

Updating Our Quest to Relieve Pain: There are new kids in town

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I have no financial disclosures or conflicts of interest with the presented material in this presentation

All price information was obtained from GoodRx in Florence County

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Objectives

1. Discuss the new pain management guidelines for adult patients.
2. Comprehensive analysis of the first non-opiate pain medication approved by the FDA called suzetrigine.
3. Review buprenorphine and how it is being used in opiate use disorder and chronic pain.
4. Discuss what the nurse practitioner needs to know when the patient is taking buprenorphine.
5. Discuss the adverse event risk of opiates and the need for intranasal naloxone.
6. Review the opiate complications in South Carolina and the most recent data on opiate-related deaths.

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Lecture Format

Part 1: Update the SC statistics of opioid harm

Part 2: What about Suzetrigine?

Part 3: Buprenorphine for chronic pain?



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First a word on opioid efficacy and safety

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OPIOIDS FOR PAIN

- Limited benefit in treating noncancer pain
- There is a decrease of -10 points on a 0-100 point scale*
- 0 = no pain
- 100 = worse pain
- For musculoskeletal pain:
- This pain relief is related to the first few days (-10)
- Has no effect after first week and a small increase in pain after 12 weeks

*NRS-101 Response scale, standard research scale NEJM 2025;393(18):1833-42 

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TAPERING OPIOIDS

- Gradual dose reduction of 5-10% of the morphine-milligram-equivalent (MME) daily dose every 2-4 weeks is the recommended approach for opioid tapering in patients with noncancer pain
- For patients on long-term therapy (≥ 1 year), slower tapers of 10% per month or longer intervals may be better tolerated

NEJM 2025;393(18):1833-42 

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UNITED STATES APPROACH

Do not discontinue opioids abruptly or rapidly reduce the dose unless there are indications of a life-threatening issue, such as warning signs of overdose (weak or conditional).

Establish goals with the patient — patient agreement and interest is likely to be key to success. Maximize the effectiveness of pain treatment with nonpharmacologic and nonopioid pharmacologic treatments (weak or conditional).

Collaborate with the patient on the tapering plan (weak or conditional).

Conduct frequent follow-up assessments — at least monthly (weak or conditional).

Use a taper slow enough to minimize withdrawal symptoms (weak or conditional).

Consider slower tapers for patients receiving long-term therapy, such as for ≥ 1 year — tapers of 10% per month or slower are likely to be better accepted than more rapid tapers (weak or conditional).

Maximize nonopioid treatments and address distress for patients struggling with tapering (weak or conditional).

Pausing and restarting a taper might be warranted for some patients (weak or conditional).

Screen for anxiety, depression, opioid misuse, or opioid use disorder and treat or refer for management (weak or conditional).

Opioid Guidelines: MMWR Recomm Rep 2022; 71: 1-95. 

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 **Part 1**

Updating the SC opioid statistics

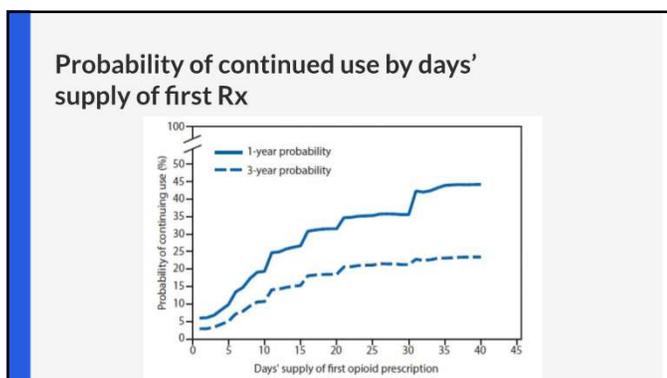
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Many reasons why we are here today!

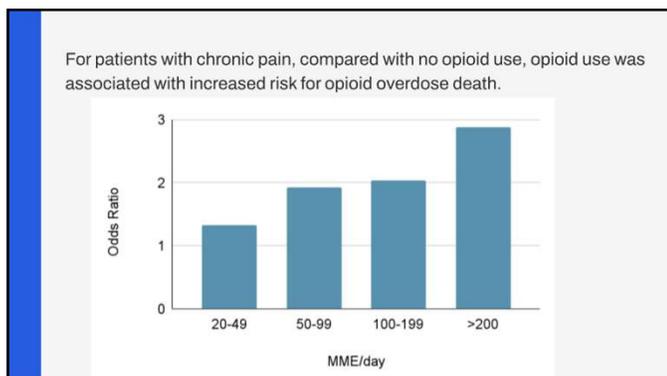
- 1990's - Pain becomes the 5th vital sign
- American Pain Association declared aggressive management of pain
- New medications were aggressively marketed that downplayed the addiction potential
- Early 2000's - patient-reported pain scores were incorporated into hospital quality metrics through post-care questionnaires
 - The Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey tied greater patient satisfaction, and by extension pain control, to increased reimbursement through Medicare, which encouraged liberal opioid prescription

Int. J. Mol. Sci. 2025, 26, 9865

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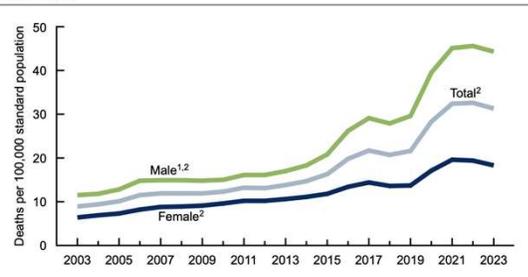


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Figure 1. Age-adjusted drug overdose death rate, by sex: United States, 2003–2023



CDC report **Drug Overdose Deaths in the United States, 2003–2023**
<https://www.cdc.gov/nchs/products/index.htm>

