

VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy (OT) for Chronic Pain

KEY ELEMENTS OF THE OT GUIDELINE

ASSESS

- » Comprehensive assessment of patient history
- » Complete assessment of pain and previous pain treatments

DETERMINE THE APPROPRIATENESS OF OT

- » Inadequate response to nondrug and nonopioid therapies
- » Identify contraindication that can not be resolved
- » Determine risk for misuse of OT
- » Determine appropriate treatment setting
- » Educate patients and family
- » Discuss written OT agreement

START AN OT TRIAL

- » Obtain patient consent
- » Initiation
- » Titration
- » Maintenance
- » Supplemental therapy

REASSESS RESPONSE TO THERAPY

- » Indication for consultation/referral
 - Adverse effects
 - Aberrant behaviors
 - Analgesia
 - Adherence
 - Activity
 - Affect

DISCONTINUE OT

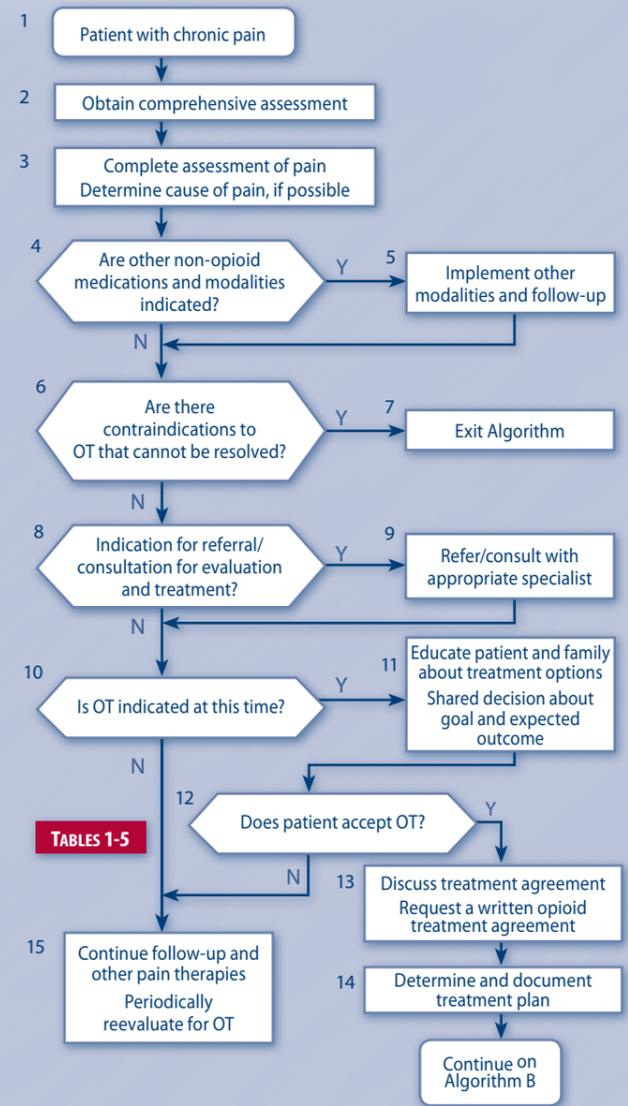
- » Maintain patient safety and comfort during the initial phase of opioid abstinence
- » Educate patient on withdrawal symptoms

Access to full guideline: <http://www.healthquality.va.gov> or <https://www.qmo.amedd.army.mil>

