ALTERNATIVES TO OPIOIDS FOR CHRONIC PAIN & OPIOID TAPERING

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OBJECTIVES:

- Describe nonopioid analgesic options for chronic nonmalignant pain
- Describe use of adjunct treatment options with brief review of evidence in the literature
- Identify the challenges of opioid tapering
- Apply strategies for the process of opioid dose reduction

IOM (Institute of Medicine) 2011. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research, Washington, DC; The National Academies Press. Available at http://iom.edu/Reports/2011/Relieving-Pain-in-America-A-Blueprint-for-TransformingPrevention-Care-Education-Research.aspx

Issued on June 30, 2011 by the Institute of Medicine's Committee on Advancing Pain Research, Care and Education.

Its findings and recommendations:

- Pain represents a public health crisis of epidemic proportions
- There is a moral imperative to address this crisis
- Solutions will require a cultural transformation in the way pain, particularly chronic pain, is understood, assessed and treated.

- 116,000,000 adults are burdened with it—that's more than 1 in 3 adults, and more than are afflicted by heart disease, diabetes and cancer combined.
- The prevalence of chronic pain will only increase as the population ages and as the effects of obesity manifest themselves in pain-related conditions like diabetes and musculoskeletal pain.
- Chronic pain costs the American economy between $ 560-635 billion in added health care and lost productivity (excluding cost of pain affecting institutionalized individuals, military personnel, and children under age 18).

CDC GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

Centers for Disease Control and Prevention
National Center for Injury Prevention and Control

Recommendation #1

- **Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.**
- **Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient.**
- **If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.**

(Recommendation category A: Evidence type: 3)

ACETAMINOPHEN

Proposed mechanisms of action:
--serotonergic pathway

--a central cyclo-oxygenase (COX)-3 mechanism

--a cannabinoid-mediated mechanism

--activity at the hypothalamus for antipyretic effect

Analgesic activity

Anti-pyretic activity

January 2011---FDA asked manufacturers of combo products to decrease acetaminophen to no more than 325 gm and recommended change to maximum daily adult dose from 4 gm to **3 gm**

ACETAMINOPHEN

No anti-inflammatory effect

No anti-platelet effect

No damage to GI mucosa

Rare renal toxicity

Hepatic toxicity (>7.5 gm to 10 gm in single dose or in 8 hour period)

Minimal drug-drug interactions but can increase antithrombotic effects of warfarin

(dose dependent > 1950 mg /week)

IV ACETAMINOPHEN

Route of admin approved by FDA in 2010

Typical dose = 1 gm IV (cost $10-$13) every 6 hours

(compared with oral dose < $0.05)

Advantages:

- Avoid first-pass hepatic metabolism
- Achieves peak concentration more quickly than oral tx (within 15 minutes vs. up to one hour)
- Blood levels up to 70% higher

Contraindications:

- severe hepatic impairment, active liver disease

IV ACETAMINOPHEN

Study reported in *Journal of Orthopedic Trauma*

- retrospective cohort study that examined effectiveness of standardized IV acetaminophen perioperative pain control protocol
- patients > 65 yo with hip fractures

- Improved pain scores (by 33%)
- Decreased opioid use (by 31%)
- Decreased length of hospital stay (by 14%)
- Decreased missed PT sessions (by 52%)

NONSELECTIVE NSAIDS

Mechanism of action:

- inhibition of COX (a key enzyme responsible for biosynthesis of prostaglandins)

Nonselective NSAIDs *inhibit* both COX-1 and COX-2

- COX-1 regulates protection of gastric mucosa, platelet function, renal function therefore inhibition is responsible for adverse effects of NSAIDs
- inhibition of COX-2 = anti-inflammatory effect of NSAIDs

NSAIDS

- Analgesic effects are dose-dependent (start with lower dose then higher strength prescription product if needed)
- They do have an *analgesic ceiling effect*, so increasing above recommended max limits only increases adverse events and doesn't provide additional pain control
- GI bleeding and CV risk begins almost immediately with starting med
- Risk of renal failure increases the longer NSAIDs are used

