

**MEDICAL TREATMENT UTILIZATION SCHEDULE (MTUS)
OPIOIDS TREATMENT GUIDELINES**

**Part 1:
Executive Summary, Introduction, and
Recommendations**

July 2015

DRAFT

Table of Contents

A1. Executive Summary 1

A2. Abbreviated Treatment Protocols..... 5

A3. Background..... 10

1. Opioids for Acute Pain (up to four weeks after injury or pain onset)..... 19

 1.1 Mild Acute Injuries (e.g., musculoskeletal strains and sprains, muscle pain, tendonitis) 19

 1.2 Moderate to Severe Acute Soft-Tissue Injuries (e.g., severely strained ligaments, severe sprains, moderate trauma, moderate to severe low back pain, moderate to severe radiculopathy) 20

 1.3 Severe Acute Injuries (e.g., fractures, crush injuries, major trauma, large burns, other injuries with significant tissue damage)..... 23

 1.4 Opioids for Post-operative Pain..... 27

2. Opioids for Subacute Pain (1–3 months)..... 29

3. Opioids for Chronic Pain and Chronic Opioid Treatment 32

 Overview of Recommendations regarding Chronic Opioid Treatment 32

 3.1. Comprehensive Evaluation and Assessment of Patient..... 34

 3.2. Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment..... 35

 3.3. Initiating and Monitoring Chronic Opioid Treatment 36

 3.3.1. Screening for Risk of Addiction or Adverse Events, Prior to Chronic Opioid Treatment 36

 3.3.2. Patient Treatment Agreement and Informed Consent 38

 3.3.3. Initiation of Chronic Opioid Treatment 39

 3.3.4. Use of CURES to Ensure Safe and Effective Opioid Use..... 39

3.3.5. Use of Tools to Monitor Patients on Chronic Opioid Treatment.....	40
3.3.6. Use of Urine Drug Testing (UDT)	41
3.3.7. Monitoring Effectiveness of Chronic Opioid Treatment.....	46
3.3.8. Opioid Titration and Dosing Threshold	49
3.3.9. Maintenance of Chronic Opioid Treatment	51
3.3.10. Treating Breakthrough Pain (BTP)	53
4. Tapering Opioids.....	53
4.1. Indications for Tapering Opioids.....	53
4.2. Methods for Tapering Opioids.....	55
5. Documentation of Morphine Equivalents	56
6. Consultation with Specialists	56
7. Concurrent Use of Benzodiazepines and Other Sedative Hypnotics.....	57
8. Methadone.....	58
9. Managing Peri-operative Pain in Workers on Chronic Opioid Treatment Undergoing Elective Surgery	59
10. Opioid Use in Catastrophic Injuries	61
11. Responsible Storage and Disposal of Opioid Medications	62
Appendices	63
Appendix A. Brief, Validated Tools.....	64
Appendix B. Written Opioid Treatment Agreement (Sample).....	80
Appendix C. Guidance on Conducting and Interpreting Urine Drug Testing (UDT)	86
Appendix D. Select Black Box Warnings: Important Safety Information on Long-Acting Opioids.....	94
Appendix E. Opioid Dose and Risk of Morbidity and Mortality	105
Appendix F. Opioid Dose Calculations.....	106
Appendix G. Summary of Screening and Monitoring Recommendations	111

Definition of Key Terms 112

Acronyms 115

References 117

DRAFT

A1. EXECUTIVE SUMMARY

Opioid misuse remains a national concern due to adverse health impacts and other unintended consequences. Yet opioids may be useful as an adjunct in the treatment of pain. The Medical Treatment Utilization Guidelines (MTUS) Opioids Treatment Guidelines provide a balance between appropriate treatment of pain among injured workers and safety in the use of opioids for that purpose.

A key difference between occupational and non-occupational guidelines is that a main goal of the former is the restoration of function to ensure early return to work. This Guideline is based on the best available medical evidence and has three main goals: (1) to provide a set of best practices and universal precautions for safe and effective prescribing of opioids for acute (lasting up to four weeks), subacute (lasting four to 12 weeks), and chronic (lasting three or more months) pain due to a work-related injury; (2) to prevent and reduce opioid-related long-term disability, morbidity, mortality, and substance misuse and abuse; and (3) to recommend opioid prescribing practices that promote functional restoration. The intended audience is primary care and specialty clinicians, providers of utilization review and independent medical review, and insurers.

The Opioids Treatment Guidelines do not address pediatric pain, labor pain, pain immediately following catastrophic injuries, or cancer/end-of-life pain. For additional information on the appropriate use of opioids for the treatment of noncancer pain that is not related to work can be found in the [Medical Board of California Guidelines for Prescribing Controlled Substances for Pain](#).

The Opioids Treatment Guidelines are divided into two parts: Part 1 contains the executive summary, abbreviated treatment protocols, background information, complete recommendations, and appendices with useful tools for clinicians. [Part 2](#) contains supplemental information consisting of a discussion of the medical evidence supporting the recommendations and a summary of recommendations from other guidelines that were reviewed.

The following are key recommended practices:

- Opioid medications are not the first line of treatment for pain and should not in general be used for mild injuries. Other therapies, such as non-opioid medication, appropriate physical activity, and complementary/alternative modalities such as yoga and acupuncture should be used first.
- Opioid medications should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or other therapies will not provide adequate pain relief or are contraindicated for medical reasons. They should only be prescribed at the lowest dose that provides pain relief, for a limited time, and with no refill, prior to re-assessment.

- Opioids for acute pain treatment should be tapered to zero within two weeks whenever possible.
 - Injured workers with severe acute pain seen in the emergency room for whom opioid therapy is warranted should receive only a short course (less than one-week supply) non-refillable prescription of opioid medication.
- If opioids are prescribed, the Controlled Substance Utilization Review and Evaluation System ([CURES](#)), California's Prescription Drug Monitoring Program should be accessed. If CURES indicates the simultaneous use of other narcotic medication, opioid use may be contraindicated.
 - Central nervous system depressants, including anti-histamines, benzodiazepines, and alcohol, should not be used simultaneously with opioids and should be discontinued before prescribing opioid medication.
 - Patients should be cautioned about the potential adverse effects of opioids, including impacts on alertness. Driving and operation of heavy equipment should be discouraged while on these medications.
 - At the time of initial prescription, and at every visit, patients should be advised regarding responsible storage and disposal of opioid medications.
 - Before prescribing opioids beyond the acute phase, providers should evaluate patients for potentially contraindicating comorbidities, continue non-opioid treatments, perform urine drug testing and evaluate the results, and carefully monitor patients for improvement in pain and function.
 - Although all doses of opioids carry risks, providers should be increasingly vigilant for doses above 80 mg/day morphine equivalent dose (MED), as the known risk of adverse events rises while the evidence for increased benefit remains weak.
 - Opioid-naïve patients (those who have not previously been treated with opioids) with acute pain treatment receiving medically necessary treatment with opioid medication should not receive doses above 80 mg/day morphine equivalent dose (MED).
 - Short-acting opioids may be indicated for a limited duration to manage moderate to severe post-operative pain and to obtain sleep, especially in the immediate post-operative period. The Opioids Treatment Guidelines also provide recommendations for patients undergoing surgery who are opioid-tolerant (already being treated with opioid medications).
 - Patients with chronic pain may be candidates for treatment with opioids if pain management and functional improvement have not been achieved with other treatment methods, including complementary modalities, and the following conditions are met:

- A comprehensive evaluation is performed.
- Screening identifies patients with high risk of addiction or serious adverse events, substance misuse, and psychosocial factors that may contribute to misuse. Such patients are not good candidates for chronic opioid treatment.
- Patients are informed about risks, benefits, and alternatives for opioids and a treatment agreement/informed consent is reviewed and signed.
- Patients undergo urine drug testing prior to initiating an opioid trial.
- A trial is conducted prior to committing to chronic opioid treatment.
- CURES is queried and the results documented; aberrant results are a contraindication to chronic opioid treatment.
- Patients on chronic opioid treatment should be carefully managed, after the following have been documented:
 - Results of questionnaire tools assessing for aberrant behavior, which may indicate the need to discontinue opioids.
 - Results of periodic urine drug testing (at point of care initially and verified by a federally certified laboratory) performed on a random basis two to four times a year during chronic treatment, and if the provider is concerned about misuse, abuse, or diversion.
 - Clinically meaningful reduction in pain and functional improvement.
- When titrating the dose of opioids used for treatment of chronic pain to achieve maximal improvement in pain and function, decisions to increase opioids should be made jointly by both the provider and the patient. It is the responsibility of the provider to inform the patient that current evidence shows a dose-related increase in adverse events.
- Clinicians should conduct semiannual attempts to wean patients whose dose has been 80 mg/day MED or higher for at least six months to lower than 80 mg/day MED.
- Clinicians may consult with or refer to a pain specialist based on clinical need:
 - To assess the risk-benefit ratio of using opioids to treat pain in complex patients or those at high risk of adverse effects.
 - At the time of a trial of chronic opioid treatment.
 - To assist with management of a patient with significant co-morbidities.
 - When significant tolerance to opioids is suspected.
 - To assist with the management of aberrant behavior or patients who have opioid use disorder.

- To assist with tapering or weaning regimens.
- To assist with management of complex issues not listed above.
- Methadone may be indicated for specific types of patients and should be initiated, titrated, and monitored cautiously by providers who have substantial experience with its use and risks.

DRAFT

A2. ABBREVIATED TREATMENT PROTOCOLS

- [Opioids for Acute Pain \(pain lasting up to 4 weeks from onset\)](#)
- [Opioids for Post-operative Pain](#)
- [Opioids for Subacute Pain \(1–3 months\)](#)
- [Opioids for Chronic Pain and Chronic Opioid Treatment \(3 months or more of treatment\)](#)

IMPORTANT NOTE ABOUT THE ABBREVIATED PROTOCOLS

The one-page summaries found on the following pages are meant to provide a *quick, general overview* of the recommendations contained within the Opioids Treatment Guidelines, but *not to replace* them. **Reviewers and health care providers should not rely exclusively on the summary recommendations**, since summary recommendations are necessarily incomplete. In order to provide medically appropriate care based on guideline recommendations, it is important to consult the main body of the guideline itself.

**Summary Recommendations — OPIOIDS FOR ACUTE PAIN
(pain lasting up to 4 weeks from onset)**

[Register for CURES](#)

Injury Type	Indication	Non-opioid Treatments	Considerations	Best Practices If Opioids Used	Monitoring	Discontinuing
MILD (e.g., strains, tendonitis, repetitive strain injuries)	Opioids NOT indicated	<p>Patients with acute pain injuries should begin with non-opioid treatments.</p> <p><i>Non-opioid pain treatments:</i></p> <ul style="list-style-type: none"> • Medications (e.g., NSAIDS, acetaminophen) unless contraindicated. 				
MODERATE TO SEVERE (e.g., severe sprains, moderate trauma, low back pain)	Opioids MAY BE indicated	<ul style="list-style-type: none"> • Rest, graded exercise, physical therapy. • Complementary treatment (e.g., acupuncture, yoga) 	<p>Only consider opioids for acute pain if non-opioid pain treatments are contraindicated or ineffective.</p> <p><i>Identify high-risk patients:</i></p> <ol style="list-style-type: none"> 1. Consult CURES. 2. Screen for comorbidities: <ul style="list-style-type: none"> • Past/present substance use disorder • Physical conditions (e.g., COPD, severe obesity, sleep disorders) • Psychological conditions (e.g., depression, PTSD) • Use of sedatives/ hypnotics (e.g., benzodiazepines) 3. Consider consulting a pain specialist for high-risk patients 	<p><i>Prior to prescribing</i></p> <ol style="list-style-type: none"> 1. Discuss with patients the benefits and risks of opioids 2. Document nature and extent of injury 3. Document level of pain and function <p><i>Prescribe only:</i></p> <ul style="list-style-type: none"> • Weaker opioids. • 1-2 week supply, without refill • One opioid at a time • Lowest effective dose, No higher than 80mg/day MED. 	<p><i>Document at every visit</i></p> <ul style="list-style-type: none"> • Consult CURES • Track and document levels of pain and function, showing clinically meaningful improvement • Document current opioid dose <p><i>Monitor closely for indications to discontinue opioids:</i></p> <ul style="list-style-type: none"> • Resolution of pain • Lack of functional improvement • Intolerance • Non-compliance 	<p>As feasible, complete opioid treatment within 2 weeks (document need for longer opioid treatment).</p> <p><i>Via tapering</i></p> <p>Use tapering (not abrupt cessation) if treatment exceeds 2 weeks.</p>
SEVERE (e.g., fractures, major trauma, large burns)	Opioids ARE indicated					

Summary Recommendations — OPIOIDS FOR POST-OPERATIVE PAIN

Important: See “Opioids for Acute Pain” for recommendations (Considerations, Monitoring, Discontinuing).

