SAFE Opioid Prescribing: ER/LA Opioids - Perspectives on Patient Assessment and Therapy Management

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Presenter Disclosure Information
The following relationships exist related to this presentation:

Charles Argoff, MD, FABPM: Speakers bureaus for Allergan, Inc.; Depomed, Inc.; Janssen Pharmaceuticals, Inc.; Millennium Laboratories, LLC; XenoPort, Inc. Advisory boards for Acorda Therapeutics, Inc.; AstraZeneca Pharmaceuticals LP; Depomed, Inc.; Insys Therapeutics Inc.; Nektilar Therapeutics; Pfizer Inc.; Purdue Pharma L.P.; QRX Pharma Ltd; Teva Pharmaceuticals Industries Ltd.; XenoPort, Inc. Research support from Eli Lilly and Company; Endo Pharmaceuticals Inc.; Forest Laboratories, Inc.

Bill McCarberg, MD: Advisor for Iroko; NeurogesX; Pfizer Inc.; Salix; Sucampo; Teva Pharmaceuticals Industries Ltd.; Zogenix, Inc.

Off-Label/Investigational Discussion
In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

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This educational activity is supported by an independent educational grant from the ER/LA Opioid Analgesic REMS Program Companies (RPC). Please see www.er-la-opioidREMS.com for a listing of the member companies. This activity is fully-compliant with the ER/LA Opioid Analgesics REMS education requirements issued by the U.S. Food & Drug Administration (FDA).

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Overall Program Learning Objectives
Upon completion of this initiative, the participants will be better able to:

Implement patient assessment strategies, including tools to assess risk of abuse, misuse, or addiction when prescribing extended-release (ER/LA) opioids

Employ approaches to safely initiate therapy, modify dose, and discontinue ER/LA opioids

Monitor patients by evaluating treatment goals and implementing periodic urine drug testing (UDT)

Employ patient education strategies about the safe use of ER/LA opioids

Identify similarities and differences among ER/LA opioids
Background:

Painkiller Overdoses = Public Health Epidemic

- Overdose deaths from opioid analgesics
  - 16,917 in 2011; >4x # in 1999
  - This represents 41% of all fatal overdoses
  - Of opioid-analgesic deaths: Benzodiazepines involved in 31%; alcohol in 19%
- Almost 1 million people ≥12 years old reported nonmedical opioid use ≥200 days in 2009-2010; 4.6 million people reported such use for 30 days or more
  - Highest prescription painkiller overdose rates in middle-aged adults
  - Highest rates in rural counties
  - Highest rates in Whites and American Indians or Alaska Natives
  - Many more Rx opioid overdose deaths in men than women
- In 2009, nearly 500,000 ED/ER visits for Rx painkillers misuse or abuse
- Direct health care costs of nonmedical prescription painkiller use: $72.5 billion annually

While improper use of any opioid can result in serious side effects, including overdose and death, risks may be greater with Rx ER/LA Opioids

The Prevalence of Chronic Pain in the United States Is High

- Approximately 100 million US adults experience chronic pain (33%)
- Numerous studies indicate undertreated pain: eg, cancer, older adults, children, minorities
- Goal: define most appropriate analgesic regimen for each person in pain, which may include the use of ER/LA opioids

Goals of Risk Evaluation and Mitigation Strategy (REMS) CME on ER/LA Opioid Analgesics

- In 2012, the US Food and Drug Administration (FDA) directed all ER/LA opioid companies to provide independent CME grants to educate prescribers and to provide information for patients to:
  - Ensure that the benefits of ER/LA opioids outweigh the risks
  - Help to reduce risk for ER/LA opioid analgesics misuse, abuse, and overdose while ensuring access to pain medication
  - Follow FDA “Blueprint” on ER/LA opioids CME to engage and educate prescribers and be in compliance with standards for continuing education for physicians and other health care professionals, including Accreditation Council for Continuing Medical Education (ACCME)