NSAIDS----SAFETY CONSIDERATIONS

GI-related

- Nausea, diarrhea, dyspepsia, constipation
- GI bleeding, ulceration, perforation
- Can occur anytime during treatment (risk may be the same for short or long term treatment)
- Elderly at greatest risk

CV events

- Thrombosis, stroke, MI
- New onset HTN
- Risk increased with prolonged therapy or in patients with existing CV disease or CV risk factors
- Contraindicated for perioperative pain in setting of CABG surgery
- Naproxen considered safest for pts at risk for CV adverse effects

NSAID GI EFFECTS CONT'D

Apparent risk of GI bleeding (highest to lowest):

Ketorolac

Piroxicam

Indomethacin

Naproxen

Ketoprofen

Meloxicam

Diclofenac

Ibuprofen

"Guidelines for prevention of NSAID-related ulcer complications"; **Am J Gastroenterol.** 2009;104(3):728-738

NSAIDS---SAFETY CONSIDERATIONS

Overall mortality incidence rate:

48 / 1000 person-years with NSAIDs

75 / 1000 person-years with opioids

Drug interactions:

ACE inhibitors = blunted antihypertensive effect

Anticoagulants = increased bleeding risk

Lithium = increases lithium levels

SELECTIVE NSAID

Celecoxib (Celebrex)

- inhibition of COX-2
- theoretical advantage of reduced GI adverse effects (since it doesn't inhibit COX-1) & similar analgesic efficacy

Indications:

Osteoarthritis, RA, JRA, ankylosing spondylitis, acute pain, primary dysmenorrhea

Dose: 50 mg to 200 mg twice a day

Still has potentially heightened risk of CV and renal problems

NSAID RISK MITIGATION

- Reduced risk of upper GI events:
  - enteric coating
  - combining with gastro-protective agents
    - Misoprostol (Cytotec)
    - H2 receptor antagonists (like ranitidine)
    - PPI's

(but this doesn't protect against lower GI, CV or renal events)

- Use lower doses
- Use NSAID with shorter half life (like diclofenac, ibuprofen)
- Avoid in high-risk patients:
  - Elderly
  - Patients with CHF, CAD, HTN, renal insufficiency, liver cirrhosis

The "Practical Pain Management" website had a helpful guide for choosing NSAIDs in the following article: https://www.practicalpainmanagement.com/treatments/pharmacological/opioids/no-perfect-medicine-what-you-need-know-about-nsaids-opioids

Table 2. Quick Guide of NSAIDs

Precautions When Using NSAIDs

Co-occurring Condition	Recommendation
Pregnancy	Schedule "C" in 1 and 2 trimesters; Schedule "D" after 28 weeks of pregnancy
History of MI, CVA	Use naproxen; avoid ibuprofen, diclofenac, and celecoxib
Hypertension	Use sulindac and celecoxib; avoid naproxen, ibuprofen, indomethacin, and piroxicam
GI problems	Use meloxicam, diclofenac, and celecoxib; avoid ketorolac, indomethacin, ibuprofen, naproxen, ketoprofen and piroxicam

ANTIDEPRESSANTS

Tricyclic antidepressants (TCAs)

Useful for neuropathic pain

Most evidence for:

Amitriptyline, desipramine, nortriptyline

Limited by side effects (antihistamine/anticholinergic actions)

- dry mouth, constipation , blurred vision, mental status changes, tachycardia, urinary hesitation

ANTIDEPRESSANTS

Selective Serotonin Reuptake Inhibitors (SSRIs)

- evidence for use in neuropathic pain conflicting, but may be useful if failed other antidepressants
- recommended for *fibromyalgia*
  - ***fluoxetine*** having most evidence for efficacy

ANTIDEPRESSANTS

Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)

- *Venlafaxine*---was the initial agent in this class, mostly used for depression
- ***Duloxetine (Cymbalta)***
  - Fibromyalgia (FDA approved)
  - Chronic musculoskeletal pain (FDA approved)
  - Neuropathic pain
  - Less CV and sexual side effects but potential to increase LFTs
- ***Milnacipran (Savella)***
  - Fibromyalgia (FDA approved)

