1 – 3pm

SAFE Opioid Prescribing

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Presenter Disclosure Information

The following relationships exist related to this presentation:

- Dr. Argoff: Advisory Board member for Acorda Therapeutics, Inc., AstraZeneca Pharmaceuticals LP, Daiichi Sankyo, Iroko Pharmaceuticals, LLC, Nektar Therapeutics, Pfizer Inc., Purdue Pharma L.P., and XenoPort, Inc. Consultant for Mallinckrodt Pharmaceuticals, Scirex Corporation, and Zogenix, Inc. Research support from Eli Lilly and Company, Endo Pharmaceuticals Inc., and Forest Laboratories, Inc. Speakers Bureau member for Allergan, Inc., Depomed, Inc., Iroko Pharmaceuticals, LLC, Janssen Pharmaceuticals, Inc., and XenoPort, Inc. Owns stock in Pfizer Inc.
- Dr. Brennan: Advisory Board member for Depomed, Inc., Insys Therapeutics Inc., Iroko Pharmaceuticals, LLC, Mallinckrodt Pharmaceuticals, Nektar Therapeutics, Purdue Pharma L.P., Teva Pharmaceuticals Industries Ltd., and Zogenix, Inc. Consultant for Purdue Pharma L.P., Teva Pharmaceuticals Industries Ltd., and Zogenix, Inc. Speakers Bureau member for Depomed, Inc., Iroko Pharmaceuticals, LLC, Johnson & Johnson, Purdue Pharma L.P., Teva Pharmaceuticals Industries Ltd., and Zogenix, Inc.

Presenter Disclosure Information

- Dr. McCarberg: Advisory Board member for AstraZeneca Pharmaceuticals LP, Collegium Pharmaceutical, Inc., Depomed, Inc., Inspirion Pharmaceuticals, LLC, Iroko Pharmaceuticals, LLC, Janssen Pharmaceuticals, Inc., Kaléo, Inc., Mallinckrodt Pharmaceuticals, Millennium Laboratories, LLC, Pfizer Inc., Salix Pharmaceuticals, Inc., Takeda Pharmaceuticals U.S.A., Inc., and Zogenix, Inc. Owns stock in BioSpecifics Technologies Corp., Galena Biopharma, Inc., Johnson & Johnson, Nektar Therapeutics, and Protein Design Labs, 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.

SAFE Opioid Prescribing

Strategies. **A**ssessment. **F**undamentals. **E**ducation

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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Overall Program Learning Objectives Sessions I–VI

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

Rx, prescription; ED/ER, emergency department/emergency room.

Chen LH, et al. NCHS Data Brief, No. 166, September 2014; Opioids drive continued increase in drug overdose deaths. Accessed May 1, 2013; www.cdc.gov/media/releases/2013/p0220_drug_overdose_deaths.htm. Accessed May 1, 2013.

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

Ensure availability of opioids for patients with pain

vs

Establish systems of control to prevent abuse

IOM (Institute of Medicine). *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. 2011; www.painpolicy.wisc.edu.

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

CME, continuing medical education.

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed February 23, 2013.

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

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed February 23, 2013.

Session I

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

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

McCarberg BH. *Postgrad Med.* 2011;123(2):119-130.

Opioid Therapy – Good Pain Management Principles

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

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

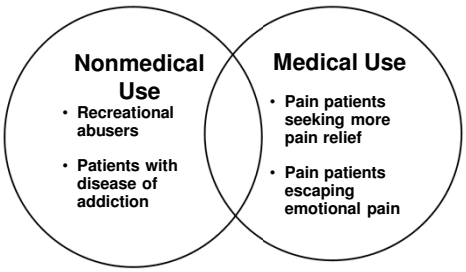
Chou R, et al. *J Pain.* 2009;10(2):113-130.

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

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed August, 2014.

Who Misuses/Abuses Opioids and Why?



