RESPONSIBLE OPIOID PRESCRIBING
ENGAGE EDUCATE PROTECT

Treating Patients with ER/LA Opioid Analgesics: Initiating, Modifying and Discontinuing Therapy

Module II

RESPONSIBLE OPIOID PRESCRIBING
ENGAGE EDUCATE PROTECT

Jeffrey A. Gudin, MD

Director
Pain Management and Palliative Care
Englewood Hospital and Medical Center
Englewood, New Jersey

Key Learning Points

- Clinicians and patients should consider initial treatment with opioids as a therapeutic trial in which to determine ongoing treatment
- Drug and dose selection are critical in opioid-naïve and nonopioid-tolerant patients
- Respiratory depression is the primary risk of ER/LA opioids
- For some ER/LA products patients MUST be opioid tolerant before prescribing certain strengths and daily doses
- All prescribers should have a plan for discontinuation of opioid therapy and understand principles of tapering

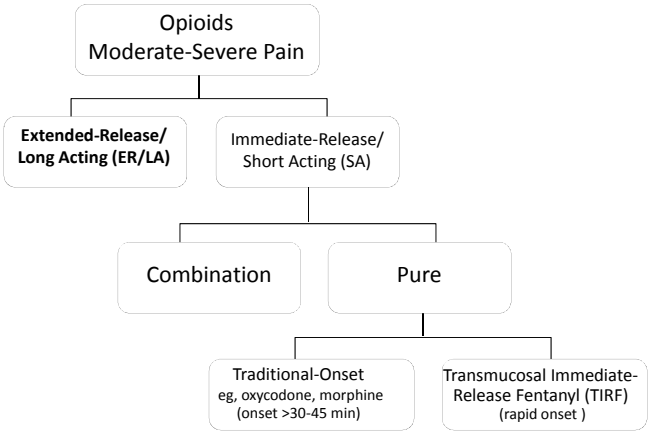
Overall Program Learning Objectives

Upon completion of this initiative, prescribers will be better able to:

- Identify and define how to assess patients for treatment with ER/LA opioid analgesics
- **Demonstrate how to initiate therapy, modify dose and discontinue use of ER/LA opioid analgesics**
- Recognize how to manage ongoing therapy with ER/LA opioid analgesics
- Employ patient and caregiver counseling about the safe use of ER/LA opioid analgesics, including proper storage and disposal
- Recall general and product-specific drug information concerning ER/LA opioid analgesics

Opioids for Pain Treatment

Classification of opioids by type



The Principle of Balance with Opioid Therapy

- Both the APS/AAPM and the WHO acknowledge that opioids are an essential treatment option in the management of patients with moderate-to-severe pain[1,2]
- However, opioids are associated with significant risks, including misuse, abuse, addiction, and overdose

APS=American Pain Society; AAPM=American Academy of Pain Medicine; WHO=World Health Organization
[1]WHO's Pain Ladder. *www.who.int/cancer/palliative/painladder/en/*. Accessed August 2011. [2]American Pain Society. Clinical Practical Guidelines. *www.americanpainsociety.org/resources/content/clinical-practical-guidelines.html*. Accessed February 12, 2014.

RESPONSIBLE OPIOID PRESCRIBING
ENGAGE EDUCATE PROTECT

Patient Assessment

Bill McCarberg, MD, FABPM
Founder
Chronic Pain Management Program
Kaiser Permanente
San Diego, California

RESPONSIBLE OPIOID PRESCRIBING
ENGAGE EDUCATE PROTECT

Initiating Therapy

General Principles of Initiating Therapy

- The initial therapeutic trial of an ER/LA opioid may last from several weeks to several months
- Considerations include progress toward meeting therapeutic goals, presence of AEs, changes in pain levels, changes in medical/psychiatric comorbidities or identification of aberrant behaviors
- The dosage should be individualized in every case
- Suspected aberrant drug-related behaviors require further evaluation and action

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

Know the Risk Factors for Opioid-Induced Respiratory Depression

- Sleep disordered breathing
- 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

Jungquist CR, et al. *Pain Manag Nurs*. 2011;12(3):180-187.

ARS Question

Opioid induced respiratory depression is the primary risk of ER/LA opioid analgesics. The greatest risk occurs in which of the following situations?