This 6-Session Activity Is FDA REMS-Compliant CME

Goals of This REMS-Compliant Education for ER/LA Opioid Analgesics

- As clinicians, WE are best positioned to balance treatment of pain against risks of serious adverse outcomes, including addiction, unintentional overdose, and death
- In this 6-session curriculum, we will review many best-practice aspects of managing ER/LA opioid analgesic therapy
  - Patient assessment
  - Therapy initiation, dose modification, and discontinuation
  - Therapy management
  - Counseling of patients and caregivers
  - General drug information
  - Product-specific drug information

Learning Objectives for Session I

Upon completion of this module, the participants will be better able to:

- Identify risk factors for opioid-related aberrant behavior
- Differentiate among tolerance, physical dependence, and addiction
Opioid Therapy in Chronic Pain Management

- Opioids ARE commonly prescribed for chronic pain
  - Efficacious for many types of pain, though not necessarily for all people who experience a certain type of pain
  - Appropriate use is KEY to safety and success
- Goals of chronic opioid therapy:
  - Improve and/or stabilize pain intensity
  - Improve function
  - Improve quality of life (QOL)
- However, significant gaps exist between guideline recommendations for safe prescribing practices of ER/LA opioids and how they are being used in practice
  - Highlights need for further education


But There Are Also Risks

- Opioid analgesics are among the most commonly misused or abused pharmaceuticals
  - Over- or under-concern by physicians, patients, and/or caregivers is disruptive to physician-patient relationship as well as to effective care
  - Other drugs also commonly abused, eg, stimulants, benzodiazepines
- Misuse:
  - Using a medication other than as directed or indicated, whether intentional or not, and whether harm results or not
    - eg, taking more than recommended dose of an opioid analgesic because pain is poorly controlled
    - eg, offering opioid analgesics to another person who is in pain
- Abuse:
  - Intentionally taking a medication for a nonmedical purpose
    - eg, taking an opioid to get high
- Both misuse and abuse are of concern
  - Can lead to an overdose
  - Common misconception that because opioid is a prescription drug it is safe


Risk Factors Associated With ER/LA Opioids

- Overdose with ER/LA formulations
- Life-threatening respiratory depression
- Abuse by patient or household contacts
- Misuse and addiction
- Physical dependence and tolerance
- Interactions with other medications and substances
- Risk of neonatal opioid withdrawal syndrome with prolonged use during pregnancy
- Inadvertent exposure by household contacts, especially children


Who Misuses/Abuses Opioids and Why?

Nonmedical Use
- Recreational abusers
- Patients with disease of addiction

Medical Use
- Pain patients seeking more pain relief
- Pain patients escaping emotional pain


Key Concepts

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance</td>
<td>State of adaptation. Exposure to a drug induces changes that result in a diminution of 1 or more of the drug’s effects over time, indicated by a need for increasing doses to achieve the same effect. Commonly occurs with opioids. Tolerance is not indicative of addiction.</td>
</tr>
<tr>
<td>Physical Dependence</td>
<td>State of adaptation manifested by drug class-specific withdrawal syndrome that can occur with abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist. Physical dependence occurs in all patients using opioids for a period of time. Physical dependence is not indicative of addiction.</td>
</tr>
<tr>
<td>Addiction</td>
<td>A primary, chronic, neurobiologic disease with genetic, psychosocial, and environmental components. Characteristic behaviors include 1 or more of the following: impaired control over drug use, compulsive use, continued use despite harm, craving.</td>
</tr>
</tbody>
</table>

Tolerance, Dependence, and Addiction — Critical Differences

What a patient who has developed tolerance to the analgesic effect of the prescribed opioid would say to you:

"The fentanyl patch that you prescribed used to work really well, and now it doesn’t seem to be easing as much of the pain as before. I am worried."

What a patient who has become opioid-dependent will typically say to you:

"I went up to the lake this weekend and forgot to take along my long-acting morphine. I was without it for 2 days. I got so sick that I went to the ER."