Key Concepts

Term	Definition
Tolerance	**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.**
Physical Dependence	**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.**
Addiction	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.

Savage SR, et al. *J Pain Symptom Manage.* 2003;26(1):655-667; Jamison RN, et al. *Clin Neuropsychol.* 2013;27(1):60-80.

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."

Tolerance, Dependence and Addiction — Critical Differences

Behavior that the addicted patient may display:

" My husband used his entire month's supply of that extended-release opioid you gave him in 1 week. He seems like a totally different person. I am very concerned."

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

www.fda.gov.

Key Concepts

Term	Definition
Abuse	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
Misuse	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
Aberrant Drug-Related Behavior	A behavior outside the boundaries of the agreed-on treatment plan

Chou R, et al. *J Pain.* 2009;10(2):113-130.

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

McCarberg BH. *Postgrad Med.* 2011;123(2):119-130; Brennan MJ, et al. *PM R.* 2010;2(6):544-558.

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

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

Webster LR, et al. *Pain Med.* 2005;6(6):432-442.

Risk Stratification and Monitoring Tools

Risk Stratification Tool (used before opioids are prescribed)	Available
Screener and Opioid Assessment for Patients with Pain (SOAPP)	www.painEDU.org
Opioid Risk Tool (ORT)	www.partnersagainstpain.com

Opioid Risk Tool (ORT)

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

Total Score Risk Category

Low Risk 0–3 Moderate Risk 4–7 High Risk ≥8

OCD, obsessive compulsive disorder.

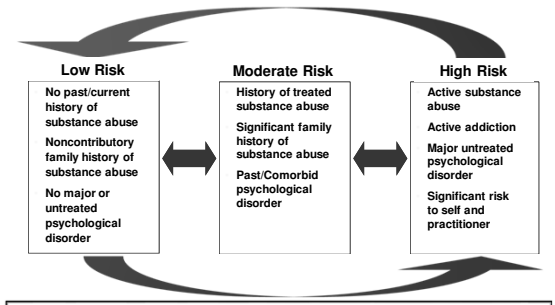
Webster LR, et al. *Pain Med.* 2005;6(6):432-442.
Opioid Risk Tool. www.partnersagainstpain.com/printouts/Opioid_Risk_Tool.pdf.
Accessed January 8, 2013. Reprinted with permission: Lynn Webster, MD.

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

Stratify Risk



Consider referring high-risk patients or any patient you have concerns about to a pain specialist

Webster LR, et al. *Pain Med.* 2005;6(6):432-442.

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

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

CR, controlled-release; MRI, magnetic resonance imaging.

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

CR, controlled-release

Peter's Score on ORT

Category	Risk Factor	Score if Female	Score if Male
Family History of Substance Abuse	Alcohol Illegal Drugs Prescription Drugs	1 2 4	(3) 3 4
Personal History of Substance Abuse	Alcohol Illegal Drugs Prescription Drugs	3 4 5	3 4 5
Age	Age 16-45 years	1	(1)
History of Preadolescent Sexual Abuse		3	0
Psychological Disease	ADD, OCD, Bipolar Disorder, Schizophrenia Depression	2 1	2 1
Total Risk Score			**4**

Total Score Risk Category

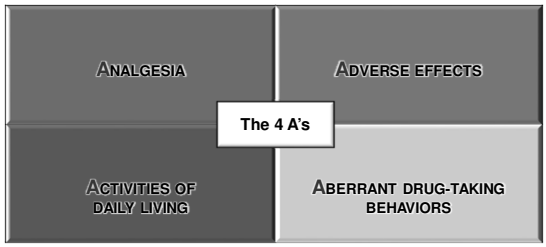
Low Risk 0–3 Moderate Risk 4–7 High Risk ≥8

Webster LR, et al. *Pain Med.* 2005;6(6):432-442.
Opioid Risk Tool. www.partnersagainstpain.com/printouts/Opioid_Risk_Tool.pdf.
Accessed January 8, 2013. Reprinted with permission: Lynn Webster, MD.

