Breaking Barriers:

Pain & Addiction Updates

Mark Garofoli, PharmD, MBA, BCGP, CPE, CTTS

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Disclosures

I have nothing to disclose concerning possible financial relationships with ineligible companies that may have a direct or indirect interest in the subject matter of this presentation.

2

Abbreviations

- MOUD (Medications for Opioid Use Disorder)
- MME (Morphine Milligram Equivalent)
- PDMP (Prescription Drug Monitoring Program)
- CS (Controlled Substance)
- UDM (Urine Drug Monitoring)
- ADF (Abuse Deterrent Formulation)

3

Personal Facts…

I have personal and professional opinions on pain management, but some things are better left NSAID.

4

Learning Objectives

1. Recall the pharmacological properties of buprenorphine.
2. Recall controlled substance "Red Flags" for prescribers and dispensers based on the National Opioid Settlement.
3. Identify the available opioid antagonist products currently available in the United States.
4. Recall the CDC Opioid Guideline Update twelve recommendations.
5. Identify pain management medications that are potentially inappropriate for utilization in older adults based on the AGS Beers Criteria
6. Recall the pharmacological properties of the most common new pain medications.

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Agenda

1. Intro
2. Addiction Updates
3. Pain Management Best Practices
4. Opioid Antagonists
5. CDC Opioid Guideline Update
6. Beers List Update
7. Newer Pain Medications

6

US Substance-Related Deaths

Substance	~US Annual Deaths
"Drugs"	80,000
Alcohol	150,000
Tobacco	500,000

https://www.drugwonfacts.org/node/1654
https://www.npr.org/2022/11/05/1134521220/alcohol-death-rate-cdc-report

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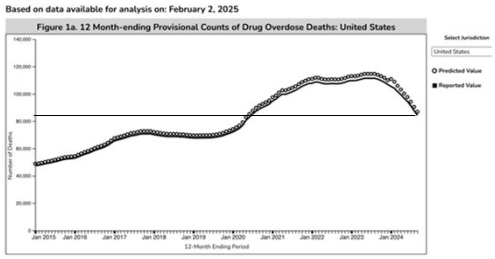
US Drug Overdose Deaths
All Drugs



https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
https://www.statista.com/chart/18744/the-number-of-drug-overdose-deaths-in-the-us/

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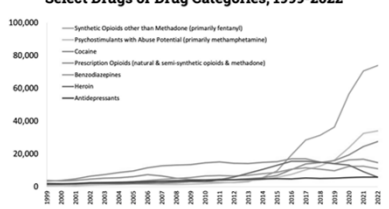
US Drug Overdose Deaths



https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates

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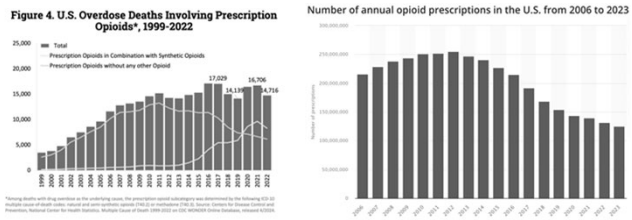
U.S. Rx Opioids
Deaths/Rx's



https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates
https://www.statista.com/statistics/752149/total-number-of-opioid-rx-prescriptions-in-us/

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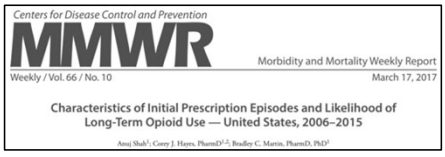
Heroin Headlines



75% of Heroin Utilizers Started with Prescription Opioids

Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use – United States, 2006-2015. Weekly / March 17, 2017 / 66(10); 265-269.

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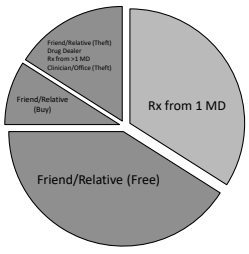
But From Where?



2017 DEA National Drug Threat Assessment https://www.dea.gov/documents/2018-060-27-2017-NDTA.pdf

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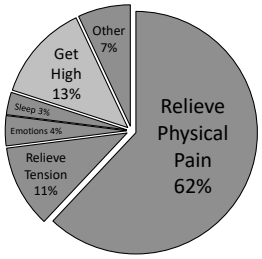
And WHY?



2018 DEA National Drug Threat Assessment (NDTA). https://www.dea.gov/documents/2018/10/02/2018-national-drug-threat-assessment-ndta

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Just Say NO

https://www.scientificamerican.com/article/why-just-say-no-doesnt-work/

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7th Grade Speeling Bee Falure

Rolaids Vs Relief

https://www.npr.org/2019/05/31/728526221/8-spelling-bee-winners-named-as-co-champions-in-historic-marathon-competition

15

Just Say KNOW

https://www.scientificamerican.com/article/why-just-say-no-doesnt-work/

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The West Virginia Way

Almost Heaven…

- Mother's Day
- Proud. Hard Working. Resilient.
- Jack Dempsey
- Jennifer Garner
- Brad Paisley
- Supersize Me (Movie)
- We are Marshall (Movie)
- Hidden Figures (Movie)
- Take Me Home, Country Roads!

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Addiction Updates MOUDs

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https://yrm.org/misunderstood-book-time/

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Buprenorphine

Pain MCG Narrative Reviews

Journal of Pain Research — Dovepress — REVIEW

Benefit-Risk Analysis of Buprenorphine for Pain Management

Martin Hale[1], Mark Garofoli[2], Robert B Raffa[3,4]

Journal of Multidisciplinary Healthcare — Dovepress — REVIEW

Frontline Perspectives on Buprenorphine for the Management of Chronic Pain

Jeremy Adler[1], Theresa Mallick-Searle[2], Mark Garofoli[3], Amanda Zimmerman[4]

Hale M, Garofoli MP, Raffa R. Benefit-Risk Analysis of Buprenorphine for Pain Management. Journal of Pain Research. 24 May 2021 Volume 2021: 14 Pages 1359—1369.
Adler J, Mallick-Searle T, Garofoli M, Zimmerman A. Frontline Perspectives on Buprenorphine for the Management of Chronic Pain. J Multidiscip Healthc. 2016;17:1375-1383

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Mu Opioid Receptor Affinity

Prescription Opioid	~K
Sufentanil	0.138
Buprenorphine	**0.216**
Hydromorphone	0.37
Naltrexone (Antagonist)	0.4 to 0.6
Oxymorphone	0.41
Levorphanol	0.42
Butorphanol	0.76
Naloxone (Antagonist)	1 to 3
Morphine	1.1
Fentanyl	1.3
Methadone	3
Diacetylmorphine	10
Hydrocodone	42
Oxycodone	25
Pentazocine	118
Codeine	734
Meperidine	450
Dextromethorphan	1,020
Tramadol	12,500

High to Low Affinity

- Affinity: "Thermodynamic Chemical Attraction to Receptor"
- NOT Intrinsic Activity (NOT effect)

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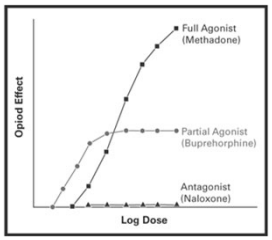
Buprenorphine

Respiratory Depression "Ceiling Effect"

Concerns

- Relapses
- Street PolyRx
- Children



Suboxone Medication Guide (Package Insert)
Roberts, James R. MD Buprenorphine: Toxicity and Overdose, Emergency Medicine News: January 2009 - Volume 31 - Issue 1 - p 7-10

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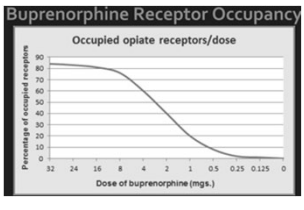
Buprenorphine

Receptor Saturation

However, did these studies involve opioid-naïve or opioid-experienced (tolerant) human brains?



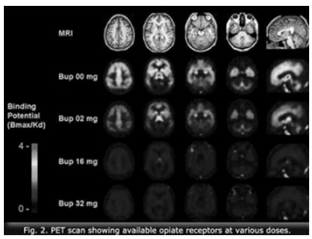


Fig. 2. PET scan showing available opiate receptors at various doses.