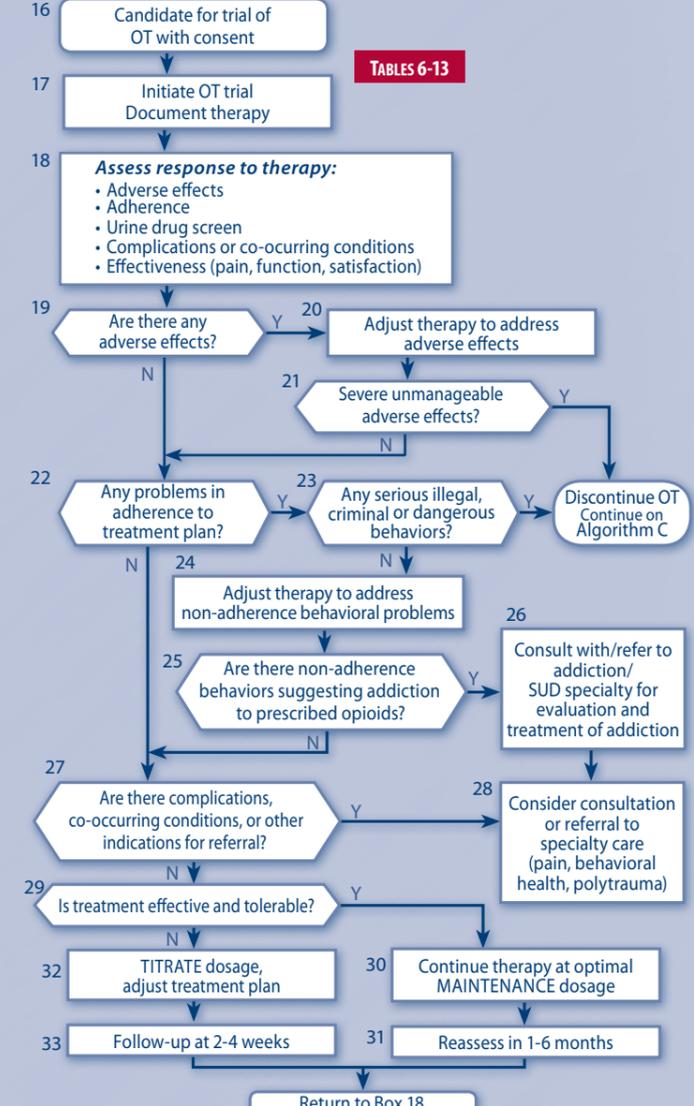
February 2009

VA/DoD Evidence-Based Practice

ALGORITHM A: Assessment



ALGORITHM B: Start OT Trial



ALGORITHM C: Discontinue OT

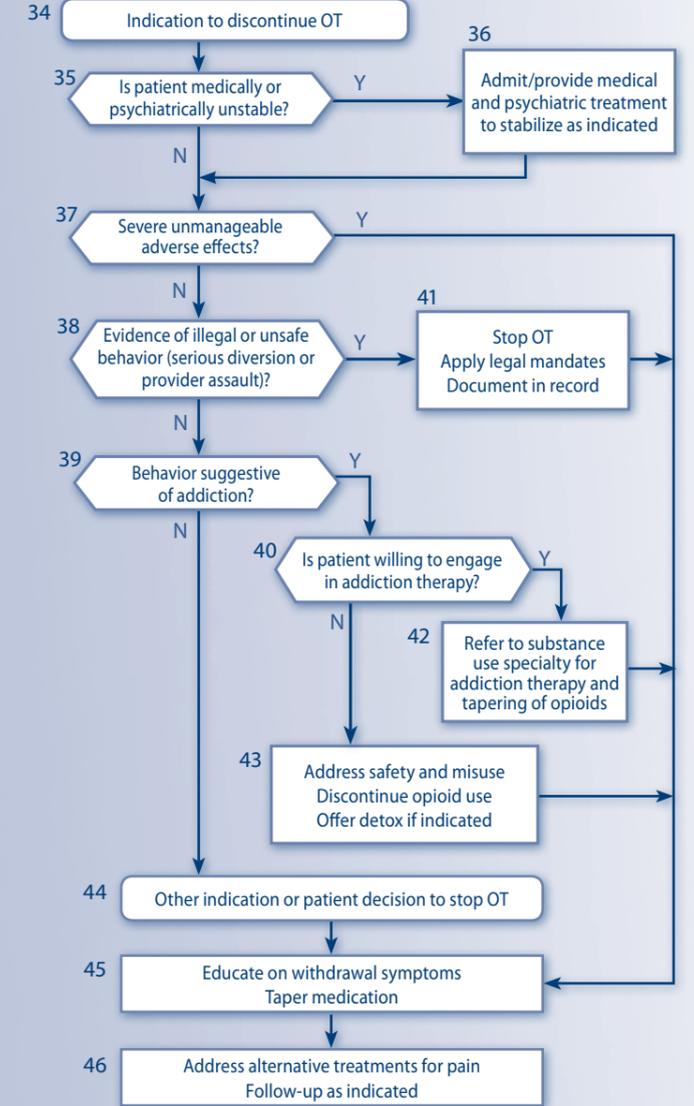


TABLE 1 Predictors of Opioid Misuse

STRONG PREDICTORS	MODERATE PREDICTORS	WEAK PREDICTORS	INCONSISTENT PREDICTORS
<ul style="list-style-type: none"> • History of alcohol and illicit substance abuse 	<ul style="list-style-type: none"> • Younger age • History of legal problems • Positive UDT 	<ul style="list-style-type: none"> • Family history of drug abuse • History of childhood sexual abuse • History of DUIs or drug convictions • Lost or stolen prescriptions • Obtaining opioids from alternate sources • High SOAPP or SOAPP-R scores 	<ul style="list-style-type: none"> • Male sex • History of an anxiety disorder • History of prescribed drug misuse • Race (nonwhite) • Education • History of MVAs • History of schizophrenia

UDT = Urine Drug Test; MVAs = Motor Vehicles Accidents; SOAPP-R = Screener and Opioid Assessment for Patients with Pain (Revised)

TABLE 2 Risks for Misuse of OT & Preferred Treatment

RISK FOR OPIOID MISUSE	CONDITION OR SITUATION	TREATMENT SETTING FOR OT
Low	<ul style="list-style-type: none"> • No history of SUD • No psychiatric comorbidity • Prior good adherence to treatments with the primary care provider • Existence of social support system 	<ul style="list-style-type: none"> • Provide OT in primary care setting
