1 – 3pm

SAFE Opioid Prescribing

SPEAKERS
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Michael Brennan, MD, FACP, FASAM

Presenter Disclosure Information

The following relationships exist related to this presentation:


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.

SAFE Opioid Prescribing

Strategies. Assessment. Fundamentals. Education

Extended-Release and Long-Acting Opioid Analgesics
Risk Evaluation and Mitigation Strategy (REMS)

Educational Grants in Support of this CME Activity

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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Pain and Palliative Care
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Swedish Medical Group
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Pain and Headache Clinic
Swedish Medical Center
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Background: Painkiller Overdoses = Public Health Epidemic

- Overdose deaths from opioid analgesics
  - 16,917 in 2011; 44,484 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 prescription painkiller overdose 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 5,000,000 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)

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

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
**Session I**

Evaluation is Essential for Safe and Effective Pain Management Using ER/LA Opioids

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**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

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**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

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**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

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**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

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**Opioid Therapy – Good Pain Management Principles**

- Evidence-based
- Multidimensional
- Based on appropriate assessment
- A dynamic process

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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>
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<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>
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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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<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..."

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

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


Risk Stratification and Monitoring Tools

<table>
<thead>
<tr>
<th>Risk Stratification Tool (used before opioids are prescribed)</th>
<th>Available</th>
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</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>

Risk Stratification Tool

<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>1</td>
</tr>
<tr>
<td></td>
<td>Illegal Drugs</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Prescription Drugs</td>
<td>3</td>
<td>3</td>
</tr>
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<td>Personal History of Substance Abuse</td>
<td>Alcohol</td>
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<td></td>
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<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Age</td>
<td>16-45 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>History of Preadolescent Sexual Abuse</td>
<td>Alcohol</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Illegal Drugs</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Psychological Disease</td>
<td>ADD, OCD, Bipolar Disorder, Schizophrenia Depression</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

Total Risk Score

Use of Risk Stratification Tools and Ongoing Monitoring KEY to Safe and Effective Opioid Use


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 five 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

Meet Peter

- 45-year-old white male, railroad worker for line maintenance and reconstruction
- S/p lumbar fusion with chronic back and leg pain
- Hx 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 7-9/10 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

Peter

History (cont)

- Physical therapy (PT), X-ray, 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

Peter – Next Steps: Make No Assumptions

- Even though the prescriber of the CR oxycodone and hydrocodone/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>
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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?
Opioid Therapy – Ongoing Monitoring

The 4 A’s

- ANALGESIA
- ADVERSE EFFECTS
- ACTIVITIES OF DAILY LIVING
- ABERRANT DRUG-TAKING BEHAVIORS

Important to remember two other “A’s”: Assessment and Action (treatment plan)


Additional Tools for Ongoing Monitoring

Current Opioid Misuse Measure (COMM) – Sample Questions

- In the past 30 days, how often have you taken your medications differently than how they are prescribed?
- In the past 30 days, how much of your time was spent thinking about opioid medications (having enough, taking them, dosing schedule, etc)?
- In the past 30 days, how often have you had to visit the Emergency Room?

Available at www.painEDU.org

Pain Assessment and Documentation Tool (PADT) – Sample Questions

- Is the patient’s functioning with the current pain reliever(s) better, the same, or worse since last assessment?
- Are patient experiencing any side effects from current pain reliever(s)?
- Check-list of potential aberrant drug-related behavior

Available at www.ucdenver.edu

Session II

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

See individual product information for additional contraindications

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

The FDA Definition of Opioid Tolerance

- 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

Be Aware

- Certain ER/LA-opioid medications should ONLY be initiated in patients who have become opioid tolerant as a result of ongoing therapy


Know The Risk Factors for Respiratory Depression

- Generally preceded by sedation and decreased respiratory rate
- Risk factors for respiratory depression include:
  - Sleep apnea or a sleep disorder diagnosis
  - Morbid obesity with a high risk of sleep apnea
  - Smoking
  - Risk increases with age (>60)
  - No recent opioid use
  - Post-surgery (particularly upper abdominal or thoracic)
  - Use of other sedating drugs (CNS depressants)
  - Preexisting cardiac or pulmonary disease or dysfunction, or major organ failure
  - Smoking


Be Aware

- Some agents should never be prescribed unless a patient is opioid tolerant
  - Duragesic (fentanyl transdermal system)
  - Exalgo (hydromorphone hydrochloride ER)

- Some agents can be prescribed to opioid-naïve patients, but not at higher doses – some ER/LA opioid doses can ONLY be used in opioid-tolerant patients