SNRIs can cause rise in blood pressure

https://www.practicalpainmanagement.com/treatments/pharmacological/medications-chronic-pain-other-agents

Table 2. Antidepressants[1,10,12,15,16]

Drug (Brand)	FDA-approved Indications	Formulations	Usual Dosing Recommendations*	Comments
Tricyclic Antidepressants				
Amitriptyline (generic)	Depression	10-, 25-, 50-, 75-, 100-, and 150-mg tablets	*Fibromyalgia:* 10 to 50 mg at bedtime *Neuropathic pain:* initial doses of 10 to 25 mg at bedtime titrated by 10 to 25 mg per week until response or a maximum of 150 mg/day	Use with caution in patients with hepatic impairment
Desipramine (Norpramin, generic)		10-, 25-, 50-, 75-, 100-, and 150-mg tablets (Norpramin, generic)	*Neuropathic pain:* initial doses of 10 to 25 mg at bedtime titrated by 10 to 25 mg per week until response or a maximum of 150 mg/day	Nortriptyline and desipramine are preferred to amitriptyline due to fewer anticholinergic side effects
Nortriptyline (Pamelor, generic)		10-, 25-, 50-, and 75-mg capsules (Pamelor, generic) 10-mg/5-mL oral solution		

ANTICONVULSANTS (MEMBRANE STABILIZERS)

EFFICACY FOR PAIN BASED ON ABILITY TO CONTROL NEURONAL EXCITABILITY

- ***Carbamazepine (Tegretol)***
  - Trigeminal neuralgia, diabetic peripheral neuropathy
- ***Oxcarbazepine (Trileptal)***
  - Neuralgia, diabetic neuropathy
- ***Lamotrigine (Lamictal)***
  - Neuropathic pain
- ***Gabapentin (Neurontin)***
  - Diabetic neuropathy, postherpetic neuralgia
- ***Pregabalin (Lyrica)***
  - Diabetic neuropathy, postherpetic neuralgia

Gabapentin & ***pregabalin*** are better tolerated, have fewer drug interactions, require less monitoring.

They can also be combined with TCA or opioid.

https://www.practicalpainmanagement.com/treatments/pharmacological/medications-chronic-pain-other-agents

Table 3. Anticonvulsants[9,10,12,18]

Drug (Brand)	FDA-approved Indications	Formulations[a]	Usual Dosing Recommendations[b]	Comments
Carbamazepine (Carbatrol, Epitol, Tegretol, generic)	Epilepsy, trigeminal neuralgia	200-mg tablets (Epitol, Tegretol, generic) 100-mg chewable tablets (Tegretol, generic) 100-, 200-, and 300-mg extended-release capsules (Carbatrol) 200- and 400-mg extended-release tablets (Tegretol XR, generic plus 100-mg Tegretol XR) 100-mg/5-mL oral suspension (Tegretol, generic)	*Neuropathic pain:* 100 mg twice daily titrated slowly to response or a maximum of 1,200 mg/day (given in divided doses)	May cause bone marrow suppression or hepatotoxicity; a CBC and LFTs should be obtained at baseline and periodically Use with caution in patients with hepatic impairment.

GABAPENTIN----MISUSE POTENTIAL

May be used at higher than recommended doses

- Can enhance the euphoria caused by an opioid (eg. Potentiate the effects of methadone)
- Used to become ‘‘intoxicated’’---capsules opened and snorted

SKELETAL MUSCLE RELAXANTS

Adjunctive medication for acute low back pain.

Data supporting efficacy in CLBP is controversial and limited.

- ***Cyclobenzaprine (Flexeril)***
  - Fibromyalgia; agent for sleep
- ***Baclofen***
  - Antispasmodic (cerebral palsy, MS); trigeminal neuralgia
- ***Tizanidine (Zanaflex)***
  - Spasticity; studied for use in low back pain

CAUTION!