Clinical Pharmacology Online Database
Neuropsychopharmacology. 2003; 28 (11): 2000–2009.
https://accuratecliniic.com/accurate-education-pain-medications-buprenorphine/

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Buprenorphine

Morphine Milligram Equivalent Factor

- March 2016 CDC Chronic Pain Opioid Guidelines
  - Buprenorphine MME Factor: 10
- January 2017 CDC Updates
  - Buprenorphine MME Factor: 30
- 2018 CDC Updates
  - Buprenorphine MME Factor: Unlisted

Clinical Pharmacology Online Database
SAMHSA. Buprenorphine Clinical Guidelines. https://www.ncbi.nlm.nih.gov/books/NBK64265/
Walsh SL, et al. Clinical Pharmacology of Buprenorphine: Ceiling Effects at High Doses. Clinical Pharmacology & Therapeutics. 1994 Mar; 55(3): 569-580. https://pubmed.ncbi.nlm.nih.gov/8143524/

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Buprenorphine
Initiations

TRADITIONAL EXAMPLE
Observe Mild to moderate opioid withdrawal (Approximate COWS >11)
Initiation of buprenorphine should start with a dose of 2mg to 4 mg
Dosages may then be increased in increments of 2 mg to 4 mg
Once initial dose is well tolerated, can titrate fairly rapidly to 24-hour stable effects
Doses average at least 8 mg per day

MICRODOSE EXAMPLE	
Day 1	0.5mg QD
Day 2	0.5mg BID
Day 3	1mg BID
Day 4	2mg BID
Day 5	3mg BID
Day 6	4mg BID
Day 7	12mg (stop other opioids)

Kampman K and Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med. Sep-Oct 2015;9(5):358-67.
Ahmed, S, Bhavsar, S, et. al. Microinduction of Buprenorphine/Naloxone: A Review of the Literature. The American Journal on Addictions, 30: 305 - 315, 2021.
Privia A. Randhawa, Rupinder Brar and Seonaid Nolan. Buprenorphine–naloxone "microdosing": an alternative induction approach for the treatment of opioid use disorder in the wake of North America's increasingly potent illicit drug

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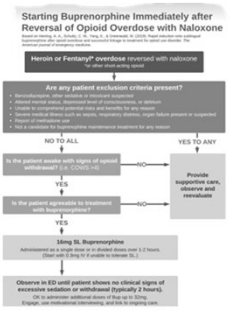
Buprenorphine
Initiations

"Macrodosing"



https://bridgetotreatment.org/resource/starting-buprenorphine-immediately-after-reversal-of-opioid-overdose-with-naloxone/

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MAT & MATE Acts

MAT Act: Buprenorphine X-Waiver eliminated

- Prescribers only need an active DEA License
- There are no limits on the number of patients for a prescriber

MATE Act: DEA renewals (q 3 years) require 8-hour Substance Use Disorder (SUD) training

https://www.medpagetoday.com/specialreports/features/102620
https://www.pewtrusts.org/en/research-and-analysis/articles/2022/12/30/president-signs bipartisan-measure-to-improve-addiction-treatment
https://www.deadiversion.usdoj.gov/pubs/docs/A-230020-Dear-Registrant-Letter-Signed.pdf

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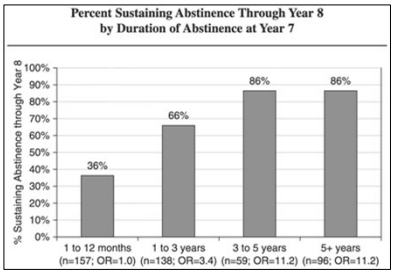
Minimum SUD Treatment???



Michael L. Dennis, Mark A. Foss, and Christy K. Scott. An Eight-Year Perspective on the Relationship Between the Duration of Abstinence and Other Aspects of Recovery. Evaluation Review 2007 31:6, 585-612

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Wouldn't Dopamine Agonists Make Sense?
Induction of Compulsions (Gambling/Sex)

Frequency of New-Onset Pathologic Compulsive Gambling or Hypersexuality After Drug Treatment of Idiopathic Parkinson Disease

J. Michael Bostwick, MD; Kathleen A. Hecksel, MD; Susanna R. Stevens, MS; James H. Bower, MD; and J. Eric Ahlskog, MD, PhD

TABLE 3. Patients With PD and Compulsive Gambling or Hypersexuality[a]

Patient No./sex/ age at PD onset (y)/ age at behavior onset (y)	Behaviors	Dose (mg/d) Pramipexole	Ropinirole	Levodopa	Other PD drug	Other psychoactive drugs at time of behavior onset (mg)
1/M/43/49	Hypersexuality[b]		15	0		Bupropion SR, 150
2/M/40/52	Pathologic gambling, compulsive lawn care	4.5		700	Selegiline, 5; amantadine, 300	Gabapentin, 900; oxycodone, 5
3/M/65/68	Pathologic gambling, hypersexuality	4.5		600		
4/F/53/53	Pathologic gambling	4.5		600		Escitalopram, 10
5/M/64/80	Hypersexuality[b]		6	850		Trazodone, 75
6/M/55/66	Hypersexuality, pathologic gambling	4.5		1400		Amiodarone, 200
7/M/41/49	Pathologic gambling, pathologic hypersexuality, increased food and alcohol consumption, compulsive hobby work		21-24	0		

[a] PD = Parkinson disease; SR = sustained release.
[b] Not clearly pathologic.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2665974/pdf/mayoclinproc_84_4_003.pdf

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Oh Oh Oh OUD

JAMA Network Open

Research Letter | Psychiatry

Semaglutide and Opioid Overdose Risk in Patients With Type 2 Diabetes and Opioid Use Disorder

William Wang, Nora D. Volkow, MD, QuangQiu Wang, MS, Nathan A. Berger, MD, Pamela B. Davis, MD, PhD, David C. Kaelber, MD, PhD, MPH, Rong Xu, PhD

Introduction

Drug overdose fatalities in the United States remain high, with an estimated 107 543 deaths in 2023, mostly from opioids.[1] Despite the effectiveness of medications for opioid use disorder (OUD) in preventing overdoses, only an estimated 25% of individuals with OUD receive them,[2] and close to 50% discontinue treatment within 6 months. There is an urgency for alternative treatments for OUD. Glucagon-like peptide-1 receptor agonists (GLP1-RAs), used for type 2 diabetes (T2D) and obesity, modulated dopamine reward signaling and decreased drug rewards, including heroin in rodents.[3] Anecdotal reports of reduced drug craving in individuals using semaglutide, a new generation GLP-1RA, along with empirical studies showed its therapeutic benefits in alcohol and nicotine use disorders.[4,5] This led us to investigate whether semaglutide could protect against overdoses in patients with OUD.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

OUD
Opioid Use Disorder

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2824054#google_vignette

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Pain Management Best Practices

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Best Practices

Patient Education
- Patient & Provider Agreements/Contracts
- Treatment Goals (Pain Reduction, Improved Function, & End of Therapy)
- Proper medication storage and disposal

Treatment Selection
- Mental Health Assessments (Psychological Evaluation & Opioid Risk Screening)
- Drug Interaction Review (Drug-Drug, PD, PK, & PGx)
- Naloxone Education

Adherence & Diversion Monitoring
- Pill Counts
- Urine Drug Monitoring
- Prescription Drug Monitoring Program (PDMP) Review
- Monitoring for Controlled Substance Red Flags

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Pain Management Goals

Pain Reduction & Function Improvement

Pain = 5th Vital Sign ???

Analgesic ???

