OPIOID PRESCRIBING: Safe Practice, Changing Lives

CHAPTER 1

WELCOME

FACULTY INFORMATION

BIO: Shorin Nemeth, DO, FACP

Dr. Nemeth is Board Certified in Internal Medicine, Hospice and Palliative Medicine, and Pain Medicine. His particular field of interest is cancer pain, but he treats all types of painful conditions. He has a holistic approach toward Pain Medicine which focuses on the biopsychosocial model. He has lectured throughout the country, been extensively involved in Resident and Fellow education, and served as a Subject Matter Expert on Pain Medicine for the American Osteopathic Association.

DISCLOSURE:

Dr. Nemeth has nothing to disclose.

NO CO*RE PARTNER HAS ANY CONFLICTS OF INTEREST TO REPORT (APPENDIX 2)
Presented by American Osteopathic Association, a member of the Collaborative for Risk Evaluation and Mitigation Strategy (REMS) Education (CO*RE), eleven interdisciplinary organizations working together to improve pain management and prevent adverse outcomes.

This educational activity is supported by an independent educational grant from the Extended-Release/Long-Acting (ER/LA) Opioid Analgesics REMS Program Companies. Please see this document for a listing of the member companies. This activity is intended to be fully compliant with the ER/LA Opioid Analgesics REMS education requirements issued by the US Food and Drug Administration.

PRODUCTS COVERED BY THIS REMS

**BRAND NAME PRODUCTS**
- Arymo ER morphine sulfate ER tablets
- Avincil morphine sulfate ER capsules
- Beprunox® transdermal patch
- Buprenex® transdermal system
- Dilaudid® extended-release tablets
- Duragesic® transdermal system
- Embeda® morphine/naltrexone ER capsules
- Exalgo® hydromorphone ER tablets
- Hysingla® ER hydrocodone ER tablets
- Kadian® morphine ER capsules
- MorphaBond® morphine ER tablets
- MS Contin® morphine ER tablets
- Nucynta® ER tapentadol ER tablets
- Opana ER oxymorphone ER tablets
- Ots-ConTril® oxycodone/naloxone ER tablets
- Targiniq ER oxycodone/naloxone ER tablets
- Troxyca ER oxycodone/naltrexone capsules
- Vansic® ER hydromorphone ER tablets
- Zohydro® ER hydrocodone ER capsules

**GENERIC PRODUCTS**
- Fentanyl ER transdermal systems
- Methadone hydrochloride tablets
- Methadone hydrochloride oral solution
- Methadone hydrochloride oral capsules
- Morphine sulfate ER tablets
- OxyContin® oxycodone ER tablets
- Oxycodone hydrochloride ER tablets

**WHY ARE WE HERE?**

CHAPTER 2
OPIOID DEATHS, TREATMENT ADMISSIONS AND PRESCRIBING

[Graph showing trends in opioid deaths, treatment admissions, and prescribing rates from 1999 to 2009.]


[Graph showing the increase in opioid deaths from 2000 to 2015.]
SOURCE: https://www.cdc.gov/drugoverdose/data/prescribing.html

PRESCRIBING PATTERNS – WE PLAY A ROLE

SOURCE: https://www.cdc.gov/drugoverdose/data/prescribing.html

OPIOID PRESCRIBING - THE PENDULUM SWINGS

PRESCRIBING BEHAVIORS

RESULTING OUTCOMES

Under-Prescribing

Unresolved Pain

Over-Prescribing

Adverse Outcomes

Appropriate Prescribing

Adequate Analgesia

BENEFITS VS. RISKS

BENEFITS

- Analgesia
  - Adequate pain control
  - Continuous, predictable (with ER/LAs)
  - Improved function
  - Quality of life

RISKS

- Overdose, especially as ER/LA formulations contain more opioids than Immediate Release
- Life-threatening respiratory depression
- Abuse by patient or household contacts
- Misuse, diversion, and addiction
- Physical dependence and tolerance
- Interactions with other meds and substances
- Risk of neonatal opioid withdrawal syndrome
- Inadvertent exposure/injection by household contacts especially children


SOURCE OF MOST RECENT RX OPIOIDS AMONG PAST-YEAR MISUSERS 2015

Source where pain relievers were obtained for most recent misuse among 12.5 million people aged 12 or older who misused prescription pain relievers in the past year: percentages, 2015

- 54% - Given by, bought from, or taken from a friend or relative
- 36% - Through a prescription or stolen from healthcare provider
- 5% - Bought from a dealer or stranger
- 5% - Some other way

FIRST SPECIFIC DRUG ASSOCIATED WITH INITIATION OF ILLICIT DRUG USE 2013

2.8 million initiates of illicit drugs
- 79.3% - Marijuana
- 12.5% - Pain Relievers
- 6.3% - Inhalants
- 5.2% - Tranquilizers
- 3.7% - Sedatives
- 2.8% - Hallucinogens
- 0.3% - Sedatives and Cocaine

SOURCE: SAMHSA Annual National Survey on Drug Use and Health, June 2015
https://www.drugabuse.gov/publications/drugfacts/nationwide-trends

THE FEDERAL PLAYERS
Many agencies involved

REMS: RISK EVALUATION AND MITIGATION STRATEGY

- On July 9, 2012, the Food and Drug Administration (FDA) approved a Risk Evaluation and Mitigation Strategy (REMS) for extended-release (ER) and long-acting (LA) opioid medications
- First time FDA has ever used accredited CE/CME as part of a REMS

CO*RE STATEMENT
Misuse, abuse, diversion, addiction, and overdose of opioids has created a serious public health epidemic in the U.S.

When prescribed well and used as prescribed, opioids can be valuable tools to effectively treat pain.

This course does not advocate for or against the use of Immediate Release (IR) or Extended-Release/Long-Acting (ER/LA) opioids. Our purpose is to provide proper education about safe prescribing practices along with effective patient education.
LEARNING OBJECTIVES

- Accurately assess patients with pain for consideration of an opioid trial
- Establish realistic goals for pain management and restoration of function
- Initiate opioid treatment (IR and ER/LA) safely and judiciously, maximizing efficacy while minimizing risks
- Monitor and re-evaluate treatment continuously; discontinue safely when appropriate
- Counsel patients and caregivers about use, misuse, abuse, diversion, and overdose
- Educate patients about safe storage and disposal of opioids
- Demonstrate working knowledge and ability to access general and specific information about opioids, especially those used in your practice

You and Your Team can have an immediate and positive impact on this crisis while also caring for your patients appropriately.

CHAPTER 3

PAIN

THE NEUROPSYCHOBIOLOGY OF PAIN
**OPIOID SITES OF ACTION IN THE BRAIN**

- Prefrontal cortex
- Nucleus accumbens
- Amygdala

**UNDERSTANDING PAIN**

- Physiologic Stimulus
  - Nociceptive
  - Neuropathic
- Biopsychosocial
- Spiritual
- Context

- Experience of Pain
  - Biopsychosocial

**THE IMPACT OF PAIN**

- Sleep disturbance
- Secondary physical problems
- Anxiety depression

**PAIN MANAGEMENT GOALS AND TREATMENT OPTIONS: A MULTI-MODAL APPROACH**

- Cognitive behavioral therapy
- Physical
- Interventional treatments
- Pharmacotherapy

- Reduce pain
- Restore function
- Self care
- Provider care

**Experience of Pain**

- Reduction
- Cultivate well being
- Pain free
- Daily activities
- Pain free
- Quality of life
CHAPTER 3 - PEARLS FOR PRACTICE

- Explain neurophysiology of pain processing to patients
- When patients understand, their concerns are validated
- Pain has biological, psychological, social, and spiritual components

CHAPTER 4 - ASSESSMENT

CHALLENGE: THE EARLY REFILL

RED FLAG: Is this misuse? Abuse?

Your patient requests an early refill for the second time in six months. Taken extra medications for headache and again for toothache. Prescription is for lower back pain.

Action:
Evaluate potential misuse. Confirm patient’s understanding of each medication’s dosage, time of day, and maximum daily dose. Ask him/her to repeat these instructions back to you. Avoid clinical terms such as “prn”. Review treatment goals and expectations. Select and document a therapy plan that is compatible with patient’s individual needs, is safe, effective and balanced. Screen for risk with Current Opioid Misuse Measure (COMM) and, if indicated, refer to addiction specialist for treatment.

PAIN ASSESSMENT

DESCRIPTION OF PAIN
Location Intensity Quality Onset/Duration Variations/Patterns/Rhythms

WHAT RELIEVES THE PAIN?

WHAT CAUSES OR INCREASES PAIN?

EFFECTS OF PAIN ON PHYSICAL, EMOTIONAL, AND PSYCHOSOCIAL FUNCTION

PATIENT’S CURRENT PAIN AND FUNCTION

**TREATMENT HISTORY**

**NON-PHARMACOLOGIC STRATEGIES AND EFFECTIVENESS**

**PHARMACOLOGIC STRATEGIES AND EFFECTIVENESS**

**PAST USE**

**CURRENT USE**

- Query state Prescription Drug Monitoring Program (PDMP) to confirm patient report

**DOSSAGE**

- For opioids currently prescribed: opioid, dose, regimen, and duration
  - Important to determine if patient is opioid tolerant

**GENERAL EFFECTIVENESS**

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**PAST MEDICAL HISTORY**

**ILLNESS RELEVANT TO (1) EFFECTS OR (2) METABOLISM OF OPIOIDS**

1. Pulmonary disease, constipation, nausea, cognitive impairment
2. Hepatic, renal disease

**ILLNESS POSSIBLY LINKED TO SUBSTANCE USE DISORDER (SUD):**

- Hepatitis
- HIV
- Tuberculosis
- Cellulitis
- STIs
- Trauma/Burns
- Cardiac Disease
- Pulmonary Disease

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**OBTAIN A COMPLETE HISTORY OF CURRENT AND PAST SUBSTANCE USE**

**RISK FACTORS FOR OPIOID ABUSE**

- Controlled medications: prescribed or non-prescribed
- Alcohol and tobacco
- History of sexual abuse
- Family history of substance abuse and psychiatric disorders
- Age (16-45 YO)

Substance abuse history does not prohibit treatment with ER/LA opioids but may require additional monitoring and expert consultation/referral

**SOCIAL HISTORY**

Employment, cultural background, social network, marital history, legal history, and other behavioral patterns

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**PHYSICAL EXAM AND ASSESSMENT**

