FACULTY INFORMATION

Yvonne D’Arcy, MS, CRNP, CNS, FAANP

Yvonne D’Arcy is a pain management & palliative care nurse practitioner with over 20 years of practice experience. She is the author of over 100 articles, ten books, and over 100 presentations. She has two AJN book of the year awards for her book on How to Manage Pain in the Elderly and The Compact Clinical Guide to Cancer Pain Management written with Pamela Davies. She speaks frequently on a variety of pain management topics. Yvonne is currently the co-chair of the AANP Pain Management Special Practice group.

DISCLOSURE:
Advisory Board for: Pfizer, Ortho-McNeil, and Astra-Zeneca
Presented by AANP a member of the Collaborative on REMS Education (CO*RE), 11 interdisciplinary organizations working together to improve pain management and prevent adverse outcomes.

This educational activity is supported by an independent educational grant from the ER/LA Opioid Analgesic REMS Program Companies. This activity is intended to be fully compliant with the ER/LA Opioid Analgesic REMS education requirements issued by the US Food & Drug Administration.
PRODUCTS COVERED BY THIS REMS

BRAND NAME PRODUCTS
- Arymo ER morphine sulfate ER tablets
- Avinza® morphine sulfate ER capsules
- Belbuca® buprenorphine buccal film
- Butrans® buprenorphine transdermal system
- Dolophine® methadone hydrochloride tablets
- Duodgesic® fentanyl transdermal system
- Embeda® morphine sulfate/naltrexone ER capsules
- Exalgo® hydromorphone hydrochloride ER tablets
- Hydelig ER (hydromorphone ER) ER tablets
- Kadian® morphine sulfate ER capsules
- Morphine ER morphine sulfate ER tablets
- MS Contin® morphine sulfate CR tablets
- Nucynta ER extended-release CR tablets
- OxyContin® oxycodone hydrochloride CR tablets
- OxyContin® oxycodone hydrochloride ER tablets
- Trigard™ oxycodeone hydrochloride/naloxone ER tablets
- Trigard™ oxycodeone ER tablets
- Trigard™ oxycodone/hydrochloride tablets
- Trigard™ oxycodone ER tablets
- Trigard™ oxycodone ER capsules
- Zohydro® hydrocodone ER capsules

GENERIC PRODUCTS
- Fentanyl ER transdermal systems
- Methadone hydrochloride tablets
- Methadone hydrochloride oral concentrate
- Methadone hydrochloride oral solution
- Morphine sulfate ER tablets
- Morphine sulfate ER capsules
- Oxycodone hydrochloride ER tablets

WHY ARE WE HERE?

CHAPTER 2
Opioid Prescribing: Safe Practice, Changing Lives

OPIOID PRESCRIBING - THE PENDULUM SWINGS

Appropriate Prescribing
- Complete elimination of pain
- Emphasis on functional goals

Under-prescribing
- Complete elimination of pain

Over-prescribing
- Emphasis on functional goals

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 IRs
- 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/ingestion by household contacts especially children


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

Source where pain relievers were obtained for most recent misuse among 12.0 million people aged 12 or older who misused prescription pain relievers in the past year: percentages, 2015

- Given by, Bought From, or Taken From a Friend or Relative: 54%
- Through a Prescription or Stolen from Healthcare Provider: 36%
- Bought From a Dealer or Stranger: 5%
- Some Other Way: 5%
FIRST SPECIFIC DRUG ASSOCIATED WITH INITIATION OF ILLICIT DRUG USE 2013

- 2.8 million initiates of illicit drugs
- 70.3% - Marijuana
- 12.5% - Pain Relievers
- 6.3% - Inhalants
- 5.2% - Tranquilizers
- 2.7% - Stimulants
- 2.6% - Hallucinogens
- 0.3% - Sedatives & Cocaine

SOURCE: https://www.drugabuse.gov/publications/drugfacts/nationwide-trends

THE FEDERAL PLAYERS

Many agencies involved

WE ARE HERE BECAUSE OF …

REMS: RISK EVALUATION 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
• Explain neurophysiology of pain processing to patients
• When patients understand, their concerns are validated
• Pain has biological, psychological, social, and spiritual components

CHAPTER 3 - PEARLS FOR PRACTICE

CHALLENGE: THE EARLY REFILL

RED FLAG: Is this misuse? Abuse?
Your patient requests an early refill for second time in six months. Took 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 them 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 to patients’ individual needs, is safe, effective and balanced. Screen for risk with COMM and, if indicated, refer to addiction specialist or 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 & PSYCHOSOCIAL FUNCTION

PATIENT’S CURRENT PAIN & FUNCTION

TREATMENT HISTORY

NON-PHARMACOLOGIC STRATEGIES & EFFECTIVENESS

PHARMACOLOGIC STRATEGIES & EFFECTIVENESS

PAST USE

CURRENT USE

• Query state PMP to confirm patient report
• Contact past providers & obtain prior medical records

DOSAGE

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

GENERAL EFFECTIVENESS

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/Blunt
• Cardiac Disease
• Pulmonary Disease
### OBTAIN A COMPLETE HISTORY OF CURRENT & PAST SUBSTANCE USE

#### RISK FACTORS FOR OPIOID ABUSE

- Prescription drugs, controlled medications (Benzodiazepine)
- Alcohol & tobacco
  - Substance abuse Hx does not prohibit treatment w/ ER/LA opioids but may require additional monitoring & expert consultation/referral
- History of sexual abuse
- Family Hx of substance abuse & psychiatric disorders
- Age (16-45 YO)

#### SOCIAL HISTORY

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

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### PHYSICAL EXAM & ASSESSMENT

Seek objective confirmatory data

Components of patient evaluation for pain:
- General: vital signs, appearance, & pain behaviors
- Neurologic exam
- Musculoskeletal Exam
  - Inspection
  - Gate & posture
  - Range of motion
  - Palpation
  - Percussion
  - Auscultation
  - Provocative maneuvers
- Cutaneous or trophic findings

Order diagnostic tests (appropriate to complaint)