Patient type	Best Practices			
	Before Surgery	During Surgery	Post-Surgery	
			In Hospital	After Discharge
Opioid naive	<ul style="list-style-type: none"> •Consult CURES. •Wean patient off benzodiazepines and other sedative-hypnotics 	No recommendations	<ul style="list-style-type: none"> •Prescribe lowest effective dose of short-acting opioids, no more than 80 mg/day MED •Prescribe for daytime use for a few days to alleviate severe pain, then taper to nocturnal use for sleep •Use opioids as adjuncts to other pain treatments (See Opioids for Acute Pain, Non-opioid Treatments). •Monitor patients with comorbidities 	<ul style="list-style-type: none"> •Limit opioid prescriptions to 2-3 weeks for less extensive procedures. •Limit opioids to 3 months for extensive procedures (See Opioids for Subacute Pain) •With rare exceptions, prescribe only for nocturnal use beyond one month •Discontinue opioids for patients with substance abuse (detected pre- or post-surgery)
Opioid tolerant	<ul style="list-style-type: none"> •Consult CURES and document current opioid dose and other medication use •Work with surgeon to establish coordinated treatment plan for managing surgical pain •Set up consult with anesthesiologist: <ul style="list-style-type: none"> ○ Most patients: 1-2 weeks before surgery ○ Patients on buprenorphine: at least 2 weeks before surgery •Set appropriate expectations for patient: assure patient opioid dose will come down to pre-operative doses or lower •Avoid escalating dosage •Consult a pain or addiction specialist for high-risk patients 	<ul style="list-style-type: none"> •Use acetaminophen, anti-inflammatory medications •Continue pre-operative opioids, and possibly use regional blocks •Consider non-opioid analgesics (e.g., gabapentin, ketamine, lidocaine) 	<ul style="list-style-type: none"> •Allow patient controlled analgesia (PCA) •Be vigilant when converting from PCA to oral opioids: AVOID “straight conversion” 	<ul style="list-style-type: none"> •No long-acting opioids (unless patient was on them previously) •Taper to pre-operative doses within 6 weeks after surgery; only continue doses higher than pre-operative levels for up to 12 weeks, with documentation to justify •Consult addiction or pain specialist as needed

**Summary Recommendations — OPIOIDS FOR SUBACUTE PAIN
(1-3 months)**

Considerations	Best Practices	Monitoring	Discontinuing
<p><i>Document results at every visit</i></p> <ul style="list-style-type: none"> •Consult CURES •Perform complete physical exam and UDT •Screen for contraindicated physical conditions (e.g., untreated sleep disorders, severe obesity, COPD) •Use validated tools to screen for depression,¹ PTSD, substance abuse^{2,3} •Advise against alcohol, sedatives/hypnotics (e.g., benzodiazepines) •Consult pain or addiction specialist when necessary 	<p><i>Prescribe</i></p> <p><i>Non-opioid treatments:</i></p> <ul style="list-style-type: none"> •Physical activity, including passive and active range motion, and physical therapy with graded exercise matched to injury •Medication (e.g., acetaminophen, NSAIDs) •Cognitive-behavioral therapy •Complementary treatment (e.g., acupuncture, massage, yoga) <p><i>Opioid treatment:</i></p> <ul style="list-style-type: none"> •Lowest effective dose of short-acting opioid producing analgesia and improved function (no more than 80mg/day MED). •Prescribe a limited supply, 1–2 weeks, with no refills <p><i>If considering chronic opioid treatment, begin a trial period of opioids to determine if chronic treatment is medically necessary</i></p> <ul style="list-style-type: none"> •Review treatment agreement; ensure patient understands risks, side effects, potential benefits and complications of treatment before signing •Set goals with patient for functional improvement and pain reduction to measure opioid efficacy during trial •For high-risk patients, document need for trial •Titrate to stable dose (See Opioids for Chronic Pain) •Trial period should last no longer than 60 days 	<p><i>At every visit</i></p> <ul style="list-style-type: none"> •Consult CURES. •Track and document levels of pain and function: clinically meaningful improvement (30% improvement in both pain and function level or worsening on attempt to wean) is desirable to continue opioid treatment. •Document current MED. •Monitor closely for adverse effects and risks. <p><i>Administer as necessary:</i></p> <ul style="list-style-type: none"> •Validated tools to screen for aberrant behavior⁴ •UDT •Consultation with pain or addiction specialist 	<p><i>Indications for tapering</i></p> <p><i>Any of the following:</i></p> <ul style="list-style-type: none"> •Resolution of pain •Lack of functional improvement •Intolerance •Non-compliance <p><i>Methods</i></p> <p>Use tapering (not abrupt cessation) to discontinue or reduce dose of opioids</p> <ul style="list-style-type: none"> •<i>Step 1:</i> 10-25% per week outpatient taper, possibly using suboxone support after patient is off opioids •<i>Step 2:</i> If Step 1 fails or comorbidities hamper efforts, inpatient detox and multidisciplinary pain program may be indicated <p><i>Duration</i></p> <p>Tapers can usually be completed in 4–10 weeks, but patients on high doses may take longer</p>

¹ The Patient Health Questionnaire-9 (PHQ-9), a tool to detect mental health conditions.

² The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) or the Opioids Risk Tool (ORT), two self-reporting questionnaires to detect high-risk patients.

³ The CAGE-AID, a self-reporting questionnaire to detect alcohol abuse.

⁴ The Current Opioid Misuse Measure (COMM) or the Prescription Opioid Misuse Index (POMI), two self-reporting questionnaires to detect current opioid abuse

**Summary Recommendations — OPIOIDS FOR CHRONIC PAIN
(3 months or more of treatment)**

Considerations	Best Practices	Monitoring	Discontinuing
<p><i>Document at every visit</i></p> <ul style="list-style-type: none"> •Consult CURES •Perform complete physical exam, UDT •Screen for contraindicated physical conditions (e.g., untreated sleep disorders, severe obesity, COPD) •Use validated tools to screen for depression,¹ PTSD, substance abuse^{2,3} •Advise against alcohol, sedatives/hypnotics (e.g., benzodiazepines) •Consult addiction or pain specialist as necessary for complex management issues 	<p><i>Optimal use of treatment agreement</i></p> <ul style="list-style-type: none"> •Review with patient treatment agreement signed prior to opioid trial (e.g., possible adverse effects; consequences of diversion, misuse or abuse; not to drive) •Ensure terms of agreement are followed •Annually review and update treatment agreement with new signatures and modify as necessary <p><i>Prescribe</i></p> <p><i>Non-opioid treatments:</i></p> <ul style="list-style-type: none"> •Physical activity, including passive and active range motion, and physical therapy with graded exercise matched to injury •Medication (e.g., acetaminophen, NSAIDs) •Cognitive-behavioral therapy •Complementary treatment (e.g., acupuncture, massage, yoga) <p><i>Opioid treatment:</i></p> <ul style="list-style-type: none"> •Lowest effective dose of short-acting opioid producing analgesia and improved function (no more than 80 mg/day MED; for those on higher doses, attempt to wean to less than 80 mg/day MED) •Avoid intravenous, intramuscular, sublingual, submucosal, and transdermal (except buprenorphine) administration of opioids for chronic pain if the patient is able to tolerate oral medication <p><i>Titration period, to find stable effective (“maintenance”) dose:</i></p> <ul style="list-style-type: none"> •Regular face-to-face visits every 4 weeks •More frequent visits (every 2 weeks) if (1) titrating doses above 80 mg/day MED, as the risk of adverse effects increases with increasing dose, or (2) provider suspects coexisting psychiatric problems, drug-behavior problems, or medical problems 	<p><i>At every visit</i></p> <ul style="list-style-type: none"> •Consult CURES •Track and document levels of pain and function: clinically meaningful improvement (30% improvement in both pain and function level or worsening on attempt to wean) is desirable to continue opioid treatment •Document current MED •Monitor for intolerance and non-compliance <p><i>Frequency of visits after titration:</i></p> <ul style="list-style-type: none"> •Monthly during the first year of opioid treatment •Quarterly thereafter <p><i>Frequency of UDTs:</i></p> <ul style="list-style-type: none"> •2x/year randomly for low-risk •Up to 4x/year randomly for high-risk or high-dose (> 80 mg/day MED) •At any unscheduled visit for opioids (e.g., ER visit) <p><i>Apply as medically necessary:</i></p> <ul style="list-style-type: none"> •Validated tools to screen for aberrant behavior⁴ •UDT •Consultation of pain or addiction specialist 	<p><i>Indications for tapering</i></p> <p><i>Any of the following:</i></p> <ul style="list-style-type: none"> •Resolution or improvement of pain. •Lack of functional improvement. •Intolerance. •Non-compliance. <p><i>Methods</i></p> <p>Use tapering (not abrupt cessation) to discontinue or reduce dose of opioids.</p> <ul style="list-style-type: none"> •<i>Step 1:</i> 10-25% per week outpatient taper, possibly using suboxone support after patient is off opioids •<i>Step 2:</i> If Step 1 fails or comorbidities hamper efforts, inpatient detox and multidisciplinary program indicated <p><i>If taper fails:</i></p> <ul style="list-style-type: none"> •Every 6 months, attempt to wean patients on high doses for more than 6 months to below 80 mg/day MED

¹ The Patient Health Questionnaire-9 (PHQ-9), a tool to detect mental health conditions.

² The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) or the Opioids Risk Tool (ORT), two self-reporting questionnaires to detect high-risk patients.

³ The CAGE-AID, a self-reporting questionnaire to detect alcohol abuse.

⁴ The Current Opioid Misuse Measure (COMM) or the Prescription Opioid Misuse Index (POMI), two self-reporting questionnaires to detect current opioid abuse

A3. BACKGROUND

The rapid rise in the use of prescription opioids has been associated with a parallel increase in the number of cases of opioid misuse/abuse and opioid-associated deaths. Coinciding with the rise in opioid use has been an increased awareness of chronic pain as a societal problem. The Opioids Treatment Guidelines are an evidence-based guide for using opioids to treat adults with work-related acute, subacute, perioperative, and chronic noncancer pain. A key goal of the Opioids Treatment Guidelines is to provide a balance between appropriate treatment of pain and safety in the use of opioids for those purposes.

Opioid analgesics are widely used to treat severe acute and peri-operative pain as well as pain due to cancer and at end-of-life. However, the use of chronic opioid therapy for noncancer chronic pain remains controversial. [1-3] While a small number of workers experience “delayed recovery” (persistent debilitation/disability, drug dependence, depression, deconditioning), they account for the majority of total disability burden and costs. Some injured workers may require opioids for the management of their acute or chronic pain. It is not the intention of the Opioids Treatment Guidelines to restrict proper medical use of opioids. However safe and responsible prescribing is necessary to avoid unintended consequences, including prolonged disability and iatrogenic morbidity and mortality.

A3.1 Burden of Pain

Pain that persists for weeks to years is a public health problem that affects more than 100 million adults in the US and reduces their quality of life. [2] The resulting costs to society are at least \$560–\$635 billion per year in direct medical expenses and lost work productivity.

A3.2 Workers’ Compensation Context

Reducing preventable disability is of the highest priority for society in general, as well as for medical practitioners, employers, and workers’ compensation professionals. While the vast majority of injured workers heal quickly and return to work, a relatively non-catastrophic injury may lead to the loss of a productive life. [1, 2, 4]

Failure to return to work early following an injury is a predictor for long-term and entrenched disability. [1] Using best practices to heal injury and illness, improve function, and encourage return to work immediately following injury is the most effective way to prevent and reduce prolonged disability. [5, 6] Preventing the transition from acute and subacute pain to chronic pain in a workers’ compensation context aligns with the goal of preventing long-term disability.

For purposes of the Opioids Treatment Guidelines, acute pain is of sudden onset and is expected to last up to four weeks (one month); in the occupational context, acute pain is linked clearly to a specific event, injury, or illness. Subacute pain is pain that lasts between four and 12 weeks (or one and three months). Chronic pain is defined as pain that lasts more than three months. [2] Thus, the actions taken immediately following injury and in the

ensuing two to three months are crucial in limiting both preventable disability and chronic pain.