Seek objective confirmatory data Components of patient evaluation for pain Order diagnostic tests (appropriate to complaint)

- General, vital signs, appearance, and pain behaviors
- Musculoskeletal exam
  - Inspection
  - Gait and posture
- Range of motion
- Palpation
- Percussion
- Auscultation
- Provocative maneuvers

- Cutaneous or trophic findings

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**RISK ASSESSMENT TOOLS**

<table>
<thead>
<tr>
<th>TOOL</th>
<th># OF ITEMS</th>
<th>ADMINISTERED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORT Opioid Risk Tool</td>
<td>5</td>
<td>patient</td>
</tr>
<tr>
<td>SOAPP® Screener and Opioid Assessment for Patients with Pain</td>
<td>14, 14, &amp; 5</td>
<td>patient</td>
</tr>
<tr>
<td>DIRE Diagnosis, Intrusability, Risk, and Efficacy score</td>
<td>7</td>
<td>clinician</td>
</tr>
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</table>

**CHARACTERIZE MISUSE ONCE OPIOID TREATMENT BEGINS**

<table>
<thead>
<tr>
<th>SCREENING TOOL</th>
<th># OF ITEMS</th>
<th>ADMINISTERED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMG Pain Medication Questionnaire</td>
<td>26</td>
<td>patient</td>
</tr>
<tr>
<td>COWRE Current Opioid Misuse Measure</td>
<td>17</td>
<td>patient</td>
</tr>
<tr>
<td>PQUI Prescription Drug Use Questionnaire</td>
<td>40</td>
<td>clinician</td>
</tr>
</tbody>
</table>

**NOT SPECIFIC TO PAIN POPULATIONS**

<table>
<thead>
<tr>
<th>SCREENING TOOL</th>
<th># OF ITEMS</th>
<th>ADMINISTERED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAGE-AID Cut Down, Annoyed, Guilty, Eye-Opener tool, Adapted to Include Drugs</td>
<td>4</td>
<td>clinician</td>
</tr>
<tr>
<td>RAFFT Relax, Alone, Friends, Family, Trouble</td>
<td>5</td>
<td>patient</td>
</tr>
<tr>
<td>DAST Drug Abuse Screening Test</td>
<td>28</td>
<td>patient</td>
</tr>
<tr>
<td>SBIRT Screening, Brief Intervention, and Referral to Treatment</td>
<td>Various</td>
<td>clinician</td>
</tr>
</tbody>
</table>

**SCREENER AND OPIOID ASSESSMENT FOR PATIENTS WITH PAIN (SOAPP®)**

Identifies patients as high, moderate, or low risk for misuse of opioids prescribed for chronic pain

**HOW IS SOAPP® ADMINISTERED?**

- Usually self-administered in waiting room, exam room, or prior to an office visit
- May be completed as part of an interview with a nurse, physician, or psychologist
- Prescribers should have a completed and scored SOAPP® while making opioid treatment decisions

**OPIOID RISK TOOL (ORT)**

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>FEMALE</th>
<th>MALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Family history of substance abuse</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2. Personal Hx of substance abuse</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>3. Age between 16 and 45 yrs</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4. Hx of preadolescent sexual abuse</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>5. Psychologic disease</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

**SCORING (RISK)**

- Score ≥ 12: high risk
- Score 8-11: moderate risk
- Score <8: low risk

**SOAPP®: 4 FORMATS AVAILABLE TO ASSESS MISUSE RISK**

- **SOAPP® V.1.0 24Q VERSION (ORIGINAL)**
  - 24 questions (14 used to score tool)
  - Add ratings for 14 “screening” questions
  - Score ≥12: high risk
  - Score 8-11: moderate risk
  - Score <8: low risk
  - 10 min. to complete

- **SOAPP® V.1.0 14Q VERSION**
  - 14 questions*
  - Add ratings for each question
  - Score ≥12: high risk
  - Score 8-11: moderate risk
  - Score <8: low risk
  - <10 min. to complete

- **SOAPP® V.1.0 5Q (SHORT-FORM) VERSION**
  - 5 questions*
  - Add ratings for each question
  - Score ≥4: increased risk
  - Score 0-4: not increased
  - <5 min. to complete

- **SOAPP® R 24Q VERSION (REVISED)**
  - 24 questions
  - Add ratings for 14 “screening” questions
  - Score ≥12: high risk
  - Score 8-11: moderate risk
  - Score ≤7: low risk
  - 10 min. to complete

*Patients rate all questions on scale of 0-4

**SOURCE:** SOAPP® Monitoring Recommendations. [https://painedu.org/soapp/SOAPP_Monitoring_Recommendations.pdf](https://painedu.org/soapp/SOAPP_Monitoring_Recommendations.pdf)

**SOAPP® Version 1.0-SF** [https://painedu.org](https://painedu.org)

**SOAPP® Version 1.0-14Q** [https://painedu.org](https://painedu.org)

**SOAPP®-R** [https://painedu.org](https://painedu.org)
Risk of opioid use disorder in patients on chronic opioid therapy (COT) for chronic non-cancer pain (CNCP) is up to 30%.

- Always highest with past history of substance use disorder (SUD) or psychiatric comorbidity.
- Recognize that patient needs and patterns shift with age.

WHAT IS THE RISK FOR MY PATIENT?

RISK AND PAIN ASSESSMENT TOOL BOXES

- PDMP
- UDT
- Risk Assessment Tools (ORT or SGAPP®)

PAIN ASSESSMENT TOOL BOX
- Pain Assessment Tools (BPI, etc.)
- Functional Assessment (SF-36, PPS, geriatric assessment, etc.)
- Pain intensity, Enjoyment of life, General activity (PEG)

Mental Health Tools (PHQ9, GAD7, etc.)
CONSIDER A TRIAL OF AN OPIOID?

- POTENTIAL BENEFITS ARE LIKELY TO OUTWEIGH RISKS
- FAILED TO ADEQUATELY RESPOND TO NON-OPIOID & NONDRUG INTERVENTIONS
- PAIN IS MODERATE TO SEVERE
- INITIATE TRIAL OF IR OPIOIDS


WHEN TO CONSIDER A TRIAL OF AN OPIOID

60-YR-OLD WITH CHRONIC DISABLING OA PAIN
- Non-opioid therapies not effective
- No psychiatric/medical comorbidity or personal/family drug abuse history
- High potential benefits relative to potential risks
- Could prescribe opioids to this patient in most settings with routine monitoring

30-YR-OLD WITH FIBROMYALGIA AND RECENT ALCOHOL USE DISORDER
- High potential risks relative to benefits (opioid therapy not first line for fibromyalgia)
- Requires intensive structure, monitoring, and management by clinician with expertise in both addiction & pain
- Not a good candidate for opioid therapy


INITIATING OPIOIDS: CDC GUIDELINE (2016)

- Begin with IR
- Prescribe the lowest effective dosage
- Use caution at any dosage, but particularly when
  - Increasing dosage to ≥50 morphine milligram equivalents (MME)/day and carefully justify a decision to titrate dosage to ≥90 MME/day
  - For acute pain, prescribe lowest effective dose of IRs, no more than needed
  - Re-evaluate risks/benefits within 1 - 4 weeks of initiation or dose escalation
  - Re-evaluate risks/benefits every 3 months; if benefits do not outweigh harms, optimize other therapies, work to taper and discontinue
- Link to the Guideline: https://www.cdc.gov/drugoverdose/prescribing/providers.html

Cancer pain, hospice, and palliative care patients are not covered by CDC Guideline

INFORMED CONSENT

When initiating a trial of opioid analgesic therapy, confirm patient understanding of informed consent to establish:

- ANALGESIC AND FUNCTIONAL GOALS OF TREATMENT
- EXPECTATIONS
- POTENTIAL RISKS
- ALTERNATIVES TO OPIOIDS

HOW TO MANAGE

- Common Adverse Effects (AEs) (e.g., constipation, nausea, sedation)
- Risks (e.g., abuse, addiction, respiratory depression, overdose)
- AEs with long-term therapy (e.g., hyperalgesia, low testosterone, irregular menses or sexual dysfunction)
**PATIENT-PRESCRIBER AGREEMENT (PPA)**

Document signed by both patient and prescriber at time an opioid is prescribed

- Clarify treatment plan and goals of treatment with patient, patient’s family, and other clinicians involved in patient’s care
- Assist in patient education
- Discuss medication safe handling, storage, and disposal
- Document patient and prescriber responsibilities

**PATIENT PROVIDER AGREEMENT (PPA)**

Reinforce expectations for appropriate and safe opioid use

- One prescriber
- Consider one pharmacy
- Safeguard
  - Do not store in medicine cabinet
  - Keep locked (medication safe)
- Do not share or sell
- Instructions for disposal when no longer needed
- Prescriber notification for any event resulting in a pain medication prescription

**MONITOR ADHERENCE AND ABERRANT BEHAVIOR**

 Routinely monitor patient adherence to treatment plan

- Recognize and document aberrant drug-related behavior
  - In addition to patient self-report also use:
    - State PDMPs
    - UDT
    - Positive for non-prescribed drugs
    - Positive for illicit substance
    - Negative for prescribed opioid
  - Family member or caregiver interviews
  - Monitoring tools such as the COMM, PADT, FMQ, or PDUQ
  - Medication reconciliation (e.g., pill counts)

**ADDRESS ABERRANT DRUG-RELATED BEHAVIOR**

Behavior outside the boundaries of agreed-on treatment plan:

- Unsanctioned dose escalations or other noncompliance with therapy on 1 or 2 occasions
- Unapproved use of the drug to treat another symptom
- Openly acquiring similar drugs from other medical sources
- Prescription forgery
- Obtaining prescription drugs from nonmedical sources

Any of these behaviors merit investigation. Proceed with caution
Adequately DOCUMENT all patient interactions, assessments, test results, and treatment plans.

**CHAPTER 4 – PEARLS FOR PRACTICE**

- Conduct a comprehensive and pain-focused history and physical
- Assess for risk of abuse and for mental health issues
- Determine if a therapeutic trial is appropriate
- Establish realistic goals for pain management and function
- Document EVERYTHING

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**CHALLENGE: THE DELAYED SURGERY**

**RED FLAG:** Patient may be stalling to continue an opioid regimen

Ms. Jones says she needs opioids to manage her pain until she can have surgery. She reports continued delays in getting to surgery. You phone the surgeon and discover that no date has been set and that she has cancelled several appointments.