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### RISK ASSESSMENT TOOLS

<table>
<thead>
<tr>
<th>TOOL</th>
<th>DATA SOURCE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENTS CONSIDERED FOR LONG-TERM OPIOID THERAPY</strong></td>
<td></td>
</tr>
<tr>
<td>Opioid Risk Tool</td>
<td>5 patient</td>
</tr>
<tr>
<td>SOAP Pain &amp; Opioid Assessment for Patients w/ Pain</td>
<td>24, 14, &amp; 5 patient</td>
</tr>
<tr>
<td>DIRE Diagnosis, Intractability, Risk, &amp; Efficacy Score</td>
<td>7 clinician</td>
</tr>
<tr>
<td><strong>CHARACTERIZE MISUSE ONCE OPIOID TREATMENTS BEGINS</strong></td>
<td></td>
</tr>
<tr>
<td>PMQ Pain Medication Questionnaire</td>
<td>35 patient</td>
</tr>
<tr>
<td>CMM Current Opioid Misuse Measure</td>
<td>17 patient</td>
</tr>
<tr>
<td>PDUG Drug Use Questionnaire</td>
<td>40 clinician</td>
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<tr>
<td><strong>NOT SPECIFIC TO PAIN POPULATIONS:</strong></td>
<td></td>
</tr>
<tr>
<td>CAGE Cut Down, Annoyed, Guilty, Eye-Opener Tool</td>
<td>4 clinician</td>
</tr>
<tr>
<td>RAFTT Relate, Alone, Friends, Family, Trouble</td>
<td>5 patient</td>
</tr>
<tr>
<td>DAST Drug Abuse Screening Test</td>
<td>24 patient</td>
</tr>
<tr>
<td>SBIRT Screening, Brief Intervention, &amp; Referral to Treatment</td>
<td>Varies clinician</td>
</tr>
</tbody>
</table>
Opioid Risk Tool (ORT)

Mark each box that applies:

1. Family history of substance abuse
   - Alcohol
   - Illegal drugs
   - Prescription drugs

2. Personal history of substance abuse
   - Alcohol
   - Illegal drugs
   - Prescription drugs

3. Age between 16 & 45 yrs

4. History of preadolescent sexual abuse

5. Psychiatric disease
   - ADD, OCD, bipolar, schizophrenia
   - Depression

Scoring Total:

0-3: low
4-7: moderate
≥8: high


Screener & Opioid Assessment for Patients With Pain (SOAPP®)

Identifies patients as at 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 & scored SOAPP® while making opioid treatment decisions


Opioids
Pain
Addiction
Opioid Prescribing: Safe Practice, Changing Lives

WHAT IS THE RISK FOR MY PATIENT?

- Risk of opioid use disorder in patients on COT for Chronic Non-Cancer Pain (CNCP) is up to 30%
- Always highest with past history of SUD or psychiatric comorbidity
- Recognize that patient needs and patterns shift with age

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PAIN AND ADDICTION

PAIN – 5 A’S
- Analgesia
- Activities/Function
- Aberrant Behavior
- Adverse Effects
- Affect

ADDITION – 5 C’S
- Control, loss of
- Compulsive use
- Craving drug
- Continued use
- Chronic problem

RISK & PAIN ASSESSMENT TOOL BOXES

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

MENTAL HEALTH TOOLS (PHQ9, GAD7, etc)

RISK ASSESSMENT TOOL BOX
- POMA
- UOT
- Risk Assessment Tools (DOT or SOAP?)

MENTAL HEALTH TOOLS (PHQ9, GAD7, etc)
CONSIDER A TRIAL OF AN OPIOID?

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


WHEN TO CONSIDER A TRIAL OF AN OPIOID

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

30-YR-OLD W/ FIBROMYALGIA & RECENT ALCOHOL USE DISORDER
- High potential risks relative to benefits (opioid therapy not 1st line for fibromyalgia)
- Requires intensive structure, monitoring, & management by clinician with expertise in both addiction & pain
- Not a good candidate for opioid therapy


INITIATING OPIOIDS: CDC GUIDELINE

- 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
  - 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 & FUNCTIONAL GOALS OF TREATMENT**

**EXPECTATIONS**

**POTENTIAL RISKS**

**ALTERNATIVES TO OPIOIDS**

**HOW TO MANAGE**
- Common AEs (e.g., constipation, nausea, sedation)
- Risks (e.g., abuse, addiction, respiratory depression, overdose)
- AEs with long-term therapy (e.g., hyperalgesia, testosterone, irregular menses or sexual dysfunction)

PATIENT-PRESCRIBER AGREEMENT (PPA)
Document signed by both patient & prescriber at time an opioid is prescribed

**CLARIFY TREATMENT PLAN & GOALS OF TREATMENT W/ PATIENT, PATIENT’S FAMILY, & OTHER CLINICIANS INVOLVED IN PATIENT’S CARE**

**ASSIST IN PATIENT EDUCATION**

**DISCUSS MEDICATION SAFE HANDLING, STORAGE, AND DISPOSAL**

**DOCUMENT PATIENT & PRESCRIBER RESPONSIBILITIES**

PATIENT PROVIDER AGREEMENT (PPA)

**REINFORCE EXPECTATIONS FOR APPROPRIATE & 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 Rx.

- Follow-up
- Monitoring
  - Random UDT & pill counts
- Refills
- Identify behaviors for discontinuation
- Exit strategy
MONITOR ADHERENCE AND ABERRANT BEHAVIOR

ROUTINE MONITOR PATIENT ADHERENCE TO TREATMENT PLAN
- Recognize & document aberrant drug-related behavior
  - In addition to patient self-report also use:
    - State PDMPs
    - UDT
      - Positive for nonprescribed drugs
      - Positive for illicit substance
      - Negative for prescribed opioid
    - Family member or caregiver interviews
    - Monitoring tools such as the COMM, PADT, PMQ, or PDUQ
    - Medication reconciliation (e.g., pill counts)

PADT = Pain Assessment & Documentation Tool

ADDRESS ABERRANT DRUG-RELATED BEHAVIOR

Behavior outside the boundaries of agreed-on treatment plan:
- Unsanctioned dose escalations or other noncompliance on 1 or 2 occasions
- Unapproved use of the drug to treat another symptom
- Openly acquiring similar drugs from other medical sources
- Multiple dose escalations or other noncompliance w/ therapy despite warnings
- 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, & treatment plans.
CHAPTER 4 – PEARLS FOR PRACTICE

• Conduct a comprehensive and pain-focused H&P
• 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

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
- Sweating, miosis, urinary retention
- Hypogonadism
- Tolerance, physical dependence, hyperalgesia
- Reward and addiction in vulnerable patients
- Death