The FDA Definition of Opioid Tolerance

- Opioid naïve vs opioid tolerant
- Patients are considered opioid tolerant if they are taking, for 1 week or longer, at least:
  - Oral morphine – 60 mg daily
  - Transdermal fentanyl – 25 mcg/h
  - Oral oxycodone – 30 mg daily
  - Oral hydromorphone – 8 mg daily
  - Oral oxymorphone – 25 mg daily
  - Equianalgesic daily dose of another opioid

Key Concepts

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<tbody>
<tr>
<td>Abuse</td>
<td>Any use of an illegal drug, or the intentional self-administration of a medication for a nonmedical purpose, such as altering one’s state of consciousness—for example, getting high</td>
</tr>
<tr>
<td>Misuse</td>
<td>Use of a medication (for a medical purpose) other than as directed or as indicated, whether willful or unintentional, and whether harm results or not</td>
</tr>
<tr>
<td>Aberrant Drug-Related Behavior</td>
<td>A behavior outside the boundaries of the agreed-on treatment plan</td>
</tr>
</tbody>
</table>

Examples of Misuse and Abuse

What patients will typically say to you:

"Sometimes in the morning I need to take extra pills just to get going..."

"My friend was visiting this weekend and had terrible back pain. I gave her one of my oxycodone pills. It really helped her. That’s OK, right?"

"That hydrocodone you gave my wife—well, it seems to make her feel a little too good sometimes. I think she’s taking more than you’ve prescribed and I’m worried about it..."

Prescribers Can Play an Active Role in Reducing the Risks Associated With Opioids

- Establish diagnosis
  - History and physical
  - Relevant diagnostic tests
- When opioids are being considered as part of acute or chronic pain treatment plan, complete an appropriate risk assessment
  - This is an active and ongoing process

Risk Factors for Opioid-Related Aberrant Behaviors

- Family history of substance abuse
  - Alcohol, illegal drugs, prescription drugs
  - Prescription drug abuse history carries greater risk
- Personal history of substance abuse
  - Alcohol, illegal drugs, prescription drugs
  - Prescription drug abuse history carries greater risk
- Age 16 to 45 years
- History of preadolescent sexual abuse
  - Increases risk for women
- Psychological disease
  - Attention deficit disorder (ADD) or depression
    - ADD carries higher risk

SOAPP — Sample Questions

Please answer the questions below, using the following scale:
0 = Never, 1 = Seldom, 2 = Sometimes, 3 = Often, 4 = Very Often

1. How often do you have mood swings? 0 1 2 3 4
2. How often do you smoke a cigarette within an hour after you wake up? 0 1 2 3 4
3. How often have you taken medication other than the way that it was prescribed? 0 1 2 3 4
4. How often have you used illegal drugs (for example, marijuana, cocaine, etc) in the past 5 years? 0 1 2 3 4
5. How often, in your lifetime, have you had legal problems or been arrested? 0 1 2 3 4

Opioid Risk Tool (ORT)

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk Factor</th>
<th>Score if Female</th>
<th>Score if Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History of Substance Abuse</td>
<td>Alcohol</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Illegal Drugs</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Prescription Drugs</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Personal History of Substance Abuse</td>
<td>Alcohol</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Illegal Drugs</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Prescription Drugs</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Age</td>
<td>Age 16-45 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>History of Preadolescent Sexual Abuse</td>
<td></td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Psychological Disease</td>
<td>ADD, OCD, Bipolar Disorder, Schizophrenia, Depression</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total Risk Score</td>
<td></td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

Test Score Risk Category
Low Risk 0-3 Moderate Risk 4-7 High Risk 8+ 

Accessed January 8, 2013. Reprinted with permission: Lynn Webster, MD.

Opioid Risk Tool (ORT) 

Risk Stratification and Monitoring Tools

<table>
<thead>
<tr>
<th>Risk Stratification Tool</th>
<th>Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screener and Opioid Assessment for Patients with Pain (SOAPP)</td>
<td><a href="http://www.painEDU.org">www.painEDU.org</a></td>
</tr>
<tr>
<td>Opioid Risk Tool (ORT)</td>
<td><a href="http://www.partnersagainstpain.com">www.partnersagainstpain.com</a></td>
</tr>
</tbody>
</table>

Meet Peter

- 45-year-old white male, railroad worker for line maintenance and reconstruction
- Suffering from chronic lower back and leg pain
- History of back pain prior to injury that led to surgery, otherwise healthy
- Still experiencing pain despite multiple treatments described below