These Opioids Treatment Guidelines have therefore focused on use of opioids in the acute, subacute, and chronic periods as critical decision points. It is important to carefully consider whether and how opioids may be used in the acute and subacute periods, since available evidence does not always warrant their use. If the evidence-based decision is to prescribe opioids, the following steps must be followed as they are crucial to worker outcomes:

1. Weigh the risks and benefits of treatment at all times.
2. Follow documentation, treatment, monitoring, and dosage recommendations described in the Opioids Treatment Guidelines for all pain phases.
3. Using extreme caution, make a transparent and planned decision with the patient's consent regarding whether to proceed from treating acute pain with opioids to treating subacute and especially chronic pain with opioids.

The Opioids Treatment Guidelines are consistent with those published by the [Medical Board of California Guidelines for Prescribing Controlled Substances for Pain](#) for the treatment of noncancer pain that is not related to work.

A3.3 Evidence of Effectiveness of Opioid Use in the Acute Period

While there are no high-quality trials to suggest that opioids are superior to other active treatments for the treatment of mild to moderate acute pain, there is evidence that short course treatment may be effective in alleviating severe acute pain. [7-12] However, non-opioid medications such as non-steroidal anti-inflammatory medications are at least equivalent if not superior for mild to moderate pain and may have fewer unwanted side effects than opioids. [7, 13-19] However, non-opioid medications also may cause adverse health effects and may not be tolerated by some patients. [20]

A3.4 Evidence of Effectiveness of Long-Term Opioid Use

Despite the lack of consistent, strong evidence for efficacy, the use of opioids for chronic noncancer pain has greatly increased over the past decade. At the time of writing the Opioids Treatment Guidelines, the question as to the long-term effectiveness and safety of opioids for the treatment of chronic noncancer pain remained unanswered. The evidence as summarized by systematic reviews as well as noted by more contemporary randomized controlled trials (RCTs) is complicated by varying conclusions. These disparate conclusions are sometimes based on the integration of new findings and, at other times, on different interpretations of the same data.

Some systematic reviews report that oral opioids are significantly more effective than placebo in treating chronic pain, with declines in pain of 30–50% and significant improvements in measures of functional status. [3, 21-23] A recent systematic review of randomized controlled trials of chronic opioid treatment found modest effects for improved pain, and small, inconsistent effects for improved function. [24] Additionally, a systematic review of pharmacological treatments for chronic low back pain found that “opioids are more effective than placebo with respect to pain and disability, with a much greater effect

size for pain than disability.” [25] Most randomized trials are no longer than four weeks in duration, with the longest trials lasting under three months.

Evidence of effectiveness for a longer time period has only been assessed in observational studies. A systematic review of longer duration observational studies of chronic opioid treatment came to the following conclusion:

[...] proper management of a type of strong painkiller (opioids) in well-selected patients with no history of substance addiction or abuse can lead to long-term pain relief for some patients with a very small (though not zero) risk of developing addiction, abuse, or other serious side effects. However, the evidence supporting these conclusions is weak, and longer-term studies are needed to identify the patients who are most likely to benefit from treatment. [3]

Furthermore, a more recent report offered the following opinion:

*Opioids can be an appropriate means of treating patients with chronic pain, particularly those with moderate to severe pain. Four of the systematic reviews we identified found that oral opioids are significantly more effective than placebo in treating chronic pain, with declines in pain in the range of 30–50%. Use of opioids for chronic pain has also been associated with significant improvements in measures of functional status (such as on SF-36). According to two of these studies, opioids are also more effective at improving pain and functional status than NSAIDs. Nevertheless, the increasing use of opioids has been accompanied by real risks of substance misuse, addiction, diversion, overdose, and death. The Institute of Medicine Report, *Relieving Pain in America*, summarizes the ongoing challenges involved in balancing effective treatment of pain against the known risks associated with opioid therapy and provides specific recommendations for national and other policy audiences. [26]*

The overall finding of greater effects of chronic opioid treatment on pain, rather than function or disability, is also true of many other treatments for chronic pain, since reduction in pain is not always associated with improvement in function and reduced disability. [27] This finding highlights the importance of combining pain treatments with efforts aimed at improving function. The Opioids Treatment Guidelines emphasize the need to balance the use of opioids to treat pain with measures of effectiveness, by monitoring pain, function, and progress towards reduced disability.

Effective treatment of pain involves using multiple modalities and a multidisciplinary approach. For guidance on the effectiveness of treatment for chronic pain with non-opioid therapies, see the [MTUS Chronic Pain Medical Treatment Guidelines](#). [28]

A3.5 Opioid Safety: Overdose, Serious Adverse Events, and Substance Misuse/Abuse

Overdose: Opioid overdose, whether intentional or unintentional, is a risk of opioid prescribing and is mainly manifested by depressed mental status, decreased respiratory rate and tidal volume, decreased bowel sounds, and pupillary constriction. Hypotension

may also accompany opioid intoxication. Patients may exhibit ataxia and audible snoring prior to more severe consequences, including collapse and death. If untreated, opioid overdose can lead to hypothermia, coma, seizure, head trauma, aspiration pneumonia, and rhabdomyolysis. Suppression of respiratory drive is one of the most serious complications, as it is most likely to lead to death.

At pharmacological doses, opioids decrease the ventilatory response to carbon dioxide (CO₂). In combination with other central nervous system (CNS) depressants, opioids can induce acute respiratory failure as defined by a decrease in the partial pressure of oxygen in arterial blood (P_aO₂). However, different opioids vary in their tendency to induce respiratory failure. For instance, methadone causes a dose-dependent decrease in P_aO₂ before hypercapnia is evident. It is believed that the different effects of various opioids is dependent on their relative affinity for discrete opioid receptors in the CNS as well as pharmacokinetic interactions between the opioid and other co-administered drugs.

In addition to suppressing central respiratory drive and response to CO₂, morphine and related drugs slow respiration by prolonging inspiration and by postponing the spontaneous termination of inspiration (“inspiratory off-switching”). Morphine suppression of phrenic nerve activity can be reversed by cholinergic agents such as physostigmine. It has been proposed that addition of anticholinergic agents in an opioid regimen may lower the toxic threshold of morphine on such mechanisms and potentially increase morbidity and mortality associated with opioid overdose. [29]

The pharmacokinetics of opioid clearance varies between patients and can also be influenced by agents that affect opioid metabolism, such as concomitant medications, herbals, and dietary supplements. Genetics, age, gender and other dietary influences can also modify opioid clearance through hepatic metabolism. In overdose, the observed half-life of opioids may increase due to changes in absorption and gastric transit. [30]

Serious Adverse Events: According to the US Centers for Disease Control and Prevention (CDC), deaths associated with prescription opioids rose from 4,000 in 1999 to over 14,000 in 2008. [31] Moreover, these deaths peaked in the age group of 25–55 years, constituting a large premature loss of productive life. [32] Additionally, an increasing number of emergency department visits and hospitalizations have been associated with prescription opioids. [33]

In addition to prescribed opioids, in the majority of opioid-associated deaths a postmortem exam reveals other drugs, including multiple opioids, antidepressants, and sedative/hypnotics (e.g., benzodiazepines). A published review of national data reports that in about half of deaths involving opioid analgesics, more than one type of drug contributed to the death. Benzodiazepines were most frequently associated with opioid analgesics deaths; other drugs included cocaine and heroin. [34] This finding emphasizes the need to exercise caution in prescribing benzodiazepines and other sedative hypnotics with opioids. (See [Section 7, Concurrent Use of Benzodiazepines and Other Sedative Hypnotics](#))

The most commonly reported adverse effects of opioid use are constipation, nausea, dyspepsia, headache, fatigue, lethargy, erectile dysfunction, and urinary retention. [3] Other

major adverse effects of opioids include myocardial infarction, allergic reactions, impairment of executive function, sleep apnea, and death.

There is controversy regarding whether opioid treatment induces increased or abnormal pain sensitivity (opioid-induced hyperalgesia). [35] The only well-controlled human study of reasonable size to date failed to show its existence. [36]

The safety profile of chronic opioid treatment also includes less common adverse effects such as endocrine disorders, neonatal abstinence syndrome, falls and fractures in the elderly, and a potential increased risk of road trauma. [37] The true incidence of these adverse effects is unknown.

Substance Misuse and Abuse: The use of opioids that were not prescribed for a medical reason has increased significantly, with one study estimating that one in 25 opioid prescriptions is used for such non-medical purposes. [38] Based on the 2010 National Survey on Drug Use and Health, more than 35 million Americans age 12 and older used an opioid analgesic for non-medical purposes at some time in their life—an increase compared to about 30 million in 2002. [39] Use of prescription opioids for non-medical purposes now surpasses that of other illicit substances—marijuana, cocaine, methamphetamine, and heroin. [40]

Despite the large numbers of patients misusing and abusing prescription opioids, the overall incidence and prevalence of substance abuse and misuse of opioids in patients treated for chronic pain remains unclear, with systematic reviews and retrospective studies reporting varying results. For instance, a recent systematic review found that the median incidence of opioid dependence syndrome was 0.5% (range 0–24%) and median prevalence was 4.5% (range 0–31%). [41] The study concluded that the “available evidence suggests that opioid analgesics for chronic pain conditions are not associated with a major risk for developing dependence.” However, another review was critical of the methodology of most of the studies attempting to assess substance misuse and abuse rates. [42] This same review suggests that earlier studies that demonstrated very low rates of substance abuse were particularly flawed. The authors identified a more contemporary study that found that 35% of longer term opioid users met the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria for a current or previous opioid use disorder. [43] It is clear that higher-quality studies are needed to more accurately characterize the incidence and prevalence of prescription opioid misuse and abuse.

While the overall incidence and prevalence of opioid misuse is not well understood, certain identified factors do predispose patients to persistent opioid use and higher rates of substance misuse and abuse. One of these factors is psychosocial distress (e.g., depression, anxiety, and post-traumatic stress disorder [PTSD]), and this finding reinforces the importance of assessing these comorbidities in patients with chronic pain being considered for chronic opioid therapy (See [Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events, Prior to Initiation of Chronic Opioid Treatment](#)). [44-46]

Coinciding with the increases in opioid-associated deaths and opioid misuse and abuse has been a substantial escalation in opioid prescribing and dosage between 2000 and 2010. [47] Opioids are currently the second most widely prescribed class of medications (statins for lowering cholesterol are the first). Indeed, the combination agents containing

hydrocodone/acetaminophen (sold under brand names including Vicodin and Norco) are the most prescribed medications in the country, at 131 million prescriptions per year. [48] This rise in sales of prescription opioids over the past decade has contributed greatly to the observed increases in serious adverse events and opioid substance misuse/abuse. It is a primary goal of the Guidelines to significantly reduce the rate of opioid-related adverse events and substance misuse and abuse.

A3.6 Scope and Target Audience for the Opioids Medical Treatment Guidelines

The target audiences for the Guidelines are primary care and medical and surgical specialty physicians, including pain specialists, caring for injured workers in the State of California and medical providers who perform utilization review and independent medical review. Employers and insurers will also find the concepts in the document useful. The Guidelines are meant to assist in the decision to initiate trials of opioid therapy for patients with acute, peri-operative, subacute, and chronic pain, and to assist in safer, more judicious and effective use of opioids if they are prescribed on a chronic basis.

A key focus of the Opioids Treatment Guidelines is to seek a balance between appropriate treatment of pain and safety in the use of opioids for that purpose. As noted in the 2011 White House Office of National Drug Control Policy comprehensive action plan on prescription drug abuse, "...any policy in this area must strike a balance between our desire to minimize abuse of prescription drugs and the need to ensure access for their legitimate use." [49]

Caution should also be exercised in extrapolating these recommendations to the non-workers' compensation population. While some of the concepts applied here are common to all patient populations, a significant difference between occupational and non-occupational guidelines is that a key goal of the former is the restoration of function to ensure early return to work.

A3.7 Core Concepts

Although the Opioids Treatment Guidelines are evidence based, consistent evidence on which to base specific treatment recommendations was lacking on many issues related to opioid prescribing. In such situations, recommendations were based on expert consensus following a critical assessment of the available literature. The Opioids Treatment Guidelines were based on the following core concepts that represent the current state of evidence, professional standards, and societal beliefs:

- Effective pain management is a professional responsibility and the duty of people in the healing professions. [2] Providing effective resources for practicing physicians to enable the delivery of best practices in community-based settings is most likely to allow effective, ongoing treatment of pain.
- Pain is influenced by a combination of biological, psychological, and social factors and requires a comprehensive approach to prevention and management. [2, 28]
- The transition from acute to subacute to chronic pain and the development of long-term disability are of particular concern in the workers' compensation system. It is of the highest public health and societal interest to prevent this transition to chronic

pain and long-term disability. Psychosocial variables are generally more accurate predictors of the development of chronic pain than biomedical findings.

