VA
U.S. Department of Veterans Affairs
Veterans Health Administration
PBM Academic Detailing Service

A QUICK REFERENCE GUIDE (2017)

Pain

Transforming the Treatment of Pain

VA PBM Academic Detailing Service

Real Provider Resources

Real Patient Results

Your Partner in Enhancing Veteran Health Outcomes

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Abbreviations

6-MAM = 6-monoacetylmorpine

APAP = acetaminophen

BEG = benzoylecognine

BP = blood pressure

CABG = coronary artery bypass graft

CBD = cannabidiol

CrCl = creatinine clearance

EC = enteric coated

EDDP = 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine

EtG = ethyl glucuronide

EtS = ethyl sulfate

GCMS = gas chromatography-mass spectrometry

GI = gastrointestinal

HR = hour(s)

IR = immediate release

MDA = 3,4-methylenedioxy-amphetamine

MDEA = 3,4-methylenedioxy-N-ethyl-amphetamine

MDMA = 3,4-methylenedioxy-methamphetamine

MEDD = morphine equivalent dose

mL = milliliter(s)

NSAID = nonsteroidal anti-inflammatory drug

ng = nanogram(s)

OEND = opioid overdose education and naloxone distribution

PDMP = prescription drug monitoring program

PPI = proton pump inhibitor

THC = tetrahydrocannabinol

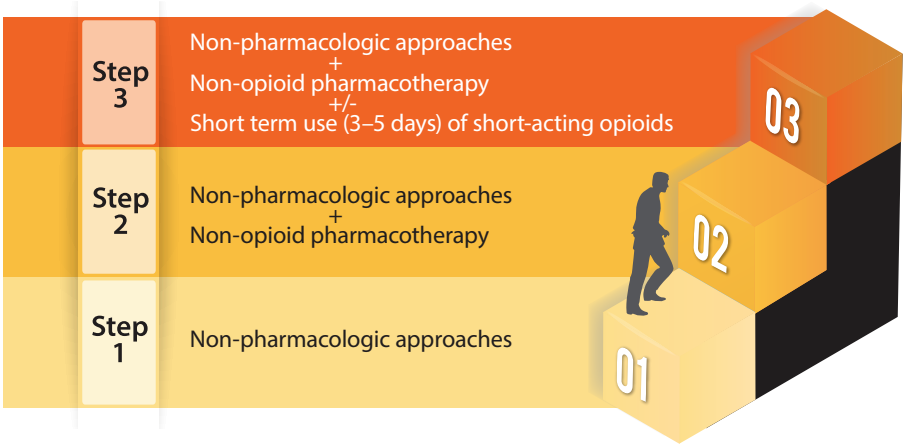
THCA = delta-9-tetrahydrocannabinol-9-carboxylic acid

UTS = urine toxicology screening

UDT = urine drug testing

XR = extended release

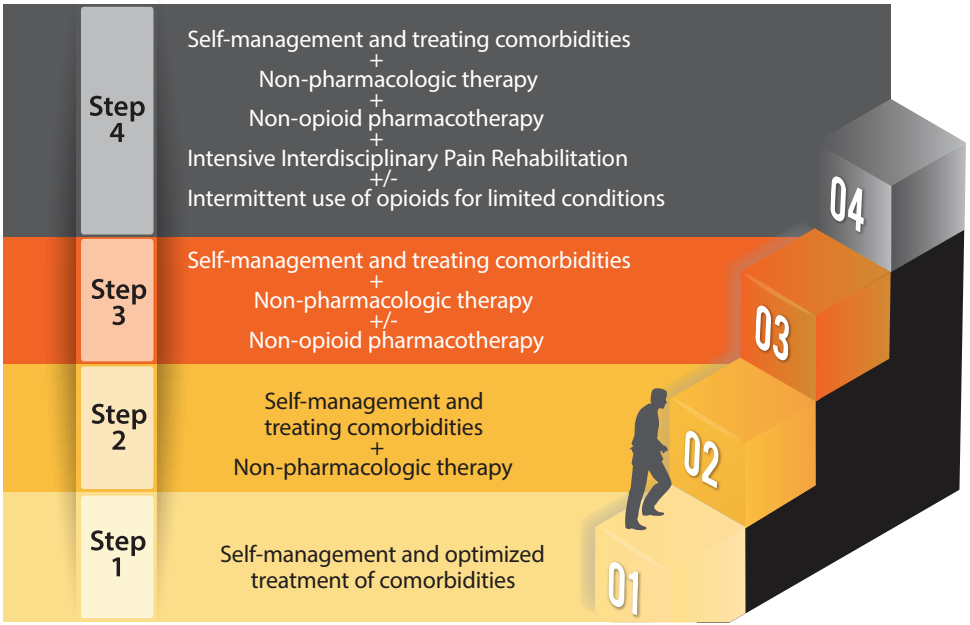
Stepwise Approach to Acute Pain Management[1–2]



Tips for Treating Acute Pain

- Reserve opioids for pain that is not expected or does not respond to Step 1 and Step 2 treatments
- Prescribe for less than 3 to 5 days then evaluate the need to continue therapy
- Use short acting opioids only