**Action:**
Set a time limit and expectation. Offer non-pharmacologic methods and non-opioid interventions for pain management. Communicate with the surgeon and advise patient to make appointment with surgeon for discussion of treatment plan.

**CHAPTER 5**

**MANAGEMENT MONITORING AND DISCONTINUING**
PART 1
MONITORING

OPIOID SIDE EFFECTS

- Respiratory depression – most serious
- Opioid-Induced Constipation (OIC) – most common
- Sedation, cognitive impairment
- Falls and fractures
- Sweating, miosis, urinary retention
- Hypogonadism
- Tolerance, physical dependence, hyperalgesia
- Addiction in vulnerable patients

Prescribers should report serious AEs to the FDA:
www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf
or 1-800-FDA-1088

OPIOID-INDUCED RESPIRATORY DEPRESSION

MORE LIKELY TO OCCUR
- In elderly, cachectic, or debilitated patients
- Contraindicated in patients with respiratory depression or conditions that increase risk
- If given concomitantly with other drugs that depress respiration
- Patients who are opioid-naive or have just had a dose increase

REDUCE RISK
- Proper dosing and titration are essential
- Do not overestimate dose when converting dosage from another opioid product
- Can result in fatal overdose with first dose
- Instruct patients to swallow tablets/capsules whole
- Dose from cut, crushed, dissolved, or chewed tablets/capsules may be fatal, particularly in opioid-naive individuals

Chief hazard of opioid agonists, including ER/LA opioids
- If not immediately recognized and treated, may lead to respiratory arrest and death
- Greatest risk: initiation of therapy or after dose increase
- Manifested by reduced urge to breathe and decreased respiration rate
- Shallow breathing
- CO₂ retention can exacerbate opioid sedating effects

Instruct patients/family members to call 911
- Managed with
- Close observation
- Supportive measures
- Opioid antagonists
- Depending on patient's clinical status

WHEN TO MOVE FROM IR TO ER/LA OPIOIDS

**PRIMARY REASONS**
- Maintain stable blood levels (steady state plasma)
- Longer duration of action
- Multiple IR doses needed to achieve effective analgesia
- Poor analgesic efficacy despite dose titration
- Less sleep disruption

**OTHER POTENTIAL REASONS**
- Patient desire or need to try a new formulation
- Cost or insurance issues
- Adherence issues
- Change in clinical status requires an opioid with different pharmacokinetics
- Problematic drug-drug interactions

CONSIDERATIONS FOR CHANGE FROM IR TO ER/LA OPIOIDS

**DRUG AND DOSE SELECTION IS CRITICAL**
Some ER/LA opioids or dosage forms are only recommended for opioid-tolerant patients
- ANY strength of transdermal fentanyl or hydromorphone ER
- Certain strengths/doses of other ER/LA products (check drug prescribing information)

**DRUG AND DOSE SELECTION IS CRITICAL**
- Monitor patients closely for respiratory depression especially within 24-72 hours of initiating therapy and increasing dosage

**MONITOR PATIENTS CLOSELY FOR RESPIRATORY DEPRESSION**
- Check ER/LA opioid product PI for minimum titration intervals
- Supplement with IR analgesics (opioids and non-opioid) if pain is not controlled during titration

**INDIVIDUALIZE DOSAGE BY TITRATION BASED ON EFFICACY, TOLERABILITY, AND PRESENCE OF AEs**
- Check ER/LA opioid product PI for minimum titration intervals
- Supplement with IR analgesics (opioids and non-opioid) if pain is not controlled during titration

**DEFINITION**
Change from an existing opioid regimen to another opioid with the goal of improving therapeutic outcomes or to avoid AEs attributed to the existing drug (e.g., myoclonus)

**RATIONALE**
Differences in pharmacologic or other effects make it likely that a switch will improve outcomes
- Effectiveness and AEs of different mu opioids vary among patients
- Patients show incomplete cross-tolerance to new opioid

- Patient tolerant to first opioid can have improved analgesia from second opioid at a dose lower than calculated from an Equianalgesic Dosing Table (EDT)

**OPIOID TOLERANCE**
If opioid tolerant caution should still be used at higher doses
- Patients considered opioid tolerant are taking at least
  - 60 mg oral morphine/day
  - 25 mcg transdermal fentanyl/hour
  - 30 mg oral oxycodone/day
  - 8 mg oral hydromorphone/day
  - 25 mg oral oxymorphone/day
- An equianalgesic dose of another opioid
Still requires caution when rotating a patient on an IR opioid to a different ER/LA opioid

**OPIOID ROTATION**

**RATIONALIZE**
- Effectiveness and AEs of different mu opioids vary among patients
- Patients show incomplete cross-tolerance to new opioid
  - Patient tolerant to first opioid can have improved analgesia from second opioid at a dose lower than calculated from an Equianalgesic Dosing Table (EDT)
EQUIANALGESIC DOSE TABLES (EDT)

Many different versions:
- Published
- Online
- Online interactive
- Smart-phone apps

Vary in terms of:
- Equianalgesic values
- Whether ranges are used

Which opioids are included: May or may not include transdermal opioids, rapid-onset fentanyl, ER/LA opioids, or opioid agonist-antagonists

EXAMPLE OF AN EDT FOR ADULTS

<table>
<thead>
<tr>
<th>DRUG</th>
<th>SC/IV Dose</th>
<th>PO Dose</th>
<th>PARENTERAL Dose</th>
<th>PO Dose</th>
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<tbody>
<tr>
<td>Morphine</td>
<td>10 mg</td>
<td>30 mg</td>
<td>2.5-5 mg SC/IV</td>
<td>5-15 mg q3-4h (IR or oral solution)</td>
</tr>
<tr>
<td></td>
<td>(3-4h)</td>
<td></td>
<td>(1-2.5-2.5 mg)</td>
<td>(2.5-7.5 mg)</td>
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<tr>
<td>Oxycodone</td>
<td>NA</td>
<td>20 mg</td>
<td>NA</td>
<td>5-10 mg q3-4</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(2.5 mg)</td>
<td>(2.5 mg)</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>NA</td>
<td>30 mg</td>
<td>NA</td>
<td>5 mg q3-4h</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(2.5 mg)</td>
<td>(2.5 mg)</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5 mg</td>
<td>7.5 mg</td>
<td>0.2-0.6 mg SC/IV</td>
<td>1.2 mg q3-4h</td>
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<td></td>
<td></td>
<td></td>
<td>(0.2 mg)</td>
<td>(0.5-1 mg)</td>
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MU OPIOIDS BIND TO MU RECEPTORS

MANY MU RECEPTOR SUBTYPES:
- Mu opioids produce subtly different pharmacologic response based on distinct activation profiles of mu receptor subtypes

MAY HELP EXPLAIN:
- Inter-patient variability in response to mu opioids
- Incomplete cross-tolerance among mu opioids

MU OPIOIDS AND INCOMPLETE CROSS-TOLERANCE

CHALLENGE DRUG:
- Cross-tolerance if tolerant to drug:
  - A
  - B
  - C
  - D

CROSS-TOLERANCE IF TOLERANT TO DRUG:
- Yes
- No
- Partial
- -
GUIDELINES FOR OPIOID ROTATION

Calculate equianalgesic dose of new opioid from EDT

<table>
<thead>
<tr>
<th>REDUCE CALCULATED EQUIANALGESIC DOSE BY 25%-50%*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SELECT % REDUCTION BASED ON CLINICAL JUDGMENT</td>
</tr>
</tbody>
</table>

CLOSER TO 50% REDUCTION
- Receiving a relatively high dose of current opioid regimen
- Elderly or medically frail

CLOSER TO 25% REDUCTION
- Does not have these characteristics
- Is changing route of administration

*75%-80% reduction for methadone

GUIDELINES FOR OPIOID ROTATION (continued)

IF SWITCHING TO METHADONE:
- Standard EDTs are less helpful in opioid rotation to methadone
- In opioid tolerant patients, methadone doses should not exceed 30-40 mg/day upon rotation
  - Consider inpatient monitoring, including serial EKG monitoring
- In opioid-naive patients, methadone should not be given as an initial drug

IF SWITCHING TO TRANSDERMAL:
- Fentanyl, calculate dose conversion based on equianalgesic dose ratios included in the PI
- Buprenorphine, follow instructions in the PI

GUIDELINE FOR OPIOID ROTATION: SUMMARY

VALUES FROM EDT

PATIENT OPIOID VALUES

SOLVE FOR X

AUTOMATICALLY REDUCE DOSE

Value of Current Opioid
Value of New Opioid

24 Hr Dose of Current Opioid
X Amount of New Opioid

Equianalgesic 24 Hr Dose of New Opioid

By 25%-50%*

Frequently assess initial response
Titrating dose of new opioid to optimize outcomes
Calculate supplemental rescue dose used for titration at 5%-15% of total daily dose

BREAKTHROUGH PAIN (BTP)

PATIENTS ON STABLE ATC OPIOIDS MAY EXPERIENCE BTP
- Disease progression or a new or unrelated pain
- Target cause or precipitating factors
- Dose for BTP: using an IR is 5%-15% of total daily opioid dose, administered at an appropriate interval
- Never use ER/LA for BTP

CONSIDER ADDING
- PRN IR opioid trial based on analysis of benefit versus risk
  - Risk for aberrant drug-related behaviors
  - High-risk: only in conjunction w/ frequent monitoring & follow-up
  - Low-risk: w/ routines follow-up & monitoring
- Non-opioid drug therapies
- Non-pharmacologic treatments

ATC = Around the Clock
BE READY TO REFER

SUBSTANCE USE DISORDER

SAMHSA substance abuse treatment facility locator
https://findtreatment.samhsa.gov/locator/

SAMHSA mental health treatment facility locator
https://findtreatment.samhsa.gov/locator/

HIGH-RISK/COMPLEX PATIENTS

Refer to pain management, check state regulations for requirements

SAMHSA = Substance Abuse and Mental Health Service Administration

RATIONALE FOR URINE DRUG TESTING (UDT)

- Urine testing is done FOR the patient not TO the patient
- Help to identify drug misuse/addiction
- Assist in assessing and documenting adherence

UDT FREQUENCY IS BASED ON CLINICAL JUDGMENT AND STATE REGULATIONS

TYPES OF UDT METHODS

Be aware of what you are testing and not testing

IMMUNOASSAY (IA) DRUG PANELS
- Either lab-based or point of care
- Identify substance as present or absent according to cutoff
- Many do not identify individual drugs within a class
- Subject to cross-reactivity and variability