The goal is NOT necessarily to eliminate pain

- S – Specific
- M – Measurable
- A – Attainable
- R – Relevant
- T – Time-Bound

➢ **The goal is to Improve Function & Reduce Pain**

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Favorite 1 to 10 Pain Scale Responses

20	Yes
13	2
8.5	3.14

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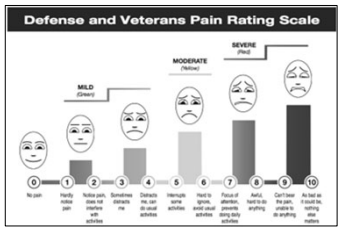
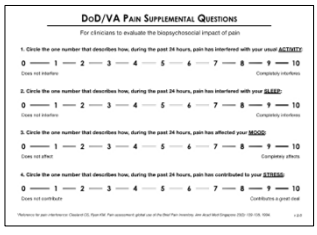
DVPRS





http://www.dvcipm.org/clinical-resources/defense-veterans-pain-rating-scale-dvprs/

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Proper Medication Storage

Bathroom Medicine Cabinets → NO
- Humidity
- Unsecure
- Typically accessed at "groggy" times of day (AM/PM)

Lockable Safe Boxes → YES
- Away from children and pets
- Secure
- Still must incorporate into daily routine

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Proper Medication Disposal
EPA

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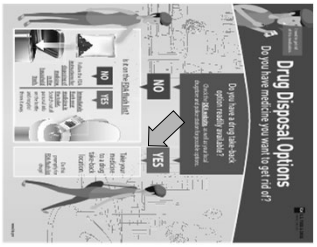
Proper Medication Disposal
FDA



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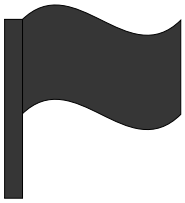
Controlled Substances Red Flags



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Publication of Red Flags

Prior to 2022
DEA Red Flags
(Court Cases)

2022
Practical Pain Management
(Now: Med Central)

2023
National Opioid Settlement

Garofoli MP. "Prescribing and Dispensing Controlled Substances: When to Pump the Brakes". Practical Pain Management. 2022;22(6). https://nationalopioidsettlement.com/

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Red Flags
National Opioid Settlement

- Teva & Allergen Settlements
- Walmart, Walgreens, & CVS Settlements
- Distributor & Janssen Settlements
- FAQs, Explanatory Charts, & Frequently Referenced Documents
- State Participation Chart & Documents

https://www.drugtopics.com/view/national-pharmacy-chain-opioid-settlements-poised-to-affect-independent-pharmacies
https://nationalopioidsettlement.com/

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Red Flags
National Opioid Settlement

- A Red Flag shall not automatically mean prescription is illegitimate, yet must be resolved
- Resolution → RPh believes legitimate diagnosis & scope
- Resolutions & Rejections → Documentation

https://nationalopioidsettlement.com/

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Red Flags
National Opioid Settlement

Red Flags (Patient)

1. CS-2 Refill Too Soon by > 3 Days
2. Doctor Shopping (CS > 4 Previous Prescribers of Separate Practices over 6 months)
3. Prescriber has > 10 documented CS refusals within 6 months
4. Previous 3 other CS from multiple prescribers with overlapping days within 30 days
5. Distance between patient's residence and pharmacy > 50 miles
6. Distance between patient's residence and prescriber > 100 miles
7. Previous 2 CS refusals within 30 days
8. Cash pay despite having prescription insurance coverage
9. >/= 3 Patients appear together for the same CS
10. Slang Term Medication Request (e.g., "Mallinckrodt blues," "M's", or "the blue pill")
11. Patient appears visibly altered, intoxicated, or incoherent

https://nationalopioidsettlement.com/

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Red Flags
National Opioid Settlement

RED FLAGS (PRESCRIPTION)

1. Fails to meet law requirements
2. Misspellings
3. Atypical Abbreviations
4. Multiple Colors of Ink or Multiple Handwritings

RED FLAGS (PRESCRIBER)

1. CS-2 + Benzodiazepine + Carisoprodol
2. Prescriber has no office within 50 miles of pharmacy
3. Prescriber utilizes preprinted or stamped prescription pads

https://nationalopioidsettlement.com/

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Corresponding Legal Responsibility

Title 21 Code of Federal Regulations

§1306.04 (a) Purpose of issue of prescription

- A prescription for a controlled substance to be effective must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice

➢The responsibility for the proper prescribing and dispensing of controlled substances is upon the prescribing practitioner, but a corresponding responsibility rests with the pharmacist who fills the prescription

https://www.deadiversion.usdoj.gov/21cfr/cfr/1300/1306_04.htm

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OBRA '90

It is an expected best practice, to not only offer patient counseling as required by OBRA 1990 law, but to proactively counsel (discuss) any and all dispensed prescriptions with respective patients.

https://www.cms.gov/files/document/patientcounselingbooklet111414pdf

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Patient Counseling At Its Best

- ~~I need you to sign here.~~
- ~~Do you have any questions?~~

➢This medication might turn your urine purple.
Pause Do you have any questions?

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Avoiding Stigmatic Communications

Stigmatic Terminology	Recommended Terminology
Aberrant Behaviors	Using Medication Not as Prescribed or Intended
Abuse	Non-Medical Use
Addict	Person with Substance-Use Disorder
Clean/Dirty Urine	Negative versus Positive, or Unexpected

https://www.samhsa.gov/capt/sites/default/files/resources/sud-stigma-tool.pdf
https://www.whitehouse.gov/sites/whitehouse.gov/files/images/Memo%20-%20Changing%20Federal%20Terminology%20Regarding%20Substance%20Use%20and%20Substance%20Use%20Disorders.pdf

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Opioid Antagonists

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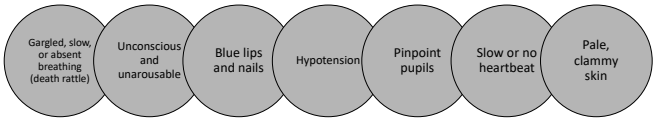
Opioid Overdose Symptoms



https://www.samhsa.gov/medication-assisted-treatment/treatment/naloxone

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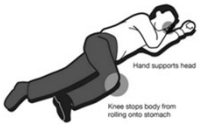
Opioid Antagonist Administration

SAMHSA Guidelines

1. Check for signs of opioid overdose
2. Call EMS to access immediate medical attention*
3. Administer antagonist (rescue position)*
4. Rescue breathe if patient not breathing
5. Stay with the person and monitor their response until emergency medical assistance arrives. After 2 to 5 minutes, repeat the dose if person is not awakening or breathing well enough (10 or more breaths per minute)



*Order depending on the source of guidance.

https://www.samhsa.gov/medication-assisted-treatment/treatment/naloxone

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Naloxone FDA "Perfect Dose" Panel

MEDPAGETODAY

Specialties COVID-19 Opinion Health Policy Meetings Special Reports Break Room Conditions Society Parts

Neurology > General Neurology

FDA Splits on Naloxone Dose

— Most agreed there was insufficient evidence to decide if 0.4-mg standard is too low

by Kristina Fiore, Associate Editor, MedPage Today October 6, 2016

A joint FDA advisory panel was split on whether the injectable 0.4-mg dose of naloxone should remain the current standard by which products containing the opioid overdose reversal drug should be measured -- though they agreed that a lack of data made their decision more challenging.

Slightly more panelists voted to increase the minimum acceptable dose rather than maintain it (15-to-13) during the joint meeting of the Anasthetic and Analgesic Drug Products Advisory Committee (AADPAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM).

No conclusion on "best" or "perfect" naloxone dose for all situations

Fiore, Kristina. "FDA Splits on Naloxone Dose." *Medical News*, MedpageToday, 6 Oct. 2016, www.medpagetoday.com/neurology/generalneurology/60632.

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Naloxone 8mg vs 4mg NS

CDC Centers for Disease Control and Prevention

Search

Morbidity and Mortality Weekly Report (*MMWR*)

Comparison of Administration of 8-Milligram and 4-Milligram Intranasal Naloxone by Law Enforcement During Response to Suspected Opioid Overdose — New York, March 2022–August 2023

Weekly / February 8, 2024 / 73(5);110–113

- No benefits to administration of 8-mg intranasal naloxone compared with 4-mg product
- 8-mg product had a significantly higher prevalence of opioid withdrawal

Payne EH, Standiff S, Rowe K, Christie JA, Dailey MW. Comparison of Administration of 8-Milligram and 4-Milligram Intranasal Naloxone by Law Enforcement During Response to Suspected Opioid Overdose — New York, March 2022–August 2023. MMWR Morb Mortal Wkly Rep 2024;73:110–113.

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Naloxone
Shelf Life

FDA announces shelf-life extension for naloxone nasal spray

Today, FDA is announcing that Emergent BioSolutions is extending the shelf-life of newly manufactured NARCAN (naloxone hydrochloride) 4 milligram (mg) Nasal Spray products from 3-years to 4-years. This action was taken at the request of the FDA and is the latest of multiple steps the Agency has recently taken to prevent overdoses and reduce overdose-related deaths by expanding access to naloxone and other overdose reversal agents.