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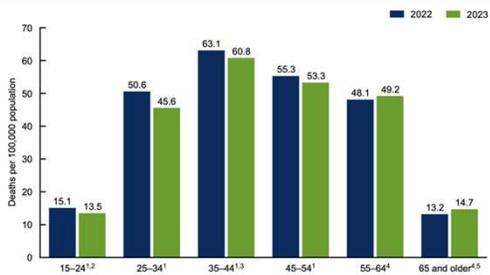
Drug Overdose Deaths

- In 2023, 105,007 drug overdose deaths occurred, resulting in an age-adjusted rate of 31.3 deaths per 100,000 standard population
- Drug overdose deaths nearly quadrupled from 8.9 in 2003 to 32.6 in 2022
- This rate has decreased to 31.3 in 2023
- From 2022 to 2023, the age-adjusted rate of:
 - Drug overdose deaths for males decreased 2.9% from 2022 to 2023
 - Rate for females decreased 5.7% (19.4 to 18.3/100,000)

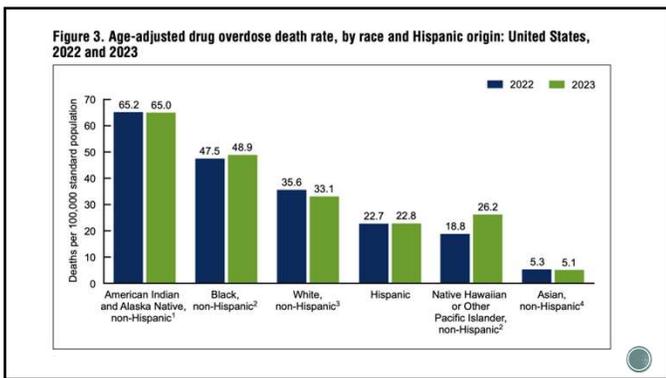
CDC report **Drug Overdose Deaths in the United States, 2003–2023**

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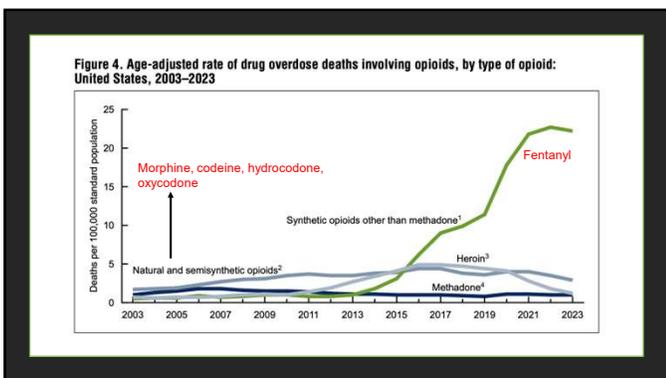
Figure 2. Drug overdose death rate, by selected age group: United States, 2022 and 2023



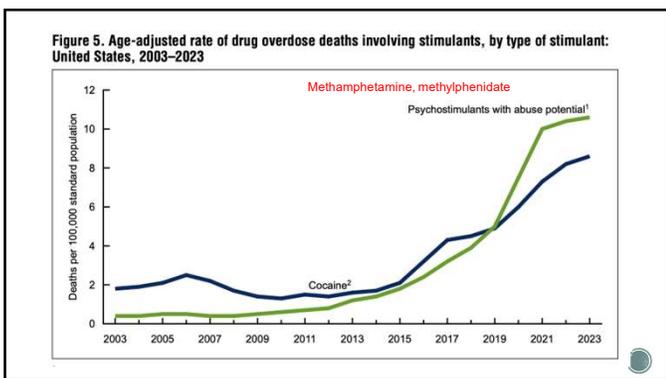
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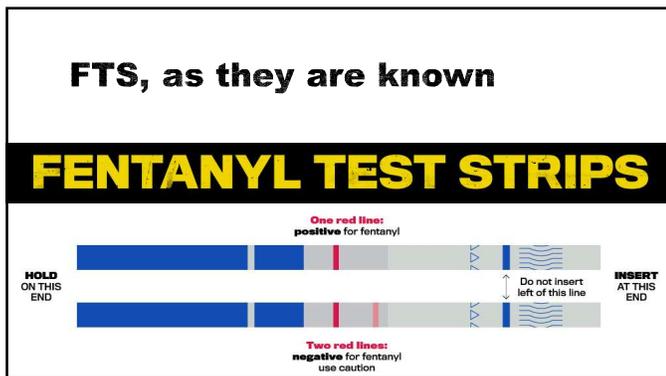
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Pitfalls

- They do not give you a quantitative amount
- They cannot differentiate with fentanyl analogs
- Large presence of diphenhydramine and or methamphetamine may interfere with results by causing false positives
- Some state list them as drug paraphernalia and are illegal
- SC has removed them as drug paraphernalia and are legal
- South Carolina Department of Alcohol and Other Drug Abuse Services (DAODAS) and South Carolina Department of Public Health (DPH) make them available

JAMA Clinical Guideline Synopsis, published online January 21, 2026

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There is hope....maybe!

Science reports that overdose deaths are down in 2023 due to a supply chain disruption out of China

Fentanyl seizures are also down

This is thought to have led to a reduction in dose

Changes in purity

Death rates in 2024 have fallen from 31 deaths to 23 deaths/100,000 (that's 26,000)

JAMA Medical News in Brief, January 23, 2026

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Self-Assessment Question 1

1. The highest county in South Carolina with the most opiate prescriptions written per capita would be?

- A. Greenville County
- B. Darlington County
- C. Lee County
- D. Charleston County
- E. Richland County

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.....AND WE ARE THE WORSE IN ...