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

Chief hazard of opioid agonists, including ER/LA opioids
- If not immediately recognized & treated, may lead to respiratory arrest & 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 w/ close observation, supportive measures, & opioid antagonists, depending on patient’s clinical status

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

**REDUCE RISK**
- Proper dosing & 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

WHEN TO MOVE FROM IR TO ER/LA OPIOIDS

**PRIMARY REASONS**
- Maintain stable blood levels
- 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 PK
- Problematic drug-drug interactions

CONSIDERATIONS FOR CHANGE FROM IR TO ER/LA OPIOIDS

**DRUG & 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 EA
- Certain strengths/doses of other ER/LA products (check drug PI)

**MONITOR PATIENTS CLOSELY FOR RESPIRATORY DEPRESSION**
Especially within 24-72 h of initiating therapy & increasing dosage

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

**REDUCE RISK**
- Proper dosing & 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
OPIOID TOLERANCE

If opioid tolerant — no restrictions on which products can be used

Patients considered opioid tolerant are taking at least

- 60 mg oral morphine/day
- 25 mcg transdermal fentanyl/hr
- 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

FOR 1 WK OR LONGER

OPIOID ROTATION

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 & 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 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>Equianalgesic Dose</th>
<th>Usual Starting Doses</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>SC/IV</td>
<td>PO</td>
</tr>
<tr>
<td>Morphine</td>
<td>10 mg 30 mg</td>
<td>2.5-5 mg SC/IV (1.25 – 2.5 mg)</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>NA 20 mg NA</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>NA 30 mg NA</td>
<td>0.2-2.5 mg SC/IV (0.2mg)</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5 mg 7.5 mg</td>
<td>0.2-0.6 mg SC/IV (0.2mg)</td>
</tr>
</tbody>
</table>

MU OPIOID RECEPTORS & INCOMPLETE CROSS-TOLERANCE

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

INCOMPLETE CROSS-TOLERANCE

<table>
<thead>
<tr>
<th>Drug</th>
<th>Receptor Subtype Selectivity</th>
<th>Cross-Tolerance if Tolerant to Drug</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>1+3</td>
<td>A - Partial</td>
</tr>
<tr>
<td>B</td>
<td>2+3</td>
<td>A - Partial</td>
</tr>
<tr>
<td>C</td>
<td>1</td>
<td>A - Yes</td>
</tr>
<tr>
<td>D</td>
<td>1+2+3</td>
<td>A - Yes</td>
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<td>B - Partial</td>
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<td>D - Partial</td>
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GUIDELINES FOR OPIOID ROTATION

REDUCE CALCULATED EQUIANALGESIC DOSE BY 25%-50%

SELECT % REDUCTION BASED ON CLINICAL JUDGMENT

CLOSER TO 50% REDUCTION IF PATIENT:

- Receiving a relatively high dose of current opioid regimen
- Elderly or medically frail

CLOSER TO 25% REDUCTION IF PATIENT:

- Does not have these characteristics
- Is changing route of administration

*75%-90% 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-naïve 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

<table>
<thead>
<tr>
<th>VALUE FROM EDT</th>
<th>PATIENT OPIOID VALUES</th>
<th>&quot;SOLVE&quot; FOR X</th>
<th>AUTOMATICALLY REDUCE DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value of Current Opioid</td>
<td>24 Hr dose of Current Opioid</td>
<td>Equivalent 24 Hr Dose of New Opioid</td>
<td>By 25% – 50%</td>
</tr>
<tr>
<td>Value of New Opioid</td>
<td>X Amount of New Opioid</td>
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</table>

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

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### BREAKTHROUGH PAIN (BTP)

**PATIENTS ON STABLE ATC OPIOIDS MAY EXPERIENCE BTP**
- Disease progression or a new or unrelated pain
- 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

**THERAPIES**
- Target cause or precipitating factors
- Nonspecific symptomatic therapies to lessen impact of 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/ routine follow-up & monitoring
- Nonopioid drug therapies
- Nonpharmacologic treatments

### BE READY TO REFER

**SUBSTANCE USE DISORDER**
- SAMHSA substance abuse treatment facility locator
  - [SAMHSA substance abuse treatment facility locator](http://findtreatment.samhsa.gov/TreatmentLocator/faces/quickSearch.jspx)
- SAMHSA mental health treatment facility locator
  - [SAMHSA mental health treatment facility locator](http://findtreatment.samhsa.gov/MHTreatmentLocator/faces/quickSearch.jspx)

**HIGH-RISK/COMPLEX PATIENTS**
- Refer to pain management, check state regulations for requirements

### 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’re testing and not testing

**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

* GC/MS=gas chromatography/mass spectrometry    - IA=immunoassay    - LC/MS=liquid chromatography/mass spectrometry


Be aware of what you’re testing and not testing

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 & pH

For most drugs it is 1-3 days

Chronic use of lipid-soluble drugs increases detection time; e.g., marijuana, dazepam, 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/Burners (Amphetamine, methamphetamine)</td>
<td>4-6 hours</td>
<td>2-3 days</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>3-8 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>
URINE SPECIMEN INTEGRITY

SPECIMEN COLOR RELATED TO CONCENTRATION

Concentrated samples more reliable than dilute samples

TEMP WITHIN 4 MIN OF VOIDING IS 90-100°F

PH FLUCTUATES WITHIN RANGE OF 4.5-8.0

CREATININE VARIATES W/ HYDRATION

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

INTERPRETATION OF UDT RESULTS

NEGATIVE RESULT

- Demonstrates recent use
  - Most drugs in urine have detection times of 1-3 d
  - Chronic use of lipid-soluble drugs: test positive for ≥1 wk
- 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
  - Bingeing, running out early
  - Other factors: eg, cessation of insurance, financial difficulties

POSITIVE RESULT

EXAMPLES OF METABOLISM OF OPIOIDS

- CODEINE → MORPHINE
- MORPHINE → 6-MAM
- 6-MAM → HYDROCODONE
- 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 on all 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 PPAs, and other tools.

PART 2
DISCONTINUING

REASONS FOR DISCONTINUING OPIOIDS

- Pain level decreases in stable patients
- Intolerable & unmanageable AES
- No progress toward therapeutic goals
- Misuse
  - 1 or 2 episodes of increasing dose without prescriber knowledge
  - Sharing medications
  - Unapproved opioid use to treat another symptom (e.g., insomnia)
- Aberrant behaviors
  - 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 & 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 and 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

Tom has back pain. He is managed by taking oxycodone [40mg BID] but wants to decrease his dose when he can, thus he requests only 20mg pills. He often brings in unused meds to show how he is trying to reduce his dose. He resists any change.