History

- Injured at work; pain on lower right side, radiating down right leg to outside of foot
  - Pain described as aching and throbbing
  - Pain severity 6/10 at rest and 7-8/10 when bending, coughing, or straining with a bowel movement
- NSAIDs, muscle relaxant, and light work duty attempted
- Patient struggled on job, complaints of severe pain

NSAID, nonsteroidal anti-inflammatory drug.
Peter

History (cont)
• Physical therapy (PT), Xray, MRI (L5-S1 disc w impingement of S1 nerve root)
• Failed steroid taper, hydrocodone, epidural steroid, more PT
• Sleep deprived, anxious, withdrawn, financially stressed
• Surgery and rehabilitation – no improvement
• Pain specialist prescribed:
  - Oxycodone CR tablets 40 mg every 12 hours
  - Hydrocodone/acetaminophen 5/300 8/day for breakthrough pain
  - Gabapentin 300 mg/ 2 tablets TID
  - Zolpidem 10 mg/HS

Returns to your office for ongoing pain management

Opioid Therapy – Ongoing Monitoring

Next Steps: Make No Assumptions

➤ Even though the prescriber of the CR oxycodone and hydrocodeone/acetaminophen has evaluated Peter’s risk for opioid misuse before initiating these drugs, should you re-assess his level of risk now that the patient is back in your care?

Yes, because the risk level can change and you want to document you have performed a risk assessment

Peter’s Score on ORT

<table>
<thead>
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<th>Risk Factor</th>
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<tr>
<td></td>
<td>Prescription Drugs</td>
<td>4</td>
<td>4</td>
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<td>Alcohol</td>
<td>3</td>
<td>3</td>
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<tr>
<td></td>
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<td>4</td>
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<td></td>
<td>Prescription Drugs</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Age</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>History of Preadolescent Sexual Abuse</td>
<td>Alcohol</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Prescription Drugs</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Psychological Disease</td>
<td>ADD, ODD, Bipolar Disorder, Schizophrenia</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Depression</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total Risk Score</td>
<td></td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

Total Score Risk Category:
Low Risk 0–3 Moderate Risk 4–7 High Risk ≥ 8


Peter – Next Steps: Make No Assumptions

➤ Complete history and physical
➤ Ask Peter about his goals for treatment:
  • Explain that complete pain relief is rarely achieved
  • Focus on functional goals, eg, return to work, work part-time, able to play golf on weekends, able to walk the dog daily
➤ Risk for aberrant drug behavior – Moderate (4 on ORT)
➤ Evaluate mental health status
➤ Peter’s Rx: oxycodone CR, hydrocodone/APAP, gabapentin, zolpidem – any other Rx? OTC? Drug-drug interactions?
➤ Re-establish care with new treatment agreement and UDT
➤ Peter’s household – What is the possibility of inadvertent exposure to the opioids you are prescribing by household contacts, especially children? Have you discussed safe storage?

Additional Tools for Ongoing Monitoring

<table>
<thead>
<tr>
<th>Current Opioid Misuse Measure (COMM) – Sample Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ In the past 30 days, how often have you taken your medications differently than how they are prescribed?</td>
</tr>
<tr>
<td>➤ In the past 30 days, how much of your time was spent thinking about opioid medications (having enough, taking them, dosing schedule, etc)?</td>
</tr>
<tr>
<td>➤ In the past 30 days, how often have you had to visit the Emergency Room?</td>
</tr>
<tr>
<td>Available at <a href="http://www.painEDU.org">www.painEDU.org</a></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pain Assessment and Documentation Tool (PADT) – Sample Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ Is the patient’s functioning with the current pain reliever(s) better, the same, or worse since last assessment?</td>
</tr>
<tr>
<td>➤ Is patient experiencing any side effects from current pain reliever(s)?</td>
</tr>
<tr>
<td>➤ Checklist of potential aberrant drug-related behavior</td>
</tr>
<tr>
<td>Available at <a href="http://www.ucdenver.edu">www.ucdenver.edu</a></td>
</tr>
</tbody>
</table>
Best Practices for How to Start Therapy with ER/LA Opioids, How to Stop, and What to Do in Between