Rate of opioid prescriptions by county

- The highest is Darlington county at 1,799 per 1000 people....#1
- Then Florence county at 1,609 per 1000....#2
- Greenville county was 1,107/1000 – that is 27th of 43 counties
- Spartanburg county was 1,260/1000 – that is 15th of 43 counties
- Calhoun county is the lowest at 334/1000

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DHEC (DPH) DASHBOARD - OPIOIDS

• Opiate Trends – Dec 1, 2023 to Dec 31, 2025

Number of Patients that were Dispensed Opioids in SC

234,000
1,616,705
 Total Patients
Down -8%
 213,000

Hover over visual to view trend line

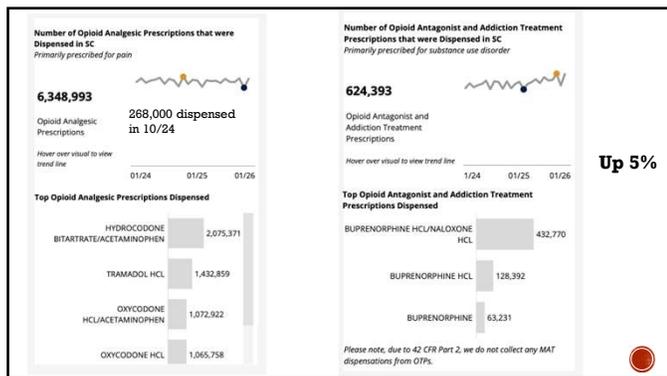
01/24 01/25 01/26

Number of Patients that were Dispensed Opioids in SC by Gender

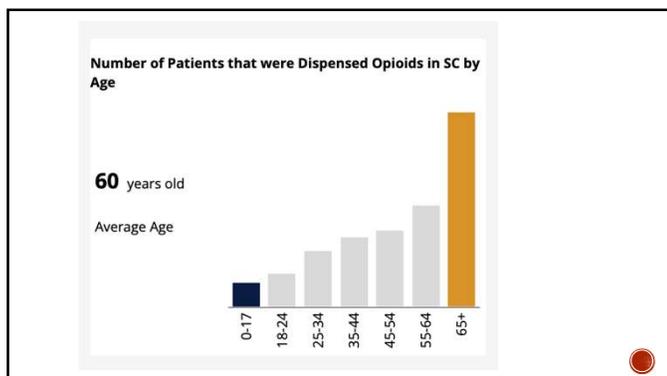
659,178 Male Patients 42.43%
 894,505 Female Patients 57.57%

South Carolina FMP Opioid Trends Dashboard
 See dph.sc.gov

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BENZODIAZEPINE USE IN SC

- Lexington county gets the benzodiazepine prize – 1,142/1000
- Darlington county is #2
- Pickens county is #3
- Florence county is #4

4,434,323 Rx filled in two years in SC

Top 5 benzo's

- Alprazolam
- Lorazepam
- Clonazepam
- Diazepam
- Temazepam

See dph.sc.gov

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STIMULANT USE IN SC

- Charleston county gets the stimulant prize – 1,626/1000
- Pickens county #2
- Florence county #3
- Greenville county #4 5,613,997 Rx filled in two years in SC
- Top stimulants
 - Adderall and salts
 - Methylphenidate
 - Lisdexamfetamine
 - Phentermine

See dph.sc.gov



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RX FILLED OVER 2023 TO 2025 IN SC

- Numbers of prescriptions filled from 12/23 to 12/25
- Opioids 6,348,993
- Benzodiazepines 4,434,323
- Stimulants 5,613,997
- Total 16,397,313
- If there are 550 pharmacies in SC, that is ~30,000 Rx filled by each pharmacy over 2 years
- That is around 60-65 fills per day for each pharmacy



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Part 2

What about Suzetrigine?

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The STEPS Approach

- Safety
- Tolerability
- Efficacy
- Price
- Simplicity

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**Suzetrigine
Journavx®**

soo-ZEH-tri-jeen / jor-NAV-ix

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Indication
Moderate to severe acute pain in **ADULTS**
First in class!!

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SUZETRICINE (JOURNAVX®)

Nav1.8 Sodium Channel Blocker

- Mechanism of Action
- It is NOT a Mu/Kappa/Delta agonist
- Blocking these sodium channels inhibits pain signaling in the peripheral nervous system
- From the work of Dr. Stephen Waxman of Yale – it's been in study since 1990
- Pakistani family of fire walkers who didn't have a gene (SCN10A) that caused pain signals to fire in their skin, thereby letting them walk on hot coals without their body recognizing it was in pain

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Suzetrigine Mechanism of Action

Afferent pain signal initiated by noxious stimulus

Fast Facts:

- IC₅₀ = 0.68 nM (human DRG)
- 31,000x selective for Nav1.8
- No activity at Nav1.5 (cardiac safe)

Int. J. Mol. Sci. 2025, 26, 8865

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There is no CNS effect making abuse unlikely

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SAFETY

**STEPS:
SUZITRIGINE**

Considered very safety – NO ADDICTION!

No issue with QT elongation so far

Tmax = 3 hours; Half-life = 24 hours; highly protein bound

Take on empty stomach – 1 hour before or 2 hours after a meal

Drug Interaction: no grapefruit juice, therefore watch strong CYP3A4 inhibitors (-azoles, HIV)

Hormonal contraceptives: watch in those on OC's - levonorgestrel and norethindrone are OK – but for any other progestin a backup method for 28 days is recommended

Avoid in severe hepatic impairment

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Pharmacology of Suzitrigine

Dosing (Oral)
100 mg loading dose then 50 mg every 12 hours

Oral Bioavailability
No published absolute value

Volume of Distribution
495 L

Elimination
~50% feces
~44% urine

CNS Safety
No signs of toxicity, dependence, or withdrawal

Cardiac Safety
No QTc prolongation or cardiovascular changes

Absorption
3.0 hr fasting
5.0 hr fed

Metabolism
CYP3A4 → M6-SUZ

90% Steady State: 3 days
Half-life: 26.6 hours

Int. J. Mol. Sci. 2025, 26, 9865

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The -trigines (are unrelated)