- Opioids can be an effective treatment for chronic noncancer pain, but their use must be balanced with potential risks.
- Opioids are not indicated in all painful conditions. Furthermore, medications alone in general (and opioids specifically) are often inadequate to manage chronic pain. Other effective pharmacological and non-pharmacological treatments should be considered, alone or in combination. [50, 51] Given chronic pain's diverse effects, interdisciplinary assessment and treatment produce the best results, especially for those with severe and persistent pain problems. [2]
- Patient care is improved with good communication and collaboration between clinicians across disciplines within primary care, between primary and specialty care physicians, and between clinicians and patients.
- The use of opioids for the treatment of pain presents risks and potential harms. Prescribers have an obligation to assess risks and minimize harms.
- Optimal implementation of the best practices described in this Guideline should include education of patients and the general public about the potential benefits and harms of opioids, and patients' and the general public's role in using opioids safely and effectively.

To reduce the overuse, misuse, and abuse of opioids, the Opioids Treatment Guidelines must be actively implemented in clinical practice; this includes the use of tools, some of which are provided as part of the Guideline. In addition, it is essential to raise public awareness about the need to improve the effectiveness and safety of opioid prescribing.

A lack of quality data on the long-term benefits, risks, and adverse effects of opioid therapy has created a strong need for more research in these areas. The Opioids Treatment Guidelines were not meant to serve as a training manual for opioid prescription. Some clinicians may need to acquire additional skills and knowledge to safely and effectively prescribe opioids for pain.

A3.8 Goals and Objectives

The goals of the recommendations in the Opioids Treatment Guidelines are as follows:

- To prevent and reduce opioid-related long-term disability, morbidity, mortality, and substance misuse and abuse.
- To provide a set of best practices and universal precautions for safe and effective prescribing of opioids for acute, subacute, and chronic pain.
- To recommend opioid-prescribing practices that promote functional restoration.

A3.9 Evidence-Based Methods

The Opioids Treatment Guidelines for the safe prescription of opioids for injured workers are based on the best available medical evidence. The methodology used is consistent with the published literature regarding guideline development. [52] Based on available resources, relevant existing evidence-based guidelines were accessed, reviewed, and evaluated and the highest level of evidence chosen for this Guideline. As of this writing, the review was restricted to guidelines available as of April 2014. Whenever possible, recommendations that were common to all or most of the guidelines reviewed received priority and were adopted as recommendations, even if they were only based on expert consensus. The guidelines that were evaluated are listed in Section A5.1 below.

Where common recommendations across guidelines were lacking, the following sequential approach was utilized:

- a. High-level evidence from high-quality therapeutic studies (i.e., from RCTs) and prognostic studies (prospective cohort studies) were adopted as recommendations. For example, specific dosing guidance was based on high quality RCTs.
- b. If no high-level evidence was available, the recommendations of a major guideline were adopted, even when other guidelines did not replicate these recommendations, as long as they aligned with the goals and objectives identified for the Opioids Treatment Guidelines. For example, this was the case for guidance on tapering.

A3.10 Guidelines Evaluated

- **American College of Occupational and Environmental Medicine (ACOEM)**
ACOEM's Guidelines for the Chronic Use of Opioids. American College of Occupational and Environmental Medicine. 2011¹[53]
- **American College of Occupational and Environmental Medicine (ACOEM)**
ACOEM's Guidelines for the Chronic Use of Opioids. American College of Occupational and Environmental Medicine. 2014. [7]
- **American Pain Society—American Academy of Pain Medicine (APS/AAPM), Chou et al**
Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. 2009.² [54]

¹ The ACOEM 2011 guideline was superseded by the revised 2014 edition of the ACOEM guideline, which came out during the development of these guidelines. In the latest version of the guideline, the 2014 version is referenced primarily.

- **American Society of Interventional Pain Physicians (ASIPP), Manchikanti et al**

American Society of Interventional Pain Physicians Guidelines for Responsible Opioid Prescribing in Chronic Noncancer pain. 2012.³ [55]

- **Canadian Guideline**

Canadian Guideline for Safe and Effective Use of Opioids for Chronic Noncancer Pain. National Opioid Use Guideline Group (NOUGG). April 30 2010 Version 4.5. [56]

- **Official Disability Guidelines (ODG)**

Work Loss Data Institute. ODG Treatment in Workers' Compensation –Pain (Chronic) (Official Disability Guidelines). (updated April 6, 2015). [57]

- **Utah**

Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain. Utah Department of Health. 2009. (Utah 2009) [58]

- **Veterans Administration/Department of Defense**

U.S. Veterans Affairs Administration Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. Version 2.0 2010. (US VA 2010) [59]

- **Washington State Workers' Compensation System**

Interagency Guideline on Opioid Dosing for Chronic Noncancer Pain. Agency Medical Directors' Group (AMDG). 2010. (WA AMDG 2010) [60]

Guideline for Prescribing Opioids to Treat Pain in Injured Workers. Washington State Department of Labor & Industries. July 1, 2013. (WA 2013) [61]

See Supplement 2 in Part 2 of the Opioids Treatment Guidelines for a summary of recommendations from the guidelines reviewed.

² Please note that since this guideline was published as a journal article, "Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain," the guideline appears in the References list under the author Chou.

³ Please note that since this guideline was published as a journal article, "American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2--guidance," the guideline appears in the Reference list under the author Manchikanti.

B. RECOMMENDATIONS

Part B of the Opioids Treatment Guidelines contains recommended practices for the use of opioids in patients with acute, subacute, post-operative, and chronic pain, as well as appendices with helpful tools for providers. The recommendations in Part B are based on a review of existing guidelines and studies from the scientific literature.

The Evidence Levels for individual studies cited as the basis for recommendations were evaluated based on the [DWC Medical Treatment Utilization Schedule \(MTUS\) Methodology for Evaluating Medical Evidence](#) and are listed in the reference section. This methodology is intended solely for the evaluation of individual studies, not guidelines; thus, the Evidence Level for recommendations based on guidelines was not evaluated. The reader is referred to the relevant guideline for further information on studies supporting these recommendations.

DRAFT

1. OPIOIDS FOR ACUTE PAIN (UP TO FOUR WEEKS AFTER INJURY OR PAIN ONSET)

The term “acute pain” is defined in this guideline as pain lasting up to four (4) weeks from the initial onset of injury.

1.1 ***Moderate to Severe Acute Soft-Tissue Injuries (e.g., severely strained ligaments, severe sprains, moderate trauma, moderate to severe low back pain, moderate to severe radiculopathy)***

A brief course of short-acting opioids is an option to provide analgesia for moderate to acute severe pain due to acute soft tissue injuries when pain is uncontrolled by other measures and/or accompanied by functional deficits. [7] The provider should ensure that the following conditions are met prior to prescribing opioids for moderate to severe soft tissue injuries:

1. Document moderate to severe soft tissue injury.
2. Document that the following additional treatments, which may be both medically indicated and more effective than opioids, have been initiated and (a) have failed and/or (b) are contraindicated and/or (c) there are reasonable expectations that only opioids will produce immediate pain relief and sleep immediately following the injury: [60]
 - Pharmacologic therapy with non-opioid pain medications (e.g., acetaminophen, NSAIDs).
 - Physical activity, including rest, passive and active range of motion, and physical therapy with graded exercise matched to the injury.
 - Complementary/alternative modalities, such as acupuncture, massage, and yoga. [62]

(See [Section 3.2, Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment](#) and refer to the MTUS Chronic Pain Treatment Guidelines)

3. Check the CURES database and document the results prior to prescribing opioids.
 - Providers in emergency departments, urgent care clinics, or other clinical settings providing initial treatment for patients with moderate to severe pain, such as those with acute fractures, should check CURES while not jeopardizing patient care and prioritizing the need to provide pain relief and comfort to the patient. It should be noted that as of this writing, there may be a delay of two to four (2–4) weeks in updating the information in CURES.
 - If CURES indicates the use of other opioid medications, but the assessment otherwise supports the use of opioids, prescribe only a limited supply of opioids at the lowest feasible dose under carefully monitored conditions. (See [Section 3.3.4, Use of CURES to Ensure Safe and Effective Opioid Use](#))

4. Provide documentation in the medical record that the following conditions that are relative contraindications to initiating opioids are not present: depression, anxiety, personality disorder, untreated sleep disorders, current or past substance abuse, drug-seeking behavior, other psychotropic medications, post-traumatic stress disorder (PTSD), cognitive impairment, chronic obstructive pulmonary disease (COPD), severe obesity, balance problems / fall risk, osteoporosis, and renal failure. If these conditions are present, written documentation must be provided to justify the use of opioids. [7, 44, 63-81]
5. Do not introduce sedative-hypnotics, including anti-histamines (H₁-blockers) and benzodiazepines, if considering prescribing opioids. Attempt to discontinue these medications in patients receiving them if prescribing opioids. [33, 80]
(See [Section 7, Concurrent Use of Benzodiazepines and Other Sedative Hypnotics](#))
 - If sedative hypnotics such as anti-histamines or benzodiazepines are being prescribed by a different treating physician (for example, for a non-industrial condition), it is important to communicate the risk to the other provider to facilitate coordinated patient care.
 - Opioid use is not recommended for patients actively performing safety-sensitive jobs. [82]
6. Provide documentation that there is no use of illicit substances or other substances that should not be taken concomitantly (e.g., sedating substances, including alcohol and benzodiazepines). [33] In individuals using illicit substances, prescription opioids should be provided only if other alternatives are not available or effective.
(See [Section 7, Concurrent Use of Benzodiazepines and Other Sedative Hypnotics](#))

If the decision is made to prescribe opioids, clinical practice should include all of the following:

1. Prescribe weaker opioids and the lowest effective dose. Stronger opioids may be considered only if weaker ones are ineffective or not tolerated. The FDA categorizes drugs into five Schedules (from I to V). [83] Schedule V drugs (weakest) have the lowest potential for abuse and Schedule I drugs (strongest) are considered to have the highest potential for abuse. [84]
2. Prescribe only one opioid at a time. The lowest dose capable of providing analgesia should be used. [85-87]
 - a. Doses for opioid-naïve patients should not exceed 80 mg/day morphine equivalent dosage (MED). [77, 88, 89]
(See [Section 3.3.8, Opioid Titration and Dosing Threshold](#))
 - b. Prescribe a short course of opioid medication (a limited supply, for one to two [1–2] weeks with no refills). [90]
3. Prescribe opioids at night or when the patient is not at work. [89]

4. Document the need to continue opioids for more than two (2) weeks, including clinically meaningful improvement in pain and function. (See [Section 3.3.7, Monitoring Effectiveness of Chronic Opioid Treatment](#))
5. Consider using screening tools for addiction or adverse events to assist with treatment decisions or recommend consultation with a pain specialist at any point prior to the 4th week of treatment with opioids, if warranted based on clinical evaluation. (See [Appendix A, Brief, Validated Tools](#); [Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events, Prior to Initiation of Chronic Opioid Treatment](#), [Section 3.3.6, Use of Urine Drug Testing](#); and [Section 6, Consultation with Specialists](#))
6. Monitor for and document indications for discontinuing opioids, including the following:
 - a. Resolution of pain or improvement to the point of not requiring opioids within the expected timeframe for the injury being treated.
 - b. Lack of improved function despite adherence to the treatment regimen.
 - c. Intolerance or severe adverse effects: it is likely that at least some side effects will occur with opioid use. The nature and severity of side effects will determine whether to discontinue the medication.
 - d. Noncompliance, surreptitious medication use, aberrant drug screening results, diversion, and consumption of medications or substances when advised to not take simultaneously.
7. Discontinue use of opioids in acute pain patients within two (2) weeks whenever possible. Patients who have been treated for more than two (2) weeks with opioids should have these medications discontinued via tapering rather than by abrupt cessation. (See [Section 4.2, Methods for Tapering Opioids](#))
8. Caution patients about the potential adverse effects of opioid medications, including impacts on alertness. Driving and operation of heavy equipment should be discouraged while on these medications. (See [Appendix B, Written Opioid Treatment Agreement \[Sample\]](#))
9. Advise patients regarding responsible storage and disposal of opioid medications at the time of initial prescription. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))

Rationale:

The physiologic benefits of effective analgesia are well described for acute severe pain. The goal is to reduce pain in the first few days following a severe injury. Thereafter, functional restoration is a specific goal for opioid use in this setting. The short- and long-term risks of opioid use outweigh the benefits if there is lack of efficacy, evidence of adverse effect, or inappropriate medication or substance use.