ER/LA Opioid

<table>
<thead>
<tr>
<th>ER/LA Opioid</th>
<th>Doses that can be used in opioid-tolerant patients ONLY</th>
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<tbody>
<tr>
<td>Avinza (morphine sulfate ER)</td>
<td>90 mg and 120 mg</td>
</tr>
<tr>
<td>Butens (buprenorphine transdermal system)</td>
<td>12 mg/h, 15 mg/h, and 20 mg/h</td>
</tr>
<tr>
<td>Embeds (morphine sulfate ER extended release)</td>
<td>100 mg and 200 mg</td>
</tr>
<tr>
<td>Kadian (morphine sulfate ER extended release)</td>
<td>100 mg and 200 mg</td>
</tr>
<tr>
<td>MS Contin (morphine sulfate controlled-release ER)</td>
<td>100 mg and 200 mg</td>
</tr>
<tr>
<td>Opiodrile (oxycodone hydrochloride ER)</td>
<td>&lt;40 mg single dose or &lt;80 mg daily</td>
</tr>
<tr>
<td>Dilaudid (hydromorphone hydrochloride)</td>
<td>2.5 mg to 10 mg every 8 to 12 hrs</td>
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<tr>
<td>Targin ER (oxycodone HCl / naltrexone HCl)</td>
<td>&lt;40 mg/30 mg single dose or &lt;80 mg/60 mg daily</td>
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<tr>
<td>Zohydro (hydrocodone bitartrate ER)</td>
<td>&lt;40 mg single dose or &lt;80 mg daily</td>
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www.fda.gov.
### Opioid Tolerance—Agents and Dosing

(Refer to full prescribing information)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exalgo (hydromorphone hydrochloride CR tablets)</td>
<td>Once a day or every 12 hours.</td>
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</tbody>
</table>
Patients who are on ER/LA opioids for pain management:

- Increase dose of ER/LA opioid
- Treat with non-opioid antinociceptives
- Treat with short-acting opioids
- Treat with slow-release opioids
- Treat with muscle relaxants
- Treat with sympathetic nervous system blockers
- Treat with alternative medication
- Treat with psychological counseling
- Treat with physical therapy

Opioid rotation is switching from one opioid to another.

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

Peter

- S/p lumbar fusion with chronic back and leg pain
- Returns to your primary care office for ongoing pain management
- Current medications:
  - Hydrocodone CR tablets 40 mg every 12 hours
  - Hydrocodone/naloxone 10/2.5 mg PO every 6-8 hours
  - Acetaminophen

- 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

Equianalgesic Dose Table – An Example

- 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.

Another Example:
Duragesic (fentanyl transdermal system)

- Recommended Initial Duragesic Dose Based Upon Daily Oral Morphine Dose

<table>
<thead>
<tr>
<th>Oral Morphine (mg/day)</th>
<th>DURAGESIC Dose (mcg/hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-120</td>
<td>50</td>
</tr>
<tr>
<td>135-224</td>
<td>75</td>
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<td>225-314</td>
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<td>250</td>
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<tr>
<td>1050-1134</td>
<td>300</td>
</tr>
</tbody>
</table>

Duragesic Full Prescribing Information. Available at www.fda.gov.
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

- Exalgo (hydromorphone HCl ER tablets)
  - Use conversion ratios in individual product-specific PI
  - Relative potency to oral morphine approximately 1:1 oral morphine to hydromorphone oral dose ratio
- Hydingla ER (hydrocodone bitartrate)
  - See individual product-specific PI for conversion recommendations from prior opioid
- Nucynta ER (tapentadol HCl ER tablets)
  - Relative potency to oral morphine approximately 3:1 oral morphine to oxycodone oral dose ratio
  - See individual product-specific PI for conversion recommendations from prior opioid
- Targin ER (oxycodone HCl/naloxone HCl tablets)
  - For relative potency to oral morphine, 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

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>No 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>Hydromorphone, methadone, meperidine, oxycodone, fentanyl, morphine, opium, and codeine, amphetamine, methamphetamine, methylnitrate, hydrocodone combination products (as of 15/9/14)</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, phendimetrazine, ketamine, anabolic steroids</td>
</tr>
<tr>
<td>IV</td>
<td>Low potential for abuse</td>
<td>Alprazolam, carisoprodol, clozaquate, clonazapam, diazepam, laranapam, midazolam, temazepam, tramadol (as of 2014), triazolam</td>
</tr>
<tr>
<td>V</td>
<td>Low potential for abuse</td>
<td>Cough preparations containing ≤ 100 mg codeine per 100 ml or per 100 g, ephedrine</td>
</tr>
</tbody>
</table>

