Opioid Use in Chronic Pain: *Building Regimens*

Online module developed by: **Emily K. Flores, PharmD, BCPS**

ETSU Health

This online module was designed as part of a Health Resources & Services Administration (HRSA) grant by faculty at ETSU Health to assist primary care providers with opioid use in chronic pain. It discusses reasonable use of opioids, concomitant nonpharmacologic and pharmacologic therapies, selection and dosing of initial opioid, and overall regimen design. Thank you for taking your time to complete this training and we hope it will benefit your patient care.

Self-assessment pre-test

- When is chronic opioid use reasonable?
- Which opioids are safest in renal decline?
- What type of opioid should be used as a regimen backbone?
- What ongoing assessments should be done once an opioid is prescribed?
- How much do you dose reduce when converting opioids?

Objectives

After reviewing these materials, learners will be able to:

- Determine if chronic opioid use is reasonable
- Select initial opioid based on patient specific factors
- Design a chronic opioid regimen including backbone, breakthrough, adjuncts, and ongoing assessments
- Utilize opioid conversions when needed

- ❑ Reasonable use
- ❑ Initial opioid
- ❑ Regimen
- ❑ Conversions

Chronic pain is pain lasting > 3 months or past the time of normal tissue healing.

- ❑ Reasonable use
- ❑ Initial opioid
- ❑ Regimen
- ❑ Conversions

Active cancer, palliative care, or end-of-life pain management differs from other chronic pain management.

Chronic pain

- Over 30% of US population has persistent or chronic pain
- Common causes
  - Spinal pain
  - Headache
  - Rheumatic conditions
  - Ischemic pain syndromes
  - Visceral pain syndromes
  - Neuropathic pain syndromes
  - Fibromyalgia

> 11.5 million Americans reported misusing opioids in 2016

https://www.cdc.gov/drugoverdose/prescribing/guideline.html

Assessment

- Patient report
- History and Physical
  - History of the pain and any preceding events
  - Thorough physical exam with attention to areas of pain
  - Evaluate patient's functional status
  - Evaluate patient's emotional response to pain
  - Evaluate for comorbid psychiatric disorders, including depression, anxiety disorder, and personality disorders
  - Patients with impaired cognitive function pre-operatively are at greater risk of chronic pain post-operatively

Chronic pain is managed with many modalities

Nonpharmacologic and non-opioid modalities should be utilized before and during opioid use … an opioid trial is a last resort *(low evidence)*

Nonpharmacologic

- Mind-body therapies
- Exercise/activity
- Acupuncture
- Low-level laser therapy
- Spinal manipulation therapy

Acetaminophen

NSAIDs

Topicals

Antidepressants

Antiepileptic agents

Cannabinoids

Nonpharmacologic interventions and nonopioid medications are preferred for chronic pain

Opioids

Nonpharmacologic interventions and nonopioid medications are continued throughout care

Reasonable use

- Common in cancer pain, palliative care, and end-of-life care
- Opioid trial
  - Patient expectations and must be continually addressed with the goals of optimal functionality and quality of life
  - Consider risk of harm or misuse
- Checklist for prescribing opioids for chronic pain
- Utilize Prescription Drug Monitoring Program (PDMP)

Risk for misuse increases if …

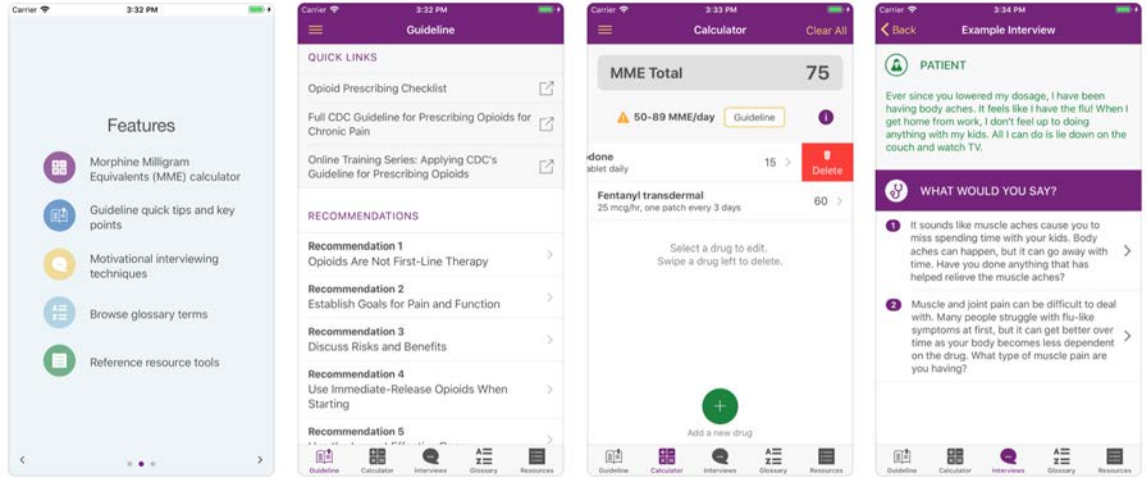
- History of substance use disorder
- Younger age
- Major depression
- Psychotropic medications