Stepwise Approach to Chronic Pain Management



Topical Agents for Acute and Chronic Musculoskeletal Pain and Neuropathic Pain[3]

Generic Name	Type of Pain	Usual Adult Dose	Maximum Dose	Comments
Diclofenac Gel 1%	Musculoskeletal	Upper extremity (hand, wrist, or elbow): 2 grams applied 4 times daily Lower extremity (foot, knee, ankle): 4 grams applied 4 times daily Do not use with oral NSAID	Upper extremity: do not exceed 8 grams a day to any single joint. Lower extremity: do not exceed 16 grams a day to any single joint.	Not evaluated for use on the spine, hip or shoulder. Risk of gastrointestinal bleeding is lower than oral diclofenac, but can occur. Dosing card provided to help measure grams for application. Contraindicated for treating preoperative pain before CABG and should be avoided for 14 days after CABG surgery.

Not all products listed may be available on VA National Formulary and may require non-formulary request or prior authorization request. To view VA National Formulary: **https://www.pbm.va.gov/PBM/NationalFormulary.asp**.

continued from page 4 (Topical Agents for Acute and Chronic Musculoskeletal Pain and Neuropathic Pain)

Generic Name	Type of Pain	Usual Adult Dose	Maximum Dose	Comments
Diclofenac Patch 1.3% **Diclofenac Topical Solution 1.5%, 2%**	Musculoskeletal	Patch: 1 patch to most painful area twice a day 1.5% solution: 40 drops to each affected knee 4 times a day 2% solution: 40 mg (2 pump actuations) to each affected knee 2 times a day Do not use with oral NSAID	Same as usual dose	Patch: Approved for treatment of acute pain due to minor strains, sprains and contusions. Solution: FDA approved for osteoarthritis of the knee. Risk of gastrointestinal bleeding is lower than oral diclofenac, but can occur. Contraindicated for treating preoperative pain before CABG and should be avoided for 14 days after CABG surgery.

Not all products listed may be available on VA National Formulary and may require non-formulary request or prior authorization request. To view VA National Formulary: **https://www.pbm.va.gov/PBM/NationalFormulary.asp**.

continued from page 4 (Topical Agents for Acute and Chronic Musculoskeletal Pain and Neuropathic Pain)

Generic Name	Type of Pain	Usual Adult Dose	Maximum Dose	Comments
Lidocaine Patch 5%	Musculoskeletal and neuropathic	1–3 patches applied once for up to 12 hours within a 24 hour period	3 patches every 12 hours	May cut patches to fit painful area. Can consider using patches every 12 hours if pain responds to patch. Systemic absorption and toxicity can occur if used on irritated or broken skin.

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continued from page 4 (Topical Agents for Acute and Chronic Musculoskeletal Pain and Neuropathic Pain)

Generic Name	Type of Pain	Usual Adult Dose	Maximum Dose	Comments
Methyl Salicylate/ Menthol Cream	Musculoskeletal	Low concentration 10–15%: Apply to affected area up to 3 to 4 times a day High concentration 16–30%: Apply to affected area up to 3 to 4 times a day	Same as usual dose	Do not use on open wounds, avoid contact with eyes or mucous membranes, do not use with a heating pad.
Methyl Salicylate 10%/Menthol 3% Patches	Musculoskeletal	1 patch every 8 to 12 hours; up to 2 patches a day	Same as usual dose	

Not all products listed may be available on VA National Formulary and may require non-formulary request or prior authorization request. To view VA National Formulary: **https://www.pbm.va.gov/PBM/NationalFormulary.asp**.

continued from page 4 (Topical Agents for Acute and Chronic Musculoskeletal Pain and Neuropathic Pain)

Generic Name	Type of Pain	Usual Adult Dose	Maximum Dose	Comments
Capsaicin Cream/ Ointment	Musculoskeletal and neuropathic	0.025%: apply thin film to affected area 2–4 times daily	0.075%: apply thin film to affected area 2–4 times daily	Wash hands after use or wear gloves to apply; do not use near eyes or mucous membranes. Requires scheduled use.

Not all products listed may be available on VA National Formulary and may require non-formulary request or prior authorization request. To view VA National Formulary: **https://www.pbm.va.gov/PBM/NationalFormulary.asp**.

Non-Opioid Agents for Acute and Chronic Musculoskeletal Pain[3]

Generic Name	Usual Adult Dose	Maximum Dose	Comments
Acetaminophen	650–1000 mg every 4–6 hours PRN	4000 mg daily in healthy patients 2000 mg daily in hepatic impairment	No platelet (<2000 mg daily) or anti-inflammatory effect. Adjust dose in alcoholic or hepatic disease.
NSAIDs			
Diclofenac EC	50–75 mg every 8–12 hours PRN	150 mg daily	Use NSAIDs with caution in renal/hepatic impairment, gastrointestinal disease, or patients receiving concurrent anticoagulants or lithium. Consider using PPI for patients at high risk for developing upper GI bleeding. Contraindicated for treating preoperative pain before CABG surgery and should be avoided for 14 days after CABG surgery.
Etodolac	200–400 mg every 6–8 hours PRN	1200 mg daily	
Ibuprofen	200–400 mg every 4–6 hours PRN	800 mg per dose or 3200 mg daily	
Meloxicam	7.5 mg once daily PRN	15 mg once daily	
Naproxen	250–500 mg every 6–12 hours PRN	1250 mg a day initial dose then 1000 mg daily	
Salsalate	500–1000 mg every 8–12 hours PRN	3000 mg daily	
Sulindac	150–200 mg every 12 hours PRN	400 mg daily	

continued from page 9 (Non-Opioid Agents for Acute and Chronic Musculoskeletal Pain)