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



Important to remember two other "A's": **A**ssessment and **A**ction (treatment plan)

Passik SD, et al. *Adv Ther.* 2000;17(2):70-83.

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?
Is 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

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed February 23, 2013.

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.

Nicholson B. *Pain Pract.* 2009;9(1):71-81; www.fda.gov.

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

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed February 23, 2013.

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

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	Snoring
Risk increases with age (>60)	No recent opioid use	Post-surgery (particularly upper abdominal or thoracic)
Use of other sedating drugs (CNS depressants)	Preexisting pulmonary or cardiac disease or dysfunction or major organ failure	Smoking

The Joint Commission. Sentinel Event Alert. August 8, 2012;49. www.jointcommission.org. Accessed February 22, 2013.

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

www.fda.gov.

Be Aware

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

www.fda.gov.

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	Doses that can be used in opioid-tolerant patients ONLY
Avinza (morphine sulfate ER)	90 mg and 120 mg
Butrans (buprenorphine transdermal system	10 mcg/h, 15 mcg/h and 20 mcg/h
Embeda (morphine sulfate ER-naltrexone)	100 mg/4 mg
Kadian (morphine sulfate ER)	100 mg and 200 mg
MS Contin (morphine sulfate controlled-release [CR])	100 mg and 200 mg
Oxycontin (oxycodone hydrochloride CR)	>40 mg single dose or >80 mg daily
Dolophine (methadone hydrochloride)	>2.5 mg to 10 mg every 8 to 12 hrs
Targiniq ER (oxycodone HCl / naloxone HCl)	>40 mg/20 mg single dose or >80 mg/40 mg daily
Zohydro (hydrocodone bitartrate ER)	>40 mg single dose or >80 mg daily

www.fda.gov.

Opioid Tolerance—Agents and Dosing

(Refer to full prescribing information)

Agent (Oral)	Selected Doses for Use in Opioid-Tolerant Patients Only
Avinza (morphine sulfate ER capsules)	**90 mg** and **120 mg** capsules for use in opioid-tolerant patients only
Embeda (morphine sulfate ER-Naltrexone capsules)	**100 mg**/**4 mg** capsule for use in opioid-tolerant patients only
Hysingla (hydrocodone bitartrate ER tablets)	Daily dose greater than or equal to **80 mg** is for use in opioit-tolerant patients only
Kadian (morphine sulfate ER capsules)	**100 mg** and **200 mg** capsules for use in opioid-tolerant patients only
MS Contin (morphine sulfate CR tablets)	**100 mg** and **200 mg** tablets for use in opioid-tolerant patients only
OxyContin (oxycodone hydrochloride CR tablets)	Single dose **greater than 40 mg** or **total daily dose greater than 80 mg** for use in opioid-tolerant patients only
Targiniq ER (oxycodone HCl/ naloxone HCl)	Single dose **greater than 40 mg**/**20 mg** or **total daily dose of 80 mg**/**40 mg** for use in opioid-tolerant patients only
Dolophine (methadone hydrochloride tablets)	**When used as first opioid analgesic, initiate** therapy with small doses, no more than **2.5 mg** to **10 mg** every 8 to 12 hours.

www.fda.gov.