CDC Opioid Guideline Mobile App

https://www.cdc.gov/drugoverdose/pdf/App_Opioid_Prescribing_Guideline-a.pdf

Free download for Android and iOs devices

https://www.cdc.gov/drugoverdose/prescribing/app.html



When is it reasonable to use an opioid trial in chronic non-cancer pain?

Answer:

If additional pain control is needed after initial nonpharmacologic interventions and nonopioid medications in patients without contraindications and if potential benefit > risk

Initial opioid selection is based on patient specific factors including allergies, organ function, age, and comorbidities …

- ✓ Reasonable use
- ❑ Initial opioid
- ❑ Regimen
- ❑ Conversions

… and is *NOT* fentanyl or methadone.

Codeine → Morphine

Hydrocodone → Hydromorphone

Oxycodone → Oxymorphone

Allergies

- **Adverse reaction**: nausea, vomiting, constipation, drowsiness, delirium, physical dependence, mild itching, QT prolongation, respiratory distress, urinary retention
- **Pseudo-allergy**: headache, hives, redness, mild itching, sweating, flushing, mild hypotension, tachycardia, sneezing
- **True allergy**: difficulty swallowing, headache, angioedemia/swelling of lips, tongue, face, or mouth, cutaneous reactions (other than hives, e.g. maculopapular rash), severe hypotension, shock, difficulty breathing

Cross reactivity

Phenanthrenes	Benzomorphans	Phenylpiperidines	Diphenylheptanes	Phenylpropyl amines
• Codeine* • **Morphine*** • **Hydrocodone** • **Hydromorphone** • **Oxycodone** • **Oxymorphone** • **Buprenorphine**	• Pentazocine (with naloxone)	• Fentanyl • Meperidine	• Methadone	• **Tramadol** • **Tapentadol**

*with a 6-hydroxyl group
→ higher incidence of nausea and hallucinations

https://www.painphysicianjournal.com/current/pdf?article=OTg3&journal=42

Organ function

Renal concerns

- Lower initial dose, careful titration
- Metabolites/accumulation risk
- Avoid meperidine
- Avoid morphine in dialysis (variable removal), adjust dose otherwise
- Buprenorphine, fentanyl, hydromorphone, and methadone (adjust if CrCl < 10 mL/min) least impacted

Hepatic concerns

- Concern based on level of impairment
- Avoid meperidine
- Lower initial dose and/or extended interval with all except fentanyl
- Fentanyl least impacted

If impairment in both, use additional caution; fentanyl is okay in both

Non-opioid organ concerns

Acetaminophen

- Renal: adjust dosing interval to Q6-8 hours
- Hepatic
  - Reduced dosing is generally a safe option
  - 2 grams/day maximum
- Combined: **likely safe at reduced total daily dose**

NSAIDs

- Renal: adjust dose and use caution
- Hepatic
  - Increased bleeding risk
  - Avoid in cirrhosis to avert renal failure
- Combined: avoid

Pediatric considerations

Codeine

- ***CONTRAINDICATED*** under 12 years
- ***Warning*** against use in age 12-18 if obese, OSA, or severe lung disease due to risk of serious breathing problems
- ***Warning*** that not recommended in breast feeding due to infant risk (excessive sleepiness, difficulty breastfeeding, or serious breathing problems)

