inject 1 mL in shoulder or thigh. • Repeat after 2-3 minutes if no or minimal response.	$
Auto-Injector	2 mg/0.4 mL	2-pack of 2 mg/0.4 mL prefilled auto-injector devices	• Inject into outer thigh as directed by voice-prompt system. • Place black side firmly on outer thigh and depress and hold for 5 seconds. • Repeat with second device in 2-3 minutes if no or minimal response.	$$$

Naloxone. In: Lexicomp Online Database. Hudson (OH): Lexicomp Inc.: 2020.
Naloxone Product Comparison. Prescribe to Prevent. Available from: https://prescribetoprevent.org/wp2015/wp-content/uploads/Naloxone-product-chart.17_04_14.pdf. Last Updated: April 2017. Accessed: September 2020.

Naloxone Access

1. Prescribed naloxone
2. Community pharmacy, via Michigan's naloxone standing order
3. Community organizations

Opioid Resources: Naloxone. State of Michigan. Available from: https://www.michigan.gov/opioids/0,9238,7-377--480835--,00.html. Last Updated: 2020. Accessed September 23, 2020.

Pharmacists as Members of the Care Team

Role of the Pharmacist

- Identify and resolve drug-related problems
- Increase patient satisfaction and reduce cost to the healthcare system
- Improve patient adherence rates for medication prescribed for chronic conditions.
- Significantly improve disease state markers (e.g., HgbA1C, BP, PHQ-9) and increase the percentage of patients meeting therapy goals.
- Manage uncomplicated chronic conditions typically managed by a physician (e.g., improve access)

De Oliveira DR, et al. Medication Therapy Management: 10 Years of Experience in a Large Integrated Health Care System. J Manag Care Pharm. 2010;16(3):185-95.
Brummel A and Carlson AM. Comprehensive Medication Management and Medication Adherence for Chronic Conditions. JMCP. 2016;22(1)56-62.
Benedict AW. Evaluation of a Pharmacist-Managed Diabetes Program in a Primary Care Setting Within an Integrated Health Care System. J Manag Care Spec Pharm. 2018;24(2):114-122.
Herbert C and Winkler H. Impact of a clinical pharmacist-managed clinic in primary care mental health integration at a Veterans Affairs health system. Mental Health Clin. 20018;8(3):105-109.

Role of the Pharmacist – Chronic Pain and Opioid Management

- Review of the state prescription drug monitoring program
- Management of laboratory screening
- Provide medication education, including that related to storage and disposal
- Distribution of naloxone and promotion/education related to use
- Opioid tapering guidance
- Patient screening and risk stratification
- Referral to treatment resources

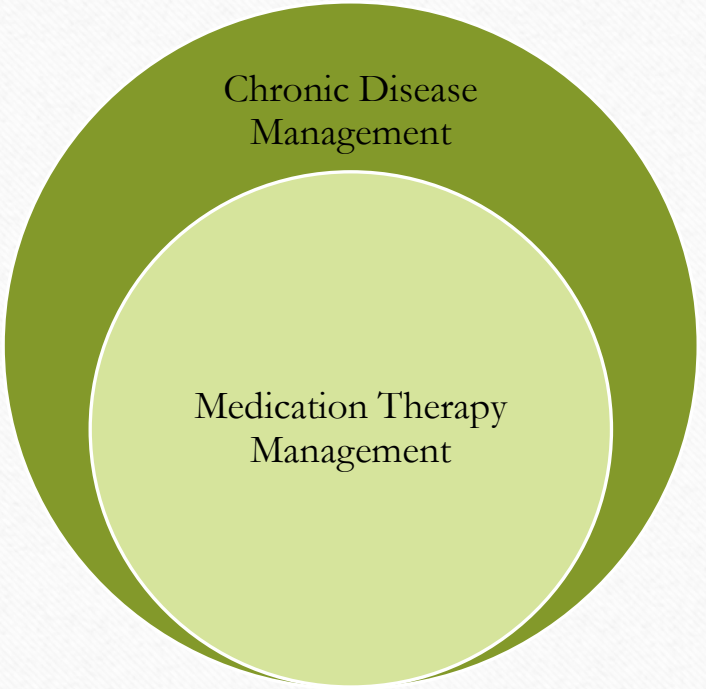
Giannitrapani KF, et al. Expanding the role of clinical pharmacists on interdisciplinary primary care teams for chronic pain and opioid management. BMC Fam Pract. 2018;19(1):107.
Chisholm-Burns, et al. The opioid crisis: Origins, trends, policies, and the roles of pharmacists. Am J Health Syst Pharm. 2019;76(7):424-435.

Models to Explore

- Centralized pharmacy team conducting medication therapy management (MTM) and/or disease state management (DSM)
- Remote pharmacist acting as a consultant
- Referral to a pharmacist operating under a collaborative practice agreement (CPA)

Centralized Pharmacy Team Conducting MTM and/or DSM

- Patients identified according to predetermined criteria
- Pharmacist activities
  - Comprehensive medication review (CMR)
  - Identification and recommendations for resolution of drug-related problems (e.g., deprescribing)
  - Patient education
  - Continuous follow up
  - Communication with care team



Norris SL, et al. Chronic Disease Management. A Definition And Systematic Approach To Component Interventions. Disease Management & Health Outcomes. 2003;11(8):477–488.

Remote Pharmacist Acting as a Consultant

- Care team reaches out to pharmacist with specific questions regarding specific patients
- Pharmacist activities
  - Provide taper schedule
  - Communication with patient, pharmacies, other prescribers, etc.
  - Patient education

Referral to a Pharmacist with a CPA

- A CPA is a legal document that creates a formal relationship between a pharmacist and a physician
  - Defines patient care functions that a pharmacist can provide
- Care team members refer individual patients to the pharmacist
- Pharmacist activities
  - Conducts follow-up calls or visits between provider visits
  - Prescribes medications (under delegated authority) to mitigate withdrawal symptoms
  - Other activities described within other previously discussed models

Collaborative Practice Agreements (CPA) and Pharmacists' Patient Care Services. APhA Foundations. Available from: https://www.aphafoundation.org/collaborative-practice-agreements. Accessed August 16, 2018.

Questions?

Claire.Nolan@miccsi.org