Opioid Tolerance—Agents and Dosing

(Refer to full prescribing information)

Agent (transdermal)	Selected Doses for Use in Opioid-Tolerant Patients Only
Butrans (buprenorphine transdermal system)	10 mcg/hr , 15 mcg/hr, and 20 mcg/hr transdermal systems are for use in opioid-tolerant patients only
Agent	**Use in Opioid-Tolerant Patients Only – All Doses**
Duragesic (fentanyl transdermal system)	**All doses** indicated for use in opioid-tolerant patients only
Exalgo (hydromorphone hydrochloride ER tablets)	**All doses** indicated for use in opioid-tolerant patients only
Agent	**Use in Opioid-Naive Patients**
Hysingla ER (hydrocodone bitartrate ER tablets)	In opioid-naïve patients, initiate treatment with 20 mg tablets every 24 hrs
Nucynta ER (tapentadol ER tablets)	In opioid-naïve patients, the initial dose is 50 mg twice a day
Opana ER (oxymorphone hydrochloride ER tablets)	In opioid-naïve patients, initiate treatment with 5 mg every 12 hours
Zohydro ER (hydrocodone bitartrate ER capsules)	In opioid-naïve patients, initiate treatment with 10 mg every 12 hours

www.fda.gov.

Initiating Therapy:
Dose Selection and Titration

Drug	Initial Dosing
Avinza (morphine sulfate ER capsules)	• Once daily • Initial dose as first analgesic (opioid-naive patients) is 30 mg once daily • Titrate using a minimum of 3-day intervals (4-day intervals for opioid-naïve patients) • **Maximum daily dose 1600 mg** (due to risk of renal toxicity)
Butrans (buprenorphine transdermal system)	• One transdermal system applied every 7 days • Initial dose as first analgesic (opioid-naïve patients) is 5 mcg/hour • Initial dose if prior total daily dose <30 mg oral morphine equivalents/day – 5 mcg/hour • When converting from 30-mg to 80-mg morphine equivalents – first taper to 30-mg morphine equivalent, then initiate with 10 mcg/hour dose • The minimum Butrans titration interval is 72 hours • **Maximum daily dose: 20 mcg/hour** (due to risk of QTc interval prolongation)

www.fda.gov.

Initiating Therapy:
Dose Selection and Titration

Drug	Initial Dosing
Dolophine (methadone HCl tablets)	• Every 8 to 12 hours • Initial dose as first opioid analgesic (opioid-naïve 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)**
Duragesic (fentanyl transdermal system)	• Every 72 hours (3 days) • Duragesic is contraindicated in opioid non-tolerant patients • 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
Embeda (morphine sulfate and naltrexone HCl) ER	• Once a day or every 12 hours • Initial dose as first opioid is 20 mg/0.8mg • Dosage adjustments may be done every 1 to 2 days

www.fda.gov.

Initiating Therapy:
Dose Selection and Titration

Drug	Initial Dosing
Exalgo (hydromorphone HCl ER tablets)	• Once a day • Not for use in opioid non-tolerant patients. Do not begin any patient on Exalgo as the first opioid • Use the conversion tables in the full prescribing information • Start patients with moderate hepatic impairment on 25% usual dosage • Start patients with moderate renal impairment on 50%, and patients with severe renal impairment on 25% usual dosage • Titrate using a minimum of 3- to 4-day intervals
Hysingla ER (hydrocodone bitartrate ER tablets)	• Once a day • For opioid-naïve patients, initiate with 20 mg tablets • Dose titration may occur every 3 to 5 days in increments of 10 mg to 20 mg • Daily doses greater than or equal to 80 mg are for opioid tolerant patients only • Start patients with severe hepatic or renal impairment on 50% initial dose

www.fda.gov.

Initiating Therapy:
Dose Selection and Titration

Drug	Initial Dosing
Nucynta ER (tapentadol HCl ER tablets)	• Every 12 hours • Use 50 mg every 12 hours as initial dose in opioid non-tolerant patients • Titrate by 50 mg increments using a minimum of 3-day intervals • **Maximum total daily dose is 500 mg**
Kadian (morphine sulfate ER capsules)	• Once a day or every 12 hours • Not recommended as a first opioid • Titrate using a minimum of 2-day intervals
MS Contin (morphine sulfate CR tablets)	• Every 8 hours or every 12 hours • Not recommended as a first opioid • Titrate using a minimum of 2-day intervals
Opana ER (oxymorphone HCl ER tablets)	• Every 12 hours; some may benefit from asymmetric dosing (higher in the AM than PM) • Use 5 mg every 12 hours as initial dose in opioid non-tolerant patients • Titrate dose at increments of 5-10 mg every 12 hours, at 3-7 day intervals • Start with lowest dose in patients with mild hepatic impairment and renal impairment (creatinine clearance <50 mL/min) and in patients older than 65 years of age