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


Session III

Evidence-Based Tools for Screening for Patients at Risk and Monitoring for Adherence to Prescribed ER/LA Opioids
Learning Objectives for Session III

Upon completion of this module, the participants will be better able to:
- Evaluate and manage adverse effects of ER/LA opioids
- Differentiate strategies for monitoring patient adherence

Key Principles of Managing Therapy With ER/LA Opioids

Use clinical evidence-based guidelines to:
- Screen for risk, including assessment of psychiatric comorbidities
- Establish analgesic and functional goals
- Use Patient Prescriber Agreements (PPAs) and monitor patient adherence
- Anticipate/manage adverse effects and periodically assess benefits and side effects
- Reevaluate patient’s underlying medical condition if clinical presentation changes over time
- Use referral sources for the treatment of abuse and addiction

Realistic Individualized Goal-Setting

- Reach agreement with patient on treatment goals
- Patient-specific goals may include 1 or more of the following
  - Pain reduction: 30% considered clinically significant
  - Improve in select functional areas:
    - eg, ability to work full time at previous or modified job; play golf once a week, walk the dog daily
  - Improved mood

What Is Typically in a Patient Prescriber Agreement (PPA)

- Understanding of risks and benefits of opioid therapy
- Taking the opioid exactly as prescribed
- One prescribing doctor and one designated pharmacy and whether or not refills will be called into pharmacy without an office visit
- Urine/serum drug testing when requested
- Pill counts at each office visit
- No early refills
- How to safeguard their opioids medication
- List of behaviors that may lead to discontinuation of opioids
- Places for signature and dating

Monitoring Patient Adherence

- Level of monitoring depends on risk stratification level determined during initial screening (using ORT or other tool)
  - State PDMPs (Prescription Drug Monitoring Programs)
  - Urine drug testing (UDT)
  - Pill counts
  - Behavioral assessment at each visit
    - If indicated, refer for substance abuse treatment
Monitoring Patient Adherence
Prescription Drug Monitoring Programs (PDMPs)

- State-run electronic databases that track dispensing of controlled substances
- Can provide clinicians with critical information about patient prescription history and identify “doctor shoppers”
- Currently available in almost all states
- No national standards for guidance; implementation of programs is variable
- Real-time data access not yet available in all states
  - Each state has its own rules and laws
  - Follow state guidelines


Monitoring Patient Adherence:
Urine Drug Testing (UDT)

- Recommended for all patients for reasons of safety and to remove the stigma associated with UDTs
- Testing does not imply a lack of trust; it is a conversation starter
- Self reports of drug use and behavioral monitoring often fail to detect abuse problems
- UDTs can identify use of prescribed opioids as well as illicit drug use
- Know limitations of UDT or laboratory that you use


Urine Drug Testing – KEY POINTS

- Know what to expect and how to interpret results
- Parent compound and or metabolite should show up in the urine
  - Oxycodone $\rightarrow$ oxymorphone
  - Hydrocodone $\rightarrow$ hydromorphone
  - Codeine $\rightarrow$ morphine
- Is the substance present that you expect?
- Are there substances present that you do not expect?
- Know what your laboratory does

Common UDT Scenarios

- Peter undergoes UDT in office and the test is negative for opioids
  - UDTs do differ
  - Certain drugs, including oxycodone, may not be detected by certain laboratory techniques
  - UDT is a conversation starter: “Why do you think your UDT is negative?”
    - Is diversion a possibility?
    - Is he binging and then running out of opioids?
    - Is he failing to take the prescribed drug because symptoms have abated?
    - Do you give him a 30-day Rx supply?


A Sample PDMP Report:
West Virginia = Board Of Pharmacy – Patient Profile

- Date 4/15/2012 Date of Birth 12-10-1966
- Beginning Date: 04-01-11 Ending Date: 04-15-12
- First Name: MIKE Last Name: OWEN

<table>
<thead>
<tr>
<th>First</th>
<th>Address</th>
<th>Zip</th>
<th>DEA</th>
<th>Name</th>
<th>Pharm</th>
<th>DEA Ph Zip</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIKE</td>
<td>319 LOWER 25526</td>
<td>5/3/2011</td>
<td>11222 APAP/HYDRO 500MG-10MG 180</td>
<td>SMITH JOE</td>
<td>DH0267890</td>
<td>TOM'S PHARM GF1234567 25526</td>
</tr>
<tr>
<td>MIKE</td>
<td>319 LOWER 25526</td>
<td>5/27/2011</td>
<td>23466 APAP/HYDRO 500MG-10MG 180</td>
<td>SMITH JOE</td>
<td>DH0267890</td>
<td>TOM'S PHARM GF1234567 25526</td>
</tr>
<tr>
<td>MIKE</td>
<td>319 LOWER 25526</td>
<td>6/4/2011</td>
<td>31111 APAP/HYDRO 500MG-10MG 180</td>
<td>SMITH JOHN</td>
<td>DH0267890</td>
<td>BILL'S PHARM AF1245687 25526</td>
</tr>
</tbody>
</table>