Generic Name	Usual Adult Dose	Maximum Dose	Comments
Non-benzodiazepine Skeletal Muscle Relaxants			
Methocarbamol	750–1500 mg every 6 hours for first 2–3 days, then use lowest effective dose, e.g., 500–1000 mg every 6–12 hours PRN	1500 mg 4 times daily	Drowsiness is common. Prescribing for a limited duration is recommended (≤7 days). Advise to avoid operating heavy machinery or driving; avoid alcohol.
Cyclobenzaprine	5 mg three times daily PRN	10 mg three times daily	
Baclofen	5–10 mg three times daily PRN	20 mg four times daily	
Tizanidine	2–4 mg every 8 hours PRN	8 mg single dose or 24 mg daily	

Antidepressants and Anticonvulsants for Musculoskeletal and Neuropathic Pain[3]

Generic Name	Usual Adult Dose	Maximum Dose	Comments
Antidepressants			
Amitriptyline	10–150 mg at bedtime	150 mg daily	Caution in elderly and patients with cardiac disease. Use no more than 75 mg at bedtime for patients over the age of 65 years old. Amitriptyline and imipramine have more anticholinergic effects than nortriptyline or desipramine. May cause QTc prolongation, avoid if QTc >450 ms.
Imipramine	10–150 mg at bedtime	150 mg daily	
Nortriptyline	10–150 mg at bedtime	150 mg daily	
Desipramine	10–150 mg at bedtime	150 mg daily	
Venlafaxine	IR: 75–150 mg twice daily XR: 75–225 mg daily	IR: 300 mg daily (divided) XR: 225 mg daily	Adjust dose based on renal function. Higher doses associated with increased blood pressure.
Duloxetine	30–60 mg daily	60 mg daily	Avoid in patients with hepatic insufficiency. Avoid with CrCl <30 mL/min. Monitor BP. Higher doses for pain have not been shown to provide additional benefit.

continued from page 11 (Antidepressants and Anticonvulsants for Musculoskeletal and Neuropathic Pain)

Generic Name	Usual Adult Dose	Maximum Dose	Comments
Antiepileptics			
Gabapentin	300 mg at bedtime and titrate to 300–900 mg every 8–12 hours	3600 mg daily in divided doses	Adjust dose based on renal function.
Pregabalin	50–150 mg every 8–12 hours	300 mg daily in divided doses	Adjust dose based on renal function. Studied up to 600 mg/day with no additional benefit in pain reduction and an increase in adverse effects.
Carbamazepine	100–200 mg every 6–12 hours	1200 mg daily in divided doses	Avoid in patients with active liver disease. Used primarily for trigeminal neuralgia. Hepatic enzyme inhibitor of CYP2C19 and inducer of CYP3A4/5, must be cautious of drug interactions. Serious dermatologic reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis reactions have been reported. Oxycarbazepine may be better tolerated than carbamazepine.
Oxcarbazepine	300 mg twice daily	1200–2400 mg daily in divided doses	

Opioids for Acute Pain[1–3]

Initial Dose: Opioid Naïve → Limit to a 3 to 5 day supply then reassess*					
Opioid	**Milligrams (mg)**	**Dose/Day**	**mg MEDD**	**Drug Prescribed**	**Initial Quantity (3 day supply)**
Codeine	15–30	2–3	6.75 to 13.5	Codeine 30 mg/APAP 300 mg	9 tablets
Hydrocodone	5–10	3	15 to 30	Hydrocodone/APAP 5/500	9 to 18 tablets
Hydromorphone IR	2	2–3	24	Hydromorphone IR 2 mg	9 tablets
Morphine IR	7.5–15	2–3	22.5 to 45	Morphine IR 15 mg	9 tablets
Oxycodone IR	5–10	2–3	22.5 to 45	Oxycodone IR 5 mg or Oxycodone 5 mg/APAP 325 mg	9 to 18 tablets
Oxymorphone IR	5	2–3	45	Oxymorphone IR 5 mg	9 tablets
Tapentadol IR	50	2–3	60	Tapentadol IR 50 mg	9 tablets
Tramadol	25–50	2–3	N/A	Tramadol 50 mg	9 tablets

*Supply should be limited to 3–5 days; however in some cases of severe pain, treatment may need to be longer.