1.2 **Mild Acute Injuries (e.g., musculoskeletal strains and sprains, muscle pain, tendonitis)**

- Opioid medications should not be used for mild injuries such as acute onset strains, sprains, muscle pain, tendonitis, and myofascial pain; opioids are also not indicated for repetitive strain injuries. [7] The following therapies should be utilized first for the aforementioned acute injuries: [60]
 - Pharmacologic therapy with non-opioid pain medications (e.g., acetaminophen, non-steroidal anti-inflammatory drugs [NSAIDs]), unless contraindicated due to history of allergy or severe adverse impact.
 - Physical activity, including rest, passive and active range of motion, and physical therapy with graded exercise matched to the injury.
 - Complementary/alternative modalities, such as acupuncture, massage, and yoga. [62] (See [Section 3.2, Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment](#); also, refer to the MTUS Chronic Pain Treatment Guidelines)
- Opioid medications should only be used for treatment of acute pain when the severity of the pain warrants that choice *and* after determining that other non-opioid pain medications or other therapies will not provide adequate pain relief or are contraindicated for medical reasons. Opioids should only be prescribed at the lowest dose that provides pain relief [85-87], for a limited time (e.g., five [5] days) and with no refill, prior to re-assessment. [7, 90]
- If the provider decides to prescribe opioids, clinical practice should include the following:
 1. Check the Controlled Substance Utilization Review and Evaluation System (CURES), California's Prescription Drug Monitoring Program (PDMP), and document findings. If CURES indicates the simultaneous use of other narcotic medication not revealed by patient history, opioid prescription may be contraindicated at this point. It should be noted that as of this writing, there may be a delay of two to four (2–4) weeks in updating the information in CURES.
 2. Prescribe weaker opioids and the lowest effective dose. Stronger opioids may be considered only if weaker ones are ineffective or not tolerated. The FDA categorizes drugs into five schedules (from I to V). [83] Schedule V drugs (weakest) have the lowest potential for abuse and Schedule I drugs (strongest) are considered to have the highest potential for abuse. [84] Long acting opioids should not be used for the treatment of acute pain. [61]
 3. Caution patients about the potential adverse effects of opioid medications, including impacts on alertness. Driving and operation of heavy equipment should be discouraged while on these medications. The use of opioids is contraindicated in patients performing safety-sensitive jobs. [82] (See Appendix B, Sample of a Written Opioid Treatment Agreement [Sample])

4. Advise patients about responsible storage and disposal of opioid medications at the time of initial prescription. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))
5. Taper patients off opioids within two weeks of initiating opioids for acute pain whenever possible. [7]

Rationale:

Based on the literature summarized in Supplement 1 of Part 2 of the Opioids Medical Treatment Guidelines, there is insufficient evidence that supports the efficacy of opioids in the acute phase for mild injuries. There is quality evidence that use of opioids can lead to adverse outcomes. All guidelines reviewed that had recommendations for the management of acute pain recommend against the use of long-acting opioids for mild acute pain.

1.3. Severe Acute Injuries (e.g., fractures, crush injuries, major trauma, large burns, other injuries with significant tissue damage)

(See also [Section 10, Opioid Use in Catastrophic Injuries](#))

Opioids are recommended for the treatment of acute, severe pain uncontrolled by other modalities and/or with functional deficits. A brief course may also be indicated for pain following severe injuries. [7, 20] Providers should ensure that the following conditions are met when prescribing opioids for severe acute injuries:

1. Document severe injury.
2. Initiate the following additional treatments, which may be more effective than opioids, and document that (a) they have failed and/or (b) are contraindicated and/or (c) there are reasonable expectations that only opioids will produce immediate pain relief and sleep immediately following the injury: [60]
 - Pharmacologic therapy with non-opioid pain medications (e.g., acetaminophen, NSAIDs).
 - Physical activity, including rest, passive and active range of motion, and physical therapy with graded exercise matched to the injury and tolerance of the patient.
 - Complementary/alternative modalities, such as acupuncture, massage, and yoga as relevant to the clinical condition. [62] (See [Section 3.2, Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment](#), and refer also to the MTUS Chronic Pain Treatment Guidelines)
3. Check the CURES database and document the results prior to prescribing opioids.
 - Providers in emergency departments, urgent care clinics, or other clinical settings providing initial treatment for patients with moderate to severe pain, such as those with acute fractures, should check CURES while not

jeopardizing patient care and prioritizing the need to provide pain relief and comfort to the patient.

- If the search indicates that other opioids are being used, the patient should be questioned about the additional medications. If the clinical assessment supports the use of additional opioids, only a limited supply should be prescribed under carefully monitored conditions.
(See [Section 3.3.4, Use of CURES to Ensure Safe and Effective Opioid Use](#))
4. Provide documentation in the medical record that the following conditions, which are relative contraindications to initiating opioids, are not present: depression, anxiety, personality disorder, untreated sleep disorders, current or past substance abuse, drug-seeking behavior, other psychotropic medications, PTSD, cognitive impairment, COPD, severe obesity, balance problems / fall risk, osteoporosis, and renal failure. If any of these conditions are present, written documentation must be provided to justify the use of opioids.
 5. Do not introduce sedative-hypnotics, including anti-histamines (H₁-blockers) and benzodiazepines, if considering prescribing opioids. Attempt to discontinue these medications in patients receiving them if prescribing opioids. [91] (See [Section 7, Concurrent Use of Benzodiazepines and Other Sedative Hypnotics](#))
 - If sedative hypnotics such as anti-histamines or benzodiazepines are being prescribed by a different treating physician (for example, for a non-industrial condition), it is important to communicate the risk to the other provider to facilitate coordinated patient care.
 6. Document that there is no use of illicit substances or of substances that should not be taken concomitantly (e.g., sedating medications including alcohol and benzodiazepines). [33] The use of illicit substances is a contraindication to opioid treatment. (See [Section 7, Concurrent Use of Benzodiazepines and Other Sedative Hypnotics](#))
 - If sedative hypnotics such as anti-histamines or benzodiazepines are being prescribed by a different treating physician (for example, for a non-industrial condition), it is important to communicate the risk to the other provider to facilitate coordinated patient care.
 - Opioid use is not recommended for patients actively performing safety-sensitive jobs. [82]
- Clinical best practices should include all of the following:
 1. Use weaker opioids and the lowest effective dose. Stronger opioids may be considered only if weaker ones are ineffective or not tolerated. The FDA categorizes drugs into five Schedules (from I to V). [83] Schedule V drugs (weakest) have the lowest potential for abuse and Schedule I drugs (strongest) are considered to have the highest potential for abuse. [84]

2. Prescribe only one opioid at a time. The lowest dose capable of providing analgesia should be used. [85-87]
 - a. Do not exceed 80 mg/day MED for opioid-naïve patients. [77, 88, 89] (See [Section 3.3.8, Opioid Titration and Dosing Threshold](#))
 - b. Prescribe a short course of opioid medication (a limited supply, for example 1–2 weeks with no refills without re-evaluation). [90]
3. Prescribe opioids at night or when not at work. Patients should be cautioned about the potential adverse effects of opioid medications, including impacts on alertness. Driving and operation of heavy equipment should be discouraged while on these medications. The use of opioids is contraindicated in patients performing safety-sensitive jobs. [82] (See [Appendix B, Sample of a Written Opioid Treatment Agreement \[Sample\]](#))
4. Document the need to continue opioids for more than two (2) weeks, including clinically meaningful improvement in pain and function. (See [Section 3.3.7, Monitoring Effectiveness of Chronic Opioid Treatment](#))
5. Consider using screening tools or obtaining a consult with a pain specialist at any point prior to the fourth week if warranted based on clinical evaluation. (See [Appendix A, Brief, Validated Tools](#); [Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events, Prior to Initiation of Chronic Opioid Treatment](#); [Section 3.3.6, Use of Urine Drug Testing](#); and [Section 6, Consultation with Specialists](#).)
6. Recommend a gradual increase in physical activity and activities of daily living as part of the treatment regimen as the patient progresses.
7. Monitor for indications for discontinuing opioids, including the following:
 - a. Resolution of pain or improvement to the point of not requiring opioids within the expected timeframe for the injury being treated.
 - b. Lack of improved function despite adherence to the treatment regimen.
 - c. Intolerance or severe adverse effects: it is likely that at least some side effects will occur with opioid use. The nature and severity of side effects should be considered when deciding whether to discontinue the medication.
 - d. Noncompliance, surreptitious medication use, aberrant drug screening results, diversion, and consumption of medications or substances when advised to not take simultaneously.
8. Discontinue use of opioids within two (2) weeks of acute pain onset whenever possible. [7] Patients who have been treated for more than two (2) weeks should have opioid doses reduced or discontinued via tapering, rather than abrupt cessation. (See [Section 3.3.8, Opioid Titration and Dosing Threshold](#).)

9. Advise patients regarding responsible storage and disposal of opioid medications at the time of initial prescription. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))

Rationale:

The physiologic benefit of treating severe acute injuries with opioids is well described. The use of opioids to treat pain must be balanced with the need to prevent misuse and adverse effects.

1.4. Opioids for Post-operative Pain

- Opioid use for a limited duration is recommended for management of post-operative pain management in addition to other treatments, especially during the immediate post-operative period and for moderate to extensive surgical procedures (e.g., arthroplasty, lumbar fusion). While continued use of opioids beyond the period of hospitalization is in general not recommended, relief of pain and discomfort is a priority. [7, 9, 12, 92] Planning for use of opioids to treat pain postoperatively should begin during pre-operative assessment.
- Considerations for prescribing opioids for post-operative pain include all of the following:
 1. Treatments with other non-opioid medications fail to provide relief or are contraindicated. Opioids are indicated to obtain sleep for evenings after surgery, and they are also indicated for daytime use to alleviate severe post-operative pain. Non-opioid medications (e.g., NSAIDs, acetaminophen) should be prescribed along with opioid medications. (See [Section 3.2, Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment](#))
 2. Prior to surgery and to prescribing opioids, the CURES database is checked and the results documented. If the search indicates that other opioids are being used, the patient should be questioned about the additional medications. If the clinical assessment supports the use of additional opioids, only a limited supply should be prescribed under carefully monitored conditions. (See [Section 9, Managing Peri-operative Pain in Workers on Chronic Opioid Treatment Undergoing Elective Surgery](#))
 3. Patients with more than one of the following conditions, which are relative contraindications for opioid use after hospital discharge, should be carefully monitored as inpatients: Anxiety, depression, personality disorder, current or past substance abuse, drug-seeking behavior, untreated sleep disorders (particularly sleep apnea), use of other psychotropic medications, PTSD, cognitive impairment, cerebrovascular disease, balance problems / fall risk, COPD, chronic hepatitis, cirrhosis, renal failure, severe obesity, and osteoporosis. [7, 44, 63-81] If patients with these conditions are prescribed opioids after discharge, written justification for their use should be provided in the medical record.
 4. Current substance abuse is a contraindication to continued opioid treatment following hospital discharge. [33]

- Clinical best practices should include all of the following:
 1. Avoid introducing sedative-hypnotics including anti-histamines (H₁-blockers) and/or benzodiazepines before surgery. Attempt to discontinue these medications in patients who are receiving them prior to surgery. [33] (See [Section 7, Concurrent Use of Benzodiazepines and Other Sedative Hypnotics](#)). Coordinate care with other providers who may be prescribing these medications.
 2. Document a complete history and physical examination. [7]
 3. Use opioids at night post-operatively, as needed for pain-interrupted sleep. Use during the daytime may generally be indicated for up to a few days to overcome severe post-operative pain, following which tapering to nocturnal use only should occur as soon as possible.
 4. Use other treatments such as NSAIDs (when the risk of bleeding is not a concern or they are not otherwise contraindicated), progressive exercises, and other modalities, with opioids as adjuncts to control post-operative pain.
 5. Prescribe opioids at the lowest dose capable of producing analgesia and improving function, as during the acute treatment phase. [85-87]
 - a. Do not exceed 80 mg/day MED for opioid naïve patients (those who are not already on higher doses of opioids). [77, 88, 89] (See [Section 3.3.8, Opioid Titration and Dosing Threshold](#)).
 - b. Use weaker opioids and the lowest effective dose. Stronger opioids may be considered only if weaker ones are ineffective or not tolerated. The FDA categorizes drugs into five Schedules (from I to V). [83] Schedule V drugs (weakest) have the lowest potential for abuse and Schedule I drugs (strongest) are considered to have the highest potential for abuse. [84]
 6. Do not extend opioid use beyond two to three (2–3) weeks for less extensive procedures.
 7. Consider use for up to three (3) months during recovery for more extensive surgical procedures. Written documentation should be provided regarding the status of pain and function.
 8. Apply the opioid use recommendations for management of subacute pain for patients treated with opioids for one to three (1–3) months post-operatively. (See [Section 2.2, Opioids for Subacute Pain](#)). With rare exceptions, only nocturnal use is recommended in the second and third months of post-operative opioid use.
 9. Use screening tools for substance (drugs and alcohol) misuse/abuse, as well as for psychosocial conditions, if opioids are continued for treatment of pain beyond four