GC/MS OR LC/MS
- Identify the presence and quantity of substance(s)
- Identify drugs not included in IA tests
- When results are contested

SPECIFIC WINDOWS OF DRUG DETECTION

How long a person excretes drug and/or metabolite(s) at a concentration above a cutoff

DETECTION TIME OF DRUGS IN URINE

Governed by various factors: e.g., dose, route of administration, metabolism, fat solubility, urine volume and pH

For most drugs it is 1-3 days

Chronic use of lipid-soluble drugs increases detection time: e.g., marijuana, diazepam, ketamine
SPECIFIC WINDOWS OF DRUG DETECTION (continued)

<table>
<thead>
<tr>
<th>Drug</th>
<th>How soon after taking drug will there be a positive drug test?</th>
<th>How long after taking drug will there continue to be a positive drug test?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana/Pot</td>
<td>1-3 hours</td>
<td>1-7 days</td>
</tr>
<tr>
<td>Crack (Cocaine)</td>
<td>2-6 hours</td>
<td>2-3 days</td>
</tr>
<tr>
<td>Heroin (Opiates)</td>
<td>2-6 hours</td>
<td>1-3 days</td>
</tr>
<tr>
<td>Speed/Uppers/</td>
<td>4-6 hours</td>
<td>2-3 days</td>
</tr>
<tr>
<td>(Amphetamine, methamphetamine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angel Dust/PCP</td>
<td>4-6 hours</td>
<td>7-14 days</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>2-7 hours</td>
<td>2-4 days</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>2-7 hours</td>
<td>1-4 days</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>2-4 hours</td>
<td>1-3 weeks</td>
</tr>
<tr>
<td>Methadone</td>
<td>8-8 hours</td>
<td>1-3 days</td>
</tr>
<tr>
<td>Tricyclic Antidepressants</td>
<td>8-12 hours</td>
<td>2-7 days</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1-3 hours</td>
<td>1-2 days</td>
</tr>
</tbody>
</table>

Source: [http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/DrugsofAbuseTests/ucm125722.htm](http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/DrugsofAbuseTests/ucm125722.htm)

URINE SPECIMEN INTEGRITY

SPECIMEN COLOR RELATED TO CONCENTRATION

Concentrated samples more reliable than dilute samples

TEMP WITHIN 4 MINUTES OF VOIDING IS 90-100ºF

PH FLUCTUATES WITHIN RANGE OF 4.5-8.0

CREATININE VARIES WITH HYDRATION

- Normal urine: >20 mg/dL
- Dilute: creatinine <20 mg/dL and specific gravity <1.003
- Creatinine <2 mg/dL not consistent with human urine

INTERPRETATION OF UDT RESULTS

POSITIVE RESULT

- Demonstrates recent use
  - Most drugs in urine have detection times of 1-3 days
  - Chronic use of lipid-soluble drugs: test positive for ≥1 week
- Does not diagnose
  - Drug addiction, physical dependence, or impairment
  - Does not provide enough information to determine
    - Exposure time, dose, or frequency of use
- Does not diagnose diversion
  - More complex than presence or absence of a drug in urine
    - May be due to maladaptive drug-taking behavior
    - Other factors: e.g., cessation of insurance, financial difficulties

NEGATIVE RESULT

- Does not diagnose recent use
- Does not provide information about drug use
- Does not provide information about drug-taking behavior
- Does not provide information about diversion

EXAMPLES OF METABOLISM OF OPIOIDS

- CODEINE ➔ MORPHINE ➔ S-MAM ➔ HEROIN
  - T½ = 25-30 MIN
- HYDROCODONE ➔ HYDROMORPHONE
- OXICODONE ➔ OXYMORPHONE
CHALLENGE: THE OFFENDED PATIENT

RED FLAG:
You decide not to request routine risk assessment for fear of creating conflict

Mrs. Lane and her family have been your patients for years. She has chronic headache and back pain treatment. When you ask her to take a UDT, she becomes upset and accuses you of not trusting her. You decide against further risk assessments because you are concerned about damaging the relationship.

Action:
Require all patients receiving opioids to follow a treatment plan and adhere to defined expectations. Create office policy for performing UDT for patients receiving opioids beyond two weeks. Practice universal precautions. Explain to patient that you must meet the standards of care that include evaluation of risk in all patients, use of PPA's, and other tools.

REASONS FOR DISCONTINUING OPIOIDS

- **PAIN LEVEL DECREASES IN STABLE PATIENTS**
- **INTOLERABLE AND UNMANAGEABLE AEs**
- **NO PROGRESS TOWARD THERAPEUTIC GOALS**
- **ABERRANT BEHAVIORS**
  - 1 or 2 episodes of increasing dose without prescriber knowledge
  - Sharing medications
  - Unapproved opioid use to treat another symptom (e.g., insomnia)
  - Use of illicit drugs or unprescribed opioids
  - Repeatedly obtaining opioids from multiple outside sources
  - Prescription forgery
  - Multiple episodes of prescription loss
  - Diversion

TAPER DOSE WHEN DISCONTINUING

- Minimize withdrawal symptoms in opioid-dependent patient, consider medications to assist with withdrawal
- May use a range of approaches from slow 10% dose reduction per week to more rapid 25%-50% reduction every few days
- If opioid use disorder or a failed taper, refer to addiction specialist or consider opioid agonist therapy
- Counseling and relaxation strategies needed
CHAPTER 5 – PEARLS FOR PRACTICE

- Establish informed consent and PPA at the beginning
- Educate the whole team: patients, families, caregivers
- Refer if necessary
- Anticipate opioid-induced respiratory depression and constipation
- Follow patients closely during times of dose adjustments
- Periodically evaluate functional outcomes
- Discontinue opioids slowly and safely

CHALLENGE: IS THIS A LAB ERROR?

RED FLAG:
The questionable Urine Drug Test
Donald has been prescribed oxycodone for six months to treat back pain. His UDT at six months comes back negative in all areas. He tells you that he is taking his meds.

Action:
Do not discharge the patient as the first action. Contact the lab and discuss the test and any metabolite or specimen integrity issues. Ask: Is this the right lab test? Repeat the UDT and document everything. Discuss with the patient.

CHALLENGE: PATIENTS WHO ARE NOT WHO THEY APPEAR

RED FLAG:
Patient wants to control their pill mg dose and taper plan
Donald has been prescribed oxycodone for six months to treat back pain. His UDT at six months comes back negative in all areas. He tells you that he is taking his meds.

Action:
Do not discharge the patient as the first action. Contact the lab and discuss the test and any metabolite or specimen integrity issues. Ask: Is this the right lab test? Repeat the UDT and document everything. Discuss with the patient.
OLDER ADULTS

RISK FOR RESPIRATORY DEPRESSION
- Age-related changes in distribution, metabolism, excretion; absorption less affected

MONITOR
- Initiation and titration
- Concomitant medications (polypharmacy)
- Falls risk, cognitive change, psychosocial status
- Reduce starting dose to 1/3 to 1/2 the usual dosage in debilitated, non-opioid-tolerant patients
- Start slow, go slow, but GO
- Patient and caregiver reliability/risk of diversion

ROUTINELY INITIATE A BOWEL REGIMEN

WOMEN WITH CHILDBEARING POTENTIAL

KNOW THE REPRODUCTIVE PLANS AND PREGNANCY STATUS OF YOUR PATIENTS
- 40% of women with childbearing potential are prescribed opioids
- Opioid exposure during pregnancy causes increased risk for fetus
- Most women do not know they are pregnant in first few weeks
- Therefore all women of childbearing age are at risk
- No adequate nor well-controlled studies of opioids for pain in pregnancy

THE PREGNANT PATIENT

Potential risk of opioid therapy to the newborn is neonatal opioid withdrawal syndrome

GIVEN THESE POTENTIAL RISKS, CLINICIANS SHOULD:
- Counsel women of childbearing potential about risks and benefits of opioid therapy during pregnancy and after delivery
- Encourage minimal/no opioid use during pregnancy, unless potential benefits outweigh risks to fetus
- Refer to a high risk OB/Gyn who will ensure appropriate treatment for the baby
- If chronic opioid therapy is used during pregnancy, anticipate and manage risks to the patient and newborn
- If using opioids on a daily basis, consider methadone or buprenorphine

CHILDREN AND ADOLESCENTS: HANDLE WITH CARE

JUDICIOUS USE OF IR FOR BRIEF THERAPY
- Pediatric analgesic trials pose challenges
- Transdermal fentanyl approved in children aged ≥12 yrs
- Oxycodeone ER dosing changes for children ≥11 yrs

ERLA OPIOID INDICATIONS ARE PRIMARILY LIFE-LIMITING CONDITIONS

WHEN PRESCRIBING ERLA OPIOIDS TO CHILDREN:
- Consult pediatric palliative care team or pediatric pain specialist or refer to a specialized multidisciplinary pain clinic
CHALLENGE: VULNERABILITY IN CO-DEPENDENT OLDER ADULTS

RED FLAG: Questionable family diversion

78-year-old Thelma comes into clinic, accompanied by grandson, who is in the exam room with you and Thelma. Thelma says her oxycodone 10 mg tablets q 4 hours is no longer working for her back pain. She asks for more medicine. You ask grandson to leave the exam room so you can examine her privately.

**Action:** Based on exam findings and her request for more medication:
- UDT and PDMP check
- Discuss whether or not it is possible her grandson, or another family member, might be using her medications.
- Patient education: Do not give opioids to another person. Store in secure place – locked. Let you know if medications are not secure or if she feels any pressure about sharing medications.