Tramadol

- ***CONTRAINDICATED*** under 12 years
- ***CONTRAINDICATED*** under 18 years for pain after tonsil and/or adenoid surgery
- ***Warning*** against use in age 12-18 if obese, OSA, or severe lung disease
- ***Warning*** that not recommended in breast feeding due to infant risk

https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-restricts-use-prescription-codeine-pain-and-cough-medicines-and

Geriatric considerations

- Opioids increase sedation and fall risk in older patients
  - Increased fracture risk?
  - Increased cardiovascular event risk?
- Uncontrolled pain limits mobility and increases depression
- Reduce initial dose and titrate slowly
- Monitor organ function and comorbid disease states
- Utilize nonpharmacologic and non-opioid adjuncts to minimize opioid requirements
- Acetaminophen and NSAID limits

Comorbidities

Disease states

- Age / Renal / Hepatic
- Respiratory / Sleep apnea
- Neuropathic
- Cardiovascular
- Depression / Mental health
- Alcohol / Substance abuse
- Pregnancy

Medications

- CNS depressants
  - Benzodiazepines
  - Skeletal muscle relaxants
  - Alcohol
- Adjuncts
- Substances of abuse

Opioid naïve starting dose

Use immediate release

	Dose	Interval
Morphine	5-10mg (initial daily dose < 50mg/day)	Q4H
Hydrocodone	2.5-5mg (with acetaminophen)	Q4-6H
Hydromorphone	1-2mg	Q4-6H
Oxycodone	2.5-5mg	Q4-6H
Oxymorphone	5-10mg	Q4-6H
Buprenorphine	75mcg	Q12-24H
Tramadol	25-50mg	Q6H
Tapentadol	50mg	Q12H

Practical Pain Management Opioid Naïve Dosing Calculator

https://opioidcalculator.practicalpainmanagement.com/

If a patient has a true allergy to morphine, which opioid would likely have the least cross reactivity?

1. Buprenorphine
2. Hydromorphone
3. Oxycodone
4. Pentazocine
5. Tramadol

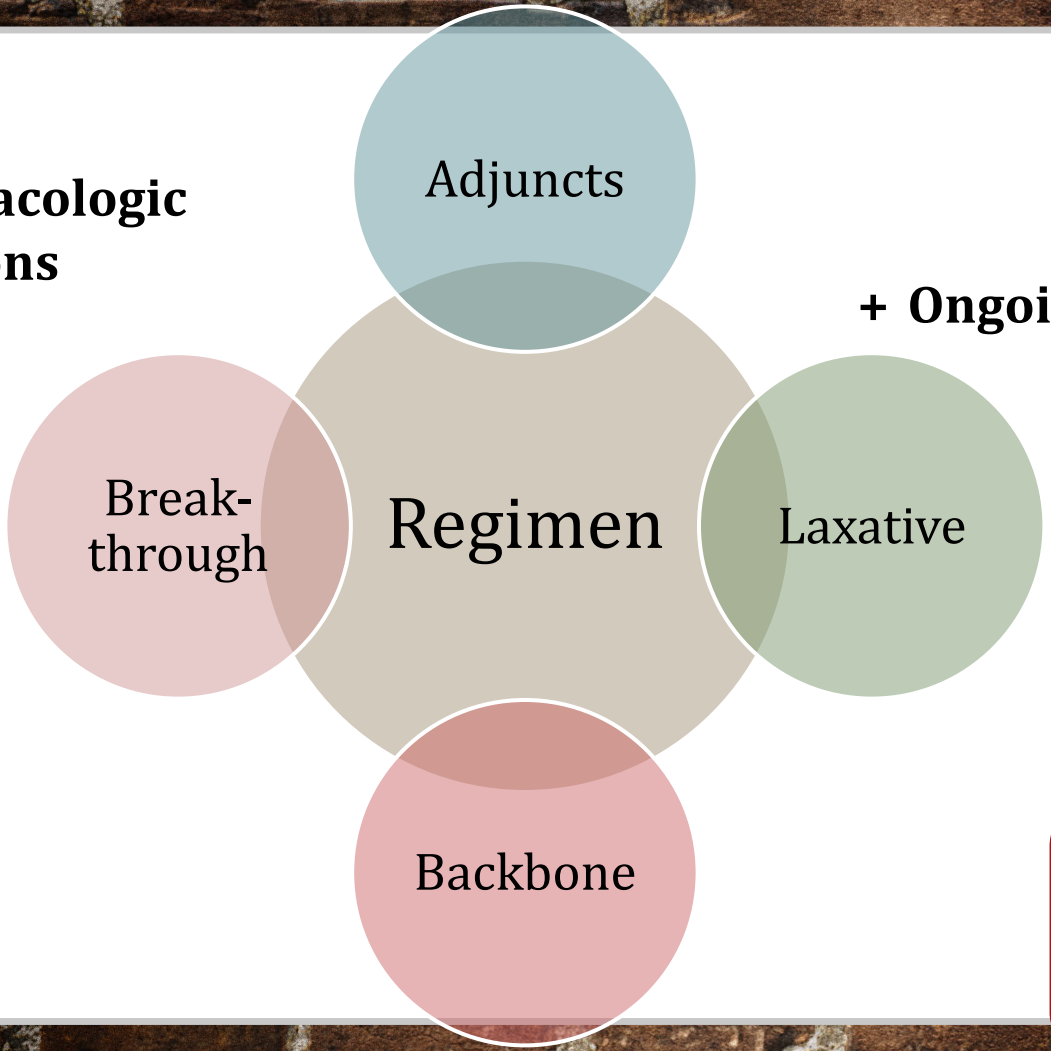
Which opioid(s) is least impacted in renal decline?