Learning Objectives for Session II

Upon completion of this module, the participants will be better able to:
- Convert patients from immediate-release to ER/LA opioids as well as from one ER/LA opioid to another
- Identify predisposing risk factors for significant respiratory depression

Key Principles of Safe Prescribing

- Know how to:
  - Identify the ER/LA opioid and dosage to use in the appropriate patient
  - Supplement pain management with immediate-release opioids and non-opioids
  - Convert patients from immediate-release to ER/LA opioids and from one ER/LA opioid to another
  - Identify the warning signs and symptoms AND PREDISPOSING RISK FACTORS for significant respiratory depression
  - Safely taper an opioid dose when therapy is no longer needed
- Keep current with regulations for opioid prescribing, both federal and those in your own state

Benefits and Limitations of ER/LA Opioids

Potential Benefits
- Provide more consistent plasma concentrations of drug compared with short-acting agents
- This minimizes serum level fluctuations that could contribute to end-of-dose breakthrough pain
- More consistent nighttime pain control
- Less clock-watching by patients
- Possible improved compliance/adherence due to a lower pill volume

Not for
- Not for as needed or “prn” use
- Not for mild pain
- Not for pain that is not expected to persist for an extended duration
- Not for acute pain
- Not for routine use in headache disorders or post-operative pain

ER/LA opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.


ER/LA Opioids – Contraindications

- Significant respiratory depression
- Acute or severe asthma in an unmonitored setting or in absence of resuscitative equipment
- Known or suspected paralytic ileus
- Hypersensitivity

Opioid-Naïve vs. Opioid-Tolerant

- Tolerance is a function of both time and dose
  - Patients who have not taken an opioid recently are considered opioid naïve
  - THESE patients are at greater risk for respiratory depression and sedation
Opioid Tolerance—Agents and Dosing
(Refer to full prescribing information)

<table>
<thead>
<tr>
<th>Agent (Transdermal)</th>
<th>Selected Doses for Use in Opioid-Tolerant Patients Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butrans (buprenorphine transdermal system)</td>
<td>10 mcg/hr to 20 mcg/hr, 15 mcg/hr to 30 mcg/hr, 20 mcg/hr to 40 mcg/hr, 25 mcg/hr to 50 mcg/hr, 30 mcg/hr to 60 mcg/hr, 40 mcg/hr to 80 mcg/hr</td>
</tr>
</tbody>
</table>

Opioid Tolerance—Agents and Dosing
(Refer to full prescribing information)

<table>
<thead>
<tr>
<th>Agent (Oral)</th>
<th>Selected Doses for Use in Opioid-Tolerant Patients Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av华人 (morphine sulfate ER capsules)</td>
<td>50 mg or 120 mg capsule for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>Embeda (morphine sulfate ER/naltrexone capsules)</td>
<td>100 mg/4 mg capsule for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>Hydromorphone (hydromorphone bitartrate ER tablets)</td>
<td>Daily dose greater than or equal to 80 mg is for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>Hydromorphone (hydromorphone ER tablets)</td>
<td>100 mg or 200 mg capsules for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>MS Contin (morphine sulfate ER tablets)</td>
<td>100 mg or 200 mg tablets for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>OxyContin (oxycodone hydrochloride CR tablets)</td>
<td>Single dose greater than 60 mg or total daily dose greater than 80 mg for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>OxyContin (oxycodone hydrochloride ER tablets)</td>
<td>Single dose greater than 40 mg, or total daily dose greater than 80 mg for use in opioid-tolerant patients only</td>
</tr>
<tr>
<td>Hydrocodone (hydrocodone HCl tablets)</td>
<td>When used as first opioid analgesic, initial therapy with small doses, no more than 2.5 mg to 10 mg every 4 to 8 hours</td>
</tr>
</tbody>
</table>

The FDA Definition of Opioid Tolerance

- Opioid naïve vs opioid tolerant
- Patients are considered opioid tolerant if they are taking, for 1 week or longer, at least:
  - Oral morphine – 60 mg daily
  - Transdermal fentanyl – 25 mcg/h
  - Oral oxycodone – 30 mg daily
  - Oral hydromorphone – 8 mg daily
  - Oral oxymorphone – 25 mg daily
  - Equianalgesic daily dose of another opioid
### Dose Selection and Titration