CHAPTER 7

KNOW YOUR FEDERAL AND STATE LAWS

FEDERAL AND STATE REGULATIONS

Comply with federal and state laws and regulations that govern the use of opioid therapy for pain

**FEDERAL**
- Code of Federal Regulations, Title 21 Section 1306: rules governing the issuance and filling of prescriptions pursuant to section 309 of the Act (21 USC 829)
- United States Code (USC) - Controlled Substances Act, Title 21, Section 829: prescriptions
  [www.deadiversion.usdoj.gov/21usc/829.htm](http://www.deadiversion.usdoj.gov/21usc/829.htm)

**STATE**
- Database of state statutes, regulations, and policies for pain management

PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

INDIVIDUAL STATE LAWS DETERMINE NOT ALL FEDERALLY LICENSED FACILITIES REPORT TO PDMPs

- Who has access to PDMP information
- Which drug schedules are monitored
- Which agency administers the PDMP
- Whether prescribers are required to register with the PDMP
- Whether prescribers are required to access PDMP information in certain circumstances
- Whether unsolicited PDMP reports are sent to prescribers
- Bordering states may be available
- Designated surrogates may have access

Link to state PDMP sites
PDMP BENEFITS

Provides full accounting of prescriptions filled by patient

- Some are available online 24/7
- Opportunity to discuss with patient
- Existing prescriptions not reported by patient
- Multiple prescribers/pharmacies
- Drugs that increase overdose risk when taken together
- Patient pays with cash (vs insurance) for controlled meds

CANNABIS

- DEA Schedule 1 ("high abuse potential"); yet state laws and regulations vary
- There is evidence that cannabis or selective cannabinoids (cannabidiol) are effective for chronic pain treatment in adults
- More research is needed
- Concern for high risk groups: children, adolescents, pregnant women

CONSIDERATIONS FOR CLINICIANS

- Use available scientific evidence, advise patients
  - Inform about potential effects; AEs mostly mild and well tolerated (cough, anxiety)
  - Screen for potential misuse/abuse, diversion
- Set treatment goals, use PPA
- Encourage patients to keep notes, discuss with them
- Document everything
- Regular re-evaluation
  - Consider periodic UDTs
  - Discontinue if not helpful moving toward goals
- Edibles are the fastest growing delivery system
- No well controlled studies on the combined use of opioids and cannabis

CHALLENGE: THE HIGH RISK PATIENT

RED FLAG:
Proceed with caution, but treat the high risk patient

18-year-old with a recurrent wound in the antecubital fossa secondary to intravenous injection. This is her third wound debridement and she is in more pain than before. She tells you if she cannot get relief from you, she will go to the street for meds.

Action:
With a drug abuse history, proceed with caution and use extra safety measures. Patient may require admission to either hospital or treatment facility while managing pain. This history does not mean you should discharge or avoid treating the patient’s pain.
CHAPTER 8
COUNSELING PATIENTS AND CAREGIVERS

USE PATIENT COUNSELING DOCUMENT

DOWNLOAD:

ORDER HARD COPIES:
www.minneapolis.cenveo.com/pcd/
SubmitOrders.aspx

SOURCE: FDA. Extended-release (Er) And Long-acting (La) Opioid Analgesics Risk Evaluation And Mitigation Strategy (Rems). Modified 06/2015

COUNSEL PATIENTS ABOUT PROPER USE

EXPLAIN
• Product-specific information about the IR or ER/LA opioid (especially when converting)
• Take opioid as prescribed
• Adhere to dose regimen
• How to handle missed doses
• Notify prescriber if pain not controlled

INSTRUCT PATIENTS/ CAREGIVERS TO
• Read the ER/LA opioid Medication Guide received from pharmacy every time an ER/LA opioid is dispensed

COUNSEL PATIENTS ABOUT PROPER USE (continued)

EXPLAIN
• Inform prescriber of ALL meds being taken
• Warn patients not to abruptly discontinue or reduce dose
• Risk of falls
• Caution with operating heavy machinery and when driving
• Sharing or selling opioids can lead to others’ deaths and is against the law

EXPLAIN
• Signs/symptoms are respiratory depression, gastrointestinal obstruction, allergic reactions

OPIOIDS CAN CAUSE DEATH EVEN WHEN TAKEN PROPERLY
COUNSEL PATIENTS ABOUT PROPER USE

EXPLAIN

- Tell patients and caregivers, medications must be kept in a locked container
- Will periodically assess for benefits, side effects, and continued need for IR/ER/LA opioids
- Need for re-evaluation of underlying medical condition if the clinical presentation changes over time

OPIOIDS SHOULD BE STORED IN A SAFE AND SECURE PLACE

- Away from children, family members, visitors, and pets
- Safe from theft

Opioids are scheduled under Controlled Substances Act and can be misused and abused

WARN PATIENTS

Never break, chew, crush, or snort an oral ER/LA tablet/capsule, or cut or tear patches prior to use
- May lead to rapid release of ER/LA opioid causing overdose and death
- If unable to swallow a capsule whole, refer to PI to determine if appropriate to sprinkle contents on applesauce or administer via feeding tube

Use of CNS depressants or alcohol with ER/LA opioids can cause overdose & death
- Use with alcohol may result in rapid release and absorption of a potentially fatal opioid dose – “dose dumping”
- Other depressants include sedative-hypnotics and anxiolytics, illegal drugs

OVERDOSE POISONING, CALL 911

- Person cannot be aroused or awakened or is unable to talk
- Any trouble with breathing, heavy snoring is warning sign
- Gurgling noises coming from mouth or throat
- Body is limp, seems lifeless; face is pale, clammy
- Fingernails or lips turn blue/purple
- Slow, unusual heartbeat or stopped heartbeat

NALOXONE

Naloxone:
- An opioid antagonist administered by injection or intranasally, or IV
- Reverses acute opioid-induced respiratory depression but will also reverse analgesia

What to do:
- Discuss an “overdose plan”
- Involve and train family, friends, partners, and/or caregivers
- Check with pharmacy if they are prescribing
- Check expiration dates and keep a viable dose on hand
- In the event of known or suspected overdose, administer naloxone and call 911

Available as:
- Naloxone kit (with syringes, needles)
- Injectable
- Nasal spray

Consider offering a naloxone prescription to all patients prescribed IR and ER/LA opioids

ABUSE-DETERRENT FORMULATION/TAMPER RESISTANT (ADF/TR) OPIOIDS

- Response to growing non-medical use problem
- An ER/LA opioid with physical barrier to deter extraction
- Less likely to be crushed, injected, or snorted
- Consider as one part of an overall strategy
- Mixed evidence on the impact of ADF/TR on misuse
- Remember overdose is still possible if taken orally in excessive amounts

SUBSTANCES PARENTS HAVE DISCUSSED WITH TEENS*

<table>
<thead>
<tr>
<th>Substance</th>
<th>% of Teens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beer/Alcohol</td>
<td>81%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>77%</td>
</tr>
<tr>
<td>Cocaine/crack</td>
<td>20%</td>
</tr>
<tr>
<td>Rx pain reliever w/o doctor’s Rx</td>
<td>23%</td>
</tr>
<tr>
<td>Any Rx drug used w/o doctor’s Rx</td>
<td>22%</td>
</tr>
<tr>
<td>Heroin</td>
<td>21%</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>21%</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>21%</td>
</tr>
<tr>
<td>Non-Rx cold/cough medicine to get high</td>
<td>15%</td>
</tr>
<tr>
<td>Steroids w/o doctor’s Rx</td>
<td>15%</td>
</tr>
<tr>
<td>Inhalants</td>
<td>14%</td>
</tr>
</tbody>
</table>

*As reported by teens

TALK WITH YOUR PATIENTS WHO ARE PARENTS

- Consider the behavior you are modeling
- 45% of parents have taken pain medications without a prescription at some point
- 14% have given their children pain medications without a prescription
- Teens report that their parents do not talk with them about prescription drug risks
  - Evidence suggests that pre-college parental conversation helps reduce high-risk substance abuse among college students

STEP 1: MONITOR
- Note how many pills in each prescription
- Keep track of dosage and refills
- Make sure everyone in the home knows

STEP 2: SECURE
- Keep meds in a safe place (locked cabinet)
- Encourage parents of your teen’s friends to secure their prescriptions

STEP 3: DISPOSE
- Discard expired or unused meds
- Consult PI for best disposal

REMEMBER...

SOURCE:
McDonald E, Kennedy-Hendrick A, McGinty E, Shields W, Barry C, Gielen A
AAP News, Pediatrics February 2017
**RX OPIOID DISPOSAL**

New “Disposal Act” expands ways for patients to dispose of unwanted/expired opioids

**DECREASES AMOUNT OF OPIOIDS INTRODUCED INTO THE ENVIRONMENT, PARTICULARLY INTO WATER**

<table>
<thead>
<tr>
<th>Collection receptacles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Call DEA Registration Call Center at 1-800-882-9539 to find a local collection receptacle</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mail-back packages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obtained from authorized collectors</td>
</tr>
</tbody>
</table>

Look for local take-back events
- Conducted by Federal, State, tribal, or local law enforcement
- Partnering with community groups

Voluntarily maintained by:
- Law enforcement
- Authorized collectors, including:
  - Manufacturer
  - Distributor
  - Reverse distributor
  - Retail or hospital/clinic pharmacy
  - Including long-term care facilities

**OTHER METHODS OF OPIOID DISPOSAL**

IF COLLECTION RECEPTACLE, MAIL-BACK PROGRAM, OR TAKE-BACK EVENT UNAVAILABLE, THROW OUT IN HOUSEHOLD TRASH

- Take drugs out of original containers
- Mix with undesirable substance
- Place in sealable bag, can, or other container
- Remove identifying info on label

**FDA: PRESCRIPTION DRUG DISPOSAL**

**FLUSH DOWN SINK/TOILET IF NO COLLECTION RECEPTACLE, MAIL-BACK PROGRAM, OR TAKE-BACK EVENT AVAILABLE**

- As soon as they are no longer needed
- Includes transdermal adhesive skin patches
  - Used patch (3 days) still contains enough opioid to harm/kill a child
  - Dispose of used patches immediately after removing from skin
- Fold patch in half so sticky sides meet, then flush down toilet
- Do NOT place used or unneeded patches in household trash
  - Butrans (buprenorphine transdermal system)
  - exception: can seal in Patch-Disposal Unit provided and dispose of in the trash

**CHAPTER 8 – PEARLS FOR PRACTICE**

- Use formal tools (PPAs, counseling document) to educate patients and caregivers
- Emphasize safe storage and disposal to patients and caregivers
- Consider co-prescribing naloxone
RED FLAG:
Patients do not safeguard their opioid medications correctly

Your patient’s daughter stole her father’s opioids from his bedside drawer to take to a “fishbowl party.” Her best friend consumed a mix of opioids and alcohol and died of an overdose.

Action:
Always counsel patients about safe drug storage; warn patients about the serious consequences of theft, misuse, and overdose. Tell patients that taking another person’s medication, even once, is against the law.