A. Initiation of therapy
B. Increasing dosage of ER/LA opioid
C. Switching ER/LA opioid
D. All the above
E. None of the above

Opioid Induced Respiratory Depression

Greatest Risk	• Initiation of therapy • Increased dose • Change of drug
Symptoms	• Reduced urge to breathe • Decreased respiration rate • Shallow breathing • CO2 retention may exacerbate opioid sedating effects
Action	• Call 911 immediately • May be treated with opioid antagonist dependent upon patient status

American Society for Pain Management Nursing Guidelines on Monitoring for Opioid-Induced Sedation and Respiratory Depression.
Jarzyna D, et al. *Disclosures Pain Manag Nurs.* 2011;12(3):118-145.

Short-acting (IR) vs Long-acting ER/LA Opioids

- Benefits of short-acting immediate-release (IR) opioids
  - Acute pain
  - Breakthrough pain
  - Dose finding
  - Ability to crush or give as a liquid
  - Those who are not yet "tolerant" to opioids

ER/LA Opioids

- Benefits of LA/ER opioids
  - Chronic pain
  - Improved treatment adherence
  - Possibility of less pain fluctuation
  - Better sleep

Initiating Treatment: Medication Selection and Dosage

- Factors to consider include:
  - Clinician experience
  - Patient experience
  - Patient health status
  - Formulation availability, cost and insurance coverage

ARS Question

Opioid naïve patients should *never* receive an ER/LA opioid.

A. True
B. False

Initiating Treatment: Opioid Naïve Patients

- Be aware which ER/LA opioid analgesics are appropriate **only** for the opioid tolerant patients
- Drug and dose selection are critical
- Some agents may be prescribed to opioid naïve patients ***but not at higher doses***
- Always refer to Prescribing Information

Monitor patients closely for signs of respiratory depression

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

Initiating Treatment: Opioid Tolerant Patients

Patients that are considered opioid tolerant are taking at least one of these doses for 1 week or longer

Opioid Tolerant Doses
60 mg oral morphine per day
25 u transdermal fentanyl per hour
30 mg oral oxycodone per day
8 mg oral hydromorphone per day
25 mg oral oxymorphone per day

An equianalgesic dose of another opioid

Refer to prescribing information on which products and which doses are indicated for use ***only*** in opioid tolerant patients

Opioid Rotation

- Opioid rotation is defined as a switch from one opioid to another in an effort to improve therapeutic response or reduce undesirable effects
- Goals:
  - Improved analgesic efficacy
  - Reduced adverse events
  - Improved functioning and QOL

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

Guidelines for Opioid Rotation: Step 1

- An automatic safety factor adjustment
  - Calculate equianalgesic dose of the new opioid based on equianalgesic dose table (EDT)
  - If switching to any other opioid other than methadone or fentanyl, apply an additional 25 to 50% lower than the calculated equianalgesic dose
    - Select a dose closer to the upper bound (50% reduction) of the reduction if the patient is receiving a relatively high dose of the current opioid regimen, is not Caucasian, or is elderly or medically frail
    - Select a dose closer to the lower bound (25% reduction) of the reduction if the patient does not have these characteristics or is undergoing a switch to a different route of systemic drug administration using the same drug

Fine PG, et al. *J Pain Symptom Manage*. 2009;38(3):418-425.

Guidelines for Opioid Rotation: Step 1

If switching to methadone:

- Apply an additional automatic dose reduction of 75% to 90% lower than the calculated equianalgesic dose
  - For individuals on very high opioid doses (eg, 1000 mg morphine equivalents/day or higher), great caution should be exercised in converting to methadone at doses of 100 mg or greater per day; consider inpatient monitoring, including serial EKG monitoring

If switching to transdermal:

- Fentanyl: calculate dose conversion based on equianalgesic dose rations included in the PI
- Buprenorphine: follow instructions in the PI

Fine PG, et al. *J Pain Symptom Manage*. 2009;38(3):418-425.

Guidelines for Opioid Rotation: Step 2

- **Additional dose adjustment based on patient characteristics**
  - Reassess pain and medical status to determine whether to apply an additional increase or decrease of 15% to 30% to increase pain control
  - Optimize outcomes by frequent assessment of initial dose and titrate to pain control
  - If a supplemental "rescue dose" is used for titration, calculate this at 5% to 15% of the total daily opioid dose
  - If an oral transmucosal fentanyl formulation is used as a rescue dose, begin dosing at one of the lower doses irrespective of the baseline opioid dose

Fine PG, et al. *J Pain Symptom Manage*. 2009;38(3):418-425.