1. Buprenorphine
2. Fentanyl
3. Hydromorphone
4. Morphine
5. Oxycodone
6. Tramadol

Which opioid(s) should not be used in a 10-year-old child after tonsillectomy?

1. Codeine
2. Hydrocodone
3. Morphine
4. Tramadol

Continue nonpharmacologic interventions



+ Ongoing assessments

- ✓ Reasonable use
- ✓ Initial opioid
- ❑ Regimen
- ❑ Conversions

CORE IM

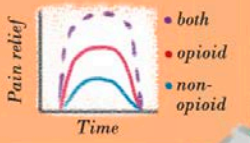
5 Pearls Podcast: Pain Management Toolbox

"The goal is to achieve tolerability of pain rather than its complete absence."

-Dr. Shani Herzig, Beth Israel Deaconess Medical Center

First, Have a Conversation:
- Characterize their pain.
- Set realistic goals for pain control.
- Use impairment in function (e.g., sleep or ability to engage in daily activities) as an endpoint.
- Talk about Multimodal Therapy...

Multimodal Therapy has a synergistic effect!



Next, Don't Forget to Complement:
Utilize physical therapy, hot and cold packs, and topicals like lidocaine patches and capsaicin cream.

Then, Cover Your Bases with Non-Opioids:
- Order standing doses of acetaminophen and/or NSAIDs.
- Ex: acetaminophen 1000mg q8h + ketorolac 15mg q6h
- Remember to treat neuropathic pain with appropriate agents such as gabapentin and pregabalin.

FYI: NSAIDs are generally safe and are often underutilized in CKD. Start with lower potency ibuprofen or naproxen in patients with cardiac, liver, and GI bleeding risk.

Finally, Use Opioids Mindfully:
- Start with the lowest PRN dose of short-acting form.
- Aim for as brief a duration of therapy as possible.
- On discharge, share your plan directly with the PCP.

https://www.coreimpodcast.com/2019/03/13/5-pearls-on-pain-management/

Adjuncts

Topicals	Acetaminophen	NSAIDs
Antidepressants	Antiepileptic agents	Cannabinoids

Laxative

Bisacodyl	• 10mg po BID
Sennokot	• 2 tabs po BID

Backbone

- Establish opioid requirements using immediate release forms
- Start low and go slow → Follow-up within 1-4 weeks
- Only continue if clinically meaningful improvement in pain and function that outweighs patient safety risks
- Only convert to ER/LA if severe, continuous pain requiring around the clock immediate release opioids daily; reduce dose
- Continue adjuncts and nonpharmacologic approaches

Breakthrough

- Use immediate release PRN as backbone and monitor dosing requirements to consider next steps in regimen
- Ask about breakthrough pain during ongoing assessments → plan PRN dosing
- Avoid combining ER/LA and immediate-release in chronic non-cancer pain

Ongoing assessments

- Calculate daily Morphine Milligram Equivalent (MME)
- Check the Prescription Drug Monitoring Program (PDMP)
- Utilize urine drug screening
- Evaluate for safety and efficacy
  - Use lowest effective dose
  - Consider overdose risk → provide naloxone
  - Significant conversation about risks/benefits of continuing opioids every 3 months

Calculate MME

1. **DETERMINE** the total daily amount of each opioid the patient takes.
2. **CONVERT** each to MMEs—multiply the dose for each opioid by the conversion factor. (*see table*)
3. **ADD** them together.