FOR SAFER USE: KNOW DRUG INTERACTIONS, PK, AND PD

CNS depressants can potentiate sedation and respiratory depression

Use with MAOIs may increase respiratory depression
Certain opioids with MAOIs can cause serotonin syndrome

Methadone and buprenorphine can prolong QTc interval

Some ER/LA products rapidly release opioid (dose dump) when exposed to alcohol
Some drug levels may increase without dose dumping

DRUG CLASS CONSIDERATIONS

FOR SAFER USE: KNOW DRUG INTERACTIONS, PK, AND PD

CNS depressants can potentiate sedation and respiratory depression

Use with MAOIs may increase respiratory depression
Certain opioids with MAOIs can cause serotonin syndrome

Methadone and buprenorphine can prolong QTc interval

Some ER/LA products rapidly release opioid (dose dump) when exposed to alcohol
Some drug levels may increase without dose dumping

TRANSDERMAL/TRANSMUCOSAL DOSAGE FORMS

Do not cut, damage, chew, or swallow

Exertion or exposure to external heat can lead to fatal overdose

Prepare skin: clip (not shave) hair & wash area with water

Monitor patients with fever for signs or symptoms of increased opioid exposure

Metal foil backings are not safe for use in MRIs

For buccal film products the film should not be applied if it is cut, damaged, or changed in any way – use entire film
**DRUG INTERACTIONS COMMON TO OPIOIDS**

- Concurrent use with other CNS depressants can increase risk of respiratory depression, hypotension, profound sedation, or coma.
- Reduce initial dose of one or both agents.
- Buprenorphine; Pentazocine, nalbuphine, butorphanol.
- May enhance neuromuscular blocking action of skeletal muscle relaxants and increase respiratory depression.
- Concurrent use of anticholinergic medication increases risk of urinary retention and severe constipation.
- May lead to paralytic ileus.
- Avoid concurrent use of partial agonists* or mixed agonist/antagonists† with full opioid agonist.
- May reduce analgesic effect and/or precipitate withdrawal.
- Concurrent use with other CNS depressants can increase risk of respiratory depression, hypotension, profound sedation, or coma.
- Reduce initial dose of one or both agents.

**DRUG INFORMATION COMMON TO OPIOIDS**

**USE IN OPIOID-TOLERANT PATIENTS**

- See individual PI for products which:
  - Have strengths or total daily doses only for use in opioid-tolerant patients.
  - Are only for use in opioid-tolerant patients at all strengths.

**CONTRAINDICATIONS**

- Significant respiratory depression.
- Acute or severe asthma in an unmonitored setting or in absence of resuscitative equipment.
- Known or suspected paralytic ileus.
- Hypersensitivity (e.g., anaphylaxis).
- See individual PI for additional contraindications.

**SPECIFIC CHARACTERISTICS**

Know for opioid products you prescribe:

- Drug substance
- Formulation
- Strength
- Dosing interval
- Key instructions
- Use in opioid-tolerant patients
- Product-specific safety concerns
- Relative potency to morphine
- Specific information about product conversions, if available
- Specific drug interactions

**SUMMARY**

Prescription opioid abuse and overdose is a national epidemic. Clinicians must play a role in prevention.

- Assess patients for treatment with IR and ER/LA opioids.
- Initiate therapy, modify dose, and discontinue use of opioids.
- Monitor ongoing therapy with IR and ER/LA opioids.
- Counsel patients and caregivers about the safe use of opioids, including proper storage and disposal.
- Be familiar with general and product-specific drug information concerning opioids.
Our session stops here, but your review continues…

Refer to Appendix 1 for specific drug information on ER/LA opioid analgesic products.

For detailed information, prescribers can refer to prescribing information available online via DailyMed at [www.dailymed.nlm.nih.gov](http://www.dailymed.nlm.nih.gov) or Drugs@FDA at [www.fda.gov/drugsatfda](http://www.fda.gov/drugsatfda).

YOUR PARTICIPATION IS IMPORTANT

Thank you for completing the post-activity assessment for this CO*RE session.

Your participation in this assessment allows CO*RE to report de-identified numbers to the FDA.

A strong show of engagement will demonstrate that clinicians have voluntarily taken this important education and are committed to patient safety and improved outcomes.

THANK YOU!

Appendix 1. Drug Specific Slides

THANK YOU!

[www.core-remso.org](http://www.core-remso.org)
Morphine Sulfate ER Tablets (Arymo ER)

Capsules 15 mg, 30 mg, 60 mg

Dosing Interval
- Every 8 or 12 hours

Key Instructions
- Initial dose in opioid-naive and opioid non-tolerant patients is 15 mg every 8 or 12 hours
- Dosage adjustment may be done every 1 to 2 days
- Take one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth

Drug Interactions
- P-gp inhibitors (e.g. quinidine) can increase the exposure of morphine by about two-fold and increase risk of respiratory depression

Opioid-tolerant
- A single dose of ARYMO ER greater than 60 mg, or total daily dose greater than 120 mg, is for use in opioid-tolerant patients only

Product-specific safety concerns
- Do not attempt to chew, crush, or dissolve. Swallow whole.
- Use with caution in patients who have difficulty in swallowing or have underlying GI disorders that may predispose them to obstruction, such as a small gastrointestinal lumen.

Morphine Sulfate ER Capsules (Avinza)

Capsules 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, and 120 mg

Dosing Interval
- Once a day

Key Instructions
- Initial dose in opioid non-tolerant patients is 30 mg
- Titrate in increments of not greater than 30 mg using a minimum of 3-4 d intervals
- Swallow capsule whole (do not chew, crush, or dissolve)
- May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing; use immediately
- MDD*: 1600 mg (renal toxicity of excipient, fumaric acid)

Drug Interactions
- Alcoholics or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose
- P-gp* inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold

Opioid-tolerant
- 90 mg & 120 mg capsules for use in opioid-tolerant patients only

Product-specific safety concerns
- None

Buprenorphine Buccal Film (Belbuca)

75 mg, 150 mg, 300 mg, 450 mg, 600 mg, 750 mg, and 900 mg

Dosing Interval
- Every 12 h (or once every 24 h for initiation in opioid naive patients & patients taking less than 30 mg oral morphine sulfate eq)

Key Instructions
- Opioid-naive pts or pts taking <30 mg oral morphine sulfate eq:
  - Initiate treatment with a 75 mg buccal film, once daily, or if tolerated, every 12 h
  - Titrate to 150 mg every 12 h no earlier than 4 d after initiation
- Individual titration to a dose that provides adequate analgesia and minimize adverse reaction should proceed in increments of 150 mg every 12 h, no more frequently than every 2-3 d
- When converting from another opioid, first taper the current opioid to no more than 30 mg oral morphine sulfate eq/day prior to initiating Belbuca
- If prior daily dose before taper was 30 mg to 89 mg oral morphine sulfate eq, initiate with 150 mg dose every 12 h
- If prior daily dose before taper was 90 mg to 150 mg oral morphine sulfate eq, initiate with 300 mg dose every 12 h
- Titration of the dose should proceed in increments of 150 mg every 12 h, no more frequently than every 4 d

Specific Drug Interactions
- CYP3A4 inhibitors may increase buprenorphine levels
- CYP3A4 inducers may decrease buprenorphine levels
- Benzodiazepines may increase respiratory depression
- Class IA and III antiarrhythmics, other potentially arrhythmogenic agents, may increase risk for QTc prolongation and torsade de pointes

Use in Opioid-Tolerant Patients
- Belbuca 600 mg, 750 mg, and 900 mg are for use following titration from lower doses of Belbuca

Product-Specific Safety Concerns
- QTc prolongation and torsade de pointes
- Hepatotoxicity

Mucositis
- Enzymatic in oral morphine has not been established
**Buprenorphine Transdermal System (Butrans)**

**Transdermal System 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, 20 mcg/hr**

**Dosing Interval**
- One transdermal system every 7 d

**Key Instructions**
- Initial dose in opioid non-tolerant patients on <30 mg morphine equivalents & in mild-moderate hepatic impairment: 5 mcg/hr
- When converting from 30 mg-80 mg morphine equivalents, first taper to 30 mg morphine equivalent, then initiate w/ 10 mcg/hr
- Titrate in 5 or 10 mcg/hr increments by using no more than 2 patches of the 5 or 10 mcg/hr system(s) w/ minimum of 72 h prior between dose adjustments. Total dose from all patches should be ≤ 20 mcg/hr
- Maximum dose: 20 mcg/hr due to risk of QTc prolongation
- Application
  - Apply only to sites indicated in PI
  - Apply to intact/non-irritated skin
  - Prep skin by clipping hair; wash site w/ water only
  - Rotate application site (min 3 wks before reapply to same site)
- Avoid exposure to heat
- Do not cut
- Dispose of patches: fold adhesive side together & flush down toilet

**Drug Interactions**
- CYP3A4 inhibitors may increase buprenorphine levels
- CYP3A4 inducers may decrease buprenorphine levels
- Benzodiazepines may increase respiratory depression
- Class IA & III antiarrhythmics, other potentially arrhythmogenic agents, may increase risk of QTc prolongation & torsade de pointe

**Opioid-tolerant**
- 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, & 20 mcg/hr for use in opioid-tolerant patients only
- QTc prolongation & torsade de pointe
- Hepatotoxicity
- Application site skin reactions

**Relative potency: oral morphine**
- Equi potency to oral morphine not established

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**Methadone Hydrochloride Tablets (Dolophine)**

**Dosing Interval**
- Every 8 to 12 h

**Key Instructions**
- Initial dose in opioid non-tolerant patients: 2.5 – 10 mg
- Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose & death. Use low doses according to table in full PI. Because of high variability in methadone metabolism, some patients may require substantially longer periods between dose increases (up to 12 d).
- High inter-patient variability in absorption, metabolism, & relative analgesic potency.
- Opioid detoxification or maintenance treatment only provided in a federally certified opioid (addiction) treatment program (CFR, Title 42, Sec 8)
- Pharmacokinetic drug-drug interactions w/ methadone are complex
  - CYP 3A4 inhibitors may decrease methadone levels
  - CYP 3A4 inducers may increase methadone levels
  - Antiarrhythm agents have little effects on methadone levels
  - Potentially arrhythmogenic agents may increase risk for QTc prolongation & torsade de pointe
  - Benzodiazepines may increase respiratory depression

**Drug Interactions**
- Refer to full PI
- QTc prolongation & torsade de pointe
- Peak respiratory depression occurs later & persists longer than analgesic effect
- Clearance may increase during pregnancy
- False-positive UDT possible
- Varies depending on patient’s prior opioid experience