**Action:**
Do not allow patient to taper on their own. Create an endpoint for the taper. See patient once a week with a seven-day supply for the tapering until they are off opioids. Document teaching, patient’s comments about the plan, UDT, pill counts, non-pharmacological modalities for pain management and their adherence to the plan.

**SPECIAL POPULATIONS**

**CHAPTER 6**

**OLDER ADULTS**

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

**MONITOR**
- Initiation & 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 low, go slow, but GO
- Patient and caregiver reliability/risk of diversion

**ROUTINE INITIATE A BOWEL REGIMEN**
WOMEN WITH CHILDBEARING POTENTIAL

KNOW THE REPRODUCTIVE PLANS & 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 don’t know they’re 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 & benefits of opioid therapy during pregnancy & after delivery
- Encourage minimal/no opioid use during pregnancy, unless potential benefits outweigh risks to fetus
- Refer to a high risk OBGyn who will insure appropriate treatment for the baby

- If chronic opioid therapy is used during pregnancy, anticipate & manage risks to the patient and newborn
- If they are using opioids on a daily basis, consider Naloxone or Buprenorphine

CHILDREN & ADOLESCENTS: HANDLE WITH CARE

JUDICIOUS USE OF IR FOR BRIEF THERAPY

SAFETY & EFFECTIVENESS OF MOST ER/LA OPIOIDS UNESTABLISHED

- Pediatric analgesic trials pose challenges
- Transdermal fentanyl approved in children aged ≥2 yrs
- Oxycodone ER dosing changes for children ≥11 yrs

ER/LA OPIOID INDICATIONS ARE PRIMARILY LIFE-LIMITING CONDITIONS

WHEN PRESCRIBING ER/LA 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 Thelma. In your exam you find bruising on right forearm. Thelma says she fell against the wall.

Action: Based on exam findings and her request for more medication:
- UDT and PDMP check
- Social service to see in clinic and at home for a vulnerable adult evaluation
- Patient education: Don’t 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 & STATE LAWS

FEDERAL & STATE REGULATIONS

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

FEDERAL
- Code of Federal Regulations, Title 21 Section 1306: rules governing the issuance & 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

STATE
- Database of state statutes, regulations, & policies for pain management
- Database of state statutes, regulations, & policies for pain management
PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

INDIVIDUAL STATE LAWS DETERMINE
- Who has access to PDMP information
- Which drug schedules are monitored
- Which agency administers the PDMP
- Whether prescribers are required to register w/ 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

NOT ALL FEDERALLY LICENSED FACILITIES REPORT TO PDMPs

PDMP BENEFITS

Provides full accounting of prescriptions filled by patient

<table>
<thead>
<tr>
<th>RECORD OF A PATIENT’S CONTROLLED SUBSTANCE PRESCRIPTIONS</th>
<th>PROVIDE WARNINGS OF POTENTIAL MISUSE/ABUSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Some are available online 24/7</td>
<td>• Existing prescriptions not reported by patient</td>
</tr>
<tr>
<td>• Opportunity to discuss w/ patient</td>
<td>• Multiple prescribers/pharmacies</td>
</tr>
<tr>
<td></td>
<td>• Drugs that increase overdose risk when taken together</td>
</tr>
<tr>
<td></td>
<td>• Patient pays for drugs of abuse w/ cash</td>
</tr>
</tbody>
</table>

State Specific Information
Michigan
www.michigan.gov/mdhhs/
Created: August 2016
Michigan Data

Overdose deaths: 1762 (2014)
Rate of prescribing: 96-143 per 100 people (2012)

Content Outline

- Prescription Drug Monitoring Program (PDMP)
- Prescriber Status and Education Requirements
- Naloxone Regulation
- Medical Marijuana Status
- Patient Prescriber Agreement and Treatment Programs

PDMP: Prescription Drug Monitoring Program

General
- Michigan Automated Prescription System (MAPS)
  www.michigan.gov/mimapsinfo
- Administered by Department of Licensing and Regulatory Affairs
- Schedule II-V are monitored
- Prescribers are required to register and input data
- Before prescribing, there is no obligation to review under certain circumstances

Access
- Prescribers, dispensers, law enforcement and judicial/prosecutorial officials; licensing/regulatory boards; state-operated Medicaid program; health care payment or benefit provider
- Prescribers cannot authorize a registered delegate

Reporting
- Must be entered into PDMP 24 hours after dispensing
- Unsolicited reports/alerts sent to prescribers
- Michigan does share data with other states' PDMP
- Out-of-state pharmacies are required to report to the patient's home state
- Patient will not be notified if their record has been accessed
Prescriber Status and Education Requirements

<table>
<thead>
<tr>
<th>Prescriber Status</th>
<th>Physician</th>
<th>Physician Assistant</th>
<th>Advanced Practice Nurse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensed</td>
<td>Schedule II-V</td>
<td>Schedule III-V</td>
<td></td>
</tr>
<tr>
<td>Education Requirements</td>
<td>None</td>
<td>None</td>
<td>1 hr/2 yrs</td>
</tr>
</tbody>
</table>

Dr. Vincent Beswick-Escanlar compiled information for a sub work group of the SAMHSA Liaison Quarterly meeting on March 10, 2016.


Naloxone Regulation

Effective date: October 2014

- Prescribers: Yes
- Dispensers: Yes
- Lay People: Yes

Prescribing Permitted:
- 3rd Party Status: Yes
- Standing Order: No

Available without a prescription: No

Who carries it: Paramedics and Advanced Emergency Techs only


Medical Marijuana Status

- It is legal to prescribe

Patient Prescriber Agreement and Treatment Programs

- A Patient Prescriber Agreement (PPA) is recommended
  http://www.namsdl.org/library/7440B2D5-788C-5D71-B596D97CE6EA4A5F

- For a list of treatment programs in this state:
  http://americanaddictioncenters.org/rehab-guide/state-funded/#how-to-find-state-funded-rehab
CANNABIS

- DEA Schedule I ("high abuse potential") yet state regulations vary
- There is good 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 while managing pain. This history does not mean you should discharge or avoid treating the patient’s pain.
CHAPTER 8
COUNSELING PATIENTS & CAREGIVERS