Calculating morphine milligram equivalents (MME)

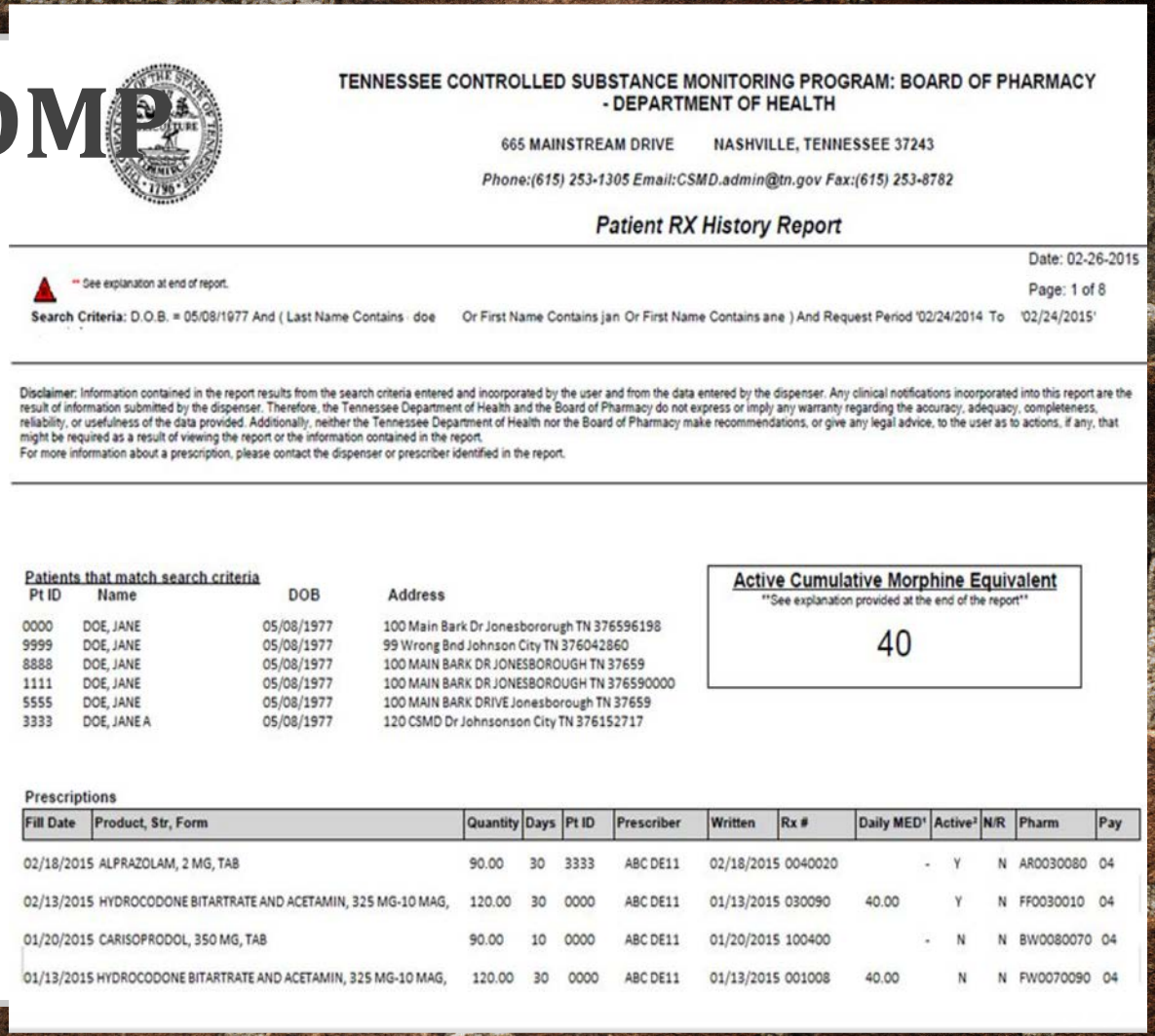
OPIOID (doses in mg/day except where noted)	CONVERSION FACTOR
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.