Nc1nc(N)c2c(c1)nc(Cl)c2Cl
lamotrigine

CC(F)(F)OC(=O)Nc1ccc(NC(=O)c2ccncc2)cc1F
suzitrigine

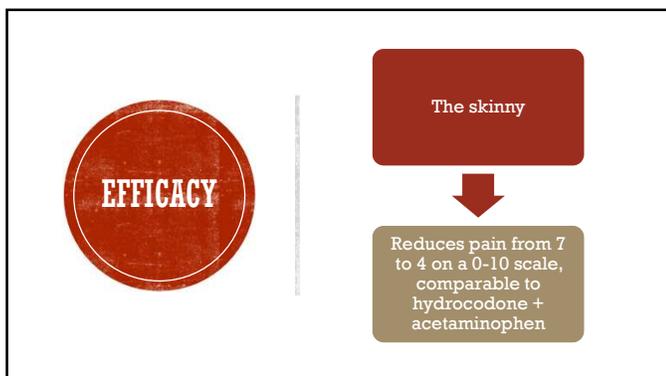
cafermed.com

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TOLERABILITY

Adverse Effect	Suzitrigine % (NNH vs placebo)	Hydrocodone/APAP	Placebo
Pruritus	2.1% (NNH 200)	3.4% (NNH 55)	1.6%
Rash	1.1% (167)	0.7% (500)	0.5%
Muscle spasm	1.3% (125)	0.7% (500)	0.5%
Increased creatine phosphokinase	1.1% (167)	0.8% (333)	0.5%
Either nausea or vomiting (data from 1 trial)	20% (N/A – or NNT 20)	33% (13)	25%

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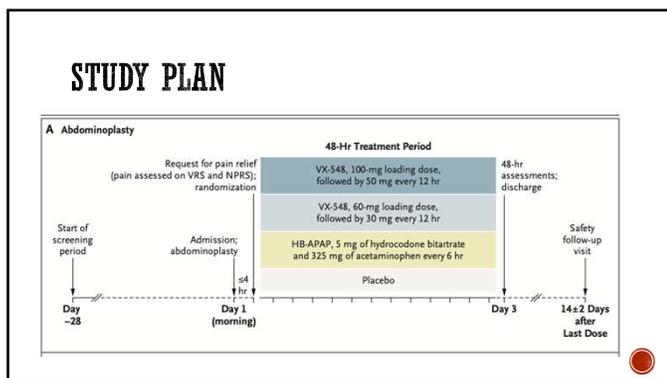
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TRIALS

N Engl J Med 2023;389:393-405

- Main studies in abdominoplasty and bunionectomy surgeries vs placebo vs hydrocodone/APAP
- Abdominoplasty
 - Most were females in both trial (98%) white (70%), black (27%), average age of 42, patient characteristics were equal
 - Mean pain score on a 0-10 scale was 7.4
 - Outcome: SPID48 Sum of the Pain Intensity Difference at 48 hours
 - The difference from baseline was assessed at each point, weighted by the amount of time elapsed and then added together to yield a score known as SPID48

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Table 2. Primary and Secondary Efficacy End Points.^a

End Point	Abdominoplasty Trial				Bunionectomy Trial				
	High-Dose VX-548 (N=76)	Middle-Dose VX-548 (N=74)	Hydrocodone Bitartrate-Acetaminophen (N=76)	Placebo (N=77)	High-Dose VX-548 (N=60)	Middle-Dose VX-548 (N=62)	Low-Dose VX-548 (N=33)	Hydrocodone Bitartrate-Acetaminophen (N=60)	Placebo (N=59)
Primary efficacy end point: SPID48									
LSM	110.5±10.3	95.1±10.4	85.2±10.3	72.7±10.2	137.8±11.5	86.9±11.3	112.9±15.5	115.6±11.5	101.0±11.6
LSM difference vs placebo	37.8±14.5	22.4±14.6	12.5±14.5	NA	36.8±16.3	-14.1±16.2	11.9±19.4	14.7±16.3	NA
95% CI of the LSM difference	9.2 to 66.4	-6.4 to 51.1	★16.1 to 41.1	NA	4.6 to 69.0	-46.1 to 17.9	★-26.2 to 50.1	★17.5 to 46.8	NA
Secondary efficacy end point: SPID24									
LSM	45.5±4.7	37.6±4.8	30.0±4.7	26.0±4.7	45.2±5.5	24.8±5.4	34.4±7.4	41.0±5.5	31.5±5.6
LSM difference from placebo	19.6±6.7	11.7±6.7	4.0±6.7	NA	13.7±7.8	-6.8±7.8	2.8±9.3	9.4±7.8	NA
95% CI of the LSM difference	6.5 to 32.7	-1.5 to 24.9	★9.1 to 17.1	NA	-1.8 to 29.1	-22.1 to 8.6	-15.5 to 21.1	★6.1 to 24.9	NA
Secondary efficacy end point: reduction in NPRS score at rest at 48 hr—no. (%)									
Participants with ≥30% reduction	46 (61) (8)	44 (59)	41 (54)(17)	37 (48)	50 (83)	39 (63)	25 (76)	41 (68)	40 (68)
Participants with ≥50% reduction	34 (45) (9)	32 (43)	32 (42)	26 (34)	40 (67)	35 (56)	24 (73)	37 (62)	36 (61)
Participants with ≥70% reduction	19 (25) (9)	14 (19)	18 (24)	11 (14)	31 (52)	24 (39)	17 (52)	30 (50)	24 (41)

(NNP – Suzi vs placebo) N Engl J Med 2023;389:393-405

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ADVERSE EVENTS IN TRIAL

- Versus Placebo
- Nausea - NNH 6
- Headache - NNH 13
 - More headache vs hydrocodone
- Constipation - NNH 25
- Dizziness - more likely with placebo

N Engl J Med 2023;389:393-405

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USE IN DENTISTRY?