USE PATIENT COUNSELING DOCUMENT
DOWNLOAD:
ORDER HARD COPIES:
www.minneapolis.cenveo.com/pcd/SubmitOrders.aspx


COUNSEL PATIENTS ABOUT PROPER USE

EXPLAIN
• Product-specific information about the prescribed IR or ER/LA opioid
• Take opioid as prescribed
• Adhere to dose regimen
• How to handle missed doses
• Notify prescriber if pain not controlled
• Call prescriber for info on handling side effects

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**

**OPIOIDS CAN CAUSE DEATH EVEN WHEN TAKEN PROPERLY**

- Inform prescriber of ALL meds being taken
- Warn patients not to abruptly discontinue or reduce dose
- Risk of falls
- Caution with operating heavy machinery & when driving
- Sharing or selling opioids can lead to others’ deaths & is against the law.
- Signs/symptoms are respiratory depression, gastrointestinal obstruction, allergic reactions

**OPIOIDS SHOULD BE STORED IN A SAFE & SECURE PLACE**

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

Opioids are scheduled under Controlled Substances Act and can be misused & 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 & 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 w/ ER/LA opioids can cause overdose & death

- Use with alcohol may result in rapid release & absorption of a potentially fatal opioid dose – “dose dumping”
- Other depressants include sedative-hypnotics & anxiolytics, illegal drugs

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OVERDOSE POISONING, CALL 911

- Person can not 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

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

ABUSE DETERRENT/TAMPER RESISTANT OPIOIDS

- Response to growing nonmedical 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
**TALK WITH YOUR PATIENTS WHO ARE PARENTS**

- Consider the behavior you are modeling
- 45% of parents have taken pain medications w/o a prescription at some point
- 14% have given their children pain medications w/o 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

**REMEMBER…**

**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

**RX OPIOID DISPOSAL**

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

- Collection receptacles
  - Call DEA Registration Call Center at 1-800-882-9539 to find a local collection receptacle
- Mail-back packages
  - Obtained from authorized collectors

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

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

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

© CO*RE 2017
OTHER METHODS OF OPIOID DISPOSAL

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

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

FDA: PRESCRIPTION DRUG DISPOSAL

- 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 exception: can seal in Patch-Disposal Unit provided & dispose of in the trash

CHAPTER 8 – PEARLS FOR PRACTICE

- Use formal tools (PPAs, counseling document) to educate patients and caregivers
- Emphasize patients and caregivers safe storage and disposal
- Consider co-prescribing Naloxone
**Challenge: The Daughter’s Party**

**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.

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**Chapter 9**

**Drug Class Considerations**

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**For Safer Use: Know Drug Interactions, PK, & PD**

- CNS depressants can potentiate sedation & respiratory depression
- Use w/ MAOIs may increase respiratory depression
- Certain opioids w/ MAOIs can cause serotonin syndrome
- Methadone & 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
- Can reduce efficacy of diuretics
- Inducing release of antidiuretic hormone
- Drugs that inhibit or induce CYP enzymes can increase or lower blood levels of some opioids
**TRANSDERMAL/TRANSMUCOSAL DOSAGE FORMS**

Do not cut, damage, chew, or swallow

- Exertion or exposure to external heat can lead to fatal overdose
- Rotate location of application
- Prepare skin: clip - not shave - hair & wash area w/ water
- Monitor patients w/ 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 anyway. Use entire film.

---

**DRUG INTERACTIONS COMMON TO OPIOIDS**

- Concurrent use w/ other CNS depressants can increase risk of respiratory depression, hypotension, profound sedation, or coma
- Reduce initial dose of one or both agents
- May enhance neuromuscular blocking action of skeletal muscle relaxants & increase respiratory depression
- Concurrent use w/ anticholinergic medication increases risk of urinary retention & 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 &/or precipitate withdrawal

* Examples: (Narcotic antagonists, buspirone, haloperidol)
† Examples: (Narcotic antagonists, naloxone, naltrexone)

For buccal film products the film should not be applied if it is cut, damaged or changed in anyway. Use entire film.

---

**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

For detailed information, refer to online PI:
- Drugs@FDA at www.fda.gov/drugs@fda

SUMMARY

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

- Assess patients for treatment w/ IR and ER/LA opioids
- Initiate therapy, modify dose & discontinue use of opioids
- Monitor ongoing therapy w/ IR and ER/LA opioids
- Counsel patients & caregivers about the safe use of opioids, including proper storage & disposal
- Be familiar w/ general & product-specific drug information concerning opioids

TO OUR LEARNERS

Our Session Stops here, but your review continues...

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

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THANK YOU!

The following individuals disclose no relevant financial relationships:

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<table>
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<th>Affiliation</th>
</tr>
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<thead>
<tr>
<th>External/Consulting Reviewer</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roberto Cardarelli, DO, MPH</td>
<td>Assistant Professor, Department of Family Medicine, University of Kentucky College of Medicine</td>
</tr>
<tr>
<td>Monica Suttles, RN</td>
<td>OMM by Design</td>
</tr>
</tbody>
</table>
### The following individuals disclose no relevant financial relationships:

#### CO*RE Partner Staff COI

<table>
<thead>
<tr>
<th>Staff Person</th>
<th>Partner Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Julie Bruno</td>
<td>American Academy of Hospice and Palliative Medicine</td>
</tr>
<tr>
<td>Michele McKay</td>
<td>American Association of Nurse Practitioners</td>
</tr>
<tr>
<td>Anne Norman</td>
<td>American Academy of Physician Assistants</td>
</tr>
<tr>
<td>Eric Peterson</td>
<td>American Osteopathic Association</td>
</tr>
<tr>
<td>Penny Yolls</td>
<td>American Society of Addiction Medicine</td>
</tr>
<tr>
<td>Marie-‐Michele Leger</td>
<td>American Psychiatric Association</td>
</tr>
<tr>
<td>Eric Peterson</td>
<td>American Academy of Physician Assistants</td>
</tr>
</tbody>
</table>

#### CO*RE Operations Organizations

<table>
<thead>
<tr>
<th>Staff Person</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cynthia Kear</td>
<td>LLC</td>
</tr>
<tr>
<td>Katie Detzler</td>
<td>LLC</td>
</tr>
<tr>
<td>Robin Haydak</td>
<td>LLC</td>
</tr>
</tbody>
</table>

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Appendix 1. Specific Drug Information for ER/LA Opioid Analgesic Products