#### Initiating Therapy:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mg</td>
<td>Once a day</td>
</tr>
<tr>
<td>6 mg</td>
<td>Every 8 to 12 hours</td>
</tr>
<tr>
<td>9 mg</td>
<td>Every 8 to 12 hours</td>
</tr>
</tbody>
</table>

#### Opioids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dosing</th>
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<tbody>
<tr>
<td>Opioids ER/LA (oral formulations)</td>
<td>Every 12 hours</td>
</tr>
<tr>
<td>Opioids ER/LA (oral formulations)</td>
<td>Initial dose as first opioid (opioid-naive patients) is 2.5 mg to 10 mg</td>
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</tbody>
</table>

#### ER/LA Opioids

<table>
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<th>Drug</th>
<th>Initial Dosing</th>
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<td>ER/LA opioids</td>
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<tr>
<td>ER/LA opioids</td>
<td>Initial dose as first opioid (opioid-naive patients) is 2.5 mg to 10 mg</td>
</tr>
</tbody>
</table>

#### Special considerations

- **Initiation of therapy:**
  - Use product-specific information for dose conversion from prior opioid.
  - Use 50% usual dosage in mild or moderate hepatic or renal impairment.
  - Titrate using no less than 72-hour intervals.

- **Supplementing ER/LA opioids:**
  - Treat with nonopioid analgesics.
  - Treat with short-acting opioids.

- **No treatment:**
  - Continue with higher dose.

- **Increase dose:**
  - Increase dose of ER/LA opioid.

- **Reduce dose:**
  - Reduce dose of ER/LA opioid.

- **Stop all ongoing analgesics (if applicable):**
  - Benefit vs risk.

---

**Notes:**

- Initial dose as first opioid (opioid-naive patients) is 2.5 mg to 10 mg.
- Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose and death. Use low doses according to the table in the full prescribing information.
- Special considerations: Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be initiated and titrated cautiously by clinicians familiar with its use and risks (Refer to Module VI).

---

**References:**

Peter

- S/p lumbar fusion with chronic back and leg pain
- Returns to your primary care office for ongoing pain management
- Current medications:
  - Oxycodone CR tablets 40 mg every 12 hours
  - Hydrocodone/acetaminophen 5/300; 8/day for breakthrough pain
  - Gabapentin 300 mg/2 tabs TID
  - Zolpidem 10 mg/HS
- Goals of therapy:
  - Work a full day
  - Sleep through the night
  - Improve daytime somnolence
- Opioid rotation may be considered if goals of therapy are not met, adverse effects are intolerable, or to lower opioid dose

Rationale for Opioid Rotation

- Opioid rotation is switching from one opioid to another
- Rationale for opioid rotation:
  - Adverse effects or toxicity of initial opioid
  - Lack of efficacy of initial opioid
  - Lowering the dose
- Rotation may work because of:
  - Incomplete cross-tolerance among opioids
  - Inter-patient variability of response based on opioid receptor genetic polymorphisms

Note: Conservative dose-conversion ratios are advised

Equianalgesic Dose Table – An Example

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Equianalgesic (mg) Dose Oral</th>
<th>Equianalgesic (mg) Dose Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30 PO</td>
<td>10 IM/IV/SQ</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>7.5 PO</td>
<td>1.5 IM/IV/SQ</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>25-30 PO</td>
<td>No Information available</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>15 PO</td>
<td>1 IM/IV/SQ; 15 PR</td>
</tr>
<tr>
<td>Levorphanol</td>
<td>4 PO</td>
<td>2 IM/IV/SQ</td>
</tr>
<tr>
<td>Methadone</td>
<td>20 PO</td>
<td>10 IM/IV/SQ</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>55-100 mcg/IV/SQ</td>
<td></td>
</tr>
</tbody>
</table>

- Hydrocodone potency ranges 1:1 to 1:2 with morphine, but safest approach is 1:1
- Be aware that individual responses may vary
- Refer to individual full prescribing information (PI) for complete information