Chinese article discussing the NAV 1.8 expression in dental pulp



Written in Chinese



Tao R, Jiang Y. [Expression of Nav1.8 in human dental pulp]. Chung Hua Kou Chiang Hsueh Tsa Chih. 2012;47(3):177-81. doi:10.3760/cma.j.issn.1002-0098.2012.03.012



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PRICE AND SIMPLICITY

- #30 = \$483 (GoodRx) = \$16 per tablet
- Initial dose: 100 mg once on an empty stomach
- Then 50 mg every 12 hours with or without food
- For moderate hepatic impairment or with moderate CYP3A4 inhibitors - same initial dosing, then 50 mg every 24 hours
- Has not been studied beyond 14 days
- Do not crush or chew

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SIMPLICITY

- Will it cause addiction? No reason to think it will. It does not cross into the CNS.
- What about the addition of NSAIDS and or acetaminophen?
- No respiratory depression
- No chance of overdose

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Utilization is low...why?

Cost, therefore low value

Needs a PA which limits time to availability

Limited indications

No trials for nonsurgical general pain at this time

No trials in chronic pain at this time

Waiting for others to use

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**FOR NOW - MORE
COMPLEMENT THAN
REPLACEMENT**



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RESEARCH IS NEEDED

- Vertex pharmaceuticals is doing other trials for other indications
- Peripheral neuropathy – looking at its use for chronic therapy
- Lumbosacral radiculopathy
- Other acute pain situations



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OTHERS ARE COMING

- Cebranopadol: Developed by Tris Pharma, this is a first-in-class dual-NMR agonist
- Pilavapadin: Lexicon Pharmaceuticals received FDA clearance in January 2026 to advance this oral medication into Phase 3 trials for diabetic peripheral neuropathic pain
- Tanezumab: A nerve growth factor (NGF) inhibitor currently in Phase 3 development for chronic low-back pain and osteoarthritis
- TNX-102 SL: This sublingual medication is being studied for fibromyalgia
- Other Nav1.8 inhibitors coming

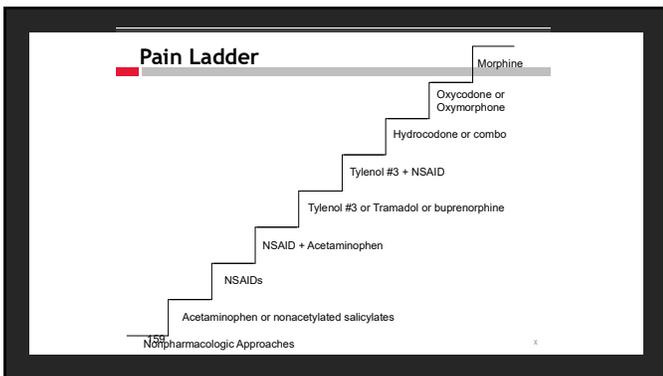
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Self-Assessment Question 2

2. From what you have learned so far about suzitrigrine where would you place it on the pain ladder?

- A. Above NSAIDs
- B. Along side of morphine
- C. Above NSAID + acetaminophen
- D. Along side of hydrocodone

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 **Part 3**

Buprenorphine for chronic pain?

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Buprenorphine

It's a revolution

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Self-Assessment Question 3

3. Buprenorphine has become very popular of late. Why?

- A. It is the drug of choice for those who can't take an NSAID
- B. It is indicated for opioid use disorder
- C. The FDA just approved it for chronic pain
- D. It can be used in combination with methadone for heroin users



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Indications

Opioid Use Disorder (OUD)

Chronic Pain
(not FDA approved except for the patch)

Opioid-induced Hyperalgesia (not FDA approved)

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Opioid Use Disorder (OUD)

It is estimated that 6-8 million adults in the USA have OUD

This has been assumed to be a result of opioid prescribing practices

In 2012 - 80 Rx's were written /100 people

2025 - we are down to 43 Rx's/100 people

Why is the death rate right at 100,000 in 2021?

Pain Practice 2025;25:e13427

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Opioid Risk Tool

Full name: _____ Date submitted: _____

This tool should be administered to patients upon an initial visit prior to beginning opioid therapy for pain management. A score of 2 or lower indicates low risk for future opioid abuse, a score of 4 to 7 indicates moderate risk for opioid abuse, and a score of 8 or higher indicates a high risk for opioid abuse.

Mark each box that applies:	<input type="radio"/> Female	<input type="radio"/> Male
Family history of substance abuse		
Alcohol	<input type="radio"/> 1	<input type="radio"/> 3
Illegal drugs	<input type="radio"/> 2	<input type="radio"/> 3
Rx drugs	<input type="radio"/> 4	<input type="radio"/> 4
Personal history of substance abuse		
Alcohol	<input type="radio"/> 3	<input type="radio"/> 3
Illegal drugs	<input type="radio"/> 4	<input type="radio"/> 4
Rx drugs	<input type="radio"/> 5	<input type="radio"/> 5
Age between 16-45 years	<input type="radio"/> 1	<input type="radio"/> 1
History of preadolescent sexual abuse	<input type="radio"/> 3	<input type="radio"/> 0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	<input type="radio"/> 2	<input type="radio"/> 2
Depression	<input type="radio"/> 1	<input type="radio"/> 1
Scoring totals		
Low risk: 0 to 3	Moderate risk: 4 to 7	High risk: 8+

Winters, L. G., & Stedman, R. M. (2003). Predicting opioid addiction in opioid-treated patients: Preliminary validation of the opioid risk tool. *Pain Med*, 4(3), 432.

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It always begins with definition!

Pain Practice 2025;25:e13427

- The American Society of Addiction Medicine defines addiction as "a treatable, chronic medical disease involving complex interactions amongst brain circuits, genetics, the environment, and the individual's life experience"
- OUD can be from mild to severe that leads to impairment or distress
- There are 3 FDA approved treatments for MOUD (Medications for OUD)
 - Buprenorphine
 - Methadone
 - Naltrexone
- It is a life-long recovery taking an average of 8 attempts at treatment for success

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Treatment of OUD is controversial

Are we just switching one addiction to another?