Center for Drug Evaluation and Research. "FDA Announces Shelf-Life Extension for Naloxone Nasal Spray." *U.S. Food and Drug Administration*, FDA, www.fda.gov/drugs/drug-safety-and-availability/fda-announces-shelf-life-extension-naloxone-nasal-spray

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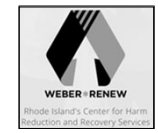
Location & Individuals

- Anyone can be trained to save a life with an opioid antagonist, yet what happens if there is none available on scene?
- Consider storing antagonist alongside AEDs, which are commonly located in public areas (malls, libraries, restaurants, and even airplanes)
- Location, Location, LOCATION!!!

55

Harm Reduction



As encountered by Pain Guy™ in Burnside Park in Providence, Rhode Island

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Naloxone Products			
Product	**Dose**	**Directions**	**Rx/OTC**
Generic Injectable	0.4mg	Inject 1mL in shoulder/thigh, may repeat in 2 to 3 min Use 3mL 23G syringe and 1" needle	Rx
Zimhi®	5mg	Inject in thigh, may repeat in 2 to 3 minutes	Rx
Auto Injector	10mg	Military Utilization	
Generic Intranasal (Kits)	1mg	Spray 1mL (half of syringe) in each nostril with atomizer, may repeat in 2 to 3 minutes	Rx
Narcan® Nasal Spray + Generic	4mg	Spray into one nostril; may repeat in 2 to 3 minute with 2nd device in alternate nostril	Rx & OTC
Kloxxado® Nasal Spray	8mg		Rx
Rivive®	3mg		OTC
Pocket Naloxone®	1 swab	Swab one nostril, may repeat in 2 to 3 minutes	OTC

Clinical Pharmacology Online Database
https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212854s000lbl.pdf
https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212854s000lbl.pdf

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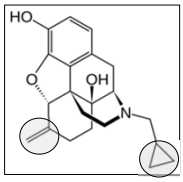
Nalmefene
Pharmacology

- Compared to Naltrexone
  - Longer t ½ (~8 Hours)
  - Greater PO bioavailability
  - Similar Mu binding affinity
- Compared to Naloxone
  - 5x Mu binding affinity

Stronger ?
Longer ?



Clinical Pharmacology Online Database

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Nalmefene
History

- 1975: Discovered
- 1995: FDA approved (Revex™) parenteral opioid overdose reversal
- 2008: Manufacturer discontinued
- 2013: European countries began approving for alcohol dependence
- 2020s: Studies for opioid overdose reversal product (US)

Clinical Pharmacology Online Database

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Nalmefene Products			
Product	**Dose**	**Directions**	**Rx/OTC**
Generic Injectable	2 mL vials (1 mg/1 mL)	Weight-Based IV Bolus or IM/SC	Rx
Zurnai® Auto-Injector	1.5mg in 0.5mL	Single-Dose Auto-Injector	Rx
Opvee® Nasal Spray	2.7mg	Spray into one nostril; may repeat in 2 to 3 minute with 2nd device in alternate nostril	Rx

Clinical Pharmacology Online Database

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Pain Guidelines

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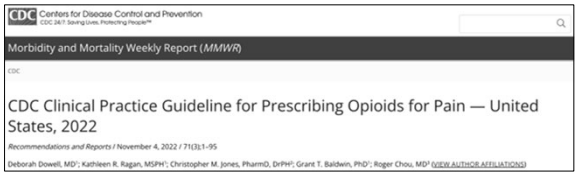
2022 CDC Opioid Guideline Update

Published Online Thursday November 3rd, 2022



https://www.regulations.gov/docket/CDC-2022-0024/document

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CDC Opioid Workgroup

2022 CDC Opioid Guideline Update

- Cunningham, Chinazo, MD, MS (Chair)
- Floyd, Frank, MD, FACP
- Habermann, Elizabeth, PhD, MPH
- Burns, Anne L., RPh
- Goertz, Christine, DC, PhD
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- Darnall, Beth, PhD
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- Perrone, Jeanmarie, MD
- Salinas, Roberto, MD, CAQ
- Smith, Wally, R., MD
- Wallace, Mark, MD
- Compton, Wilson, MD, MPE (Ex-Officio)
- Mundkur, Mallika, MD, MPH (Ex-Officio)
- Gandotra, Neeraj, MD (Ex-Officio)
- Rudd, Stephen, MD, FAAFP, CPPS (Ex-Officio)
- Ross, Melanie R., MPH, MCHES (Designated Federal Officer)

https://www.cdc.gov/injury/hsr/opioid-workgroup-2019.html#:~:text=The%20Opioid%20Workgroup%20(OWG)%20of,prepared%20by%20CDC)%20and%20a

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2022 CDC Opioid Guideline Updates

What's Updated???

1. Settings (All Outpatient)
2. Expanded Time Frames (Acute, Subacute, and Chronic)
3. Specific Pain Conditions
   - OA, Neuropathic, Fibromyalgia, DPN, & PHN
   - Not including palliative, cancer, nor sickle cell
4. Taper only when appropriate & only gradually (Avoid rapid tapers)
5. Massaged MME limits and thresholds wording
   - Updated Hydromorphone, Methadone, & Tramadol MME Factors

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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2022 CDC Opioid Guideline Update

12 Recommendations

1.	Nonopioid therapies are effective for many common types of acute pain	Opioid Yes/No
2.	Nonopioid therapies are preferred for subacute and chronic pain	
3.	Utilize Immediate-Release (IR) before Extended-Release (ER) opioids	Opioid Selection
4.	Start low, go slow, and avoid increasing to high-risk dosage levels	
5.	Current high-risk opioid dosages: continually reassess risk/benefits, only taper gradually if risks > benefits	
6.	When opioids are utilized in acute pain, only provide for expected duration	Duration & Follow-Up
7.	Reevaluate chronic/subacute opioid utilization at least every 3 months (within 1 to 4 weeks initially)	
8.	Opioid risk screening and naloxone education	Risk Reduction
9.	PDMP review initially and periodically	
10.	Toxicology testing (UDM)	
11.	Caution with opioid/benzo combinations (or opioids with any CNS depressant)	
12.	Arrange MOUD for patients with OUD	

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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2022 CDC Opioid Guideline Updates

Section 1: Recommendation 1

➢ Nonopioid therapies are at least as effective as opioids for many common types of acute pain

- Maximize Non-Rx and Non-Opioid Treatments
- Only utilize Rx Opioid when Benefits > Risks
- Discuss benefits & risks of opioid therapy with patient
- Reference: AHRQ Review Article of 183 RCTs

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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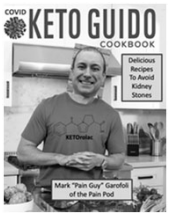
Opioids in Acute Pain

Kidney Stones



- 8 trials w/ ~2K Patients with kidney stone pain
  - Opioids
    - 1 Trial: Morphine
    - 7 Trials: Meperidine (Not commonly utilized in U.S.)
  - NSAIDs
    - 1 Trial: Indomethacin
    - 4 Trials: Ketorolac
    - 3 Trials: Diclofenac
  - Summary
    - Opioid therapy *probably* less effective than NSAIDs for kidney stone pain
    - Less effective than APAP for kidney stone pain

❖All single dose Inpatient IV Therapy, yet guideline scope: OUTPATIENT ???

Chou R, Wagner J, Ahmed AY, et al. Treatments for Acute Pain: A Systematic Review [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2020 Dec.