Incomplete Cross-Tolerance

- Pharmacologic phenomenon whereby tolerance developed to the effects of one drug translates into tolerance to other drugs from the same class
- Incomplete cross-tolerance: Failure to develop complete cross-tolerance, increasing the likelihood of therapeutic effects as well as adverse effects
- It is known to occur among opioids
- Mechanism behind opioid rotation
- Also reason for caution in converting from one opioid to another

Converting Patients From Immediate-Release to ER/LA Opioids or to Another ER/LA Agent

- Guidelines for select agents
  - Butrans (buprenorphine transdermal system)
    - Converting from 30-mg to 80-mg morphine equivalents:
      - First taper to 30-mg-morphine equivalent per day
      - Then initiate with 10-mg/hr dose
    - Dolophine (methadone HCl tablets)
      - Converting opioid-tolerant patients using equianalgesic tables can result in overdose and death.
      - To minimize risk, use low doses according to table in full PI
      - Note: Relative potency to oral morphine varies, depending on patient’s prior opioid experience
    - Duragesic (fentanyl transdermal system)
      - For relative potency to oral morphine, see individual product-specific PI for conversion recommendations from prior opioid

Always refer to full prescribing information (PI)
### Federal DEA Controlled Substance Schedules: ER/LA-Opioids are Schedule II

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Not currently accepted medical use in the U.S.; high potential for abuse</td>
<td>Heroin, LSD, marijuana, peyote, methaqualone, Ecstasy</td>
</tr>
<tr>
<td>II</td>
<td>High potential for abuse, which may lead to severe psychological or physical dependence</td>
<td>Hydrocodone, methadone, meperidine, oxycodone, oxymorphone, hydromorphone combination products (as of 10/6/14)</td>
</tr>
<tr>
<td>III</td>
<td>Potential for abuse, which may lead to moderate or low physical dependence or high psychological dependence</td>
<td>Products containing ≤ 50 mg codeine per dose, buprenorphine, benzphetamine, phenetermine, ketamine, anabolic steroids</td>
</tr>
<tr>
<td>IV</td>
<td>Low potential for abuse</td>
<td>Alprazolam, carisoprodol, clonazepam, clonazapate, diazepam, lorazepam, midazolam, temazepam, tramadol (as of 2014), triazolam</td>
</tr>
<tr>
<td>V</td>
<td>Low potential for abuse</td>
<td>Cough preparations containing ≤ 200 mg codeine per 100 ml or per 100 g, esgabine</td>
</tr>
</tbody>
</table>

State Laws/Regulations Vary. KNOW YOUR OWN STATE Rx REQUIREMENTS


### Converting Patients From Immediate-Release to ER/LA Opioids or to Another ER/LA Agent

- Exalgo (hydromorphone HCl ER tablets)
  - Use conversion ratios in individual product-specific PI
  - Relative potency to oral morphine approximately 2:1 oral to hydromorphone
- Hysingla ER (hydrocodone bitartrate)
  - See individual product-specific PI for conversion recommendations from prior opioid
- Nucynta ER (tapentadol HCl ER tablets)
  - Equi potency to oral morphine not established
- Opana ER (oxymorphone HCl ER tablets)
  - Relative potency to oral morphine approximately 3:1 oral to oxymorphone and dose ratio
- OxyContin (oxycodone HCl CR tablets)
  - Relative potency to oral morphine approximately 2:1 oral to oxycodone oral dose ratio
- Targin ER (oxycodone HCl/naloxone HCl tablets)
  - See individual product-specific PI for conversion recommendations from prior opioid


### Tapering and Discontinuing ER/LA Opioid Analgesics

- When ER/LA opioid analgesic is no longer required, gradually titrate downward to prevent signs and symptoms of withdrawal in the physically dependent patient
- Do not abruptly discontinue these products
  - Decrease original dose by 10% per week
- Abrupt discontinuation of chronic opioids may cause withdrawal characterized by:
  - Stomach cramps, diarrhea, rhinorrhea, sweating, elevated heart rate, increased blood pressure, irritability, dysphoria, hyperalgesia, and insomnia


Always refer to full prescribing information (PI)