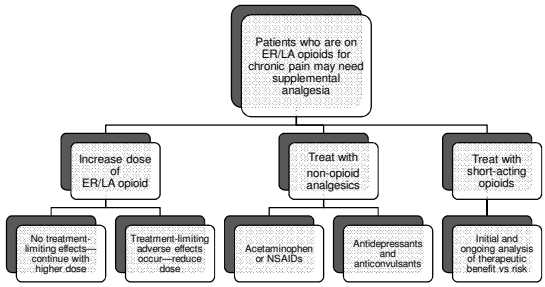
www.fda.gov.

Initiating Therapy:
Dose Selection and Titration

Drug	Initial Dosing
OxyContin (oxycodone HCl CR tablets)	• Every 12 hours • Initiate treatment with 10 mg every 12 hours in opioid non-tolerant patients • Titrate using a minimum of 1- to 2-day intervals • Hepatic impairment: start with one-third to one-half usual dosage • Renal impairment (creatinine clearance <60 mL/min): start with one-half usual dosage
Targiniq ER (oxycodone hydrocloride / naloxone hydrochloride tablets)	• Every 12 hours • For opioid-naïve patients, initiate with 10 mg/5 mg tablet every 12 hours • Titrate using a minimum of 1 to 2 day intervals • Contraindicated in moderate and severe hepatic impairment. Start with one-third to one-half dose in mild hepatic impairment. Start with one-half dose in renal impairment
Zohydro ER (hydrocodone bitartrate ER capsules)	• Every 12 hours • For opioid-naïve patients, initiate with 10 mg capsule every 12 hours • Titrate dose at increments of 10 mg every 12 hours, at 3-7 day intervals • Start with low initial dose in patients with renal impairment and severe hepatic impairment

www.fda.gov.

Supplementing ER/LA Opioids



Zeppetella G. *Curr Opin Support Palliat Care.* 2009;3:1-6; Prommer E, et al. *Patient Prefer Adherence.* 2012;6:465-475; Chou R, et al. *J Pain.* 2009;10(2):113-130; Burton AW. Medscape. June 15, 2005. www.medscape.org/viewarticle/506124. Accessed September 7, 2012; Rhiner MI, et al. *J Support Oncol.* 2010;8:232-238.

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

Fine PG, et al. *J Pain Symptom Manage.* 2009 Se;38(3):418-25; Chou R, et al. *J Pain.* 2009;10(2):113-130.

Equianalgesic Dose Table – An Example

Opioid	Equianalgesic (mg) Dose Oral	Equianalgesic (mg) Dose Other
Morphine	60 PO	10 IM/IV/SQ
Hydromorphone	7.5 PO	1.5 IM/IV/SQ
Oxycodone	20-30 PO	No information available
Oxymorphone	15 PO	1 IM/IV/SQ; 10 PR
Levorphanol	4 PO	2 IM/IV/SQ
Methadone	20 PO	10 IM/IV/SQ
Fentanyl		50-100 mcg IV/SQ

- 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

Knotkova H, et al. *J Pain Symptom Manage.* 2009;38(3):426-439.

Another Example:
Duragesic (fentanyl transdermal system)

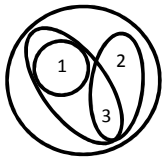
- Recommended Initial Duragesic Dose Based Upon Daily Oral Morphine Dose

Oral 24-hour Morphine (mg/day)	DURAGESIC Dose (mcg/hour)
60-134	25
135-224	50
225-314	75
315-404	100
405-494	125
495-584	150
585-674	175
675-764	200
765-854	225
855-944	250
945-1034	275
1035-1124	300

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



Chou R, et al. *J Pain.* 2009;10(2):113-130.