67

2022 CDC Opioid Guideline Updates

Section 1: Recommendation 2

➢Non-Opioids Preferred For Subacute & Chronic Pain

- Maximize Non-Rx and Non-Opioid Treatments
- Only utilize Rx Opioid when Benefits > Risks
- Discuss Benefits & Risks Of Opioid Therapy with Patient
- Discuss Opioid Discontinuation if Risks Eventually > Benefits

➢Non-Opioid Options Should Have Insurance Coverage

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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2022 CDC Opioid Guideline Updates

Section 1: Recommendation 2

Osteoarthritis	Neuropathic Pain	Fibromyalgia
Non-Rx → Topical NSAIDs → Duloxetine or NSAIDs	TCAs, SNRIs, Gabapentin, Pregabalin, Oxcarbazepine, Capsaicin Patches, & Lidocaine Patches	TCAs, SNRIs, NSAIDs, Gabapentin, & Pregabalin (Duloxetine, Milnacipran, & Pregabalin are FDA-approved)

DPN	PHN
Duloxetine & pregabalin (FDA-Approved)	Pregabalin & gabapentin (FDA-Approved)

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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2022 CDC Opioid Guideline Updates

Section 2: Recommendation 3

➢Opioid Initiation: IR Before ER/LA

- ER/LA opioids should be reserved for severe, continuous pain
  - FDA: Some ER/LA opioids only after IR opioids daily for at least 1 week
- Be careful with opioid rotation & renal/hepatic dysfunction
- Methadone should not be 1st Line option for ER/LA Rx pain opioid
- TD Fentanyl only with clinicians aware of dosing/absorption

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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2022 CDC Opioid Guideline Updates

Section 2: Recommendation 4

➢Opioid Initiation: Start Low, Go Slow

- Many patients do not experience benefit in pain and function from ≥50 MME/day but are exposed to progressive risk

➢Opioid-Naïve Starting Dose:

- 5 to 10 MME single dose, or 20 to 30 MME/Day

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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MME Factors

2022 CDC Guidelines

Rx Opioid	MME Factor
Codeine	0.15
Fentanyl (Transdermal)	2.4
Hydrocodone	1.0
Hydromorphone	5.0
Methadone	4.7
Morphine	1.0
Oxycodone	1.5
Oxymorphone	3.0
Tapentadol	0.4
Tramadol	0.2

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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MME Practice Case #1

Oxycodone

Ms. Faye Kinet is prescribed oxycodone 40mg BID for the management of chronic lower back pain. How many Morphine Milligram Equivalents (MMEs) per day are being utilized?

40mg tablet x 2/Day = 80mg/Day
80mg/Day x 1.5 (MME Factor) = 120 MME/Day

120 MMEs/Day

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

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MME Practice Case #2

Tramadol

Thomas Payne is utilizing tramadol 50mg QID PRN. How many Morphine Milligram Equivalents (MMEs) per day are being utilized?

Tramadol 50mg tablet x 4/Day= 200mg/Day
200mg/Day x 0.2 (MME Factor) = 40 MMEs/Day

40 MMEs/Day

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

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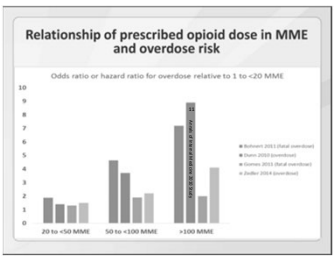
MME Potential Limitations

- **Patient Variability**
  - Age, Height, Weight
  - Genetics
  - Hepatic/Renal Function
  - Medications, etc.
- **Conversion Estimates**
- **Dose-Response Curves**
  - Respiratory Depression
  - Analgesia
- **Formulation Bioavailability Variability**
- **Mixed-Action Opioids**
- **Tolerance**
- **Methadone**
  - 2016: 4/8/10/12
  - 2022: 4.7 (Source 2008)
- **Transdermal Fentanyl**
  - Before 2016: Variable

75

MMEs & Overdose Risk



https://i1.wp.com/hs-facts.org/wp-content/uploads/2017/04/Opioid-dose-vs-overdose-risk.jpg

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2022 CDC Opioid Guideline Updates

Section 2: Recommendation 5

- If Opioid Risks > Benefits: Optimize Other Tx's (& *Gradually* Taper Opioid)
  - 10% Monthly, and may need to pause/restart (rapid tapers only if life threatening)
  - Counsel on decreased tolerance (Overdose risk with previous doses)
- Payers, health systems, & state medical boards should *not* use this clinical practice guideline to set rigid standards

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1-95.

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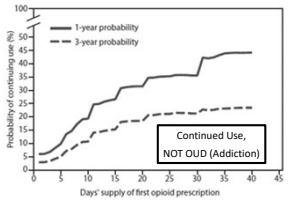
2022 CDC Opioid Guideline Updates
Section 3: Recommendation 6

➢Acute Pain

Utilize no greater quantity than needed for the pain's expected duration



Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.
Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015. MMWR Morb Mortal Wkly Rep 2017;66:265–269.

79

2022 CDC Opioid Guideline Updates
Section 3: Recommendation 7

➢Regular Follow-Up

- Evaluate Risks/Benefits within 1 to 4 weeks of opioid initiation or dosage escalation
- Regularly reevaluate Risks/Benefits of continued utilization

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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2022 CDC Opioid Guideline Updates
Section 4: Recommendation 8

➢Opioid Risk Assessment (Initially & Continually)

➢Naloxone Education (*ALREADY DISCUSSED*)

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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Opioid Risk Screenings

	Opioid-Naïve	Opioid-Experienced
Self	• Drug Abuse Screening Test (DAST) • Screener and Opioid Assessment for Patients with Pain (SOAPP)	• Current Opioid Misuse Measure (COMM) • Pain Medication Questionnaire (PMQ) • Prescription Drug Use Questionnaire, Patient (PDUQp)
Provider	• Opioid Risk Tool (ORT) • Opioid Risk Tool for Substance-Use Disorder (ORT-SUD) • Diagnosis, Intractability, Risk, and Efficacy Score (DIRE)	• Prescription Drug Use Questionnaire (PDUQ)

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2022 CDC Opioid Guideline Updates
Section 4: Recommendation 9

➢PDMP Review: Initially & minimum q 3 months

- Part of the overall risk reduction strategy (not sole)
- Assess Complete Opioid Daily Dosage & Risks
- PDMP Risk Scores are not validated (to clinical outcomes such as overdose) and should not supplant clinical judgement
- Clinicians should not dismiss patients based on PDMP alone

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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2022 CDC Opioid Guideline Updates
Section 4: Recommendation 10

➢Consider Urine Drug Monitoring (Subacute/Chronic Pain)

- Screening vs. Testing
- Not Punitive (Should not dismiss based on UDM alone)

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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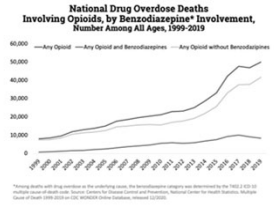
2022 CDC Opioid Guideline Updates
Section 4: Recommendation 11

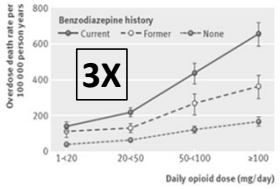
- Caution with Opioids & Benzos (Risks vs Benefits)
- Incidents of the combo do occur
  - Patient utilizing chronic Benzo experiencing Acute Pain, etc.
- Benzo's require a personalized gradual taper to avoid withdrawal symptoms (seizures, etc.)

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

85

Opioids & Benzos





https://www.drugabuse.gov/drug-topics/opioids/benzodiazepines-opioids
Tae Won Park, et al. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. BMJ 2015;350:h2698

86

2022 CDC Opioid Guideline Updates
Section 4: Recommendation 12

- OUD → MOUD
- This is a Pain Guideline Right?

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

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Beers Criteria Update

88

Aging Anatomy & Physiology

Cardiovascular
- Heart wall thickens, HR decreases, & Systolic BP increases

Pulmonary
- Chest wall thickens & Central airways widen = Decreased pulmonary Flow

Central Nervous System (CNS)
- Brain Size & BBB decreases

Endocrine
- Kidney size decreases GFR decreases

Hepatic System
- Liver Mass & CYP450 decreases

Immune System
- Entire immune system function decreases

Gastrointestinal
- Gastric emptying frequency decreases
- Gastric emptying time duration increases

Overall Body
- Body water/muscle ratio decreases
- Body fat increases

http://www.merckmanuals.com/professional/geriatrics.html

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Painful Paperwork

- Living Wills
  - Advanced Directives for healthcare, life sustainment, treatment, etc.
- Power of Attorney
  - Invalid if patient becomes incompetent
- Durable Power of Attorney
  - Valid if patient becomes incompetent
- Durable Power of Attorney for Healthcare Decisions
  - Valid if patient becomes incapacitated
- DNR Orders
  - Do Not Resuscitate Orders, made by patient while competent
  - Made by Family/Practitioner if not competent

http://www.merckmanuals.com/professional/geriatrics.html

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Geriatric Medication Toolbelt

Medication Selection & Utilization Tools for Patients >/= 65yo	
AGS Beers	American Geriatrics Society Beers List
STOPP	Screening Tool of Older Peoples Prescriptions
START	Screening Tool to Alert to Right Treatment
FORTA	Fit fOR The Aged
MAI	Medication Appropriateness Index
ADS	Anticholinergic Drug Scale
ACB	Anticholinergic Cognitive Burden Scale
ARS	Anticholinergic Risk Scale

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2023 AGS Beers List Update


SPECIAL ARTICLE

Journal of the American Geriatrics Society

American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults

By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023; 1–30.