Calculating Milligram Morphine Equivalent Daily Dose (MEDD)[2]

Opioid Agent	Conversion Factor	How to Calculate
Codeine	0.15	1. Determine the total daily dose (TDD) of all opioids. 2. Convert to mg MEDD by multiplying the TDD of each opioid by their conversion factor. 3. Add all opioids together. Example: Veteran taking Oxycodone SR 20 mg three times daily and Hydrocodone/APAP 10/325 mg 4 tablets a day. Oxycodone 60 mg daily x 1.5 = 90 Hydrocodone/APAP 40 mg daily x 1 = 40 Total mg MEDD = 130
Tapentadol	0.4	
Morphine	1	
Hydrocodone	1	
Oxycodone	1.5	
Fentanyl Transdermal (in mcg/hr)	2.4	
Oxymorphone	3	
Hydromorphone	4	
Methadone **1–20 mg/day** **21–40 mg/day** **41–60 mg/day** **≥61–80 mg/day**	 4 8 10 12	

This is only an estimate and cannot account for individual variability in genetics and pharmacokinetics. Do not use the calculated MEDD when converting from one opioid to another. When converting opioids, the new opioid dose is usually substantially lower than the calculated MEDD dose (33–50% less) to avoid accidental overdose.

Considerations When Prescribing Methadone[2,4]

Dose Titration

- Wait at least 5–7 days before increasing the dose

QTc Prolongation

- Avoid use if QTc is >500 ms
- Caution if QTc 450–500 ms

Patients with Risk of QTc Prolongation or History of >450 ms

- Baseline ECG then repeat 2–4 weeks after starting
- ECG after dose changes
- ECG when methadone dose >30 mg/day and again if reaching 100 mg/day
- Consider alternative if QTc 450–500 ms or if patient has new risk factors or signs/symptoms suggestive of arrhythmia

Patients Not Known to be at High Risk of QTc Prolongation

- Baseline ECG in past 12 months
- ECG when methadone dose >30 mg/day and again if reaching 100 mg/day
- New risk factors or signs/symptoms suggestive of arrhythmia

Methadone is not a first-line treatment for chronic pain. It has unique pharmacokinetics that make it different from other opioids and should only be prescribed by an experienced provider or in consultation with a specialist.

Methadone Dosing Strategies[4–11]

Methadone Dosing Strategies							
Dosing strategies for patients receiving codeine preparations or no previous opioid: • Gradual titration - Start with 2.5 mg every 8 to 12 hours; may start at a lower dose using methadone solution 1 mg/ml - Increase dose by 2.5 to 7.5 mg (in divided doses), no more often than every 5–7 days - Start low and go slow							
Dosing strategies for patients taking opioids chronically: • Determine the equianalgesic dose							
Morphine (mg/day)	<30	31–99	100–299	300–499	500–999	1000–1200	>1200
Morphine: Methadone	2:1*	4:1*	8:1*	12:1*	15:1*	20:1*	Consult*

*Methadone conversions should only be performed by an experienced provider or in consultation with a specialist.

continued from page 16 (Methadone Dosing Strategies)

Methadone Dosing Strategies

Dosing strategies for patients taking opioids chronically (cont.):

- Rapid conversion
  - Discontinue the previous opioid
  - Start calculated methadone dose on day 1
  - Titrating strategies
    - Dose titration 2.5 mg every 8 hours after 5–7 days OR
    - Calculate how much opioid was used for breakthrough pain on days 5, 6 and 7 and use the average amount, convert to mg methadone and increase accordingly. Do not use methadone as needed. Opioids for breakthrough pain include oxycodone with or without acetaminophen, hydrocodone/acetaminophen, and immediate release morphine
- Stepwise conversion – may be a better option with high doses
  - Dose of previous opioid is reduced by 1/3 and replaced with 1/3 of the calculated methadone dose (in 3 divided doses)
  - After several days to weeks reduce original opioid by an additional 1/3 and the methadone dose is increased by 1/3
  - After several days to weeks the remaining 1/3 of the previous opioid is discontinued and the methadone dose is increased to the initial calculated dose

*Methadone conversions should only be performed by an experienced provider or in consultation with a specialist.

Monitoring Patients on Chronic Opioid Therapy—Perform at Each Follow Up Visit[1,2]

Assess

- Function, risks and benefits of opioid therapy
- Adverse effects
- Progress toward functional treatment goals
- Adherence to treatment plan
- Complications or co-occurring conditions (medical, mental health, and/or SUD)

Complete Risk Mitigation Strategies

- Urine drug testing (UDT)
- Prescription drug monitoring program (PDMP)
- Monitoring for overdose and suicidality
- Opioid overdose education and naloxone distribution (OEND)

Discuss expectations and optimize comprehensive pain care plan

Evaluate for opioid taper

Follow up should be performed at least every 3 months if opioid dose is stable and more frequently if needed based on risk factors.

Assess Baseline Pain and Function—PEG Scale[12]

Pain, enjoyment, general activity scale (**PEG** Scale)—scale from 0–10.