Carisoprodol (Soma) is a popular muscle relaxant with an active byproduct metabolite, meprobamate—a barbiturate—that is potentially addictive.

Potentially lethal 3-drug combination:

- Hydrocodone (Vicodin, Lortab, Norco, Lorcet)
- Carisoprodol (Soma)
- Alprazolam (Xanax)

TOPICAL PAIN MEDICATION

- ***Lidocaine***
  - 5% topical patch
  - Local analgesia with few systemic effects
  - Studied for postherpetic neuralgia
  - For neuropathies in specific area
- ***Capsaicin***
  - Believed to reduce pain thru modulation of substance P (neurotransmitter for pain impulses)
  - Topical OTC formulations
    - Musculoskeletal pain
    - 0.075% strength shown effective for diabetic neuropathy
  - Prescription 8% topical patch
    - Has to be applied by healthcare professional; lasts 3 months
    - Postherpetic neuralgia

ACCUPUNCTURE

Randomized trial & meta-analysis

- improves pain and function in chronic LBP and knee OA more than controls do, but no more than shams do
- evidence suggests efficacy for short-term pain relief in neck disorders, lateral epicondylitis, rotator cuff tendonitis, fibromyalgia, myofascial pain

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)

Pulsed current to relieve pain thru stimulating nerve fibers to inhibit pain transmission to the brain based on gate control theory

Consider for:

Fibromyalgia, short term knee OA, chronic neck pain

Lacks evidence for:
chronic LBP

CANNABIDIOL (CBD)

Cannabis sativa

- main component is delta-9 THC & first cannabinoid to be discovered
  - Mimics endogenous cannabinoid neurotransmitters by binding at CB1 & CB2 receptors
- cannabidiol is a major phytocannabinoid isolated from the plant
  - Does not activate the CB1 & CB2 receptors which likely accounts for lack of psychotropic activity or "non-intoxicating" effect

CANNABIDIOL (CBD)

Pharmacological effects:

- Reduces inflammation
- Neuroprotective
- Relieves pain
- Relieves anxiety
- Antidepressant
- Causes vasodilation
- Antioxidant
- Reduces cancer cell growth
- Reduces tumoral angiogenic process

CANNABIDIOL (CBD)

Some current areas of study:

Alzheimer's disease

Parkinson's

Multiple sclerosis

Epilepsy

Pain

Anxiety

Depression

Cancer

Rheumatoid arthritis

Diabetic complications

NUTRITION & PAIN--- CONSIDERATIONS

- **Vitamin D**
  - Low levels proposed as explanation of dull, persistent, generalized aches, pains, weakness; associated with inflammation & susceptibility to illness
- **Amino Acids**
  - Can supplementation optimize endogenous opiates (endorphins)?
- **Turmeric**
  - Curcumin is active component
  - Studies have explored anti-inflammatory properties
- **Ginger**
  - Functions as anti-inflammatory (disrupts COX-2 pathway)

NUTRITION & PAIN--- CONSIDERATIONS

Diet

How does food impact inflammatory processes?

- "pro-inflammatory foods" ?

  (sugar, processed cereals, fried foods, red meat)

- anti-oxidants? Omega-3 ?

Consider asking about diet in your chronic pain patient:

- What is daily protein consumption? (often low)
- Do they skip breakfast?
- Amount of sugars & carbohydrates during the rest of the day? (eg "comfort foods")

"ALTERNATIVES TO OPIOIDS IN THE "PHARMACOLOGIC MANAGEMENT OF CHRONIC PAIN SYNDROMES: A NARRATIVE REVIEW OF RANDOMIZED, CONTROLLED, AND BLINDED CLINICAL TRIALS"

A.NICOL, R. HURLEY, H. BENZON; ANESTHESIA-ANALGESIA 2017

- 9566 studies were obtained thru literature search and 271 met inclusion criteria
  - Studies that compared nonopioid med to placebo or another medication
  - Prospective, randomized, controlled and blinded design
  - Primary outcome: impact on pain severity, functional status, proportion of patients with response
- Chronic low back pain is one of the most commonly encountered conditions in clinical practice---there are no on-label FDA approved medications for this condition