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2019 AGS Beers List (10 Tables)

Table	Descriptions
1	Designations Of Quality Of Evidence And Strength Of Recommendations
2	Potentially Inappropriate Medication Use In Older Adults (PIMs)
3	PIMs Due To Drug-disease Or Drug-syndrome Interactions That May Exacerbate The Disease/Syndrome
4	PIMs: Drugs To Be Used With Caution In Older Adults
5	Potentially Inappropriate Drug-Drug Interactions That Should Be Avoided In Older Adults
6	Medications to Avoid or Have Dosage Reduced With Varying Levels of Kidney Function in Older Adults
7	Drugs With Strong Anticholinergic Properties
8	Medications/Criteria Removed Since Previous AGS Beers List
9	Medications/Criteria Added Since Previous AGS Beers List
10	Medications/Criteria Modified Since Previous AGS Beers List

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023; 1–30.

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Table 1: PIMs (Pain Related)

Drug Class	Alternative(s)
TCA's: ALL except Doxepin </= 6 mg/day Paroxetine Barbiturates (Butalbital/Phenobarbital) Benzodiazepines (ALL) Z-Hypnotics Eszopiclone, Zaleplon, & Zolpidem	SSRI's (Not Paroxetine) SNRI's Bupropion Trazodone Topicals (Neuro Pain)

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023; 1–30.

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Table 1: PIMs (Pain Related)

Drug Class	Alternative(s)
• Meperidine • Muscle Relaxants (Spasmodics) • Carisoprodol, Chlorzoxazone, Cyclobenzaprine, Metaxalone, Methocarbamol, & Orphenadrine • Non-Selective NSAIDs (all except celecoxib)	Non-Pharm APAP Celecoxib Topicals Antispasticity Agents (baclofen/tizanidine)

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023; 1–30.

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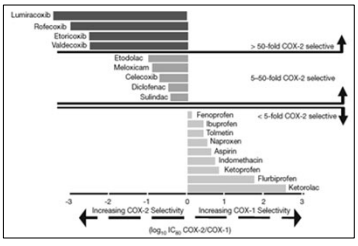
COX Selectivity



COX-1 to COX-2 Ratio	
Flurbiprofen	10.27
Ketoprofen	8.16
Fenoprofen	5.14
Tolmetin	3.93
Aspirin	3.12
Oxaprozin	2.52
Naproxen	1.79
Indomethacin	1.78
Ibuprofen	1.69
Ketorolac	1.64
Piroxicam	0.79
Nabumetone	0.64
Etodolac	0.11
Celecoxib	0.11
Meloxicam	0.09
Mefenamic acid	0.08
Diclofenac	0.05
Rofecoxib	0.05

Herndon, C. et al. Management of Chronic Nonmalignant Pain with Nonsteroidal Anti-inflammatory Drugs. Pharmacotherapy. 2006; 26 (6): 788-805.

Feldman, M. et al. Do Cyclooxygenase-2 Inhibitors Provide Benefits Similar to Those of Traditional Nonsteroidal Anti-Inflammatory Drugs with Less Gastrointestinal Toxicity. Ann Intern Med. 2000; 132: 134-143.

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COX-1 & COX-2

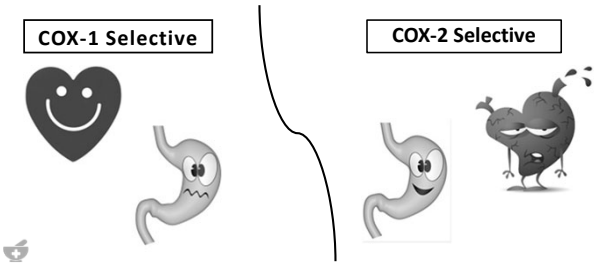

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Table 3: PIMs Due to Disease/Syndrome

Pain Related

- Heart Failure (Avoid NSAIDs)
- Syncope (Avoid Tertiary TCAs: Amitriptyline, Imipramine, Clomipramine, Doxepin)
- Delirium (Avoid Opioids, Benzo's, Corticosteroids, etc.)
- Dementia (Avoid Anticholinergics, Antipsychotics, Benzo's, & Z-Hypnotics)
- History of Falls/Fractures (Avoid Benzo's, Opioids, Z-Hypnotics, TCAs, SSRIs, & SNRIs)
- Gastric/Duodenal Ulcer (Avoid NSAIDs except celecoxib)
- CKD Stages 4 & 5 (Avoid all NSAIDs)

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023; 1- 30.

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Table 4: Medications to Use with Caution in Elderly

Pain Related

- Antipsychotics
- Mirtazapine
- SNRIs
- SSRIs
- TCAs
- Tramadol

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023; 1- 30.

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Table 5: Drug/Drug Interactions

Pain Related

- Multiple Anticholinergic Medications (Cognitive Decline, delirium, & falls/fractures)
- Opioids & Benzos/Gabapentinoids (Sedation/Overdose)
- >/= 3 CNS Active Medications (Falls/Fractures)
  - Antidepressants, Antipsychotics, Antiepileptics, Benzos, Z-Hypnotics, Muscle Relaxants, & Opioids

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101

If Not Anything, Then Something?

Patient by patient scenarios

- Clinical judgment
- Monitoring
- Documentation

102

BioPsychoSocial Model of Pain

https://www.physio-pedia.com/Biopsychosocial_Model

103

New Pain Medications

The Opioids

104

Tamayta, Toemaatoe, Opiate, Opioid

Opiate
"Natural"
Thebaine
Morphine
Codeine

Opioid
"Semi/Synthetic"
Heroin
Hydrocodone
Oxycodone
Fentanyl

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Opioid Structural Classes

Structural Class	Phenanthrenes		Benzomorphan	Diphenylheptanes	Phenylpiperidines	Phenylpropylamines	New Entity
Rings	5 Rings	4 Rings	3 Rings	2 Rings	2 Rings	1 Ring	4 Rings
Structure							
Medication(s)	Opium Codeine Diacetylmorphine Hydrocodone Hydromorphone Benz-Hydrocodone Morphine Oxycodone Oxymorphone Naloxone Naltrexone Nalmefene Buprenorphine	Butorphanol Levorphanol	Pentazocine	Methadone Propoxyphene	Fentanyl/Analogs Sufentanil Meperidine Diphenoxylate Loperamide	Tapentadol Tramadol	Oliceridine

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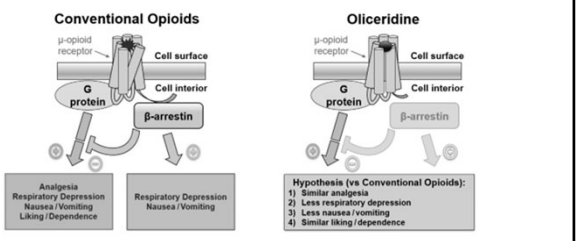
Oliceridine

Specificity Matters



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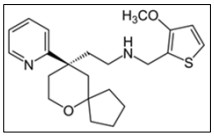
Oliceridine

OLINVYK™

- IV administration only (No Dilution)
- Dosing
  - Initial dose of 1.5 mg
  - Max single subsequent doses of 3 mg
  - Max cumulative daily dose of 27 mg
- ➢Oliceridine 1 mg IV ≈ morphine 5 mg IV
- CYP 2D6 & 3A4 Primary Metabolism
- Bolus & PCA Dosing
- No Renal & Hepatic Dosage Adjustment