Some sell buprenorphine for other street meds (heroin, fentanyl, etc)

Not all agree!!

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Consolidated Appropriations Act of 2023

X-waiver was eliminated to emulate France's success in reducing morbidity and mortality associated with OUD

Need for prescriber education (practical and philosophical)

The Door Opens

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OPIOID USE DISORDER
MOUD THERAPY GOALS:

- Prevent withdrawal
- Reduce cravings
- Minimize euphoria
- Reduce risk of euphoria
- Reduce infectious disease

JAMA Clinical Guidelines Synopsis, January 21, 2026

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WHAT WE KNOW SO FAR

- 2021 meta-analysis of 30 studies, n = 562,714
- Medications – either methadone or buprenorphine
- All-cause mortality was reduced in those on treatment vs no treatment
- 11 deaths / 1000 persons on treatment
- 24 deaths / 1000 persons not on treatment
- Methadone had higher rates of death at 4 weeks and more overdose than those treated with buprenorphine (OR = 3 in first 4 weeks)

JAMA Psychiatry 2021;78(9):979-993

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WHAT WE KNOW SO FAR

- 2023 meta-analysis of 83 studies + 193 observational studies, n = 155,111
- Medications – retention rates for 6 months with methadone or buprenorphine
- In the RCT's only
- Retention rates:
 - Methadone 66%
 - Buprenorphine 53%

Lancet Psychiatry 2023;10(6):386-402

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IMPROVED RETENTION RATES

- Retention rates go up when primary care gets involved vs treatment centers
- 86% in primary care vs 67% in treatment centers
- Integrated care is the key for success
 - Nurses, social workers, psychologist
 - When this is not available, treatment centers are encouraged
- “Withdrawal management without long-term addiction treatment for patients with OUD is associated with increased risk of relapse, opioid-related morbidity and death.”

JAMA Clinical Guidelines Synopsis, January 21, 2026

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Facts

- FDA approved for Opioid Use Disorder treatment in an office-based setting
- Overdose with buprenorphine in adults is less common
- Risk for overdose
 - Those individuals without tolerance (naïve)
 - Those using other substances like alcohol or benzodiazepines
- Buprenorphine should be part of a comprehensive management program that includes psychosocial support.....but it should not be withheld in the absence of psychosocial support

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Pharmacotherapy

- Buprenorphine acts as a partial mixed opioid agonist at the μ -receptor
- It is an antagonist at the κ -receptor
- It has a higher affinity for the μ -receptor than other opioids
- It can precipitate withdrawal symptoms in those actively using other opioids
- It is dosed daily, has a long half-life, and prevents withdrawal in opioid dependent patients

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Pharmacotherapy

- Formulations - tablet, sublingual film, injectable
- Many formulations contain naloxone to prevent injection diversion
 - This formulation is the preferred treatment medication
- The buprenorphine only version is often used with pregnant women to decrease potential fetal exposure to naloxone, however this has been recently challenged
- The buprenorphine only version is best for chronic pain treatment

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Pain Receptors

Drug	Mu	Delta	Kappa
Morphine	+	0	+
Buprenorphine	P	0	-
Pentazocine	P	0	+
Naloxone	-	-	-

Buprenorphine has a high affinity for the Mu-receptor
P = partial Pain Physician 2012; 15:ES59-ES66

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SAFETY - The Plateau Effect

A

Fentanyl

B

Buprenorphine

British Journal of Anaesthesia
Volume 94, Issue 6, June 2005, Pages 825-834

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Issue #1

Buprenorphine has a very high affinity for the mu receptor and will displace any other opioid on the receptor, thereby causing precipitated opioid withdrawal

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Issue #2

Discontinuing buprenorphine increases risk of overdose death upon return to illicit opioid use

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Issue #3

Alcohol or benzodiazepines + buprenorphine increases the risk of overdose and death

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Issue #4

Tell your physician if you are having a procedure that may require pain medication

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Tolerability

- Buprenorphine's side effects may be less intense than those of full agonist
- Similar to other opioids
- Possible side effects: Oral numbness, constipation, tongue pain, oral mucosal erythema, vomiting, intoxication, disturbance in attention, palpitations, insomnia, opioid withdrawal syndrome, sweating, and blurred vision

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Table 4. The most common adverse effects during the 4-week clinical trial using buprenorphine 16 mg daily (17).

Headache	36.4%	Vasodilation	9.3%
Withdrawal Symptoms	25.2%	Vomiting	7.5%
Generalized Pain	22.4%	Chills	7.5%
Nausea	15%	Asthenia	6.5%
Insomnia	14%	Infection	5.6%
Sweating Or Diaphoresis	14%	Rhinitis	4.7%
Constipation	12.1%	Diarrhea	3.7%
Abdominal Pain	11.2%	Back Pain	3.7%

Pain Physician 2012; 15:ES59-ES66

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Efficacy Summary

- Managing opioid use disorder and withdrawal (heroin and other opiates) – 27 trials
- Usually compared with clonidine or methadone
- Buprenorphine is more effective at patients being more likely to complete treatment withdrawal – NNT 4 (CI = 4-6)
 - From 14 trials
 - Less signs and symptoms of withdrawal
 - Stay in treatment longer
 - Experience fewer side effects
- Methadone - appear to be equally effective vs buprenorphine

Cochrane Review 2017, Issue 2, No.CD002025

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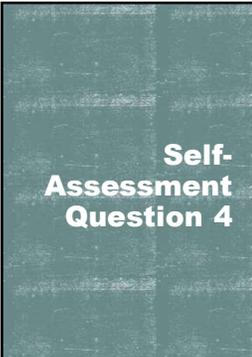


Efficacy Summary

- Cancer Pain Management
- 19 trials
- Available evidence is not conclusive
- Many authors rank it as a fourth-line agent behind morphine, oxycodone, fentanyl for cancer pain
- Transdermal buprenorphine is less effective

Cochrane Review 2018, Issue 3, No.CD009596

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Self-Assessment Question 4

4. Buprenorphine comes in a patch formulation. It is indicated in chronic pain. What is its advantage?

- A. It absorbs well in the fat under the skin and increases its efficacy
- B. It does not cause constipation
- C. It can be prescribed in opiate naive patients
- D. Best used when patient does not respond to transdermal fentanyl

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BUPRENORPHINE
PATCH
(THE NEW
DARVOCET®?)