CHRONIC LOW BACK PAIN--Effective Medications based on the included studies	
Medication	FDA Off-Label
Acetaminophen	None
NSAIDs	Naproxen, celecoxib, diclofenac, piroxicam, indomethacin
Amine Reuptake Inhibitors (ARI's) (TCA's, SSRI's, SNRI's)	Desipramine, nortriptyline, doxepin, duloxetine, maprotiline
Membrane stabilizers (anticonvulsant drug class)	Topiramate
Muscle relaxant	Carisoprodol, cyclobenzaprine, diazepam
ARI/opioid	Tramadol, Tapentadol
Topical capsaicin	Capsaicin cream
Local anesthetic	None
NMDA antagonists (amantadine)	None
Miscellaneous	Botulinum toxin type A

FIBROMYALGIA---Effective Medications based on the included studies		
Medication	FDA On-Label	FDA Off-Label
NSAIDs	None	None
Amine Reuptake Inhibitors (ARI's) (TCA's, SSRI's, SNRI's)	Duloxetine, milnacipran	Amitriptyline, fluoxetine, paroxetine
Membrane stabilizers (anticonvulsant drug class)	Pregabalin	Gabapentin
Muscle relaxant	None	Cyclobenzaprine
ARI/opioid	None	Tramadol/APAP
Opioid antagonists	None	Low dose naltrexone
Local anesthetic	None	None
NMDA antagonists (amantadine)	None	Memantine
Miscellaneous	None	Nabilone

RADICULAR PAIN---Effective Medications based on the included studies	
Medication	FDA Off-Label
Amine Reuptake Inhibitors (ARI's) (TCA's, SSRI's, SNRI's)	Duloxetine, milnacipran, amitriptyline
Membrane stabilizers (anticonvulsant drug class)	None
Topical (nonlocal anesthetic)	None
ARI/opioid	None
Local anesthetic	None
NMDA antagonists (amantadine)	None
Miscellaneous	Indomethacin

NONINVASIVE TREATMENTS FOR CHRONIC LOW BACK PAIN---CLINICAL PRACTICE GUIDELINES AMERICAN COLLEGE OF PHYSICIANS

Table 2. The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

Magnitude of effect:
Pain----measured with an analog scale
Function---measured with Oswestry Disability Index

Intervention	**Quality of Evidence**	**Improved pain**	**Improved function**
Exercise	Moderate	Small effect	Small effect
Acupuncture	Moderate	Moderate effect	No to moderate effect
Mindfulness	Moderate	Small effect	Small effect
Tai chi	Low	Moderate effect	Small effect
Yoga	Low	Small to moderate	Small to moderate
Electromyography Biofeedback	Low	Moderate effect	
Cognitive behavioral therapy	Low	Moderate effect	
Spinal manipulation	Low	Small effect	

OPIOID TAPERING

OPIOID TAPERING

When to consider:

- ❑ Poor pain relief or functioning despite reasonable increase in opioid dose
- ❑ Significant adverse effects
- ❑ Not adhering to treatment recommendations
- ❑ Deterioration in physical, emotional or social functioning
- ❑ Underlying condition changes (eg. pain improves)

THE CHALLENGE OF OPIOID TAPERING

Patient barriers:

- Overall low self-perceived risk of opioid overdose. They attributed reports of overdose to intent or risky behavior.
- Rated importance of treatment of current pain higher than the future potential risk of opioid use
- Pessimism about non-opioid therapies
- Fear of opioid withdrawal symptoms

"Patients' Perspectives on Tapering of Chronic Opioid Therapy: A Qualitative study"J.Frank et al. **Pain Medicine**. Vol 17, Issue 10, 1October2016,pp 1838-1847.

OPIOID TAPERING

M. Matthias, et al (Department of Medicine, Indiana University School of Medicine) conducted a qualitative analysis of audio-recorded primary care clinic visits with patients taking opioids for chronic pain. They also conducted in-depth interviews with patients and PCPs to identify communication challenges.