For the ER/LA opioids you frequently use, know:
• Formulation availability
• Dosing intervals
• Key instructions
• Drug interactions
• Opioid-tolerant information
• Product specific adverse reactions
• Relative potency: morphine

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-naïve 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**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Once a day</th>
</tr>
</thead>
</table>
|  **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** | • 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** | • 90 mg & 120 mg capsules for use in opioid-tolerant patients only |
| **Product-specific safety concerns** | • None |

* MDD=maximum daily dose; P-gp= P-glycoprotein

### Buprenorphine Buccal Film (Belbuca)

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

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Every 12 h (or once every 24 h for initiation in opioid naive patients &amp; patients taking less than 30 mg oral morphine sulfate eq)</th>
</tr>
</thead>
</table>
|  **Key instructions** | • Opioid-naive pts or pts taking <30 mg oral morphine sulfate eq: Initiate treatment with a 75 mcg buccal film, once daily, or if tolerated, every 12 h  
- Titrate to 150 mcg every 12 h no earlier than 4 d after initiation  
- Individual titration to a dose that provides adequate analgesia and minimizes adverse reaction should proceed in increments of 150 mcg every 12 h, no more frequently than every 4 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 mcg dose every 12 h  
- If prior daily dose before taper was 90 mg to 160 mg oral morphine sulfate eq, initiate with 300 mcg dose every 12 h  
- Titration of the dose should proceed in increments of 150 mcg every 12 h, no more frequently than every 4 d |

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### Buprenorphine Buccal Film (Belbuca) continued

#### Key instructions
- Maximum dose: 900 mcg every 12 h due to the potential for QTc prolongation
- Severe Hepatic Impairment: Reduce the starting and incremental dose by half that of patients with normal liver function
- Oral Mucositis: Reduce the starting and incremental dose by half that of patients without mucositis
- Do not use if the package seal is broken or the film is cut, damaged, or changed in any way

#### 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 mcg, 750 mcg, and 900 mcg are for use following titration from lower doses of Belbuca

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

#### Relative Potency: Oral Morphine
- Equipotency to 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/h
- When converting from 30 mg-80 mg morphine equivalents, first taper to 30 mg morphine equivalent, then initiate w/ 10 mcg/h
- Titrate in 5 or 10 mcg/h increments by using no more than 2 patches of the 5 or 10 mcg/h system(s) w/ minimum of 72 h prior between dose adjustments. Total dose from all patches should be ≤20 mcg/h
- Maximum dose: 20 mcg/h 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)
  - Do not cut
- Avoid exposure to heat
- Dispose of patches: fold adhesive side together & flush down toilet
### Buprenorphine Transdermal System (Butrans) continued

<table>
<thead>
<tr>
<th>Drug interactions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• CYP3A4 inhibitors may increase buprenorphine levels</td>
<td></td>
</tr>
<tr>
<td>• CYP3A4 inducers may decrease buprenorphine levels</td>
<td></td>
</tr>
<tr>
<td>• Benzodiazepines may increase respiratory depression</td>
<td></td>
</tr>
<tr>
<td>• Class IA &amp; III antiarrythmics, other potentially arrhythmogenic agents, may increase risk of QTc prolongation &amp; torsade de pointe</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• 7.5 mcg/h, 10 mcg/h, 15 mcg/h, &amp; 20 mcg/h for use in opioid-tolerant patients only</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product-specific safety concerns</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• QTc prolongation &amp; torsade de pointe</td>
<td></td>
</tr>
<tr>
<td>• Hepatotoxicity</td>
<td></td>
</tr>
<tr>
<td>• Application site skin reactions</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative potency: oral morphine</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Equipotency to oral morphine not established</td>
<td></td>
</tr>
</tbody>
</table>

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### Methadone Hydrochloride Tablets (Dolophine)

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Every 8 to 12 h</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key instructions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Initial dose in opioid non-tolerant patients: 2.5 – 10 mg</td>
<td></td>
</tr>
<tr>
<td>• Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose &amp; death. Use low doses according to table in full PI</td>
<td></td>
</tr>
<tr>
<td>• Titrate slowly with dose increases no more frequent than every 3-5 d. Because of high variability in methadone metabolism, some patients may require substantially longer periods between dose increases (up to 12 d).</td>
<td></td>
</tr>
<tr>
<td>• High inter-patient variability in absorption, metabolism, &amp; relative analgesic potency</td>
<td></td>
</tr>
<tr>
<td>• Opioid detoxification or maintenance treatment only provided in a federally certified opioid (addiction) treatment program (CFR, Title 42, Sec 8)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug interactions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pharmacokinetic drug-drug interactions w/ methadone are complex</td>
<td></td>
</tr>
<tr>
<td>− CYP 450 inducers may decrease methadone levels</td>
<td></td>
</tr>
<tr>
<td>− CYP 450 inhibitors may increase methadone levels</td>
<td></td>
</tr>
<tr>
<td>− Anti-retroviral agents have mixed effects on methadone levels</td>
<td></td>
</tr>
<tr>
<td>• Potentially arrhythmogenic agents may increase risk for QTc prolongation &amp; torsade de pointe</td>
<td></td>
</tr>
<tr>
<td>• Benzodiazepines may increase respiratory depression</td>
<td></td>
</tr>
</tbody>
</table>

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## Methadone Hydrochloride Tablets (Dolophine) continued

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
<th>• Refer to full PI</th>
</tr>
</thead>
</table>
| Product-specific safety concerns | - QTc prolongation & torsade de pointe  
- Peak respiratory depression occurs later & persists longer than analgesic effect  
- Clearance may increase during pregnancy  
- False-positive UDT possible |
| Relative potency: oral morphine | • Varies depending on patient's prior opioid experience |

## Fentanyl Transdermal System (Duragesic)

12, 25, 37.5*, 50, 62.5*, 75, 87.5*, and 100 mcg/hr  
(*These strengths are available only in generic form)

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Every 72 h (3 d)</th>
</tr>
</thead>
</table>
| 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 |
**Fentanyl Transdermal System (Duragesic), continued**