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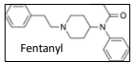
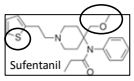
Sufentanil
Dsuvia®

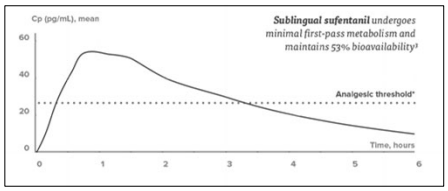
- Each 30mcg tablet is 3mm, blue, & flat-faced
- Dosage is 1 SL tablet, minimum of 1-hour between doses
- Do not exceed 12 tablets in 24 hours (360mcg)
- Use beyond 72 hours has not been studied
- 30mcg Sufentanil SL Tablet = 5 MMEs (MME Factor ~500)
- CYP-3A4 Substrate
- Minimize talking & avoid food/drink for 10 minutes post dosage
- Provide ice chips if excessive dry mouth prior to administration

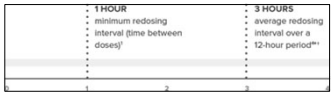




109

Sufentanil
Dsuvia®



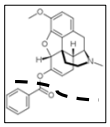


110

Benz-hydrocodone/APAP
Apadaz®

- Prodrug covalently bonded with benzoic acid
  - Benzoic Acid: Typical food preservative
  - Ligand-Activated Technology (LAT®)
  - Also being studied with a methylphenidate prodrug
- NOT FDA approved as an abuse-deterrent formulation (ADF) opioid
- Indicated for the short-term (*no more than 14 days*) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate

Benzhydrocodone/APAP 6.12/325mg = hydrocodone/APAP 7.5/325mg



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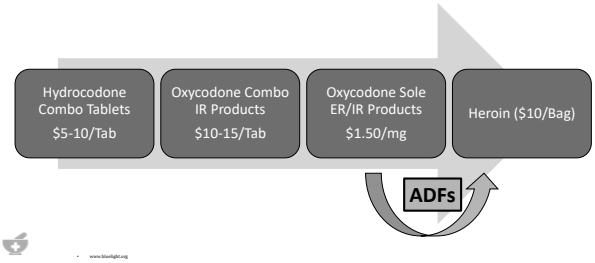
Opioid Abuse Transition



- www.bluelight.org
- Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015. Weekly / March 17, 2017 / 66(10); 265–269.

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Abuse-Deterrent Formulations

ADF Type	Description
1. Physical Barrier	Prevent chewing, crushing, cutting, grating, or grinding
2. Chemical Barrier	Resist extraction of the opioid through use of common solvents including water, alcohol or other organic solvents
3. Agonist/Antagonist Combinations	Antagonist is added to the formulation to interfere with release if taken in any other way than it was intended
4. Aversion	Substances are added to the dosage form to produce an unpleasant effect if the dosage form is manipulated prior to ingestion or if a higher dosage than directed is used
5. Delivery System	Alternative delivery systems that are more difficult to manipulate (such as a depot injectable, an implant, or transdermal application)
6. Prodrug	Medication contains a prodrug that lacks opioid activity until it has been transformed in the gastrointestinal tract
7. Combination of the above	

Webster L, Gudin J. Review of Opioid Abuse-Deterrent Formulations: Impact and Barriers to Access. J Pain Res. 2024 Jun 5;17:1989-2000.

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FDA ADF Studies

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

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Category 3
Abuse Potential Studies

Physically Manipulation	Routes of Administration
Cutting Grafting Milling Chewing +/- Heat	Ingestion (Oral Route) Injection (Parenteral Route) Insufflation (Nasal Route) Smoking (Inhalation Route)

https://www.fda.gov/downloads/Drugs/.../Guidances/UCM492172.pdf

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Category 3
Abuse Potential Studies

In Vitro Studies (Lab)	In Vivo Studies (Body)
Extractability studies	Nasal and oral PK
Performed at both room temp and elevated temp	Multiple strengths tested
Solvents • Level 1: deionized water • Level 2: vinegar, 0.2% baking soda solution, 40% ethanol, & carbonated drink • Level 3: 100% ethanol, 100% isopropyl alcohol, acetone, 0.1 N HCl, & 0.1N NaOH	Agonist/Antagonist Levels

https://www.fda.gov/downloads/Drugs/.../Guidances/UCM492172.pdf

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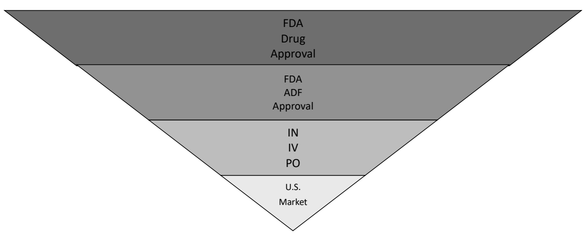
ADF Opioid Availability Cascade



https://www.fda.gov/downloads/Drugs/.../Guidances/UCM492172.pdf

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Abuse Deterrent Formulation (ADF) Opioids "Attempts"			
Active Ingredient	**Product**	**FDA ADF Approval**	**Formulation**
oxycodone	Xtampza ER®	IN, IV, & PO Chew	Capsule
	Xartemis ER® (+APAP)	-	IR/ER Tablet
	OxyContin®	IN & IV	Tablet
	Troxyca®	IN, IV, PO Crush	Capsule
	Targiniq®	-	Tablet
	Oxaydo®	-	IR Tablet
	RoxyBond®	IN & IV	IR Tablet
tapentadol	Nucynta ER®	-	Tablet
hydromorphone	Exalgo®	-	Tablet
morphine	Embeda®	IN & PO Crush	Tablet
	Arymo®	IV	Tablet
	MorphaBond®	IN & IV	Tablet
hydrocodone	Hysingla®	IN, IV, & PO Chew	Tablet
	Zohydro ER®	-	Capsule
	Vantrela ER®	IV	Tablet
	Hydromet®	-	Liquid
	Tussigon®	-	Tablet
benzhydrocodone	Apadaz®	-	Tablet
pentazocine	Talwin NX®	-	Tablet
Oxymorphone	Opana ER®	-	Tablet

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411218/
https://www.sciencedirect.com/science/article/pii/S0378517316304884
https://www.futuremedicine.com/doi/pdf/10.2217/pmt-2015-0005
https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm

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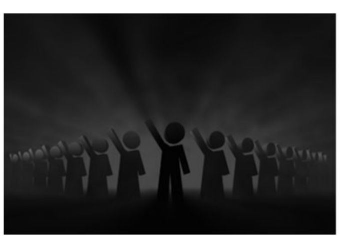
So, Who Made the Cut?…Pun Intended



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FDA Approved ADF Opioids on US Market (2025)

Medicine	Product	FDA ADF Approval			Formulation	Generic Available
hydrocodone	Hysingla®	IN	IV	PO Chew	ER Tablet	Yes
oxycodone	OxyContin®	IN	IV	n/a	ER Tablet	Yes
	Xtampza ER®	IN	IV	PO Chew	ER Capsule	No
	RoxyBond®	IN	IV	PO Chew	***IR Tablet***	No

Adapted from Clinical Pharmacology Online Database.