"I'm Not Gonna Pull the Rug out From Under You": Patient-Provider Communication About Opioid Tapering. M. Matthias, et al. **The Journal of Pain**, Vol 18, No 11 (November), 2017:pp1365-1373.

THEMES THAT EMERGED:

- **Explaining**
  - Patients needed to understand *individualized* reasons for tapering
- **Negotiating**
  - Patients needed to have input
- **Managing difficult conversations**
  - When patients & providers didn't reach shared understanding—difficulties arose
- **Nonabandonment**
  - Patients needed to know that their providers would not abandon them during the tapering process

Approaching opioid taper.

Reason for taper	Length of taper	Interventions:
Substance Use Disorder See DSM 5 criteria for Opioid Use Disorder	No taper	Immediate referral as needed. (1) inpatient detox may be indicated. (2) inpatient vs outpatient treatment with medication-assisted treatment (MAT). Offer naloxone.
Diversion	No taper	Determine need based on actual use of opioids
At risk for severe harm	Weeks	(1) Inpatient withdrawal management OR (2) Outpatient opioid taper Offer naloxone.
Lack of functional improvement; pain condition not opioid responsive	Months	Outpatient opioid taper Offer naloxone.

BEFORE TAPERING:

The Plan:

- pain management
  - adjuncts for chronic pain
- co-morbidity management
  - Mental health---addressing depression and anxiety
  - Sleep
  - Other medical conditions
- follow up
  - Visit frequency; point of contact
- Withdrawal management, if needed

MEDICOLEGAL CONSIDERATIONS:

Be clear in your documentation

- this is a **prescription opioid *taper* or *wean***

"Detoxification" = implies a diagnosis of substance use disorder (SUD) & requires special licensure

Overdose risk

discuss loss of tolerance with patient & risk of OD if they suddenly go back to previous doses

offer Naloxone

TAPERING

- The daily dose to prevent acute withdrawal is approximately 25% of the previous day's dose

Protocols to consider:

- CDC 2016
  - 10% per week
  - 10% per month if long-term (eg. over 2 years)
- VA/DoD 2017
  - 5-20% per 28 days

Example from VA Opioid Taper Decision Tool

Example Tapers for Opioids[5-9]			
Slowest Taper (over years)	**Slower Taper (over months or years)**	**Faster Taper (over weeks)****	**Rapid Taper (over days)****
Reduce by 2 to 10% every 4 to 8 weeks with pauses in taper as needed *Consider for patients taking high doses of long-acting opioids for many years*	Reduce by 5 to 20% every 4 weeks with pauses in taper as needed **MOST COMMON TAPER**	Reduce by 10 to 20% every week	Reduce by 20 to 50% of first dose if needed, then reduce by 10 to 20% every day

TAPERING

If patient is on both long-acting and short-acting opioids, which should be tapered first?

We don't have good evidence.

Example of a taper schedule with Excel spreadsheet that calculates weekly doses

https://www.hca.wa.gov/search/site/taper%20schedule?section=%2A

Initial Total Dose

Opioid Type	Baseline Opioid	Current mg/Day	Current MED/Day	% of Total MED
Short Acting			0	
Long Acting			0	
	Total Morphine Equianalgesic Dose		0	

First taper Short Acting Narcotics q week if > 10% of total MED if combined with a long acting opioid.