(4) weeks post-operatively. (See [Section 3.3.1.1, Screening for Drug Misuse/Abuse](#), and [Section 3.3.1.2, Screening for Alcohol Misuse/Abuse](#)) If aberrant results are obtained, providers should consider obtaining a consult with a pain specialist or conducting urine drug screening. (See [Section 6, Consultation with Specialists](#), and [Section 3.3.6, Use of Urine Drug Testing](#))

10. Schedule periodic outpatient visits following discharge to monitor efficacy, adverse effects, compliance and surreptitious medication use. Towards this end, providers should document their assessments and may consider using screening tools, obtaining a consult with a pain specialist, or conducting urine drug screening at any point, if they feel it is warranted based on clinical evaluation.
11. Monitor for indications for discontinuing opioids, including all of the following:
 - a. Meaningful resolution of pain and function to the point of not requiring opioids within the expected timeframe for the injury being treated.
 - b. Lack of improved function despite adherence to the treatment regimen.
 - c. Intolerance or severe adverse effects. It is likely that at least some side effects will occur with opioid use; the nature and severity of side effects should be considered when deciding whether to discontinue the medication.
 - d. Noncompliance, surreptitious medication use, aberrant drug screening results, diversion, and consumption of medications or substances when advised to not take simultaneously.
12. Discontinue opioids via tapering, as opposed to abrupt cessation, in patients who have been treated with opioids for more than two weeks. When tapering, patients should be monitored to ensure that pain and function do not worsen. Transition to non-opioid medications if needed. [7] (See [Section 4, Tapering Opioids](#))
13. Caution patients about the potential adverse effects of opioid medications, including impacts on alertness. Driving and operation of heavy equipment should be discouraged while on these medications. The use of opioids is contraindicated in patients performing safety-sensitive jobs. [82] (See [Appendix B, Written Opioid Treatment Agreement \[Sample\]](#))
14. Advise patients regarding responsible storage and disposal of opioid medications at time of discharge. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))

See [Section 9, Managing Peri-operative Pain in Workers on Chronic Opioid Treatment Undergoing Elective Surgery](#), for management of patients who are being treated with opioids prior to surgery.

Rationale:

Sufficient pain control during the post-operative phase is needed to ensure rapid and adequate recovery of function. Opioid use should be limited to the dose and duration

needed to assist improvement of pain and function.

2. OPIOIDS FOR SUBACUTE PAIN (1–3 MONTHS)

If pain extends beyond the acute phase, i.e., beyond one (1) month following onset, a multidisciplinary approach to treatment should be continued (or initiated if not yet used), including cognitive-behavioral therapy, activity coaching, graded exercise, and other treatments such as acupuncture. (See [Section 3.2, Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment](#))

If opioids are being considered beyond the acute phase, these clinical practices should be followed:

1. Document a complete history and physical.
2. Screen for risk using validated tools if medically indicated, if this has not already been done in the acute pain phase. (See [Section 3.3.5, Use of Tools to Monitor Patients on Chronic Opioid Treatment](#)) During the subacute pain phase, a consult with a pain specialist may be obtained for complex management and/or if warranted based on clinical evaluation. (See [Section 6, Consultation with Specialists](#))
3. Administer a baseline urine drug test (UDT) in the office toward the beginning of the subacute period, four to six (4–6) weeks from onset of opioid treatment. (See [Section 3.3.6, Use of Urine Drug Testing](#)) Aberrant results (e.g., those indicating diversion, use of illicit substances, or controlled medications which have not been prescribed) should be evaluated further, addressed with the patient, and written justification provided in the medical record regarding the necessity for continued opioid use. (See [Appendix C, Guidance on Conducting and Interpreting Urine Drug Testing](#)) A history of opioid use disorder or substance use disorder is a relative contraindication to continued opioid use during the subacute phase. Prior to prescribing opioids beyond six (6) weeks to patients with a history of substance use disorder, consult an addiction specialist.
4. Note the following contraindications to continued opioid treatment:
 - a. Current substance use disorder is a contraindication to opioid prescription. If other alternatives are not an option, provide written documentation and consult an addiction specialist to assess the need to use opioids. [61]
 - b. The following conditions are relative contraindications to continuing opioids during the subacute phase: Depression, anxiety, personality disorder, untreated sleep disorders, past substance abuse, drug-seeking behavior, other psychotropic medications, PTSD, cognitive impairment, COPD, severe obesity, balance problems / fall risk, osteoporosis, and renal failure. If any of these conditions are present, written documentation should be provided in the medical record to justify the use of opioids. [7, 44, 63-81]

5. Continue non-opioid treatments as medically indicated:

- Pharmacologic therapy with non-opioid pain medications (e.g., acetaminophen, NSAIDs).
- Physical activity, including rest, passive and active range of motion, and physical therapy with graded exercise matched to the injury.
- Behavioral therapy and complementary/alternative modalities. Refer to the MTUS Chronic Pain Treatment Guidelines.

(See [Section 3.2, Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment](#))

6. Consult CURES again to ensure that the use of prescribed narcotics continues to be consistent with the history and prescription record.
7. Continue documenting clinically meaningful improvement in pain and function during opioid use during the subacute phase. (See [Section 3.3.7, Monitoring Effectiveness of Chronic Opioid Treatment](#))
8. Remind patients at each visit that they should not take benzodiazepines or other sedative-hypnotics or drink alcohol while on opioids. Discontinue opioids via tapering (see 11. below), or taper sedative-hypnotics and/or benzodiazepines if the patient is found to be taking them against provider's advice. Coordinate care with other providers who may be prescribing these medications.
9. Prescribe opioids at the lowest dose capable of producing analgesia and improving function, as during the acute treatment phase. [85-87]
- a. Do not exceed a dose of 80 mg/day MED for opioid-naïve patients (those who are not already on higher doses of opioids). [77, 88, 89]
 - b. Use weaker opioids and the lowest effective dose. Stronger opioids may be considered only if weaker ones are ineffective or not tolerated. The FDA categorizes drugs into five Schedules (from I to V). [83] Schedule V drugs (weakest) have the lowest potential for abuse and Schedule I drugs (strongest) are considered to have the highest potential for abuse. [84]
10. Monitor for indications for discontinuing opioids, including all of the following:
- a. Resolution of pain or improvement to the point of not requiring opioids within the expected timeframe for the injury being treated.
 - b. Lack of improved function despite adherence to the treatment regimen.
 - c. Intolerance or severe adverse effects: it is likely that at least some side effects will occur with opioid use. The nature and severity of side effects should be considered when deciding whether to discontinue the medication.

- d. Noncompliance, surreptitious medication use, aberrant drug screening results, diversion, and consumption of medications or substances when advised to not take simultaneously.
11. If discontinuing opioids, do so via tapering, rather than abrupt cessation, in patients who have been treated with opioids for more than two (2) weeks. (See [Section 4, Tapering Opioids](#))
12. Caution patients about the potential adverse effects of opioid medications, including impacts on alertness. Driving and operation of heavy equipment should be discouraged while on these medications. The use of opioids is contraindicated in patients performing safety-sensitive jobs. [82] (See [Appendix B, Written Opioid Treatment Agreement \[Sample\]](#))
13. Advise patients at each evaluation regarding responsible storage and disposal of opioid medications. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))

Rationale:

With rare exceptions, resolution of pain and resumption of regular function is anticipated after four to six (4–6) weeks. The provider should carefully consider non-opioid alternative treatments and document the absence of factors that would increase the risk of harm prior to continuing opioid use.

3. OPIOIDS FOR CHRONIC PAIN AND CHRONIC OPIOID TREATMENT

The term “chronic pain” is defined in this guideline as pain lasting longer than three (3) months from the initial onset of injury pain (i.e., over 12 weeks). Patients with chronic pain may be candidates for treatment with opioids if pain management and functional improvement have not been achieved with a multidisciplinary treatment approach, including passive and active movement, cognitive behavioral therapy, and other practices such as acupuncture. Patients who require treatment with opioids to relieve pain or improve function for durations longer than three (3) months are considered as being on chronic opioid treatment.

Overview of Recommendations regarding Chronic Opioid Treatment

Steps that should be taken by prescribing providers who are considering chronic opioid treatment are listed below and described in more detail in [Section 3.3, Initiating and Monitoring Chronic Opioid Treatment](#). [7]

- Prior to initiating opioids for chronic pain or chronic opioid treatment, the following steps should be taken and documentation provided in the medical record:
 1. Perform a comprehensive evaluation and assessment that includes a relevant history and physical exam. [56] (See [Section 3.1, Comprehensive Evaluation and Assessment of Patient](#))

2. Consider alternative treatments. (See [Section 3.2, Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment](#))
 3. Screen for risk of addiction or adverse events. (See [Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events, Prior to Initiation of Chronic Opioid Treatment](#))
 - a. Screen for drug misuse/abuse. (See [Section 3.3.1.1, Screening for Drug Misuse/Abuse](#))
 - b. Screen for alcohol misuse/abuse. (See [Section 3.3.1.2, Screening for Alcohol Misuse/Abuse](#))
 - c. Screen for additional psychosocial factors contributing to substance misuse/abuse. (See [Section 3.3.1.3, Screening for Additional Psychosocial Factors Contributing to Substance Misuse/Abuse](#))
 4. Complete patient treatment agreement / informed consent and discuss with patient. (See [Section 3.3.2, Patient Treatment Agreement and Informed Consent](#), and [Appendix B, Written Opioid Treatment Agreement \[Sample\]](#))
 5. Initiate a trial period of opioid treatment. (See [Section 3.3.3, Initiation of Chronic Opioid Treatment](#))
- Based on the above, if the decision is made to initiate chronic opioid therapy, the following medically indicated steps should be taken as part of best clinical practice:
 1. Check CURES to ensure that narcotic medications are not being prescribed by other providers. (See [Section 3.3.4, Use of CURES to Ensure Safe and Effective Opioid Use](#)) If CURES indicates the simultaneous use of other narcotic medication not revealed by patient history, justification should be provided for chronic opioid therapy.
 2. Use questionnaires and other validated screening tools to monitor chronic opioid therapy. These tools are intended to be integrated into a provider's assessment of a patient and should not be used alone to determine treatment in the absence of clinical evaluation. (See [Section 3.3.5, Use of Tools to Monitor Patients on Chronic Opioid Treatment](#), and [Appendix A1, Tools to Screen for High-Risk Patients](#)) Consider obtaining a consult with a pain specialist if warranted based on clinical evaluation. (See [Section 6, Consultation with Specialists](#))
 3. Use urine drug testing for initiation and monitoring of chronic opioid therapy. (See [Section 3.3.6, Use of Urine Drug Testing](#), and [Appendix C, Guidance on Conducting and Interpreting Urine Drug Testing](#))
 4. Monitor the effectiveness of chronic opioid therapy by tracking pain and function. (See [Section 3.3.7, Monitoring Effectiveness of Chronic Opioid Treatment](#), and [Appendix A2, Tools for Tracking Pain and Function: Pain Interference Scales](#))
 5. Monitor and adjust dose of patients on chronic opioid therapy. (See [Section 3.3.8, Opioid Titration and Dosing Threshold](#), and [Appendix F, Opioid Dose Calculations](#))

6. Monitor and make dose adjustments during the maintenance period.
(See [Section 3.3.9, Maintenance of Chronic Opioid Treatment](#), and [Appendix F, Opioid Dose Calculations](#))
7. Make regular efforts to taper opioids. When tapering, patients should be monitored to ensure that pain and function do not worsen. (See [Section 4, Tapering Opioids](#))

3.1. Comprehensive Evaluation and Assessment of Patient

Evaluation and assessment prior to initiating treatment with opioid medications beyond the subacute period (more than three [3] months after initiation of opioid treatment) should include all of the following, which should be documented in the medical record: [7, 53-61]

1. Identify the cause of the pain and develop an appropriate differential diagnosis.
2. Assess prior treatments for the current condition, including their effectiveness, adverse effects, and appropriateness.
3. Consider obtaining a consult with the appropriate specialist (i.e., pain, psychiatry, or other medical specialty) if warranted based on clinical evaluation.
(See [Section 6, Consultation with Specialists](#))
4. Assess the severity of pain (using a numerical rating scale), pain interference (using pain inventory instruments), and function (using validated patient reported questionnaires), even if this has been done during the acute or subacute periods of treatment. This will establish a baseline and thus serve as a basis to track outcomes of chronic opioid treatment. (See [Appendix A2, Tools for Tracking Pain and Function: Pain Interference Scales](#))
5. Assess psychological and social factors and comorbid medical or mental health conditions that may compromise the safe use of opioids to treat chronic pain. (See subsections of [Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events, Prior to Initiation of Chronic Opioid Treatment](#), and [Appendix A1, Tools to Screen for High-Risk Patients](#)) These comorbid factors include the following:
 - Psychiatric conditions (e.g., depression, anxiety, PTSD) that may impact pain treatment in general and chronic opioid treatment specifically. (See [Section 3.3.1.3, Screening for Additional Psychosocial Factors Contributing to Substance Misuse/Abuse](#), and the Patient Health Questionnaire in [Appendix A1, Tools to Screen for High-Risk Patients](#))
 - A history of substance abuse, misuse, or addiction. (See [Section 3.3.1.1, Screening for Drug Misuse/Abuse](#); [Section 3.3.1.2, Screening for Alcohol Misuse/Abuse](#); and [Appendix A1, Tools to Screen for High-Risk Patients](#))
 - Use of current medications that might negatively interact with other medications used for pain treatment. Particular attention should be given to identifying use of benzodiazepines or other sedative-hypnotics, which should not be prescribed simultaneously with opioids. Do not introduce these

medications if considering prescribing opioids. Attempt to discontinue these medications in patients receiving them if prescribing opioids. (See [Section 7, Concurrent Use of Benzodiazepines and Other Sedative Hypnotics](#)) Coordinate care with other providers who may be prescribing these medications.