Moderate	<ul style="list-style-type: none"> • History of substance use • History or cooccurring psychiatric disorder • History of suicide attempt • Any positive UDT • Any history of legal problems • Young age (less than 25) 	<ul style="list-style-type: none"> • Primary care with escalated monitoring and caution • Consider consultation with SUD or Behavioral health specialty
High	<ul style="list-style-type: none"> • Unstable or untreated substance use or mental health disorder • Persistent or repeated troublesome aberrant behavior or history of ADRB 	<ul style="list-style-type: none"> • Advanced structured pain clinic/ program • Co-managed with Substance Use Disorder or Mental Health Specialty

TABLE 3 Absolute Contraindications to OT

OT TRIAL SHOULD NOT BE INITIATED IN THE FOLLOWING SITUATIONS

- Severe respiratory instability
- Acute psychiatric instability or uncontrolled suicide risk
- Diagnosed non-nicotinic Substance Use Disorder (DSM-IV criteria) not in remission and not in treatment
- True allergy to opioid agents (cannot be resolved by switching agents)
- Co-administration of drug capable of inducing life-limiting drug-drug interaction
- QTc interval > 500 millisecond for using methadone
- Active diversion of controlled substances (providing the medication to someone for whom it was not intended)
- Prior adequate trials of specific opioids that were discontinued due to intolerance, serious adverse effects that cannot be treated, or lack of efficacy

TABLE 4 Indications for Referral to Specialty

Consider consultation or referral to addiction specialty for evaluation and treatment in the following conditions:

- Demonstration of behaviors suggesting addiction to prescribed opioids or substance use disorders
- Patients with a significant chronic or substantiated pain who develop addiction behaviors in the context of chronic OT
- Uncontrolled substance use disorder (excluding nicotine)
- Behaviors characteristic of compulsive drug use (addiction) to either opioids or other drugs or alcohol should be referred to an addiction specialty
- Complex conditions who manifest behaviors characteristic of addiction with multiple co-occurring psychiatric disorders
- Need for tapering of opioids or unable to tolerate tapering after discontinuation of OT.
- Consider consultation with a SUD specialist to evaluate the risk of recurrent substance abuse or to assist with ongoing management.
- Refer patient for psychosocial treatments specific to prescription medication addiction/abuse. These can include addiction counselors comfortable with such topics, and self-help organizations (Pills Anonymous/ PA, the National Chronic Pain Outreach association, and other similar organizations).

TABLE 5 Types of Serious and Dangerous Behaviors

ILLEGAL OR CRIMINAL BEHAVIOR

- Active diversion (selling or provision of drugs to others)
- Prescription forgery
- Stealing, "borrowing", or buying drugs from others

DANGEROUS BEHAVIOR

- Motor vehicle crash /arrest related to opioid or illicit drug or alcohol intoxication or effects
- Intentional or unintentional overdose or suicide attempt
- Assaultive behaviors
- Aggressive/threatening/belligerent behavior in the clinic

TABLE 6 Short-Acting, Orally Administered Opioids

SHORT-ACTING OPIOID †	INITIAL DOSAGE	DOSAGE TITRATION	ANALGESIC: ONSET (MIN) PEAK (MIN) DURATION (H)
Codeine (alone or in combination with APAP or ASA)	30 mg every 4 to 6 h	<ul style="list-style-type: none"> Increase dose as needed and tolerated to a maximum of 360 mg/day (4000 mg/day APAP; 2000 mg/day APAP in chronic alcoholics) Ceiling effect occurs at doses >60 mg/dose 	15 to 30 30 to 60 4 to 6
Hydrocodone (in combination with APAP, ASA, or IBU)	5 to 10 mg every 4 to 6 h	<ul style="list-style-type: none"> Increase dose as needed and tolerated Maximum dose: 60 mg/day (4000 mg/day APAP; 2000 mg/day APAP in chronic alcoholics) for hydrocodone + APAP combination, or 37.5 mg/day (1000 mg/day IBU) for hydrocodone + IBU combination 	15 to 30 30 to 60 4 to 8
Hydromorphone	2 mg every 4 to 6 h	<ul style="list-style-type: none"> Individually titrate as needed and tolerated; doses ≥ 4 mg every 4 to 6 h may be necessary 	15 to 30 30 to 60 4 to 6
Morphine	10 to 30 mg every 4 h	<ul style="list-style-type: none"> Individually titrate as needed and tolerated 	15 to 60 60 to 90 2 to 6
Oxycodone (alone or in combination with APAP or ASA)	5 mg every 6 h	<ul style="list-style-type: none"> Increase dose as needed and tolerated For combination products, maximum dose is limited by APAP or ASA content (4000 mg/day for both; 2000 mg/day APAP in chronic alcoholics) 	10 to 15 30 to 60 3 to 6
Oxymorphone	10 to 20 mg every 4 to 6 h (may start at 5 mg to improve tolerability)	<ul style="list-style-type: none"> Individually titrate as needed and tolerated 	34 to 45 — 4

TABLE 6 Short-Acting, Orally Administered Opioids (Continued)

SHORT-ACTING OPIOID †	INITIAL DOSAGE	DOSAGE TITRATION	ANALGESIC: ONSET (MIN) PEAK (MIN) DURATION (H)
Tapentadol	50 mg every 4 to 6 h	<ul style="list-style-type: none"> Subsequent dose is 50, 75, or 100 mg every 4 to 6 h, adjusted to analgesia and tolerability Second dose may be given 1 h after the first dose if necessary Max recommended dose: 700 mg on first day, 600 mg on subsequent days. 	— 60 4 to 6
Tramadol ^{STOP} (alone or in combination with APAP)	25 mg every morning	<ul style="list-style-type: none"> Increase by 25 mg as separate doses every 3 day to 100 mg/day (25 mg every 6 h) Subsequent increments of 50 mg/day may be made every 3 day to 200 mg/day (50 mg every 6 h) After titration, may give 50 to 100 mg every 4 to 6 h Maximum daily dose: 400 mg/day (Maximum 4000 mg/day APAP; 2000 mg/day APAP in chronic alcoholics) 	< 60 ~120 to 240 3 to 6