1. What number best describes your **P**ain on average in the past week?
   [__1 2 3 4 5 6 7 8 9 10____]
   No pain **Bad as you can imagine**

2. What number best describes how, during the past week, pain has interfered with your **E**njoyment of life?
   [__1 2 3 4 5 6 7 8 9 10____]
   Does not interfere **Completely interferes**

3. What number best describes how, during the past week, pain has interfered with your **G**eneral activity?
   [__1 2 3 4 5 6 7 8 9 10____]
   Does not interfere **Completely interferes**

Risk Mitigation Strategies for Patients on Chronic Opioids[1,2,5]

Opioid Risk	Recommended Frequency UDT	Recommended Frequency PDMP
All Patients	At least once yearly	Once a year at minimum; prescribers must follow requirements by their state of licensure.
Higher Risk Patients • Opioid doses ≥ to 90 mg MEDD • Concomitant benzodiazepine use • OUD	At least every 3 months	Every prescription.
Aberrant Behavior • Lost or stolen prescriptions • Taking larger than prescribed doses • Frequent emergency department visits • Demanding increased doses • Using opioids or other controlled substances that are not prescribed	At the time of the visit or when the Veteran presents with the aberrant behavior; address behaviors in person	At time of visit. It is important to address aberrant behaviors in person.

continued from page 20 (Risk Mitigation Strategies for Patients on Chronic Opioids)

UDT Results—Red Flags

The following should be viewed as a **"red flag"**, requiring confirmation testing and intervention (see interpreting UDT page 29):

- Negative for opioid(s) prescribed
- Positive for prescription medications not prescribed (e.g., opioids, benzodiazepines, stimulants)
- Positive for illicit drugs (e.g., methamphetamine, cocaine or its metabolites)
- Positive for alcohol or its metabolites

If confirmatory drug test substantiates the **"red flag"** (e.g., positive for amphetamines) AND is:

- **Positive for prescribed opioids**: have a discussion with the patient, come up with a plan (consider a slow taper and consultation with/referral to an addiction treatment program).
- **Negative for prescribed opioids**: have a discussion with the patient, come up with a plan (consider consultation with/referral to an addiction treatment program; tapering of prescribed opioid not necessary if patient not taking prescribed opioid).

Urine Drug Testing Methods[5,13–15]

Type of Test	Logistics	Pearls
Initial Screening Test		
Immunoassay*	• Inexpensive • Fast • Widely available	• High sensitivity, low specificity (higher potential for false positives) • Opiate screen not sensitive for semisynthetic (e.g., oxycodone) or synthetic opioids (e.g., fentanyl)
Confirmatory Test		
Gas Chromatography-Mass Spectrometry (GCMS)**	• Expensive • Time consuming	• High sensitivity, high specificity • Detects medication even if concentration low • Allows detection of a specific drug/metabolite
Liquid Chromatography-Mass Spectrometry (LCMS)	• Less expensive than GCMS • Faster than GCMS	

*Immunoassay tests have high predictive values for tetrahydrocannabinol (THC), the testing component of marijuana, and also for cocaine, but lower predictive values for opioids and amphetamines. **GMCS is considered the criterion standard for confirmatory testing.

continued from page 22 (Urine Drug Testing Methods)

Normal Characteristics of a Urine Sample

- Temperature within 4 minutes of voiding: 90°–100°F
- pH: 4.5–8.0
- Creatinine: >20 mg/dL
- Specific gravity: >1.003
- Nitrates: <500 mcg/dL
- Volume: ≥30 mL

Urine Drug Testing Specimen Validity

- Urine samples that are adulterated, substituted, or diluted may avoid detection of drug use
- Urine collected in the early morning is most concentrated and most reliable
- Excessive water intake and diuretic use can lead to diluted urine samples (creatinine <20 mg/dL)
- THC assays are sensitive to adulterants (e.g., Visine eye drops)

Urine Drug Testing (UDT) Federal Work Place Cut Off Values*[13–20]

Substance	Initial Drug Test Level (immunoassay) (ng/mL)	Confirmatory Drug Test Level (GC–MS) (ng/mL)	Confirmatory Test Analyte	Detection Period After Last Dose**
Regular UDT				
Amphetamines	500	250 250	Amphetamine Methamphetamine	1–3 days
Cocaine Metabolites	150	100	BEG	1–3 days
Marijuana Metabolites	50	15	THCA	2–8 days single use 20–30 days chronic use***
Opioid Metabolites	2000***	2000*** 2000***	Codeine Morphine	2–3 days opiates 3–5 minutes heroin
Phencyclidine (PDP)	25	25	Phencyclidine	Detection time 2–8 days

*Updated Federal Work Place Cut Off Values to start October 2017. **Detection time for most drugs in urine is 1–3 days; ***Long-term use of lipid-soluble drugs (THC, diazepam) can be detected for a longer period of time; ****Testing levels for opiates were raised from 300 ng/mL to 2000 ng/mL to reduce detection from foods containing poppy seeds.

continued from page 24 (Urine Drug Testing (UDT) Federal Work Place Cut Off Values)