Equianalgesic Reference Tables†

Equianalgesic Opioid Dosing

Drug	Equianalgesic Doses (mg)	
	Parenteral	Oral
Morphine	10	30
Buprenorphine	0.3	0.4 (sl)
Codeine	100	200
Fentanyl	0.1	NA
Hydrocodone	NA	30
Hydromorphone	1.5	7.5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tramadol	100*	120

*Not available in the US

Available in many forms:
- Online
- Apps
- Published

Variability on content:
- Equianalgesic values
- Ranges may/may not be provided
- Which opioids are included

†**Ask your Pharmacist for Guidance**

McPherson ML. *Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing.* American Society of Health-System Pharmacists, Bethesda, MD, 2010.

Equianalgesic Tables: Limitations Exist

- Based on single dose potency studies which do not factor in:
  - Chronic dosing
  - High opioid doses
  - Other routes of administration
  - Different pain types
  - Comorbidities/clinical status which may affect pharmacokinetics
  - Gender, ethnicity, age, concomitant medications
  - Direction of switch
  - Incomplete cross-tolerance

Pasternak GW. *Trends Pharmacol Sci*. 2001;22:67-70.

Utilizing Equianalgesic Tables…

- Always be conservative in dosing
- Treat the individual patient
- Follow conversion instructions found in individual ER/LA opioid package insert
- Monitor patient response

Pasternak GW. *Trends Pharmacol Sci*. 2001;22:67-70.

Drug-Drug Interactions

- Pharmacokinetic drug interactions may result in higher or lower blood levels of opioid resulting in:
  - Excess effects (including toxicity)
  - Loss of analgesia
  - Misinterpretation of urine drug testing
- CYP 450 enzymes account for almost 50% of overall elimination of commonly used drugs, including opioids

Tanaka E. *J Clin Pharm Ther.* 1998;23(6):403-416.

Patients usually have a variable response to medications

⇩

ESPECIALLY TO ANALGESICS

⇩

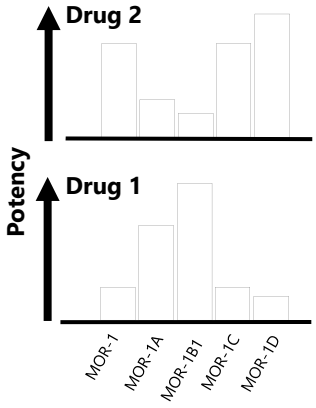
ESPECIALLY TO OPIOIDS

Multiple Opioid Receptors

- The opioid system comprises four subtypes of receptor:
  - Classical receptor subtypes: mu, delta, kappa
  - Non-classical receptor subtype: nociceptin
- Opioid receptors all have selective endogenous peptides and have sensitivity to naloxone
- Analgesia elicited by opioids used clinically act predominately via the mu receptor

McDonald J, et al. *Contin Educ Anaesth Crit Care Pain*. 2005;5(1):22-25.

Mu Opioid Receptors and Cross-Tolerance



- Mu opioids produce subtly different pharmacologic response based on distinct activation profiles of mu receptor subtypes
- May help explain:
  - Inter-patient variability in response to mu opioids
  - Incomplete cross-tolerance among mu opioids

Pasternak GW. *Pain Med*. 2012;13 Suppl 1:S4-11.

Incomplete Cross Tolerance

- **Cross Tolerance:** Tolerance to effects of one drug translates to tolerance to other drugs in the same class
- **Incomplete cross-tolerance:** Failure to develop complete cross tolerance
  - Altered therapeutic response
  - May not predict adverse effects
- Rationale behind opioid rotation
- Caution in opioid conversion

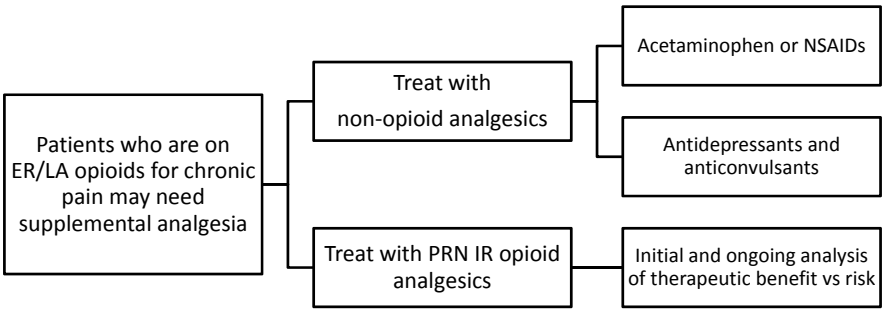
Pasternak GW. *Trends Pharmacol Sci*. 2001;22:67-70.