THIS GUIDELINE DOES NOT RECOMMEND THE USE OF LONG-ACTING OPIOID AGONISTS FOR AS-NEEDED (P.R.N.) ADMINISTRATION

TABLE 7 Use of Long-Acting Opioids

LONG-ACTING OPIOID †	INITIAL ORAL DOSAGE	DOSAGE TITRATION	ANALGESIC: ONSET (MIN) PEAK (MIN) DURATION (H)
Fentanyl Transdermal System	25 mcg/h transdermally every 72 h	<ul style="list-style-type: none"> Increments should be based on supplemental opioid doses, using a ratio of 12 mcg/h transdermal fentanyl for every 45 mg/24 h of supplemental oral morphine equivalent Make increments at least 3 day after initial dose then not more often than every 6 day thereafter as necessary 	12 to 18 (h) 24 to 72 (h) 48 to 72
	CONTRAINDICATED in non-opioid tolerant patients		
	12 mcg/h dose has not been evaluated as an initial dose		

TABLE 7 Use of Long-Acting Opioids (Continued)

LONG-ACTING OPIOID †	INITIAL ORAL DOSAGE	DOSAGE TITRATION	ANALGESIC: ONSET (MIN) PEAK (MIN) DURATION (H)
Methadone	2.5 to 10 mg orally every 8 to 12 h	<ul style="list-style-type: none"> Increments of 2.5 mg every 8 h may be made every 5 to 7 days Start low and go slow 	30 to 60 — 4 to 12
	More frequent administration (every 6 h) may be necessary during initiation to maintain analgesia	<p>NOTE: USE EXTREME CAUTION TO AVOID OVERDOSAGE DUE TO LONG PLASMA HALF-LIFE. ANALGESIC DURATION INCREASES WITH CONTINUED USE AND CUMULATIVE EFFECTS</p>	
Morphine CR/ SR ER	15 mg every 8 to 12 h (CR/SR) to 30 mg every 24 h (ER)	<ul style="list-style-type: none"> Total daily increments of < 30 to 40 mg/day may be made every 2 days 	30 to 60 30 to 60 8 to 24
Oxycodone CR	10 mg orally every 12 h	<ul style="list-style-type: none"> May increase to 20 mg every 12 h after 1 or 2 days Thereafter, the total daily dose may be increased by 25% to 50% of the current dose every 1 or 2 days 	30 to 60 90 to 180 8 to 12
Oxymorphone ER	5 mg orally every 12 h	<ul style="list-style-type: none"> May increase by 5 to 10 mg every 12 h, every 3 to 7 days 	— 1 (fasted state) —
Tramadol ER ^{STOP}	100 mg once daily	<ul style="list-style-type: none"> Increase by 100 mg every 5 days based on analgesia and tolerability. Max dose: 300 mg/day 	— 12 h 24 h
<i>Controlled Release (CR) / Sustained Release (SR) / Extended Release (ER)</i>			
<i>P.O. = Per Os (orally); t.d. = Transdermally</i>			
<i>† Check local formulary for available formulations</i>			

TABLE 7A Opioid Recommendations for Special Populations

FOR USE IN PATIENT WITH SWALLOWING DIFFICULTY:

- Fentanyl Transdermal
- Hydromorphone (Oral solution, Rectal suppository)
- Methadone (Oral solution)
- Morphine (Oral solution, Rectal suppository)
- Oxycodone (Oral solution)

FOR USE IN PATIENT WITH GI MALABSORPTION:

- Fentanyl Transdermal
- Hydromorphone (Rectal suppository)
- Morphine (Rectal suppository)

TABLE 8 OT Titrate to Effect

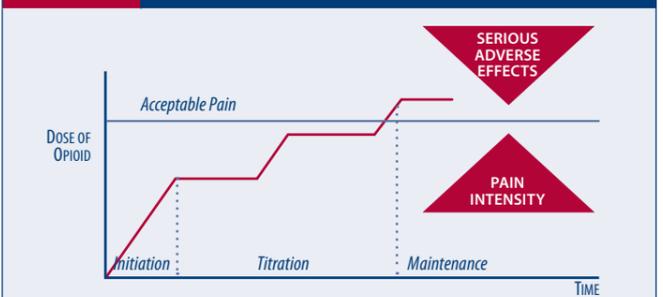


TABLE 9 Time Drugs of Abuse Can be Detected in Urine

Opioid	Time
Codeine	48 hours
Heroin (morphine)	48 hours
Hydromorphone	2-4 days
Methadone	3 days
Morphine	48-72 hours
Oxycodone	2-4 days

TABLE 10 Supplemental Therapy

TYPE OF THERAPY	DESCRIPTION OF PAIN EPISODE
Rescue	Insufficient analgesia during dosage titration
Breakthrough Pain	Unpredictable exacerbation of chronic pain otherwise controlled on stable maintenance doses of opioid
Incident Pain	Predictable, activity-related exacerbation of chronic pain otherwise controlled on stable maintenance doses of opioid

TABLE 11 Opioids for Chronic Pain in Special Populations

MEDICATION	HEPATIC DYSFUNCTION	RENAL DYSFUNCTION	RENAL DIALYSIS	ELDERLY OR DEBILITATED	PATIENTS WITH SEIZURES	PREGNANCY RISK CATEGORY (a)	LACTATION (b)
Codeine (b)	X	▲ & ↓	X	▲ & ↓		C*†	▲
Fentanyl Transdermal	▲ & ↓	▲ & ↓	▲	▲ & ↓		C†	UC (c)
Hydrocodone		▲ & ↓	▲	▲ & ↓		C†	PC
Hydromorphone	▲ & ↓	▲ & ↓	RBD	▲ & ↓		B†	PC
Methadone (d)	▲ & ↓	▲ & ↓	▲	▲ & ↓		B†	PC
Morphine		↓ OR X	▲ OR X RBD	▲ & ↓		C†	PC
Oxycodone		▲ & ↓	X ND	▲ & ↓		B†	PC
Oxymorphone	X	▲ & ↓	▲ RBD	▲ & ↓		B†	PC
Tapentadol	▲	↓ OR X	X (e) ND	▲ & ↓	▲	C†	X (f)
Tramadol ^{STOP}	▲ & ↓	▲ & ↓	X RBD	▲ & ↓	X	C†	PC

X = Not Recommended ▲ = Use Caution ↓ = Reduce Dose RBD = Removed by Dialysis ND = No Data

Pregnancy Lactation Risk: B = No evidence of risk in humans; C = Risk cannot be ruled out, but potential benefits may justify potential risk; UC = Usually compatible; either not excreted into human breast milk in clinically significant amounts or not expected to cause toxicity in infant; PC = Probably compatible; no or limited human data; * human data suggest risk; † human data suggest risk in 3rd trimester; ‡ Risk category D if prolonged periods or high doses at term

(a) Estimates of risk of OT in pregnancy and while breastfeeding may be based on expectations of intermittent or short-term use; use of chronic OT during pregnancy or while breastfeeding should be approached with caution.