Substance	Initial Drug Test Level (immunoassay) (ng/mL)	Confirmatory Drug Test Level (GC–MS) (ng/mL)	Confirmatory Test Analyte	Detection Period After Last Dose**
Extended UDT				
Alcohol	N/A	N/A	EtG, EtS	12 hours
6-Monoacetylmorphine (6-MAM) - metabolite of heroin	10	10	6-Monoacetylmorphine (6-MAM)	12–24 hours
Barbiturates	300	200	Butalbital, phenobarbital, secobarbital, amobarbital/ pentobarbital	1 day for short-acting up to 30 days for phenobarbital
Benzodiazepines	300	200	Alprazolam, diazepam, clonazepam, lorazepam, etc.	3 days for short-acting 30 days for long-acting***

*Updated Federal Work Place Cut Off Values to start October 2017. **Detection time for most drugs in urine is 1–3 days; ***Long-term use of lipid-soluble drugs (THC, diazepam) can be detected for a longer period of time; ****Testing levels for opiates were raised from 300 ng/mL to 2000 ng/mL to reduce detection from foods containing poppy seeds.

continued from page 24 (Urine Drug Testing (UDT) Federal Work Place Cut Off Values)

Substance	Initial Drug Test Level (immunoassay) (ng/mL)	Confirmatory Drug Test Level (GC–MS) (ng/mL)	Confirmatory Test Analyte	Detection Period After Last Dose**
Hydrocodone	300	100	Hydrocodone	2–4 days
Hydromorphone		100	Hydromorphone	
Methadone	300	200	EDDP	3–6 days
Methamphetamine	500	250	Methamphetamine	3–4 days
MDMA		250	MDMA	
MDA		250	MDA	
Oxycodone	100	100	Oxycodone	2–4 days
Oxymorphone		100	Oxymorphone	

*Updated Federal Work Place Cut Off Values to start October 2017. **Detection time for most drugs in urine is 1–3 days; ***Long-term use of lipid-soluble drugs (THC, diazepam) can be detected for a longer period of time; ****Testing levels for opiates were raised from 300 ng/mL to 2000 ng/mL to reduce detection from foods containing poppy seeds.

Summary of Agents Potentially Contributing to False Positives[13–18]

Substance	Agents Potentially Causing False Positives			
Marijuana Metabolites	• dronabinol • efavirenzproton	• NSAIDs* • proton pump inhibitors	• hemp foods: tea, oil** • THC/CBD topicals	
Cocaine Metabolites	• coca leaf teas	• topical anesthetics containing cocaine		
Opioid Metabolites	• dextromethorphan • fluoroquinolones	• levofloxacin • ofloxacin	• poppy seeds • poppy oil	• rifampin • quinine
Amphetamines/ Methamphetamine (High Rate of False Positives)	• amantadine • benzphetamine • brompheniramine • bupropion • chlorpromazine • desipramine • dextroamphetamine	• doxepin • ephedrine • fluoxetine • isometheptene • isoxsuprine • labetalol • l-methamphetamine (OTC nasal inhaler)	• methylphenidate • MDMA • phentermine • phenylephrine • phenyl-propanolamine • promethazine • pseudoephedrine	• ranitidine • selegiline • thioridazine • trazodone • trimethobenzamide • trimipramine

*NSAIDs resulting in false-positive for marijuana mainly consist of ibuprofen and naproxen and modern tests do not result in false positives;
**THC concentrations in hemp products are typically low enough to prevent positive immunoassay results.

continued from page 27 (Summary of Agents Potentially Contributing to False Positives)

Substance	Agents Potentially Causing False Positives
Benzodiazepines	• oxaprozin • sertraline
Barbiturates	• ibuprofen • naproxen
Methadone	• chlorpromazine • clomipramine • diphenhydramine • doxylamine • ibuprofen • quetiapine • thioridazine • verapamil
Alcohol	• mouthwash • short-chain alcohols • OTC cough products • (isopropyl alcohol)

*NSAIDs resulting in false-positive for marijuana mainly consist of ibuprofen and naproxen and modern tests do not result in false positives;
**THC concentrations in hemp products are typically low enough to prevent positive immunoassay results.

Interpreting Urine Drug Testing[5,13–15]

Drug or Class	Expected Results	Considerations
Alcohol	Alcohol	• Testing for ETOH metabolites, ethyl glucuronide or ethyl sulfate, can identify alcohol up to 80 hours after consumption
Amphetamines	Immunoassay–amphetamines, methamphetamines or MDMA Confirmatory–amphetamines, methamphetamines or MDMA	• Immunoassay tests are highly cross-reactive; therefore confirmatory testing is required and can identify which amphetamine is present
Benzodiazepines	Immunoassay–unconjugated oxazepam or its metabolites Confirmatory–alprazolam, diazepam, clonazepam, lorazepam, etc.	• Immunoassays for benzodiazepines have a 28% overall false negative rate • Confirmatory testing is needed when use is expected or suspected (alprazolam, clonazepam and lorazepam often not detected by immunoassay)
Barbiturates	Confirmatory–butalbital, phenobarbital, secobarbital, amobarbital/pentobarbital	• Presence of a barbiturate in urine at >200 mg/mL indicates use of 1 of these drugs.