Week	Day	Total mg/day: dosage schedule	MED of Short Acting Opioid	Week	Day	Total mg/day: dosage schedule	MED of Short Acting Opioid
1	1-7	0	0	6	36-42	0	0
2	8-14	0	0	7	43-49	0	0
3	15-21	0	0	8	50-56	0	0
4	22-28	0	0	9	57-63	0	0
5	29-35	0	0	10	64-70	0	

SHORT TERM RISK OF TAPERING: WITHDRAWAL SYNDROME

- Starts within 2 to 3 half-lives after the last dose.
  - HTN, tachycardia, restlessness, sweating, tremor
  - GI symptoms (nausea, cramping, diarrhea)
  - Anorexia, insomnia, hot flashes, dizziness
  - Mood swings
- Improves in 1-2 weeks.
- *Sensory hyperalgesia* may appear immediately after discontinuation of long-term opioid treatment
- Subjective symptoms can be enhanced by anxiety
- Symptoms of anxiety can be interpreted as withdrawal

Autonomic symptoms (sweating, tachycardia, myoclonus)	**First line** • Clonidine 0.1 to 0.2 mg oral every 6 to 8 hours; hold dose if blood pressure <90/60 mmHg (0.1 to 0.2 mg 2 to 4 times daily is commonly used in the outpatient setting) – Recommend test dose (0.1 mg oral) with blood pressure check 1 hour post dose; obtain daily blood pressure checks; increasing dose requires additional blood pressure checks – Re-evaluate in 3 to 7 days; taper to stop; average duration 15 days **Alternatives** • Baclofen 5 mg 3 times daily may increase to 40 mg total daily dose – Re-evaluate in 3 to 7 days; average duration 15 days – May continue after acute withdrawal to help decrease cravings – Should be tapered when it is discontinued • Gabapentin start at 100 to 300 mg and titrate to 1800 to 2100 mg divided in 2 to 3 daily doses* – Can help reduce withdrawal symptoms and help with pain, anxiety, and sleep • Tizanidine 4 mg three times daily, can increase to 8 mg three times daily
Anxiety, dysphoria, lacrimation, rhinorrhea	• Hydroxyzine 25 to 50 mg three times a day as needed • Diphenhydramine 25 mg every 6 hours as needed**
Myalgias	• NSAIDs (e.g., naproxen 375 to 500 mg twice daily or ibuprofen 400 to 600 mg four times daily)*** • Acetaminophen 650 mg every 6 hours as needed • Topical medications like menthol/methylsalicylate cream, lidocaine cream/ointment
Sleep disturbance	• Trazodone 25 to 300 mg orally at bedtime
Nausea	• Prochlorperazine 5 to 10 mg every 4 hours as needed • Promethazine 25 mg orally or rectally every 6 hours as needed • Ondansetron 4 mg every 6 hours as needed

SECONDARY ABSTINENCE SYNDROME

- Can last up to 6 months
  - General malaise
  - Fatigue
  - Decreased well-being
  - Poor tolerance to stress
  - Craving for opioids

TRAMADOL

Parent drug & metabolite are partial agonists at the mu receptor.

Tramadol inhibits the reuptake of norepinephrine & serotonin

(reuptake inhibition of NE plays role in neuropathic pain of the descending pathway)

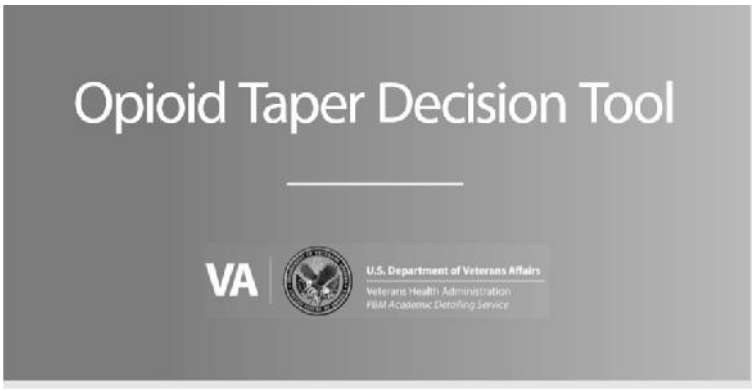
Withdrawal:

- anxiety, sweating, insomnia
- more like serotonin withdrawal:
  - mood swings, vertigo, insomnia, fatigue

Clonidine not as helpful

Consider fluoxetine 10-20 mg daily

- https://www.pbm.va.gov/AcademicDetailingService/Documents/Pain_Opioid_Taper_Tool_IB_10_939_P96820.pdf



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