120

Oxycodone IR ADF
RoxyBond™

- Oxycodone IR 5mg, 15mg, & 30mg
- 1-to-1 Dosing Conversion with Oxycodone IR
- SentryBond™ Technology
  - Resists Physical Manipulation
  - Resists Chemical Extraction
  - Resists manipulation or transformation for injection

https://www.roxybond.com/

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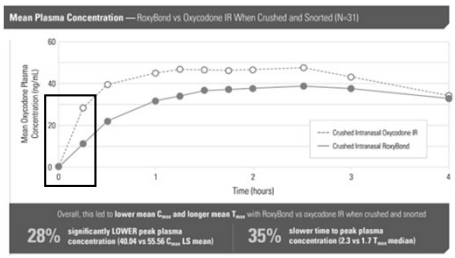
Oxycodone IR ADF
RoxyBond™



https://www.roxybond.com/

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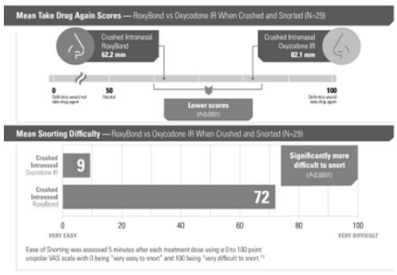
Oxycodone IR ADF
RoxyBond™



https://www.roxybond.com/

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New Pain Medications
The Non-Opioid

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Journavx™
suzetrigine

- Non-Opioid
- NaV1.8 Antagonist (Blocks action potential that typically shifts Na into cell)
- FDA Approval: Moderate-to-Severe (NPS 4 to 10) Acute Pain in Adults
- Dosage:
  - 100mg, 50mg q12 x 3, then 50mg QD (<14d)
  - 1st Dose: 1 hour before 2 hours after food; Subsequent doses +/- food
- 3A Substrate
- $15/pill

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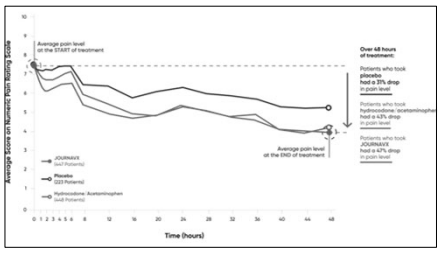
Journavx™
Tummy Tuck Trial



https://www.journavx.com/How-it-works

ADEs (<~2%)
- Itching
- Rash
- Muscle Spasms
- CPK Increase

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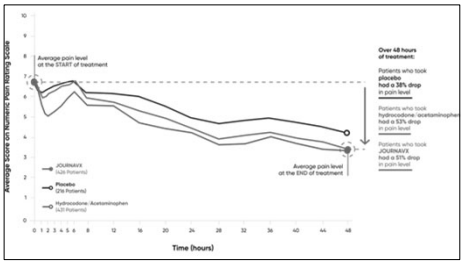
Journavx™
Bunion Removal Trial



https://www.journavx.com/#how-it-works

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Summary

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Patient CARE

People Respect What You Inspect, Not What You Expect

An Ounce of Prevention, is Worth a Pound of Treatment

Never Stop Learning

Hippocratic Oath: Do No Harm

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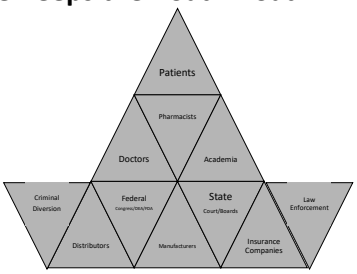
Everyone Keeps the Boat Afloat



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Resources

- 2023 Beers Criteria Update
- 2022 CDC Opioid Guideline Update
- 2016 West Virginia Safe & Effective Management of Pain (SEMP) Guidelines (Updating in 2025)
- https://www.nationalopioidsettlement.com/

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Key Takeaways

- MAT Act eliminated buprenorphine "X Waiver"
- Buprenorphine is a partial Mu agonist with a respiratory depression ceiling effect
- Controlled Substance Red Flags in the National Opioid Settlement include, but are not limited to:
  - CS-2 Refill Too Soon by > 3 Days
  - Doctor Shopping (CS > 4 Previous Prescribers of Separate Practices over 6 months)
  - Distance between patient's residence and pharmacy > 50 miles
  - Distance between patient's residence and prescriber > 100 miles
  - Prescriber has no office within 50 miles of pharmacy
  - Cash pay despite having prescription insurance coverage
  - CS-2 + Benzodiazepine + Carisoprodol
- Opioid overdose symptoms include gargled, slow, or absent breathing (death rattle); being unconscious & unarousable; blue lips & nails (hypoxia); hypotension; pinpoint pupils; slow/no heartbeat; & pale clammy skin
- Naloxone is a highly lipophilic, low oral bioavailability, short duration of action mu-opioid antagonist which is FDA approved for opioid agonist overdose (respiratory depression)
- Nalmefene is a mu-opioid antagonist that has great oral bioavailability, a longer half-life compared to naltrexone, 5-times the mu-opioid receptor affinity of naloxone, and is available as injectable, auto-injector, and intranasal products, with nasal administration mirroring that of naloxone prepackage nasal products (1st Dose being 1 spray in one nostril)

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Key Takeaways

- The CDC recommends prescription opioid utilization considerations including utilization of immediate-release (IR) before extended-release (ER) opioids; a start low, go slow dosage strategy, and avoid increasing to high-risk dosage levels; reevaluating risks versus benefits for legacy or inherited patient utilizing high-risk prescription opioid dosages; when prescription opioid tapering is appropriate, only utilize a gradual tapering; when opioids are utilized in acute pain, only provide for expected duration; & to reevaluate chronic/subacute opioid utilization at least every 3 months (within 1 to 4 weeks initially)
- The CDC recommends universal pain management best practices including opioid risk screening, naloxone education, PDMP review, urine drug monitoring, avoidance of opioid and other sedatives combinations, and offering MOUD for patient with OUD
- Meperidine is the only opioid on the Beers Criteria List of Potentially Inappropriate Medications (PIMs) for all geriatric patients, yet for patients with a history of falls, all opioids are on the PIMs list
- The FDA-approved ADF opioid medications available on the U.S. market include the hydrocodone product of Hysingla® and the three oxycodone products of OxyContin®, Xtampza ER®, & RoxyBond®
- Suzetrigine is a Non-Opioid NaV1.8 Antagonist FDA Approval: Moderate-to-Severe (NPS 4 to 10) Acute Pain in Adults

133

Question 1

1. Which of the following described current buprenorphine regulations?
   a) There is no "X-Waiver" nor provider patient limits
   b) There is no "X-Waiver" but a provider patient limit of 100
   c) There is an "X-Waiver" with a provider patient limit of 100
   d) There is an "X-Waiver" with a provider patient limit of 250

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Question 2

1. According to the National Opioid Settlement, which of the following are controlled substance red flags?
   a) 60 miles between patient's residence and pharmacy
   b) 60 miles between patient's residence and prescriber
   c) 75 miles between patient's residence and prescriber
   d) 30 miles between pharmacy and prescriber

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Question 3

1. According to the National Opioid Settlement, which of the following are controlled substance red flags?
   a) Oxycodone, Diazepam, & Zolpidem
   b) Oxycodone, Diazepam, & Carisoprodol
   c) Hydrocodone, Morphine, & Alprazolam
   d) Hydrocodone, Tramadol, & Zolpidem

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Question 4

1. Which of the following naloxone products is available as both prescription and over-the-counter?
   a) 5mg Injectable
   b) 10mg Auto Injector
   c) 4mg Nasal Spray
   d) 8mg Nasal Spray

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Question 5

1. What is the dose of the nalmefene nasal spray products available with a prescription?
   a) 2.7mg
   b) 3.6mg
   c) 5.4mg
   d) 7.6mg

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Question 6

1. According to the CDC Opioid Guideline update, what is a recommended gradual opioid taper (when appropriate)?
   a) 10% Monthly
   b) 10% Weekly
   c) 15% Monthly
   d) 15% Weekly

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Question 7

1. According to the most recent AGS Beers Criteria, which of the following NSAIDs is recommended for an older adult without any comorbidities?
   a) Celecoxib
   b) Diclofenac
   c) Ibuprofen
   d) Naproxen

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Question 8

1. Which of the following medications has a novel mechanism of action aiming to avoid the B-Arrestin portion of the Opioid Mu Receptor?
   a) Buprenorphine
   b) Levorphanol
   c) Oliceridine
   d) Pentazocine

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Question 9

1. Which prescription opioid is is an FDA-Approved immediate-release ADF product?
   a) Hysingla ®
   b) OxyContin ®
   c) RoxyBond ®
   d) Xtampza ®

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Question 10

1. What are appropriate patient counseling points for the non-opioid Journavx®?
   a) Take with a full glass of water to avoid hypernatremia
   b) Take 1 hour before or 2 hours after food
   c) Take 2 hours before or 1 hour after food
   d) Review for Significant interaction with 2C9 NSAIDs

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CE Evaluation Access Code

Capital Letters, No Spaces

Please complete the online evaluation by **03/16/2025**

Note: CE credit will be reported to NABP CPE Monitor within 4-6 weeks

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www.painguy.us

SCAN ME

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Pain & Addiction Updates

Mark Garofoli, PharmD, MBA, BCGP, CPE, CTTS

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