https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

Check the PDMP

- At initiation & regularly
- Review medications, quantities, dates, prescribers, pharmacies



TENNESSEE CONTROLLED SUBSTANCE MONITORING PROGRAM: BOARD OF PHARMACY - DEPARTMENT OF HEALTH

665 MAINSTREAM DRIVE NASHVILLE, TENNESSEE 37243

Phone:(615) 253-1305 Email:CSMD.admin@tn.gov Fax:(615) 253-8782

Patient RX History Report

Date: 02-26-2015

Page: 1 of 8

** See explanation at end of report.

Search Criteria: D.O.B. = 05/08/1977 And (Last Name Contains doe Or First Name Contains jan Or First Name Contains ane) And Request Period '02/24/2014 To '02/24/2015'

Disclaimer: Information contained in the report results from the search criteria entered and incorporated by the user and from the data entered by the dispenser. Any clinical notifications incorporated into this report are the result of information submitted by the dispenser. Therefore, the Tennessee Department of Health and the Board of Pharmacy do not express or imply any warranty regarding the accuracy, adequacy, completeness, reliability, or usefulness of the data provided. Additionally, neither the Tennessee Department of Health nor the Board of Pharmacy make recommendations, or give any legal advice, to the user as to actions, if any, that might be required as a result of viewing the report or the information contained in the report.
For more information about a prescription, please contact the dispenser or prescriber identified in the report.

Patients that match search criteria

Pt ID	Name	DOB	Address
0000	DOE, JANE	05/08/1977	100 Main Bark Dr Jonesbororugh TN 376596198
9999	DOE, JANE	05/08/1977	99 Wrong Bnd Johnson City TN 376042860
8888	DOE, JANE	05/08/1977	100 MAIN BARK DR JONESBOROUGH TN 37659
1111	DOE, JANE	05/08/1977	100 MAIN BARK DR JONESBOROUGH TN 376590000
5555	DOE, JANE	05/08/1977	100 MAIN BARK DRIVE Jonesborough TN 37659
3333	DOE, JANE A	05/08/1977	120 CSMD Dr Johnsonson City TN 376152717

Active Cumulative Morphine Equivalent
See explanation provided at the end of the report
40

Prescriptions

Fill Date	Product, Str, Form	Quantity	Days	Pt ID	Prescriber	Written	Rx #	Daily MED[1]	Active[2]	N/R	Pharm	Pay
02/18/2015	ALPRAZOLAM, 2 MG, TAB	90.00	30	3333	ABC DE11	02/18/2015	0040020	-	Y	N	AR0030080	04
02/13/2015	HYDROCODONE BITARTRATE AND ACETAMIN, 325 MG-10 MAG,	120.00	30	0000	ABC DE11	01/13/2015	030090	40.00	Y	N	FF0030010	04
01/20/2015	CARISOPRODOL, 350 MG, TAB	90.00	10	0000	ABC DE11	01/20/2015	100400	-	N	N	BW0080070	04
01/13/2015	HYDROCODONE BITARTRATE AND ACETAMIN, 325 MG-10 MAG,	120.00	30	0000	ABC DE11	01/13/2015	001008	40.00	N	N	FW0070090	04

Overdose risk increases if …

- History of overdose
- ≥ 50 MME/day
- Concurrent benzodiazepine use
- Multiple prescribers

Naloxone!

Arrange for medication-assisted treatment (MAT) in combination with behavioral therapies if opioid use disorder presents.

Polypharmacy concerns with opioids must be recognized.
Avoiding other drugs of abuse and CNS depressants is recommended.
Monitoring adherence on all regimen components and comorbid treatments is important.

What are the components to include when building an opioid regimen in chronic non-cancer pain?

Answer:

Nonpharmacologics

Adjunct(s)

Laxative

Backbone opioid of immediate release formulation

Ongoing assessments

What should be prescribers check with every initial opioid prescription and at least every 3 months with ongoing treatment?