Supplemental Analgesia for Patients on ER/LA Opioids

- Patients who are on stable doses of around-the-clock ER/LA opioids may need supplemental analgesia:
  - Disease progression
  - Incidental pain
  - Idiopathic pain
  - Pain associated with end of dose

Mishra S et al. *Indian J Palliat Care*. 2009;15(1):14-18.

Supplemental Therapeutic Strategies



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

RESPONSIBLE OPIOID PRESCRIBING
ENGAGE EDUCATE PROTECT

Discontinuing Use of ER/LA Opioid Analgesics

When to Consider Discontinuation of ER/LA Opioid Therapy

- Patient makes no progress toward meeting therapeutic goals
- Intolerable AEs that cannot be resolved
- Repeated drug-related aberrant behaviors
  - Use of illicit drugs or unprescribed opioids
  - Repeatedly obtaining opioids from multiple unauthorized source
  - Prescription forgery
- Non-adherence
  - Unauthorized dose escalation
  - Sharing medication
  - Misuse

Tapering and Discontinuing Opioids. *www.healthquality.va.gov/cot/OpioidTaperingFactSheet23May2013v1.pdf*

Methods of Discontinuation of Treatment

- Taper dosing upon discontinuation
  - Avoid withdrawal symptoms when opioid dependent
  - Rehabilitation support advised for patients with aberrant behavior
- Follow discontinuation instructions as described in the individual ER/LA opioid package insert

Tapering and Discontinuing Opioids. *www.healthquality.va.gov/cot/OpioidTaperingFactSheet23May2013v1.pdf*

Taper Protocols

- Appropriate reduction rates vary
  - Slow: 10% weekly
  - More rapid: 25-50% weekly
- Reduction rates vary in accordance with:
  - Reasons for discontinuation
  - Medical/psychiatric comorbidities
  - Dose (slower rate for lower doses)
  - Withdrawal symptoms upon initial reduction

Tapering and Discontinuing Opioids. *www.healthquality.va.gov/cot/OpioidTaperingFactSheet23May2013v1.pdf*

Federal and State Regulations that Govern Use of Opioid Therapy for Pain

Rx for legitimate medical purpose

While acting in "usual course of professional practice"

While exercising "appropriate degree of medical supervision" over individual patient

While following other federal and state laws, clinical standards of care, and professional guidelines

DEA obligations when prescribing controlled medications

FDA approved REMS guidance*

Facilitates compliance with good clinical practice (subject to individual REMS requirements)

Guides practitioners in key documentation points when prescribing controlled medications

Be familiar with your own state requirements

*Check with qualified legal counsel for overall compliance requirements

Complying with State and Federal Laws

Code of Federal Regulations, Title 21 Section 1306: rules governing the issuance and filling of prescriptions pursuant to section 309 of the Act (21 USC 829)

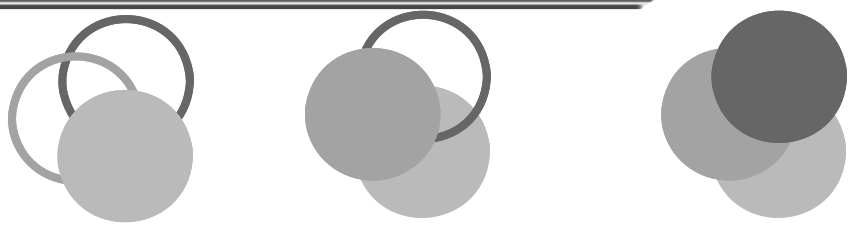
www.deadiversion.usdoj.gov/21cfr/cfr/2106cfrt.htm

United States Code (USC) - Controlled Substances Act, Title 21, Section 829

www.deadiversion.usdoj.gov/21cfr/21usc/829.htm

www.emergingsolutionsinpain.com

Summary



Engage	Educate	Protect
Altering treatment plans in consultation with patients and in response to current treatment	Initiating, modifying and discontinuing opioid therapy Adverse event monitoring Use of EDT	Appropriate patient selection Documentation Follow guidance on dosing, modifications and discontinuation

Thank you for completing Module 2.

You must answer the post-test questions at the end of this module before moving on to Module 3

You must complete all six modules in order to print your CE certificate