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-mcg/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)

www.fda.gov.

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 5:1 oral morphine to hydromorphone oral dose ratio
- Hysingla ER (hydrocodone bitartrate)
  - See individual product-specific PI for conversion recommendations from prior opioid
- Nucynta ER (tapentadol HCl ER tablets)
  - Equipotency to oral morphine not established
- Opana ER (oxymorphone HCl ER tablets)
  - Relative potency to oral morphine approximately 3:1 oral morphine to oxymorphone oral dose ratio
- OxyContin (oxycodone HCl CR tablets)
  - Relative potency to oral morphine approximately 2:1 oral morphine to oxycodone oral dose ratio
- Targiniq ER (oxycodone HCl/naloxone HCl tablets)
  - See individual product-specific PI for conversion recommendations from prior opioid
- Zohydro ER (hydrocodone bitartrate)
  - For relative potency to oral morphine, see individual product-specific PI for conversion recommendations from prior opioid

Always refer to full prescribing information (PI)

www.fda.gov.

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

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed February 23, 2013; Manchikanti L et al. *Pain Phys.* 2012;15(3 suppl):S67-S116; Morgan MM, et al. *Br J Pharmacol.* 2011;164(4):1322-1334.

Federal DEA Controlled Substance Schedules: ER/LA-Opioids are Schedule II

Sch	Description	Examples
I	No currently accepted medical use in the U.S.; high potential for abuse	Heroin, LSD, marijuana, peyote, methaqualone, Ecstasy
II	**High potential for abuse, which may lead to severe psychological or physical dependence**	**Hydromorphone, methadone, meperidine, oxycodone, fentanyl, morphine, opium, and codeine, amphetamine, methamphetamine, methylphenidate, hydrocodone combination products (as of 10/6/14)**
III	Potential for abuse, which may lead to moderate or low physical dependence or high psychological dependence	Products containing ≤ 90 mg codeine per dose, buprenorphine, benzphetamine, phendimetrazine, ketamine, anabolic steroids
IV	Low potential for abuse	Alprazolam, carisoprodol, clonazepm, clorazepate, diazepam, lorazepam, midazolam, temazepam, tramadol (as of 2014), triazolam
V	Low potential for abuse	Cough preparations containing ≤ 200 mg codeine per 100 ml or per 100 g, ezogabine

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

DEA Diversion Control. Available at www.deadiversion.usdoj.gov/schedules/index.htm. Accessed Aug, 2014

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

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed February 23, 2013.

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
    - Explain to patient that complete pain relief rarely achieved
  - Improvement 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

Patient Prescriber Agreement (PPA)

- Clinical evidence and guidelines support use of agreements
- Any of following can be used as a PPA:
  - Informed consent documents
  - Treatment agreement documents
  - PPA available for download at no cost*
- Benefits
  - Informed decision making with patient
  - Enables clear and mutual understanding of goals and expectations and respective responsibilities of patient and clinician
  - Can be jointly signed during patient visit

*eg, www.caresalliance.org.

Chou R, et al. *J Pain.* 2009;10(2):113-130.

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

Chou R, et al. *J Pain.* 2009;10(2):113-130.

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

Chou R, et al. *J Pain.* 2009;10(2):113-130.

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

Dahl J. *J Pain.* April 2012;13:Abstract 245; Dahl J, et al. *J Pain.* April 2012;13:Abstract 246.