1. Morphine Milligram Equivalent (MME)
2. Prescription Drug Monitoring Program (PDMP)
3. Urine Drug Screen (UDS)

Establish opioid requirements using _____ release formulations.

Answer:

Establish opioid requirements using immediate release formulations.

Opioid dose conversion

If needing to switch due to patient safety or efficacy:

1. Add up total daily dose of current opioid
2. If IV convert to PO within the same opioid
3. Decrease the oral daily dose by 25-50%
4. Convert between oral formulations of the two opioids
5. Design new regimen using available strengths and recommended intervals

Practical Pain Management Opioid Conversion Calculator

https://opioidcalculator.practicalpainmanagement.com/

- ✓ Reasonable use
- ✓ Initial opioid
- ✓ Regimen
- ❑ Conversions

- Hydrocodone 7.5/325mg 2 tabs TID (45mg/day)
- Remove acetaminophen (1,950mg/day)
- Hydromorphone 2mg, 4mg, 8mg IM tablets
- 30% reduction → 7.9mg Hydromorphone
- Hydromorphone 2mg po Q6H

Additional caution is warranted with conversion to/from Fentanyl or Methadone and among Fentanyl dosage forms.

Opioid dosing tips

- Reduce maintenance dose by **~ 25%** when switching to sustained-release agent due to improved pharmacodynamics/physiology
- Reduce opioid dose **25-50%** when switching between opioids due to incomplete cross tolerance and interpatient variability
  - More if controlled pain or sedation, less if uncontrolled pain
  - Then use equianalgesic dose based on morphine equivalents
- Combination analgesics may not be feasible in severe pain due to dosing restrictions on non-opioid component

- ✓ Reasonable use
- ✓ Initial opioid
- ✓ Regimen
- ✓ Conversions

Mark (58 yo male) has chronic back pain and is on opioid therapy. How would you convert Morphine 10mg po Q4H PRN (taking 4 doses daily) to Oxycodone (due to nausea)?

Practical Pain Management Opioid Conversion Calculator
https://opioidcalculator.practicalpainmanagement.com/

Answer:

40mg morphine → 20mg oxycodone

(25% reduction)

5mg, 10mg, 15mg, 20mg, 30mg IM tablets

Oxycodone 5mg Q6H PRN

Self-assessment post-test

- When is chronic opioid use reasonable?
- Which opioids are safest in renal decline?
- What type of opioid should be used as a regimen backbone?
- What ongoing assessments should be done once an opioid is prescribed?
- How much do you dose reduce when converting opioids?

Objectives

After reviewing these materials, learners will be able to:

- Determine if chronic opioid use is reasonable
- Select initial opioid based on patient specific factors
- Design a chronic opioid regimen including backbone, breakthrough, adjuncts, and ongoing assessments
- Utilize opioid conversions when needed

- ✓ Reasonable use
- ✓ Initial opioid
- ✓ Regimen
- ✓ Conversions

Questions or feedback?

florese@etsu.edu

References

- Fudin J. Opioid Allergy, Pseudo-allergy, or Adverse Effect? Pharmacy Times 2018. Available online at: https://www.pharmacytimes.com/contributor/jeffrey-fudin/2018/03/opioid-allergy-pseudo-allergy-or-adverse-effect
- Trescot AM, Datta S, Lee M, and Hansen H. Opioid Pharmacology. Pain Physician 2008: Opioid Special Issue: 11: S133-S153. Available online at: https://www.painphysicianjournal.com/current/pdf?article=OTg3&journal=42
- Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1external icon.
- Nix E, Majeroni BA. Pain Management (chronic non-malignant). Essential Evidence Plus. Last Updated 02-21-2020. Accessed 05-24-2020.

Additional Resources

- CDC Guideline for Prescribing Opioids for Chronic Pain resource page: https://www.cdc.gov/drugoverdose/prescribing/guideline.html
- Tennessee Medical Association Opioid Resource Center: https://www.tnmed.org/opioids
- Opioid Tapering online module: https://sites.google.com/view/opioidtapering/taper-approach
- Benzodiazepine Tapering online module: https://sites.google.com/view/benzodiazepinetapering/benzodiazepine-tapering