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### Fentanyl Transdermal System (Duragesic)

**Dosing Interval**
- Every 72 h (3 d)

**Key Instructions**
- Use product-specific information for dose conversion from prior opioid
- Hepatic or renal impairment: use 50% of dose if mild/moderate, avoid use if severe
- Application: apply to intact/non-irritated/non-irradiated skin on a flat surface
- Prep skin by clipping hair, washing site w/ water only
- Rotate site of application
- Titrate using a minimum of 72 h intervals between dose adjustments
- Do not cut
- Avoid exposure to heat
- Avoid accidental contact when holding or caring for children
- Dispose of used/unused patches: fold adhesive side together & flush down toilet

**Specific contraindications:**
- Patients who are not opioid-tolerant

**Drug interactions**
- CYP3A4 inhibitors may increase fentanyl exposure
- CYP3A4 inducers may decrease fentanyl exposure
- Discontinuation of concomitant CYP P450 3A4 inducer may increase fentanyl plasma concentration

**Opioid-tolerant**
- All doses indicated for opioid-tolerant patients only

**Product-specific safety concerns**
- Accidental exposure due to secondary exposure to unwashed/unclothed application site
- Increased drug exposure w/ increased core body temp or fever
- Bradycardia
- Application site skin reactions

**Relative potency:**
- See individual PI for conversion recommendations from prior opioid

**Relative potency:**
- Oral morphine: see individual product information

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### Morphine Sulfate ER-Naltrexone (Embeda)

**Capsules**
- 20 mg/0.8 mg, 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg, 3.2 mg, 100 mg/4 mg

**Dosing Interval**
- Once a day or every 12 h

**Key instructions**
- Initial dose as first opioid: 20 mg/0.8 mg
- Titrate using a minimum of 1-2 d intervals
- Swallow capsules whole (do not chew, crush, or dissolve)
- Crushing or chewing will release morphine, possibly resulting in fatal overdose, & naltrexone, possibly resulting in withdrawal symptoms
- May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately

**Drug interactions**
- Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose
- P-gp inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold

**Opioid tolerant**
- 100 mg/4 mg capsule for use in opioid-tolerant patients only

**Product-specific adverse reactions**
- None

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### Hydromorphone Hydrochloride (Exalgo)

**ER Tablets**
- 8 mg, 12 mg, 16 mg, 32 mg

**Dosing Interval**
- Once a day

**Key instructions**
- Use conversion ratios in individual PI
- Start patients w/ moderate hepatic impairment on 25% dose prescribed for patient w/ normal function
- Renal impairment: start patients w/ moderate on 50% & patients w/ severe on 25% dose prescribed for patient w/ normal function
- Titrate in increments of 4-8 mg using a minimum of 3-4 d intervals
- Swallow tablets whole (do not chew, crush, or dissolve)
- Do not use in patients w/ sulfite allergy (contains sodium metabisulfite)

**Drug interactions**
- None

**Opioid tolerant**
- All doses indicated for opioid-tolerant patients only

**Product specific adverse reactions**
- Allergic manifestations to sulfite component
- ~5:1 oral morphine to hydromorphone oral dose ratio, use conversion recommendations in individual product information
Hydrocodone Bitartrate (Hysingla ER)

**Dosing**
- Once a day

**Key Instructions**
- Opioid-naïve patients: initiate treatment with 20 mg orally once daily.
- During titration, adjust the dose in increments of 10 mg to 20 mg every 3 to 5 days until adequate analgesia is achieved.
- Swallow tablets whole (do not chew, crush, or dissolve).
- Consider use of an alternative analgesic in patients who have difficulty swallowing or have underlying gastrointestinal disorders that may predispose them to obstruction.
- Take one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth.
- Use 1/2 of the initial dose and monitor closely for adverse events, such as respiratory depression and sedation, when administering Hysingla ER to patients with severe hepatic impairment or patients with moderate to severe renal impairment.

**Drug Interactions**
- CYP3A4 inhibitors may increase hydrocodone exposure.
- CYP3A4 inducers may decrease hydrocodone exposure.
- Concomitant use of Hysingla ER with strong laxatives (e.g., Lactulose) that rapidly increase GI motility may decrease hydrocodone absorption and result in decreased hydrocodone plasma levels.
- The use of MAO inhibitors or tricyclic antidepressants with Hysingla ER may increase the effect of either the antidepressant or Hysingla ER.

**Opioid-tolerant**
- A single dose ≥ 80 mg is only for use in opioid tolerant patients.

**Product-specific safety concerns**
- Use with caution in patients with difficulty swallowing the tablet or underlying gastrointestinal disorders that may predispose patients to obstruction.
- Esophageal obstruction, dysphagia, and choking have been reported with Hysingla ER.
- In nursing mothers, discontinue nursing or discontinue drug. QTc prolongation has been observed with Hysingla ER following daily doses of 160 mg.
- Avoid use in patients with congenital long QTc syndrome. This observation should be considered in making clinical decisions regarding patient monitoring when prescribing Hysingla ER in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, or who are taking medications that are known to prolong the QTc interval.
- In patients who develop QTc prolongation, consider reducing the dose.

**Relative potency:**
- Oral morphine

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Morphine Sulfate (Kadian)

**Dosing Interval**
- Once a day or every 12 h

**Key Instructions**
- PI recommends not using as first opioid
- Titrate using minimum of 2-d intervals
- Swallow capsules whole (do not chew, crush, or dissolve)
- May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately

**Specific Drug Interactions**
- Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose of morphine
- P-gp inhibitors (e.g., quinidine) may increase the absorption/exposure of morphine sulfate by ~2-fold

**Opioid-tolerant**
- Morphine 100 mg tablets are for use in opioid-tolerant patients only

---

Morphine Sulfate (MorphaBond)

**Dosing Interval**
- Every 8 h or every 12 h

**Key Instructions**
- Product information recommends not using as first opioid
- Titrate using a minimum of 1 – 2 d intervals
- Swallow tablets whole (do not chew, crush, or dissolve)

**Specific Drug Interactions**
- P-gp inhibitors (e.g., quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold

**Opioid-tolerant**
- MorphaBond 100 mg tablets are for use in opioid-tolerant patients only

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### Morphine Sulfate (MS Contin)

**ER Tablets 15 mg, 30 mg, 60 mg, 100 mg, 200 mg**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>Every 8 h or every 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key instructions</td>
<td>Product information recommends not using as first opioid.</td>
</tr>
<tr>
<td></td>
<td>Titrate using a minimum of 1-2 d intervals</td>
</tr>
<tr>
<td></td>
<td>Swallow tablets whole (do not chew, crush, or dissolve)</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>P-gp inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold</td>
</tr>
<tr>
<td>Opioid-tolerant</td>
<td>100 mg &amp; 200 mg tablet strengths for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>Product-specific safety concerns</td>
<td>None</td>
</tr>
</tbody>
</table>

### Tapentadol (Nucynta ER)

**ER Tablets 50 mg, 100 mg, 150 mg, 200 mg, 250 mg**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>Every 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key instructions</td>
<td></td>
</tr>
<tr>
<td>Drug interactions</td>
<td>Alcoholic beverages or medications w/ alcohol may result in rapid release &amp; absorption of a potentially fatal dose of tapentadol</td>
</tr>
<tr>
<td>Opioid-tolerant</td>
<td>No product-specific considerations</td>
</tr>
<tr>
<td>Product-specific safety concerns</td>
<td>Risk of serotonin syndrome, Angio-edema</td>
</tr>
<tr>
<td>Relative potency: oral morphine</td>
<td>Equi-potency to oral morphine has not been established</td>
</tr>
</tbody>
</table>

### Oxymorphone Hydrochloride (Opana ER)

**ER Tablets 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>Every 12 h dosing, some may benefit from asymmetric (different dose given in AM than in PM) dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key instructions</td>
<td>Use 5 mg every 12 h as initial dose in opioid non-tolerant patients &amp; patients w/ mild hepatic impairment &amp; renal impairment (creatinine clearance &lt;60 mL/min) &amp; patients &gt;65 yrs</td>
</tr>
<tr>
<td></td>
<td>Swallow tablets whole (do not chew, crush, or dissolve)</td>
</tr>
<tr>
<td></td>
<td>Take 1 tablet at a time, w/ enough water to ensure complete swallowing immediately after placing in mouth</td>
</tr>
<tr>
<td></td>
<td>Titrate in increments of 5-10 mg using a minimum of 3-7 d intervals</td>
</tr>
<tr>
<td></td>
<td>Contraindicated in moderate &amp; severe hepatic impairment</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>Alcoholic beverages or medications w/ alcohol may result in absorption of a potentially fatal dose of oxymorphone</td>
</tr>
<tr>
<td>Opioid-tolerant</td>
<td>No product-specific considerations</td>
</tr>
<tr>
<td>Product-specific safety concerns</td>
<td>Use with caution in patients who have difficulty swallowing or underlying GI disorders that may predispose to obstruction (e.g. small gastrointestinal lumen)</td>
</tr>
<tr>
<td>Relative potency: oral morphine</td>
<td>Approximately 3:1 oral morphine to oxymorphone oral dose ratio</td>
</tr>
</tbody>
</table>

### Oxycodone Hydrochloride (OxyContin)

**ER Tablets 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg and 80 mg**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>Every 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key instructions</td>
<td>Initial dose in opioid-naïve and non-tolerant patients: 10 mg every 12 h</td>
</tr>
<tr>
<td></td>
<td>Titrate using a minimum of 1-2 d intervals</td>
</tr>
<tr>
<td></td>
<td>Hepatic impairment: start w/ ⅓—½ usual dosage</td>
</tr>
<tr>
<td></td>
<td>Renal impairment (creatinine clearance &lt;60 mL/min): start w/ ½ usual dosage</td>
</tr>
<tr>
<td></td>
<td>Consider other analgesics in patients w/ difficulty swallowing or underlying GI disorders that predispose to obstruction. Swallow tablets whole (do not chew, crush, or dissolve)</td>
</tr>
<tr>
<td></td>
<td>Take 1 tablet at a time, w/ enough water to ensure complete swallowing immediately after placing in mouth</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>Alcoholic beverages or medications w/ alcohol may increase oxycodone exposure</td>
</tr>
<tr>
<td>Opioid-tolerant</td>
<td>For Adults: Single dose &gt;40 mg or total daily dose &gt;80 mg for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>Product-specific safety concerns</td>
<td>Choking, gagging, regurgitation, tablets stuck in throat, difficulty swallowing tablet</td>
</tr>
<tr>
<td>Relative potency: oral morphine</td>
<td>Approximately 2:1 oral morphine to oxycodone oral dose ratio</td>
</tr>
</tbody>
</table>
Oxycodone Hydrochloride (OxyContin) continued

<table>
<thead>
<tr>
<th>Key Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For Adults:</strong></td>
</tr>
<tr>
<td>- Single dose greater than 80 mg or total daily dose greater than 200 mg are for use in patients for whom tolerance to an opioid of comparable potency has been established.</td>
</tr>
<tr>
<td>- When a dose increase is clinically indicated, the total daily oxycodone dose can usually be increased by 25% to 50% of the current dose.</td>
</tr>
</tbody>
</table>

**For Pediatric Patients (11 years and older):**
- For use in opioid-tolerant pediatric patients already receiving and tolerating opioid therapy for at least five (5) consecutive days with a minimum of 20 mg/day of oxycodone or its equivalent for at least 2 days immediately preceding dosing with OxyContin ER. |
- If needed, pediatric dose may be increased in 1 to 2 day intervals. |
- When a dose increase is clinically indicated, the total daily oxycodone dose can usually be increased by 25% of the current daily dose. |

**IMPORTANT:**
- Opioids are rarely indicated or used to treat pediatric patients with chronic pain. |
- The recent FDA approval for this oxycodone formulation was NOT intended to increase prescribing or use of this drug in pediatric pain treatment. Review the product information and adhere to best practices in the literature.