<table>
<thead>
<tr>
<th>Key instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Specific contraindications:</strong></td>
</tr>
<tr>
<td>- Patients who are not opioid-tolerant</td>
</tr>
<tr>
<td>- Management of</td>
</tr>
<tr>
<td>- Acute or intermittent pain, or patients who require opioid analgesia for a short time</td>
</tr>
<tr>
<td>- Post-operative pain, out-patient, or day surgery</td>
</tr>
<tr>
<td>- Mild pain</td>
</tr>
<tr>
<td>- CYP3A4 inhibitors may increase fentanyl exposure</td>
</tr>
<tr>
<td>- CYP3A4 inducers may decrease fentanyl exposure</td>
</tr>
<tr>
<td>- Discontinuation of concomitant CYP P450 3A4 inducer may increase fentanyl plasma concentration</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
</tr>
</thead>
<tbody>
<tr>
<td>All doses indicated for opioid-tolerant patients only</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Accidental exposure due to secondary exposure to unwashed/unclothed application site</td>
</tr>
<tr>
<td>- Increased drug exposure w/ increased core body temp or fever</td>
</tr>
<tr>
<td>- Bradycardia</td>
</tr>
<tr>
<td>- Application site skin reactions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product-specific safety concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>- See individual PI for conversion recommendations from prior opioid</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative potency: oral morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Morphine Sulfate ER-Naltrexone (Embeda)</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Dosing interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Once a day or every 12 h</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Alcoholic beverages or medications w/ alcohol may result in rapid release &amp; absorption of potentially fatal dose</td>
</tr>
<tr>
<td>- P-gp inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 100 mg/4 mg capsule for use in opioid-tolerant patients only</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product-specific safety concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>- None</td>
</tr>
</tbody>
</table>
### Hydromorphone Hydrochloride (Exalgo)

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

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Once a day</th>
</tr>
</thead>
</table>

| 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 are indicated for opioid-tolerant patients only |
| Product-specific adverse reactions | • Allergic manifestations to sulfite component |
| Relative potency: oral morphine | • ~5:1 oral morphine to hydromorphone oral dose ratio, use conversion recommendations in individual product information |

### Hydrocodone Bitartrate (Hysingla ER)

**ER Tablets, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg, 120 mg**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Once a day</th>
</tr>
</thead>
</table>

| Key instructions | • Opioid-naive 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. |

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### Hydrocodone Bitartrate (Hysingla ER) Continued

**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**
- See individual PI for conversion recommendations from prior opioid.

### Morphine Sulfate (Kadian)

**ER Capsules 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 80 mg, 100 mg, 130 mg, 150 mg, 200 mg**

**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

**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 absorption/exposure of morphine by ~2-fold

**Opioid-tolerant**
- 100 mg, 130 mg, 150 mg, 200 mg capsules for use in opioid-tolerant patients only

**Product-specific safety concerns**
- None
### Morphine Sulfate (MorphaBond)
ER Tablets 15 mg, 30 mg, 60 mg, 100 mg

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Every 8 h or every 12h</th>
</tr>
</thead>
</table>
| 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 |
| Product-specific safety concerns | • None |

### Morphine Sulfate (MS Contin)
ER Tablets 15 mg, 30 mg, 60 mg, 100 mg, 200mg

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Every 8 h or every 12 h</th>
</tr>
</thead>
</table>
| 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) |
| Drug interactions | • P-gp inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold |
| Opioid-tolerant | • 100 mg & 200 mg tablet strengths for use in opioid-tolerant patients only |
| Product-specific safety concerns | • None |
**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>
</table>
| Key instructions | • 50 mg every 12 h is initial dose in opioid non-tolerant patients  
• Titrate by 50 mg increments using minimum of 3-d intervals  
• MDD: 500 mg  
• Swallow tablets whole (do not chew, crush, or dissolve)  
• Take 1 tablet at a time w/ enough water to ensure complete swallowing immediately after placing in mouth  
• Dose once/d in moderate hepatic impairment (100 mg/d max)  
• Avoid use in severe hepatic & renal impairment |
| Drug interactions | • Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of a potentially fatal dose of tapentadol  
• Contraindicated in patients taking MAOIs |
| Opioid-tolerant | • No product-specific considerations |
| Product-specific safety concerns | • Risk of serotonin syndrome  
• Angio-edema |
| Relative potency: oral morphine | • Equipotency to oral morphine has not been established |

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**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>
</table>
| Key instructions | • Use 5 mg every 12 h as initial dose in opioid non-tolerant patients & patients w/ mild hepatic impairment & renal impairment (creatinine clearance <50 mL/min) & patients >65 yrs  
• Swallow tablets whole (do not chew, crush, or dissolve)  
• Take 1 tablet at a time, w/ enough water to ensure complete swallowing immediately after placing in mouth  
• Titrate in increments of 5-10 mg using a minimum of 3-7 d intervals  
• Contraindicated in moderate & severe hepatic impairment |
| Drug interactions | • Alcoholic beverages or medications w/ alcohol may result in absorption of a potentially fatal dose of oxymorphone |
| Opioid-tolerant | • No product-specific considerations |
| Product-specific safety concerns | • Use with caution in patients who have difficulty swallowing or underlying GI disorders that may predispose to obstruction (e.g. small gastrointestinal lumen) |
| Relative potency: oral morphine | • Approximately 3:1 oral morphine to oxymorphone oral dose ratio |
### Oxycodone Hydrochloride (OxyContin)

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

#### Key instructions

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Every 12 h</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key instructions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Initial dose in opioid-naive and non-tolerant patients: 10 mg every 12 h</td>
<td></td>
</tr>
<tr>
<td>• Titrate using a minimum of 1-2 d intervals</td>
<td></td>
</tr>
<tr>
<td>• Hepatic impairment: start w/ ¼-½ 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>
<tr>
<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>
<td></td>
</tr>
<tr>
<td>• Take 1 tablet at a time, w/ enough water to ensure complete swallowing immediately after placing in mouth</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug interactions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• CYP3A4 inhibitors may increase oxycodone exposure</td>
<td></td>
</tr>
<tr>
<td>• CYP3A4 inducers may decrease oxycodone exposure</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• For Adults: Single dose &gt;40 mg or total daily dose &gt;80 mg for use in opioid-tolerant patients only</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product-specific safety concerns</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Choking, gagging, regurgitation, tablets stuck in throat, difficulty swallowing tablet</td>
<td></td>
</tr>
<tr>
<td>• Contraindicated in patients w/ GI obstruction</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative potency: oral morphine</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Approximately 2:1 oral morphine to oxycodone oral dose ratio</td>
<td></td>
</tr>
</tbody>
</table>

**For Adults:**

- Single dose greater than 40 mg or total daily dose greater than 80 mg are for use in adult patients in whom tolerance to an opioid of comparable tolerance has been established.
- When a dose increase is clinically indicated, the total daily oxycodone dose usually can be increased by 25% to 50% of the current dose.