(b) Codeine is metabolized to morphine by CYP 2D6; both pass into breast milk in small amounts usually considered insignificant; however, caution in known or suspected ultra rapid metabolizers of CYP 2D6; 2006 case report of death in a nursing infant of CYP 2D6 ultra rapid metabolizer mother associated with high morphine levels in breast milk (Koren et al, 2006)

(c) Manufacturer does not recommend use while breast feeding; classified as compatible by the American Academy of Pediatrics

(d) Caution: For use in patients with prolonged QTc: Methadone is the only long-acting opioid available as an oral solution. See full guideline for Dosing Recommendations.

(e) Less effective with decrease CYP 2D6 activity.

(f) Per product information.

TABLE 12 Equianalgesic and Conversion Doses for Patients Previously Receiving Other Opioids

OPIOID AGENT	EST. ORAL EQUIANALGESIC DOSE (MG)	INITIAL CONVERSION DOSE (NOT EQUIANALGESIC)
Codeine	180 to 200 ‡	30 mg every 4 to 6 h
Fentanyl	— transdermal	For converting ONLY to fentanyl from another opioid, use about 12 mcg/h fentanyl transdermally for every 45 mg of oral morphine or equivalent (see Table 7, Initial Fentanyl Transdermal Dosage)
Hydrocodone	30	50% to 67% of estimated oral equianalgesic dose
Hydromorphone	7.5	50% to 67% of estimated oral equianalgesic dose
Methadone	20 acute 2 to 4 chronic	Methadone-to-morphine dosage proportion (%) is dependent on morphine-equivalent dose of previous opioid
Morphine	30	50% to 67% of estimated oral equianalgesic dose
Oxycodone	15 to 20 ‡	50% to 67% of estimated oral equianalgesic dose
Oxymorphone	10	50% to 67% of estimated oral equianalgesic dose
Tapentadol	ND(50 to 100)†	50 to 100 mg every 4 to 6 h
Tramadol ^{STOP}	ND(50 to 100)†	25 mg every morning

ND = No Data

Many other equianalgesic dosing tables are available that may provide equivalent doses different from those shown here.

† The initial dose of the new drug applies to patients who are not tolerant to the new opioid and should be given at 50% to 67% of the calculated dose for all potent opioids except fentanyl and methadone to allow for incomplete cross-tolerance (the new drug may have more relative analgesic efficacy and more adverse effects). For methadone, use dosage proportions (%) based on the morphine equivalent dose of previous opioid (also see Methadone Dosing Recommendations for Treatment of Chronic Pain). Initial doses should be individualized. The patient's medical condition, the potency, dose, and type of previous opioid, the patient's degree of opioid exposure and tolerance, the patient's past analgesic response and adverse experiences, and the accuracy and reliability of opioid conversion factors may all influence the choice of starting dose. For fentanyl, see Table 8.

‡ When converting from weak opioid analgesics to stronger opioids, use the recommended initial doses of the new opioid for opioid-naïve patients. Doses of tapentadol and tramadol should NOT be considered equianalgesic to the doses of pure agonists. Equianalgesic doses have not been established for conversions between either tapentadol or tramadol and pure opioid agonists.

TABLE 13 Opioid Conversion Instructions

- Determine the total 24-hour dose of the current opioid.
 - Using the estimated equianalgesic dose, calculate the equivalent dose of new analgesic for the desired route of administration.
 - When converting to a different opioid, for most agents, the starting conversion dose of the new opioid should be 50% to 67% of the equianalgesic dose because of incomplete cross-tolerance. (For fentanyl, see conversion doses in Table E5).
 - Take the 24-hour starting dose of the new opioid and divide by the frequency of administration to give the new dose for the new route.
- Consider rescue opioid therapy during the conversion process.**

IMPORTANT NOTE: For active duty DoD personnel cared for at VA facilities (e.g. convalescent leave or Poly Trauma center care) or transitioning to permanent VA care, it is imperative VA provide and continue their DoD prescribed medications, regardless of formulary status until return of care to DoD or evaluated by their permanent VA provider. Ref VA Pharmacy Benefits

^{STOP} See FDA Warning: Tramadol has warning regarding suicide and overdose risks. † Check local formulary for available formulations.