- The presence of any medical factors that could complicate treatment of pain in general or increase risks of adverse events with chronic opioid treatment, including any pertinent laboratory tests specific to the patient's circumstances. If not already identified in the acute phase, assess for the following conditions: Depression, anxiety, personality disorder, untreated sleep disorders (particularly sleep apnea), current or past substance abuse, drug-seeking behavior, other psychotropic medications, PTSD, cognitive impairment, medication allergies, cardiac disease, COPD, chronic hepatitis, cirrhosis, cerebrovascular disease, severe obesity, balance problems / fall risk, osteoporosis, and renal failure. [7, 44, 63-81]

These conditions are relative contraindications to chronic opioid therapy, and in their presence, written documentation should be provided in the medical record to justify the use of these medications and show that other alternatives have been considered and are not feasible.

- Social factors that may impact pain management including: employment, job satisfaction, marital history, social network, and history of legal problems. [7]

Rationale:

There is agreement across guidelines that the potentially serious adverse effects of chronic opioid treatment warrant comprehensive assessment to avoid potential complications.

3.2. Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment

Non-opioid alternative therapies for pain treatment should be tried whenever possible before resorting to chronic opioid therapy. [7, 57-60] In addition, these treatment modalities should be continued even if opioids are used for relieving chronic pain:

- Pharmacologic therapy with non-opioid pain medications (e.g., acetaminophen, NSAIDs).
- Physical activity, including rest, passive and active range of motion, and physical therapy/occupational therapy with graded exercise matched to the injury.
- Complementary/alternative modalities, such as acupuncture, massage, and yoga. [62]
- Consultation with an appropriate specialist based on clinical assessment to evaluate the need for and provide necessary care, including, but not limited to

psychological, cognitive-behavioral therapy, addiction counseling, and specialized pain management with non-opioid alternatives.

Refer to the MTUS Chronic Pain Medical Treatment Guidelines of California's Division of Workers' Compensation (DWC) to find specific recommendations for non-opioid treatment of chronic pain including, but not limited to, the above. [28]

Rationale:

The guidelines reviewed as well as the [National Institutes for Health](#) offer consistent recommendations that alternative treatments for chronic pain are often medically indicated and offer benefits and promote recovery without many of the side effects of opioid treatment.

3.3 Initiating and Monitoring Chronic Opioid Treatment

3.3.1. Screening for Risk of Addiction or Adverse Events, Prior to Chronic Opioid Treatment

Every major guideline reviewed (See Supplement 2 in Part 2 of the Opioids Medical Treatment Guidelines) recommends using validated tools to assess the risk of addiction or adverse events in patients who are candidates for chronic opioid therapy. Most of these recommendations are based on expert consensus, since research on use of these tools is relatively sparse. [7, 53-61]

3.3.1.1 Screening for Drug Misuse/Abuse

1. Perform screening for drug misuse or abuse in two situations, the first of which will be the focus of this section:
 - a. Prior to initiating a trial of chronic opioid treatment, screening should be performed to predict the probability of a patient engaging in drug misuse/abuse when prescribed opioids for chronic pain.
 - b. During the opioid trial or during chronic opioid treatment, screening should be performed, as needed, to identify current abuse/misuse of opioid medications. (See [Section 3.3.5, Use of Tools to Monitor Patients on Chronic Opioid Treatment](#))
2. Use validated screening tools for predicting the risk of drug misuse, or others, before beginning chronic opioid treatment, and document the results. Providers may use one or more validated questionnaires, such as the following, that rely on self-reporting to predict which chronic pain patients will be at greatest risk for problems with long-term opioid medications: the Opioids Risk Tool (ORT), Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R⁴), and Patient Medication Questionnaire (PMQ).

⁴ <http://www.painedu.org/soap.asp>

- ORT is a brief, gender-specific instrument made up of five questions that address these topics: (1) Family history of substance abuse; (2) Personal history of substance abuse; (3) Age (between 16 and 45 years); (4) History of preadolescent sexual abuse in females; and (5) Psychiatric history (ADD, OCD, bipolar, schizophrenia, and depression). (See this tool in [Appendix A1, Tools to Screen for High-Risk Patients](#))
 - Like ORT, the SOAPP-R is designed to predict which patients will be at high risk of aberrant behavior on chronic opioid treatment. [93] SOAPP-R is superior to the tool that preceded it (SOAPP), because SOAPP-R is more subtle and does not ask patients to admit to socially unacceptable behavior. A score of 18 or higher indicates high risk.
3. Initiate chronic opioid treatment only if the screening tools identify a predicted increased risk for substance misuse/abuse and other alternatives are not viable; in this case, provide documentation in the medical record that attempts are being made to address the identified risks.
 4. Consider administering a urine drug test if the screening tools suggest current drug misuse or abuse. (See [Section 3.3.6, Use of Urine Drug Testing](#), and [Appendix C, Guidance on Conducting and Interpreting Urine Drug Testing](#)) In addition, consider obtaining a consult with an addiction specialist.
 5. Avoid routine genomic testing to predict adverse effects of opioids, including the potential for abuse, as this type of testing not recommended. [54, 94]

Rationale:

A personal history of illicit drug and alcohol use are predictors of opioid misuse or abuse. The literature indicates that validated screening tools may be used to identify patients who may be currently misusing opioids as well as those at risk for future misuse; the results of this screening will help to guide decision making for chronic pain treatment. Evidence that genetic testing reliably predicts the potential for abuse is currently lacking.

3.3.1.2 Screening for Alcohol Misuse/Abuse

1. Complete and document the results of the CAGE-AID questionnaire prior to initiating a trial of chronic opioid treatment. (See this questionnaire in [Appendix A1, Tools to Screen for High-Risk Patients](#))
2. Provide documentation, if the screening tools identify a predicted increased risk for alcohol misuse/abuse, to address the identified risks prior to initiating or continuing chronic opioid treatment.
3. Consult with an addiction specialist as warranted by documented clinical assessment.

Rationale:

Most current guidelines agree on this approach.

3.3.1.3 Screening for Additional Psychosocial Factors Contributing to Substance Misuse/Abuse

1. Use a validated tool to screen for depressive symptoms (e.g., PHQ-9) to document results prior to initiating a trial of chronic opioid treatment. [60] (See this tool in [Appendix A1, Tools to Screen for High-Risk Patients](#))
2. Assess and document the presence of other mental health conditions such as anxiety disorder, severe sleep disorder, PTSD or suicidal ideation.
3. Document mental health conditions identified by screening tools and obtain a consultation with a licensed mental health professional prior to initiating a trial of chronic opioid treatment.
4. Do not initiate chronic opioid treatment during acute psychiatric instability or if suicide risk is identified. Instead, refer patient to the appropriate mental health professional.

Rationale:

Mental health disorders are a strong risk factor for both misuse/abuse and opioid overdose events. [44-46, 95, 96] Several guidelines provide strong recommendations to screen for these conditions prior to initiating chronic opioid treatment. [7, 59, 60]

3.3.2. Patient Treatment Agreement and Informed Consent

A patient treatment agreement is a method for informing patients about potential risks and benefits of opioid use, as well as relative responsibilities in the provider/patient relationship. [57-61] In addition, an agreement allows the provider to obtain permission from the patient to conduct necessary testing, such as random urine drug tests. Both the patient and provider sign the agreement after reviewing its contents.

1. Both the treating health care provider and patient should sign a written patient treatment agreement adhering to the principles described in the above section prior to initiating a trial of chronic opioid treatment. (See [Appendix B, Written Opioid Treatment Agreement \[Sample\]](#))
2. Address all of the following in the treatment agreement:
 - a. Details of the opioid trial. (See [Section, 3.3.3, Initiation of Chronic Opioid Treatment](#))
 - b. Alternative therapies available and potential adverse effects of opioid treatment.
 - c. Activity limitations during opioid treatment (e.g., driving, operating machinery).
 - d. Consequences to the patient if evidence of diversion, misuse, or abuse comes to light.
 - e. Responsible storage and disposal of opioid medications.

3. Update the treatment agreement annually with new signatures.
 - a. Revisit the treatment agreement more frequently if warranted and modified if needed.
 - b. Modify the treatment agreement update it as necessary if the patient does not adhere to the treatment plan.
4. Document in the medical record any misuse, abuse, or diversion that is identified while the patient agreement is in effect. Provide documentation if the original agreement terms are modified addressing the issue of concern and why and how the original agreement was modified.

Rationale:

The use of a treatment agreement is recommended to document patient understanding, involvement in their care, and agreement with expectations during opioid treatment.

3.3.3. Initiation of Chronic Opioid Treatment

Initiation of opioids for the treatment of chronic pain should be considered a trial to assess efficacy (degree and duration of pain reduction, improvements in function, quality of life) and side effects. [7, 54, 57, 59] The trial of opioid treatment for a period up to several weeks, and not more than three (3) months, should not be considered a commitment to long-term therapy.

The following clinical practices are recommended for initiating chronic opioid therapy [97]:

- Describe initiation of opioids as a therapeutic trial for a limited period of time (typically no more than 60 days).
- Explain that progress will be carefully monitored for both benefit and harm, considering both the efficacy (pain reduction, improvement in function and quality of life) and adverse effects of opioid treatment.
- Prescribe the lowest possible dose initially and titrate to effect.
- Begin chronic opioid therapy with a short-acting opioid. Consider longer-acting only if the shorter-acting medications are not effective.

The following clinical best practices should be followed:

1. Consult CURES prior to the opioid trial. CURES may also be consulted during the trial period, based on provider's assessment of need. (See [Section 3.3.4, Use of CURES to Ensure Safe and Effective Opioid Use](#))
2. Conduct urine drug screening prior to the trial. Urine drug screening may be repeated during the trial period, based on the provider's assessment of need. (See [Section 3.3.6, Use of Urine Drug Testing](#), and [Appendix C, Guidance on Conducting and Interpreting Urine Drug Testing](#))

3. Use screening tools prior to the trial to identify patients at high risk of aberrant behavior, if these have not already been administered. Other screening tools to identify concurrent abuse may be used during the trial period, based on the provider's assessment of need. (See [Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events, Prior to Initiation of Chronic Opioid Treatment](#); [Section 3.3.5, Use of Tools to Monitor Patients on Chronic Opioid Treatment](#); and [Appendix A1, Tools to Screen for High-Risk Patients](#))
4. Complete a written patient treatment agreement adhering to the principles described in the above section. The agreement should be signed by both the treating health care provider and patient. It is prudent to share the signed agreement with other health care providers treating the patient. (See the [Section 3.3.2, Patient Treatment Agreement and Informed Consent](#); [Appendix B, Written Opioid Treatment Agreement \[Sample\]](#); and [Appendix G, Summary of Screening and Monitoring Recommendations](#))
5. Intravenous, intramuscular, sublingual, submucosal, and transdermal (except buprenorphine [Suboxone]) administration of opioids for chronic pain are not indicated if the patient is able to tolerate oral medication. [98, 99]

Rationale:

A trial period of opioid use prior to initiating chronic treatment is a precautionary recommendation. By assessing and documenting pain relief and functional improvement, titrating dose appropriately, and establishing appropriate patient expectations during a trial period, providers can minimize potential adverse impacts. [97]

3.3.4. Use of CURES to Ensure Safe and Effective Opioid Use

CURES is California's Prescription Drug Monitoring Program (PDMP). Most guidelines recommend consulting such programs as part of opioid treatment. [51, 58, 59, 100] Providers should query the CURES database and document results in the following situations:

1. Prior to providing an initial prescription for an opioid (i.e., for acute pain, particularly mild pain, as well as before surgery). Refer to earlier sections ([Section 1.2, Moderate to Severe Acute Soft-Tissue Injuries](#), and [Section 1.3, Severe Acute Injuries](#)) to see specific recommendations for checking CURES prior to treating patients with acute severe pain.
2. At the start of the subacute phase, (i.e., four [4] weeks following initial injury).
3. Periodically, based upon risk of diversion, misuse or abuse, if chronic opioid treatment is continued. The following schedule is recommended:
 - Before initiation of and at some point during the trial period for chronic opioid treatment.
 - At least quarterly during titration to a "maintenance dose."
 - At least annually during maintenance.