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Oxycodone Hydrochloride/Naltrexone Hydrochloride (Targiniq ER)

<table>
<thead>
<tr>
<th>Dosing Interval</th>
<th>Every 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key instructions</td>
<td></td>
</tr>
<tr>
<td>- Opioid-naive patients: initiate treatment w/ 10mg/5mg every 12 h</td>
<td></td>
</tr>
<tr>
<td>- Titrated using min of 1-2-d intervals</td>
<td></td>
</tr>
<tr>
<td>- Do not exceed 60 mg/30 mg total daily dose (40 mg/20 mg q12h)</td>
<td></td>
</tr>
<tr>
<td>- May be taken w/ or without food</td>
<td></td>
</tr>
<tr>
<td>- Swallow whole. Do not chew, crush, split, or dissolve; this will release oxycodone (possible fatal overdose) &amp; naltrexone (possible withdrawal)</td>
<td></td>
</tr>
<tr>
<td>- Hepatic impairment: contraindicated in moderate-severe impairment. In patients w/ mild impairment, start w/ ½ to ⅔ usual dosage</td>
<td></td>
</tr>
<tr>
<td>- Renal impairment (creatinine clearance &lt;60 mL/min): start w/ ½ usual dosage</td>
<td></td>
</tr>
</tbody>
</table>

**Drug interactions:**
- CYP3A4 inhibitors may increase oxycodone exposure |
- CYP3A4 inducers may increase oxycodone exposure |

**Opioid-tolerant**
- Single dose >60 mg/30 mg or total daily dose of 120 mg/60 mg for opioid-tolerant patients only |

**Product-specific safety concerns**
- Contraindicated in patients w/ moderate-severe hepatic impairment |

**Relative potency: oral morphine**
- See individual PI for conversion recommendations from prior opioids

---

Oxycodone Hydrochloride (OxyContin)

<table>
<thead>
<tr>
<th>Dosing Interval</th>
<th>Every 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key instructions</td>
<td></td>
</tr>
<tr>
<td>- Opioid-naive patients: initiate treatment w/ 10mg/5mg every 12 h</td>
<td></td>
</tr>
<tr>
<td>- Titrated using min of 1-2-d intervals</td>
<td></td>
</tr>
<tr>
<td>- Do not exceed 60 mg/30 mg total daily dose (40 mg/20 mg q12h)</td>
<td></td>
</tr>
<tr>
<td>- May be taken w/ or without food</td>
<td></td>
</tr>
<tr>
<td>- Swallow whole. Do not chew, crush, split, or dissolve; this will release oxycodone (possible fatal overdose) &amp; naltrexone (possible withdrawal)</td>
<td></td>
</tr>
<tr>
<td>- Hepatic impairment: contraindicated in moderate-severe impairment. In patients w/ mild impairment, start w/ ½ to ⅔ usual dosage</td>
<td></td>
</tr>
<tr>
<td>- Renal impairment (creatinine clearance &lt;60 mL/min): start w/ ½ usual dosage</td>
<td></td>
</tr>
</tbody>
</table>

**Drug interactions:**
- CYP3A4 inhibitors may increase hydrocodone exposure |
- CYP3A4 inducers may increase hydrocodone exposure |

**Opioid-tolerant**
- A 90 mg tablet, a single dose greater than 60 mg, or a total daily dose >120 mg are for use in opioid-tolerant patients only |

**Product-specific safety concerns**
- None |

**Relative potency: oral morphine**
- See individual product information for conversion recommendations from prior opioid

---

Hydrocodone Bitartrate (Vantrela ER)

<table>
<thead>
<tr>
<th>Dosing Interval</th>
<th>Every 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key instructions</td>
<td></td>
</tr>
<tr>
<td>- Opioid-naive patients: initiate treatment w/ 15 mg every 12 h</td>
<td></td>
</tr>
<tr>
<td>- Titrated using min of 1-2-d intervals</td>
<td></td>
</tr>
<tr>
<td>- Do not exceed 45 mg total daily dose (30 mg q12h)</td>
<td></td>
</tr>
<tr>
<td>- May be taken w/ or without food</td>
<td></td>
</tr>
<tr>
<td>- Swallow capsules whole. Do not chew, crush, or dissolve</td>
<td></td>
</tr>
<tr>
<td>- Mild or moderate hepatic and moderate to severe renal impairment: initiate therapy with ½ recommended initial dose. If a dose &lt;15 mg needed, use alternative options</td>
<td></td>
</tr>
</tbody>
</table>

**Drug interactions:**
- CYP3A4 inhibitors may increase hydrocodone exposure |
- CYP3A4 inducers may decrease hydrocodone exposure |

**Opioid-tolerant**
- A 90 mg tablet, a single dose greater than 60 mg, or a total daily dose >120 mg are for use in opioid-tolerant patients only |

**Product-specific safety concerns**
- None |

**Relative potency: oral morphine**
- See individual product information for conversion recommendations from prior opioid

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# Oxycodone (Xtampza ER)

**ER Capsules 9 mg, 13.5 mg, 18 mg, 27 mg, 36 mg**

## Dosing Interval
- Every 12 h

## Key Instructions
- Opioid naïve and non-tolerant, initiate with 9 mg every 12 h
- Titrate using a minimum of 1-2-d intervals
- Take with same amount of food in order to ensure consistent plasma levels
- Maximum daily dose: 288 mg (8 x 36 mg), safety of excipients not established for higher doses
- May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately
- May also be administered through a NG or G feeding tube
- Hepatic impairment: initiate therapy at 1/3 to ½ usual dose
- Renal impairment: creatinine clearance <60 mL/min, follow conservative approach

## Drug Interactions
- CYP3A4 inhibitors may increase hydrocodone exposure
- CYP3A4 inducers may decrease hydrocodone exposure

## Opioid-tolerant
- A single dose >36 mg or a total daily dose >72 mg for opioid-tolerant patients only

## Product-specific safety concerns
- None

## Relative potency: oral morphine
- There are no established conversion ratios for Xtampza ER, defined by clinical trials

# Naloxone (Narcan)

**IM or SQ: onset 2-5 minutes, duration >45 min**

## Key Instructions
- Monitor respiratory rate
- Monitor level of consciousness for 3-4 hours after expected peak of blood concentrations
- Note that reversal of analgesia will occur

## Drug Interactions
- Larger doses required to reverse effects of buprenorphine, butorphanol, nalbuphine, or pentazocine

## Opioid-tolerant
- Assess signs and symptoms of opioid withdrawal, may occur w/i 2 min – 2 hrs
- Vomiting, restlessness, abdominal cramps, increased BP, temperature
- Severity depends on naloxone dose, opioid involved & degree of dependence

## Product-specific safety concerns
- Ventricular arrhythmias, hypertension, hypotension, nausea & vomiting
- As naloxone plasma levels decrease, sedation from opioid overdose may increase

# Hydrocodone Bitartrate (Zohydro ER)

**ER Capsules 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg**

## Dosing Interval
- Every 12 h

## Key Instructions
- Initial dose in opioid non-tolerant patient is 10 mg
- Titrate in increments of 10 mg using a min of 3-7-d intervals
- Swallow capsules whole (do not chew, crush, or dissolve)

## Drug Interactions
- Alcoholic beverages or medications containing alcohol may result in rapid release & absorption of a potentially fatal dose of hydrocodone
- CYP3A4 inhibitors may increase hydrocodone exposure
- CYP3A4 inducers may decrease hydrocodone exposure

## Opioid-tolerant
- Single dose >40 mg or total daily dose >80 mg for use in opioid-tolerant patients only

## Product-specific safety concerns
- None

## Relative potency: oral morphine
- Approximately 1.5:1 oral morphine to hydrocodone oral dose ratio
The following individuals disclose no relevant financial relationships:

**Faculty Advisory Panel & Reviewer COI**

<table>
<thead>
<tr>
<th>Faculty Advisory Panel</th>
<th>Affiliation</th>
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<tbody>
<tr>
<td>David Bazzo, MD</td>
<td>Clinical Professor of Family Medicine, University of California San Diego, School of Medicine</td>
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**External / Consulting Reviewers**

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<td>Roberto Cardarelli, DO, MPH</td>
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<tr>
<td>Nancy K. Hines</td>
<td>Chief, National Opioid Policy Institute</td>
</tr>
</tbody>
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**The following individuals disclose no relevant financial relationships:**

**CO*RE Partner Staff COI**

<table>
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<th>Former Affiliation</th>
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<tbody>
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<td>Julie House</td>
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<td>Nancy Mahler</td>
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<td>Stephanie Traina</td>
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<td>American Society of Addictive Medicine</td>
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<td>Jesse Mariano</td>
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<td>Staci Keenan</td>
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**The following individuals disclose no relevant financial relationships:**

**CO*RE Operations Organizations**

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<td>Katie Gielke</td>
<td>Forefront Collaborative</td>
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<td>Robin Hoopfer</td>
<td>HoopferTy, LLC</td>
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