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 =nbsp Ending Date: 04-15-12
- First Name: MIKE Last Name: =OWEN

First Name	Address	Zip	Fill date	Rx no.	Product Name	Strength	Qty	Doctor Name	Doctor DEA	Pharm Name	Pharm DEA	Ph Zip
MIKE	319 LOWER	25526	4/2/2011	11222	APAP/HYDRO	500MG-10MG	180	SMITH JOE	DH0267890	TOM'S PHARM	GF1234567	25526
MIKE	319 LOWER	25526	5/3/2011	19976	APAP/HYDRO	500MG-10MG	180	SMITH JOE	DH0267890	TOM'S PHARM	GF1234567	25526
MIKE	319 LOWER	25526	5/27/2011	23466	APAP/HYDRO	500MG-10MG	180	SMITH JOE	DH0267890	TOM'S PHARM	GF1234567	25526
MIKE	319 LOWER	25526	6/4/2011	31111	APAP/HYDRO	500MG-10MG	180	JOHN JOHN	DH0267890	BILL'S PHARM	AF1245687	25526

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

Katz NP, et al. *Anesth Analg.* 2003;97(4):1097-1102; Heit HA, et al. *J Pain Symptom Manage.* 2004;27(3):260-267.

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 → oxymorphone
  - Hydrocodone → hydromorphone
  - Codeine → 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 bingeing 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?

Heit HA, et al. *J Pain Symptom Manage.* 2004;27(3):260-267.

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

Common UDT Scenarios

- Patient reports no relief on codeine and UDT is negative
- Possible explanations include
  - Laboratory error
  - Diversion
  - Patient is a slow metabolizer of codeine

Heit HA, et al. *J Pain Symptom Manage.* 2004;27(3):260-267.

Screening vs Confirmatory UDTs

	SCREENING	CONFIRMATORY
ANALYSIS TECHNIQUE	Immunoassay	GC-MS or HPLC
SENSITIVITY (POWER TO DETECT A CLASS OF DRUGS)	Low or none when testing for semi-synthetic or synthetic opioids	High
SPECIFICITY (POWER TO DETECT AN INDIVIDUAL DRUG)	Varies (can result in false-positives or false-negatives)	High
TURNAROUND	Rapid	Slow
OTHER	Intended for a drug-free population. May not be useful in pain medicine.	Legally defensible results

GC-MS, gas chromatograph mass spectrometer; HPLC, high performance liquid chromatography.
www.opioidrisk.com.

Anticipating and Managing Adverse Effects

Adverse Effect	Treatment
Nausea and vomiting	Anti-emetics; Switch opioids*
Sedation	Lower dose (if possible); Add nonsedating co-analgesic; Add stimulant or attention enhancer
Constipation	Treat prophylactically with stool softeners, bowel stimulants; Nonpharmacologic measures

*Opioid switching is an option for any adverse effect.

Swegle JM, et al. *Am Fam Physician.* 2006;74(8):1347-1354. Chou R, et al. *J Pain.* 2009;10(2):113-130.

Anticipating and Managing Adverse Effects

Adverse Effect	Treatment
Itching	Antipruritic therapy (eg, antihistamines)
Endocrine dysfunction/Reduced libido/Loss of menstrual period	Endocrine monitoring; Testosterone replacement; Endocrine consultation
Edema and sweating	Switch opioids*
Dizziness	Antivertigo agents
Confusion	Titrate dose

*Opioid switching is an option for any adverse effect.

Swegle JM, et al. *Am Fam Physician.* 2006;74(8):1347-1354; Chou R, et al. *J Pain.* 2009;10(2):113-130.

Anticipating and Managing Adverse Events

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

Brush DE. *J Med Toxicol.* 2012 Dec;8(4):387-92; Dimsdale JE et al. *J Clin Sleep Med.* 2007 Feb 15;3(1):33-6

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.

Manchikanti L, et al. *Pain Physician.* 2012;15(3 suppl):S67-S116.

ER/LA Opioid Analgesics in Pregnancy

- Be aware of the pregnancy status of your patient
- There re 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

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

Chou R, et al. *J Pain.* 2009;10(2):113-130.

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/opoidabuse/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