Common UDT Scenarios

- Patient on LA morphine undergoes UDT. Test results positive for morphine and hydromorphone
- Possible explanations include:
  - Patient using another opioid obtained from another physician
  - Hydromorphone is a trace metabolite of morphine found only when very high morphine concentrations are present
Common UDT Scenarios

- Patient being treated with hydrocodone has UDT positive for hydrocodone and hydromorphone
- After hydrocodone use, urine may be positive for:
  - Hydrocodone only
  - Hydrocodone and hydromorphone (metabolite)
  - Hydromorphone only

**Screening vs Confirmatory UDTs**

<table>
<thead>
<tr>
<th>ANALYSIS TECHNIQUE</th>
<th>SCREENING</th>
<th>CONFIRMATORY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (ability to detect a class of drugs)</td>
<td>Low or none when testing for semi-synthetic or synthetic opioids</td>
<td>High</td>
</tr>
<tr>
<td>Specificity (ability to detect an individual drug)</td>
<td>Variability can result in false-positives or false-negatives</td>
<td>High</td>
</tr>
<tr>
<td>Turnaround</td>
<td>Rapid</td>
<td>Slow</td>
</tr>
<tr>
<td>OTHER</td>
<td>Intended for a drug-free population. May not be useful in pain medicine.</td>
<td>Legally defensible results</td>
</tr>
</tbody>
</table>

GC-MS, gas chromatograph mass spectrometer; HPLC, high performance liquid chromatography


Anticipating and Managing Adverse Effects

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea and vomiting</td>
<td>Anti-emetic; switch totramadol*</td>
</tr>
<tr>
<td>Sedation</td>
<td>Lower dose if possible; add non-narcotic co-analgesics; add stimulant or attention enhancer</td>
</tr>
<tr>
<td>Constipation</td>
<td>Treat pharmacologically with stool softeners, bowel stimulants; nonpharmacologic measures</td>
</tr>
</tbody>
</table>

*Opioid switching is an option for any adverse effect.


Emerging issues

- Hyperalgesia
  - An increased response to a normally painful stimulus
  - May occur at higher doses
- Sleep
  - Central and obstructive sleep apnea
  - Sleep architecture

Respiratory Depression – The Most Serious Adverse Effect

- Most serious adverse effect associated with opioids is RESPIRATORY DEPRESSION
- Occurs when
  - Initial doses are too high
  - Therapy is titrated too rapidly
  - Drug-drug interactions
  - Opioids combined with other drugs that may potentiate opioid-induced respiratory depression
    - Benzodiazepines
    - Herbals
    - OTC preparations that contain diphenhydramine
- More common in patients with sleep apnea
- Respiratory depression may be fatal

OTC, over-the-counter.

Reevaluating the Patient’s Condition

- Reevaluate if the presentation changes to determine if opioid therapy continues to be effective or necessary
- Reevaluate or refer if there is new pain
- Continue opioid therapy if appropriate analgesia and functional status improvements are maintained


ER/LA Opioid Analgesics in Pregnancy

- Be aware of the pregnancy status of your patient
- There are no adequate and well-controlled studies of ER/LA opioids in pregnant women
- ER/LA opioids should be used in pregnancy only if the potential benefit justifies the risk to the fetus
- If opioid use is required, advise the patient of risk of neonatal opioid withdrawal syndrome

What to Do if Your Patient Needs Treatment for Abuse and Addiction

- Know treatment centers in your area
- Work out a plan with the center you are referring to
- With a clear indication of abuse or addiction, discontinue prescribing of opioids

Referral Sources for Abuse and Addiction Treatment

- Balancing Pain Management and Prescription Opioid Abuse
  Available at www.cdc.gov/primarycare/materials/opioidabuse/index.html
- Find Substance Abuse and Mental Health Treatment
  Available at www.samhsa.gov/treatment
- National Institute on Drug Abuse
  Available at www.nida.nih.gov
- American Council for Drug Education
  Available at www.acde.org
- American Academy of Addiction Psychiatry
  - Providers’ Clinical Support System for Opioid Therapies:
    www.pcss-o.org
  - Providers’ Clinical Support System for Medication Assisted Treatment:
    www.pcssmat.org