▪ **Indication**

- Moderate to severe chronic pain
- Continuous formulation patch
- CIII schedule
- Takes up to 3 days to see efficacy
 - See quantifiable levels in 17 hours
 - Half-life is 26 hours

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BUPRENORPHINE (BUTRANS®)

Efficacy	Low back pain trial improvement was modest	Comparative trials 6 mcg vs 20 mcg/hr
<ul style="list-style-type: none"> • N=5,415 patient experience • Can be used in opiate naive patients • Four 12-week trials • Two of the 4 trials showed no efficacy over placebo 	<ul style="list-style-type: none"> • NNT 10 for 50% reduction in pain scores vs placebo • ~10% stopped therapy due to the lack of effect in trials 	<ul style="list-style-type: none"> • 30% reduction in pain scores of higher dose

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BUPRENORPHINE (BUTRANS®)

- **Price**
 - Expensive brand name ~\$120.00/patch
 - 5 mcg/hr; 7.5 mcg/hr; 10 mcg/hr; 15 mcg/hr; 20 mcg/hr
 - Now generic
- **Dosing**
 - Weekly patch, apply to upper arm, chest, back or side
 - Alternate site application
 - Avoid external heat sources
 - Do not cut
 - Can tape edges if needed
 - Available in box of #4 with 4 patch-disposable units

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- **Generic Buprenex® and Generic Subutex®**
 - Buprenorphine SL tab 2mg #60 = \$35
 - Buprenorphine SL tab 8mg #60 = \$42-\$65
- **Buprenorphine buccal film 150mcg #30 = \$150 (generic Buprenex®)**
 - Film 75, 150, 300, 450, 600, 750, 900 mcg films (increase in price)
- **Buprenorphine 8 mg/2 mg film #14 = \$35 (Brand name is Suboxone)**
 - Films – 2 mg/0.5 mg; 4 mg/1 mg; 8 mg/2 mg; 12 mg/3 mg
 - SL Tabs – 2 mg/0.5 mg #60 - \$80
 - SL Tabs – 8 mg/2 mg #60 - \$113
- **Generic Butrans® patch (once weekly)**
 - 10 mcg #4 = \$65
 - 20 mcg #4 = \$100

Price - GoodRx

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Simplicity

- Long half-life, so once daily dosing
- Low level of physical dependence
- If a patient withdraws from stopping buprenorphine, after long-term use – symptoms are usually mild over a few weeks
- Does not affect sex hormones like traditional opioids (lowers FSH/LH levels, testosterone)
- Safe in the elderly
- Safe with renal impairment

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In the Older Adult

- Recommended in renal impaired patients and those on dialysis
 - Dose should be 25-50% of the initial dose
- Lower risk of falls
- Lower risk of fractures
- Evaluate dose
- Start low and go slow
 - 0.2 mg SL every 8 hours, titrate to 0.4 mg as needed
 - For patch: start lowest dose and increase as needed (5 mcg patch)

Drugs & Aging 2024; 41:959-76

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Simplicity OUD Induction

- The dose of buprenorphine depends on the severity of withdrawal symptoms, and the history of last opioid use
- Long-acting opioids, such as methadone, require at least 48-72 hours since last use before initiating buprenorphine
- Short acting opioids (for example, heroin) require approximately 12 hours since last use for sufficient withdrawal to occur in order to safely initiate treatment
- Some opioid such as fentanyl may require greater than 12 hours
- Clinical presentation should guide this decision as individual presentations will vary

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Wesson & Ling, J Psychoactive Drugs, 2003 Apr-Jun;35(2):253-9.