**For Pediatric Patients (11 years and older):**

- For use only in opioid tolerant pediatric patients already receiving and tolerating opioids for at least five (5) consecutive days with a minimum of 20 mg per day of oxycodone or its equivalent for at least 2 days immediately preceding dosing with Oxycontin ER.

- Renal impairment (creatinine clearance <60 mL/min): start w/ ½ usual dosage
- If needed, pediatric dose may be adjusted in 1 to 2 day intervals.
- When a dose increase is clinically indicated, the total daily oxycodone dose usually can 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.
### Oxycodone Hydrochloride/Naloxone Hydrochloride (Targiniq ER)

**Dosing interval**
- Every 12 h

<table>
<thead>
<tr>
<th>Key instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid-naive patients:</strong> initiate treatment w/ 10mg/5mg every 12 h</td>
</tr>
<tr>
<td>Titrate using min of 1-2 d intervals</td>
</tr>
<tr>
<td>Do not exceed 80 mg/40 mg total daily dose (40 mg/20 mg q12h)</td>
</tr>
<tr>
<td>May be taken w/ or without food</td>
</tr>
<tr>
<td>Swallow whole. Do not chew, crush, split, or dissolve: this will release oxycodone (possible fatal overdose) &amp; naloxone (possible withdrawal)</td>
</tr>
<tr>
<td>Hepatic impairment: contraindicated in moderate-severe impairment. In patients w/ mild impairment, start w/ ⅓-½ usual dosage</td>
</tr>
<tr>
<td>Renal impairment (creatinine clearance &lt;60 mL/min): start w/ ½ usual dosage</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug interactions</th>
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</thead>
<tbody>
<tr>
<td>CYP3A4 inhibitors may increase oxycodone exposure</td>
</tr>
<tr>
<td>CYP3A4 inducers may decrease oxycodone exposure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose &gt;40 mg/20 mg or total daily dose of 80 mg/40 mg for opioid-tolerant patients only</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product-specific safety concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraindicated in patients w/ moderate-severe hepatic impairment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative potency: oral morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>See individual PI for conversion recommendations from prior opioids</td>
</tr>
</tbody>
</table>

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### Oxycodone Hydrochloride/Naltrexone Hydrochloride (Troxvca ER)

**Dosing interval**
- Every 12 h

<table>
<thead>
<tr>
<th>Key instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid-naive &amp; non-tolerant patient:</strong> is 10/1.2 mg, every 12 h</td>
</tr>
<tr>
<td>Total daily dose may be adjusted by 20/2.4 mg every 2-3 d</td>
</tr>
<tr>
<td>Swallow capsules whole (do not chew, crush, or dissolve); possible fatal overdose, and naltrexone (possible withdrawal)</td>
</tr>
<tr>
<td>May open capsule &amp; sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately</td>
</tr>
<tr>
<td>Do not administer through NG or G tube</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP3A4 inhibitors may increase hydrocodone exposure</td>
</tr>
<tr>
<td>CYP3A4 inducers may decrease hydrocodone exposure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose &gt;40/4.8 mg or total daily dose &gt;80/9.6 mg for use in opioid-tolerant patients only</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product-specific safety concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative potency: oral morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>See individual product information for conversion recommendations from prior opioid</td>
</tr>
</tbody>
</table>
### Hydrocodone Bitartrate (Vantrela ER)

**ER Tablets 15 mg, 30 mg, 45 mg, 60 mg, 90 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 naive and non-tolerant patient is 15 mg every 12 h. Dose can be increased to next higher dose every 3-7 d&lt;br&gt;• Swallow capsules whole (do not chew, crush, or dissolve)&lt;br&gt;• 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>
</tr>
<tr>
<td>Drug interactions</td>
<td>• CYP3A4 inhibitors may increase hydrocodone exposure&lt;br&gt;• CYP3A4 inducers may decrease hydrocodone exposure</td>
</tr>
<tr>
<td>Opioid-tolerant</td>
<td>• A 90 mg tablet, a single dose greater than 60 mg, or a total daily dose &gt;120 mg are for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>Product-specific safety concerns</td>
<td>• None</td>
</tr>
<tr>
<td>Relative potency: oral morphine</td>
<td>• See individual product information for conversion recommendations from prior opioid</td>
</tr>
</tbody>
</table>

### Oxycodone (Xtampza ER)

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

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Every 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key instructions</td>
<td>• Opioid naive and non-tolerant, initiate with 9 mg every 12 h&lt;br&gt;• Titrate using a minimum of 1-2 d intervals&lt;br&gt;• Take with same amt of food in order to ensure consistent plasma levels&lt;br&gt;• Maximum daily dose: 288 mg (8 x 36 mg), safety of excipients not established for higher doses&lt;br&gt;• May open capsule &amp; sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately&lt;br&gt;• May also be administered through a NG or G feeding tube&lt;br&gt;• Hepatic impairment: initiate therapy at 1/3 to ½ usual dose&lt;br&gt;• Renal impairment: creatinine clearance &lt;60 mL/min, follow conservative approach</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>• CYP3A4 inhibitors may increase hydrocodone exposure&lt;br&gt;• CYP3A4 inducers may decrease hydrocodone exposure</td>
</tr>
<tr>
<td>Opioid-tolerant</td>
<td>• A single dose &gt;36 mg or a total daily dose &gt;72 mg for opioid-tolerant patients only</td>
</tr>
<tr>
<td>Product-specific safety concerns</td>
<td>• None</td>
</tr>
<tr>
<td>Relative potency: oral morphine</td>
<td>• There are no established conversion ratios for Xtampza ER, defined by clinical trials</td>
</tr>
</tbody>
</table>
**Naloxone (Narcan)**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>IM or SQ: onset 2-5 minutes, duration &gt;45 min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV: onset 1-2 min, duration 45 minutes</td>
</tr>
<tr>
<td></td>
<td>IN: onset 2-3 min, duration ~ 2 hours</td>
</tr>
</tbody>
</table>

| 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 |

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**Hydrocodone Bitartrate (Zohydro ER)**

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

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>Every 12 h</th>
</tr>
</thead>
</table>

| 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 |

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