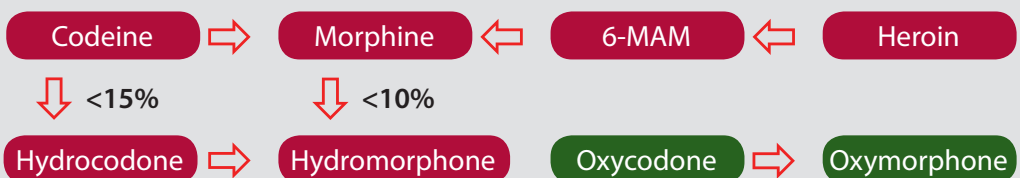
Note: Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details.

continued from page 29 (Interpreting Urine Drug Testing)

Drug or Class	Expected Results	Considerations
Cocaine Metabolites	Immunoassay–cocaine or benzoylecgonine (BEG)	• Cocaine's primary metabolite, BEG, has low cross-reactivity with other substances and is highly predictive of cocaine use • A positive result should be interpreted as recent exposure to cocaine
Opioids or "opiates"- Natural (from opium)		
Codeine	Opiates Immunoassay–positive Confirmatory–codeine, possibly morphine and hydrocodone	• Immunoassays for "opiates" are responsive to morphine and codeine but do not identify an individual substance • Codeine is metabolized to morphine and small quantities of hydrocodone

Note: Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details.

continued from page 29 (Interpreting Urine Drug Testing)

Drug or Class	Expected Results	Considerations
Opioids or "opiates"- Natural (from opium)		
Morphine	Opiates Immunoassay–positive Confirmatory–morphine, possibly hydromorphone	• Immunoassays for "opiates" are responsive to morphine and codeine but do not identify an individual substance • Morphine (<10%) may be metabolized to hydromorphone
Heroin	Opiates Immunoassay–positive Confirmatory–heroin (6–MAM), morphine, possibly codeine	• 6-MAM is pathognomonic for heroin use, detection 12–24 hrs • Heroin is metabolized to morphine
Opioid Metabolic Pathways:		

Note: Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details.

continued from page 29 (Interpreting Urine Drug Testing)

Drug or Class	Expected Results	Considerations
Opioids-Semisynthetic (derived from opium)		
Hydrocodone	Opiates Immunoassay–positive Confirmatory–hydrocodone, possibly hydromorphone	• "Opiates" immunoassay may detect semisynthetic opioids - hydrocodone > hydromorphone > oxycodone • Negative result does not exclude use and confirmatory testing (GCMS or LCMS) is required • Hydrocodone is metabolized in small amounts to hydromorphone, both may be found in urine • Oxycodone is metabolized to oxymorphone, both may be found in urine • Hydromorphone and oxymorphone use does not result in positive screens for hydrocodone and oxycodone, respectively
Hydromorphone	Opiates Immunoassay–may be positive Confirmatory–hydromorphone	
Oxycodone	Opiates Immunoassay–may be positive Oxycodone Immunoassay–positive Confirmatory–oxycodone possibly oxymorphone	
Oxymorphone	Oxycodone Immunoassay–positive Confirmatory–oxymorphone	
Buprenorphine	Opiates immunoassay–typically negative Confirmatory–buprenorphine, norbuprenorphine	

Note: Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details.

continued from page 29 (Interpreting Urine Drug Testing)

Drug or Class	Expected Results	Considerations
Opioids-Synthetic (man-made)		
Fentanyl	Opiates immunoassay–negative Fentanyl immunoassay–positive Confirmatory–Fentanyl and norfentanyl	• Current "opiates" immunoassays do not detect synthetic opioids • Confirmatory testing (GCMS or LCMS) is needed
Meperidine	Opiates immunoassay–negative Confirmatory–normeperidine, possibly meteridine	
Methadone	Opiates immunoassay–negative Methadone Immunoassay–positive Confirmatory–methadone, EDDP	

Note: Each facility may have its own order sets and lab policies and procedures. Contact your lab for additional details.

Common Adverse Effects for Opioid Analgesics and Suggested Management[1]

Adverse Effect	Suggested Management
Pruritus	• Rule out allergic reaction • Consider treatment with antihistamine • Itching may resolve spontaneously despite continuation of therapy
Sedation	• Rule out other causes • Reduce or temporarily hold dose with or without addition of coanalgesic to prevent respiratory depression • Add or increase non–sedating adjuvant for additional pain relief
Constipation	• Assess for constipation at every visit • Initiate bowel stimulant and a stool softner and increase liquids, dietary fiber (bulk forming laxatives NOT recommended), and exercise • If initial regimen is inadequate, mild hyperosmotics, saline and emollient laxatives may be added • If possible, reduce or discontinue other drugs that may cause or contribute to constipation

Less Common Adverse Effects[1]