COWS Clinical Opiate Withdrawal Scale

<p>Rating Pulse Rate: _____ beats/minute</p> <p>Diastolic blood pressure: _____ mmHg for one minute</p> <p>0 Pulse rate 80 or below</p> <p>1 Pulse rate 81-100</p> <p>2 Pulse rate 101-120</p> <p>3 Pulse rate greater than 120</p> <p>Sweating: <i>over past 1-2 hours not accounted for by room temperature or patient activity</i></p> <p>0 No report of chills or flushing</p> <p>1 Subjective report of chills or flushing</p> <p>2 Flushed or observable moisture on face</p> <p>3 Drench of sweat on torso or face</p> <p>4 Sweat covering all face</p> <p>Postures: <i>Observation during assessment</i></p> <p>0 Able to sit still</p> <p>1 Reports difficulty sitting still, barely able to do so</p> <p>2 Frequent shifting or continuous movements of legs/torso</p> <p>3 Unable to sit still for more than a few seconds</p> <p>Pupil size:</p> <p>0 Pupils pinned or normal size for room light</p> <p>1 Pupils possibly larger than normal for room light</p> <p>2 Pupils markedly dilated</p> <p>3 Pupils so dilated that only the rim of the iris is visible</p> <p>Raise or Joint aches: <i>If patient was having pain previously, only the additional component on hand, or report with rest or stand</i></p> <p>0 Not present</p> <p>1 Mild diffuse discomfort</p> <p>2 Patient reports severe diffuse aching of joints/muscles</p> <p>3 Patient is rubbing joints or muscles and/or unable to sit still because of discomfort</p> <p>Heavy nose or tearing: <i>Not assessed for 10-15 min symptoms or after give</i></p> <p>0 Not present</p> <p>1 Tears running or noticeably moist eye</p> <p>2 Nose running or tearing</p> <p>3 Nose continuously running or tears streaming down cheeks</p>	<p>GI upset: <i>over last 1-2 hours</i></p> <p>0 No GI symptoms</p> <p>1 Stomach cramps</p> <p>2 Nausea or loose stool</p> <p>3 Vomiting or diarrhea</p> <p>4 Multiple episodes of diarrhea or vomiting</p> <p>Tremor: <i>observation of non-affected hands</i></p> <p>0 No tremor</p> <p>1 Tremor can be felt, but not observed</p> <p>2 Slight tremor observable</p> <p>3 Coarse tremor or muscle twitching</p> <p>Yawning: <i>Observation during assessment</i></p> <p>0 No yawning</p> <p>1 Yawning once or twice during assessment</p> <p>2 Yawning three or more times during assessment</p> <p>3 Yawning several consecutive times</p> <p>Anxiety or irritability:</p> <p>0 None</p> <p>1 Patient reports increasing irritability or anxieties</p> <p>2 Patient obviously irritable/anxious</p> <p>3 Patient is hostile or agitated that participation in the assessment is difficult</p> <p>Overlook skin:</p> <p>0 Skin is smooth</p> <p>1 Flaccidity of skin can be felt or hair is standing up on arms</p> <p>2 Prominent piloerection</p> <p>Total Score: _____</p> <p>The total score is the sum of all 11 items</p> <p>Establish of patient completing Assessment:</p>
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Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

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Injection Formulation CIII

- Sublocade® (extended-release injection)
- Indicated for adults with moderate to severe opioid addiction whose withdrawal symptoms are controlled by oral buprenorphine for at least 7 days
- Monthly dose – at least 26 days apart
- 300 mg induction for at least 2 months, then 100 mg maintenance
- Upon injection, it forms a gel under the skin and becomes a depot

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Injection Formulation CIII

- Brixadi® (extended-release injection) indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of a transmucosal buprenorphine product or who are already being treated with buprenorphine
- BRIXADI (weekly) is available in 8 mg/0.16 mL, 16 mg/0.32 mL, 24 mg/0.48 mL, and 32 mg/0.64 mL
- BRIXADI (monthly) is available in 64 mg/0.18 mL, 96 mg/0.27 mL, and 128 mg/0.36 mL
- Prefilled syringes – different formulations

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Buprenorphine Case

- Patient X has just had a procedure that may require pain medication. You always prescribe ibuprofen and acetaminophen, but you often add low dose oxycodone for those just in case moments.
- You note that the patient currently takes buprenorphine 8 mg daily. He uses it for opioid use disorder.
- What to do? Do you give him the oxycodone?

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Buprenorphine Case

- You can give him oxycodone – lowest dose necessary for the shortest time
 - No trial has documented the respiratory depression concern of the addition
 - No trial has shown that exposure leads to old habits
 - Untreated pain has been the trigger of return to old habits
 - Always taper off the oxycodone (give instructions)
- You may decide not to give him the oxycodone and split the buprenorphine to 4 mg twice a day to help with analgesia
 - The analgesic half-life of buprenorphine is 4-8 hours
- Add the ibu's + acetaminophen

Pain Prac 2025;25:e113427

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When to consider the SWITCH!

Patient no longer benefits from opioid

Patient experiences harms from long-term opioids

Opioid naïve who are high risk for OUD

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Making the Switch

- Two ways:
 1. Stop full agonist and wait for withdrawal then start
 2. Overlap method:
 - Start low dose buprenorphine and continue full agonist
 - Taper full agonist and increase buprenorphine

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Bup Protocol

- Option 1:**
 - Stop full agonist and wait for withdrawal (~12-24 hours)
 - Start buprenorphine 2 mf BID
- Option 2:**
 - Day 1 - 0.5 mg buprenorphine (bup) daily
 - Day 2 - 0.5 mg bup twice a day
 - Day 3 - 1 mg bup twice aa day
 - Day 4 - 2 mg bup BID
 - Day 5 - 4 mg bup BID and stop full agonist (you can taper the full agonist beginning on day 4)

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QUOTES - NALOXONE

- For all patients who are prescribed opioid pain relievers, health care professionals should discuss the availability of naloxone
- Consider for high risk OUD ,
 - benzodiazepines or other medicines that
 - history of opioid use disorder
 - those who have experienced a previous opioid overdose
 - those at risk for accidental ingestion or opioid overdose



Original Prescription Strength
Easy to Use
Can Save a Life
Designed to quickly reverse the effects of an overdose of opioid emergency
2 Single-Dose Nasal Spray Devices
0.005 fl oz (0.1 mL each) For each nostril

Cost OTC - \$45 for 2 doses

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Generic Name and Form	Strength(s)/Brand Name and Estimated Cost	Considerations
Nalmefene Injection	-1.5 mg (Zimbal) - \$50/autoinjector -2 mg - \$30/vial	-Approved for pts 12 years and older -Can be given subcut, IM, or IV
Nalmefene Nasal Spray	-2.7 mg (Opvee) - \$98/two doses	-Approved for pts 12 years and older -Alternate nostrils with multiple doses
Naloxone Injection	-0.4 mg/mL - \$20/vial -2 mg/2 mL - \$31/prefilled syringe -5 mg/0.5 mL (Zimhi) - \$62/prefilled syringe	-Approved for any age (dose dependent) -Can be given subcut, IM, or IV
Naloxone Nasal Spray	-3 mg (Rivive) - \$36/two doses (OTC) -4 mg - \$102/two doses (Rx) - \$45/two doses (OTC) -8 mg (Kloxxado) - \$125/two doses	-Approved for any age (dose dependent) -Alternate nostrils with multiple doses

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