Adverse Effect	Signs and Symptoms	Protocol for Management
Respiratory Depression	Drowsiness; slow shallow, breathing; difficulty staying awake; difficulty awakening; loud or unusual snoring	• Hold opioid completely • Avoid other CNS depressants (esp. benzodiazepines) • Alert family members/care takers of the signs and symptoms
Opioid-induced Endocrinopathy	Loss of libido; impotence; fatigue; mood alterations; loss of muscle mass; abnormal menses; infertility	• Ask patients about symptoms at each visit • Determine cause of symptoms (consult endocrinologist)
Hallucinations/ Dysphoria	Confusion; bad dreams; hallucinations; restlessness; agitation	• Evaluate for underlying cause • Eliminate non-essential CNS acting medications (e.g., corticosteroids, anticholinergics) • If symptoms persist consider consultation with mental health professional or switch medications

continued from page 35 (Less Common Adverse Effects)

Adverse Effect	Signs and Symptoms	Protocol for Management
Sleep, Disordered Breathing	Loud snoring; irregular pauses in breathing; excessive daytime sleepiness; morning headaches; depression; impaired concentration	• Strongly consider stopping opioid and obtain sleep study • Instruct patient to avoid alcohol and medications that cause drowsiness • Obstructive sleep apnea: instruct to sleep on side; see dentist about mouthpiece to assist breathing
Osteoporosis	Bone fracture	• Monitor bone density in patients at risk
Immune Dysfunction	Severe fatigue; muscle and joint pain that worsens following exertion; decreased immunoglobulins	• Obtains labs and consult with immunologist

Example of Opioid Tapers[21–26]

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.	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.

Tips on Tapers

1. In most patients, use the slower taper of 5–20% reduction every 4 weeks.
2. If Veteran is having withdrawal symptoms using a slower taper, then reduce the speed and follow the slowest taper of 2–10% reduction every 4 to 8 weeks.
3. Faster tapers may be necessary in situations where risk of overdose and harm are present.
4. Consider hospital admission when rapid tapers are used due to significant withdrawal and risk of patient seeking opioids from alternative sources.
5. Communicate the plan clearly to the Veteran, preferably in person, and provide written instructions. Do not mail instructions about tapering without first communicating directly with the patient.

Follow Up with the Veteran During the Taper[26]

Follow Up	Slowest Taper over years	Slower Taper over months or years	Faster Taper over weeks	Rapid Taper over days
When	1 to 4 weeks after starting taper then monthly before each reduction.	1 to 4 weeks after starting taper then monthly before each reduction.	Weekly before each dose reduction.	Daily before each dose reduction or if available offer inpatient admission.
Who	PACT Team*			
How	Clinic and/or telephone**	Clinic and/or telephone**	Clinic and/or telephone**	Hospital, clinic or telephone**
What	Patient function,*** pain intensity, sleep, physical activity, personal goals, and stress level.			

*Follow up for tapering is recommended to be a team function with various team members taking on roles in which they have demonstrated specific competencies. Mental health practitioners may need to be included in the follow up plan. **Providers will need to determine whether a telephone or in-clinic appointment is appropriate based on the risk category of the Veteran. A Veteran with high risk due to a medical condition may have decompensation during the taper and may require a clinic visit. If there are issues with the Veteran obtaining outside prescriptions or they are displaying other aberrant behaviors during the taper, providing follow up in a clinic visit may be more optimal than a telephone visit. ***Quality of Life Scale for patients with pain: **https://www.theacpa.org/uploads/documents/Quality_of_Life_Scale.pdf**.

Benzodiazepine Dosage Equivalents and Taper Schedules[27]

Benzodiazepine	Approx. Dosage Equivalents	Elimination Half-life (hours)	Example Taper: Lorazepam 4 mg bid (Convert to 40 mg diazepam daily)	
Chlordiazepoxide	25 mg	>100 hr	Milestones: Week 2: ↓ dose by 25% Week 4: ↓ dose by 25% Weeks 5–8: Hold dose 1 month Weeks 9–15: ↓ dose by 25% every two weeks	Week 1: 35 mg/day Week 2: 30 mg/day (25% of initial dose) Week 3: 25 mg/day Week 4: 20 mg/day (50% of initial dose) Weeks 5–8: Continue at 20 mg/day for 1 month Weeks 9–10: 15 mg/day Weeks 11–12: 10 mg/day Weeks 13–14: 5 mg/day Week 15: Discontinue
Diazepam	10 mg	>100 hr		
Clonazepam	1 mg	20–50 hr		
Lorazepam	2 mg	10–20 hr		
Alprazolam	1 mg	12–15 hr		
Temazepam	15 mg	10–20 hr		

Shorter taper (e.g., 3 months): Reduce dose by 50% the first 4 weeks then maintain on that dose for 1–2 months then reduce dose by 5% every 2 weeks.
Longer taper (e.g., 6 months): 10–25% every 4 weeks.

Switching to a longer acting benzodiazepine may be considered if clinically appropriate; in geriatric patients consider tapering the short acting agent until withdrawal symptoms are seen then switch to a longer acting agent; high dose alprazolam may not have complete cross tolerance, and a gradual switch to diazepam or clonazepam before taper may be appropriate; other treatment modalities should be considered (e.g., antidepressants for anxiety) if clinically appropriate.

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Notes

U.S. Department of Veterans Affairs

This reference guide was created to be used as a tool for VA providers and is available to use from the Academic Detailing SharePoint. These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

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