- More often for patients at high risk for substance abuse.
- If an unscheduled healthcare appointment results in an additional prescription for opioids. Providers in emergency departments, urgent care clinics, or other clinical settings providing treatment for patients with moderate to severe pain should check CURES while not jeopardizing patient care and prioritizing the need to provide pain relief and comfort to the patient.

Rationale:

Evidence-based and expert, consensus-derived guidelines reviewed recommend evaluating current opioid use before a provider writes the first prescription. Studies suggest that approximately 5% of new claimants entering the workers' compensation system have received opioid prescriptions prior to injury. Of these, about 40% were already receiving chronic opioid treatment. [61] The goal of checking CURES after starting a trial of opioids is to verify that the patient has not received additional prescriptions since starting the trial. [58] Accessing CURES periodically during chronic treatment, or if an unexpected visit or event occurs, aids in verifying appropriate use and identifying misuse. [101, 102]

3.3.5. Use of Tools to Monitor Patients on Chronic Opioid Treatment

Tools such as the Current Opioid Misuse Measurement (COMM) and the Prescription Opioid Misuse Index (POMI) should be used in combination with clinical assessment to assess for current aberrant behavior during chronic opioid treatment to determine whether chronic opioid treatment should be discontinued. [57] The COMM and POMI are self-report questionnaires designed to identify *current* abuse/misuse of opioids in patients who are on chronic opioid treatment. [103-105] (See [Section 4.1, Indications for Tapering Opioids](#))

- The COMM has 17 items and its authors recommend using it in tandem with the SOAPP-R. (See [Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events, Prior to Chronic Opioid Treatment](#)) A score of 9 or higher on the COMM indicates a high risk of current aberrant medication related behavior.

Rationale:

While there are no definitive studies to recommend any one tool over another, the use of validated screening instruments is an aid to clinical assessments in identifying aberrant behavior related to opioid treatment.

3.3.6. Use of Urine Drug Testing (UDT)

Periodic drug testing is useful in assessing adherence to the treatment plan and in detecting the use of non-prescribed substances. While various biologic media may be used for drug testing, urine is preferred because it is convenient to collect and store, and testing is cost-effective and relatively easy to obtain. Several guidelines recommend UDT as part of the evaluation to determine whether chronic opioid treatment should be embarked upon following a trial of opioids. [57, 59-61]

1. UDT process:

Develop and follow standardized protocols in consultation with the testing laboratory to ensure proper collection, handling, storage, and shipping of urine specimens. [106] Procedures should ensure compliance with local, state, and federal requirements pertaining to laboratory testing, such as the Clinical Laboratory Improvement Amendments (CLIA⁵). When UDT is conducted as part of pain treatment, forensic standards (such as those required by the Department of Transportation for employer drug testing programs) are generally not needed, so it is not necessary to observe specimen collection and follow chain-of-custody protocols.⁶ [97, 107]

2. Types of UDT:

- An initial UDT may be performed at the location where the specimen is collected. The standard practice includes a measurement of temperature, specific gravity, and a select panel of drugs. Point of collection (POC) screening with an immunoassay should be considered the initial test for multiple drug classes to obtain rapid results. [108, 109] As of this writing, POC UDTs have the following limitations: (1) ethanol (alcohol) and some prescribed opioids (e.g., fentanyl and oxycodone) cannot be detected; (2) they do not detect the presence of benzodiazepines with much accuracy; and (3) they are subject to false positive and negative results. [110]
- Testing performed in federally-certified laboratories uses a two-step testing process, enzyme-mediated immunoassay followed by gas chromatography mass spectrometry (GC/MS) or liquid chromatography mass spectrometry (LC/MS/MS). If POC testing has been performed, laboratory-based immunoassays do not need to be repeated.
- Both POC screening and lab-based immunoassay tests are subject to false negative and false positive results. Confirmatory testing by a laboratory with GC/MS or LC/MS should be utilized for the following conditions: (1) POC testing was negative for

⁵ “Congress passed the Clinical Laboratory Improvement Amendments (CLIA) in 1988 establishing quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed. A laboratory is any facility that does laboratory testing on specimens derived from humans to give information for the diagnosis, prevention, treatment of disease, or impairment of, or assessment of health.”

<http://www.fda.gov/medicaldevices/deviceregulationandguidance/ivdregulatoryassistance/ucm124105.htm>
(Accessed on February 12, 2014.)

“The Clinical Laboratory Improvement Amendments of 1988 (CLIA) law specified that laboratory requirements be based on the complexity of the test performed and established provisions for categorizing a test as waived. Tests may be waived from regulatory oversight if they meet certain requirements established by the statute. The section of the statute specifying the criteria for categorizing a test as waived was excerpted without elaboration in the regulations at 42. CFR 493.15(b) and 493.15(c) contains a list of these waived tests.”

<http://www.fda.gov/medicaldevices/deviceregulationandguidance/ivdregulatoryassistance/ucm124202.htm>
(Accessed on February 12, 2014.)

⁶ <http://www.dot.gov/odapc/mro>

prescribed drugs, (2) POC testing was positive for opioids that were not prescribed by any treating physicians, or (3) POC testing indicated illicit substances. [109]

3. What to test

Consider testing for drugs in addition to the prescribed opiate medication, depending on the clinical circumstances, using laboratory-based GC/MS or LC/MS/MS. [60] For further guidance on UDT, refer to [Appendix C, Guidance on Conducting and Interpreting Urine Drug Testing](#).

Some drugs that may be considered as part of urine drug testing are listed in Table 1 on the next page. (Please note that this is not a comprehensive list of drugs that can be detected in urine.) Prior to ordering and interpreting these tests, it is essential to be informed of sensitivities, half-lives, metabolic pathways, and levels of detection.

Table 1. Drugs to Consider Testing for as Part of Urine Drug Panel⁷

Most Common	May Also be Considered
Prescribed and additional opioids	Alcohol*
Benzodiazepines	Barbiturates
Cocaine	Cannabinoids
Methadone	Fentanyl
Methamphetamine	PCP

* Ethyl glucuronide (EtG) is recommended for detection of alcohol beyond the acute exposure period. See: <http://store.samhsa.gov/shin/content/SMA12-4686/SMA12-4686.pdf>

⁷ Table adapted from information in the Washington State Agency Medical Director's Group Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain, 2011 (page 13) and the Southern Oregon Opioid Prescribing Guidelines, 2013 (page 14). See also [Clinical Drug Testing in Primary Care \(SAMSHA, 2012\)](#).

4. Frequency of UDT:

Urine drug screening should be performed at the following phases to document absence of opioids (noncompliance), presence of unprescribed drugs (prescription drug abuse), and/or presence of illicit drugs. [57]

- a. Administer a baseline UDT prior to initiating a trial of chronic opioid treatment, usually during the subacute phase. [61] Urine drug screening may be repeated during the trial period, based on the provider's assessment of need. [7]
- b. Conduct UDT on a random basis during chronic opioid treatment, and adjust in frequency as relevant after assessment for risk of abuse, misuse, or diversion. [7, 54, 56-59, 61, 106]
- c. Perform UDT at least two (2) times annually on all patients on chronic opioid treatment and on some patients up to four (4) times a year as warranted, especially patients taking doses greater than 80 mg/day MED. [7]
- d. Consider adjusting the frequency of UDTs based upon risk assessment. The frequency recommended below may be adjusted after documenting the following:
 - Provider concern for misuse, abuse, or diversion.
 - Basis for this concern: Why is there concern for misuse, abuse or diversion?
 - What are the drugs or drug classes of concern?

The recommended timing and frequency of UDT is summarized in Table 2:

Table 2. Timing and Frequency of UDT

Rationale for UDT	Timing of UDT
Based on duration of opioid treatment	
During the subacute phase of treatment	1-3 months after opioids are started to treat acute injury, to determine baseline prior to initiating opioid trial period
Chronic opioid treatment	Prior to initiating a trial (if not begun during subacute phase); additional tests during the trial, based on assessment of need
	On a <i>random</i> basis during chronic treatment; adjusted in frequency as relevant after assessment for risk of abuse, misuse or diversion (see below)
	At least 2 times a year in all patients on chronic opioid treatment and up to 4 times a year, as warranted, especially for those taking doses greater than 80 mg/day MED
	At any unscheduled visit for opioids to the emergency room
Based on Physician's Documented Assessment of Risk of Misuse	
Low	2 times a year
Moderate	2–4 times a year
High	4 times a year

5. How to use the results of urine drug screening:

- a. Document in the medical record and discuss the results with the patient if the initial UDT detects opioids or illicit substances.
- b. Document in the medical record if UDT indicates illicit substance use and opioid treatment still appears the best option after weighing the potential adverse impacts and alternatives. Documentation should include why detection of the unexpected substances does not prevent treatment with opioids, particularly chronic opioid therapy.
- c. Discuss the findings with the patient and discontinue opioid treatment via tapering, rather than abrupt cessation, if two-step UDT in a certified laboratory

confirms that the patient is not taking the prescribed medications and medication diversion is suspected.

It is important that all test results that suggest opioid misuse or abuse be discussed with the patient. These discussions should occur in a positive, supportive fashion, to encourage trust in the provider and healthy behaviors. The test results, discussion with the patient, and the reason continued opioid treatment is needed should be documented in the medical record. [97] Consultation with a pain or addiction specialist may be considered as warranted based on documentation of clinical need.

Rationale:

Every major guideline reviewed makes similar recommendations for the frequency and use of urine drug screening. There is fair evidence that UDTs (1) provide diagnostic accuracy, (2) identify patients who are noncompliant or abusing prescription drugs or illicit drugs, and (3) may decrease prescription drug abuse or illicit drug use when patients are in chronic pain management therapy. [55]

3.3.7. Monitoring Effectiveness of Chronic Opioid Treatment

3.3.7.1 Tracking Pain and Function to Monitor Effectiveness of Chronic Opioid Treatment

Every guideline reviewed recommends documentation of pain and function specifically as the principal method to determine effectiveness. [7, 53-61] (See Supplement 2 in Part 2 of the Opioids Medical Treatment Guidelines)

Monitoring the effectiveness of opioids and giving strong consideration to weighing the risks and benefits throughout the period of opioid use are crucial to maximizing potential benefit and avoiding serious short- or long-term adverse consequences.

Several methods are used for tracking pain and function. To provide valid comparisons, pain and function should be consistently tracked with the same validated instruments each time. Providers should not rely solely on informal inquiry or observation, physical therapy notes, and similar nonstandard and scientifically unvalidated methods, because they are unreliable and lead to inconsistent tracking of effectiveness across practice types and systems. In order to track pain intensity, most guidelines rely on a 10-point scale, such as a numerical rating scale or visual analog scale. The most valid and consistent method for tracking function is to routinely measure physical function by documenting actual physical performance, including exertional capacity, degree of flexibility, and improved strength.

An additional or alternate method is to track the types of physical function most meaningful to the patient, such as the ability to stand, sit, lift, and carry.

1. Document the following outcomes when assessing the effectiveness of chronic opioid treatment:
 - a. Reduction in level of pain via a brief validated instrument (e.g., numerical rating scale where 0 = no pain and 10 = worst pain imaginable). Use the same validated instrument(s) each time. (See [Appendix A2, Tools for Tracking Pain and Function](#))
 - b. Functional improvement attributable to the use of opioids via a validated instrument (e.g., the Graded Chronic Pain Scale [GCPS], the Brief Pain Inventory [BPI], the Multidimensional Pain Inventory [MPI], and the Pain Severity Scale of the SF-12⁸). Pain interference scales (GCPS and BPI) are brief and sensitive, but do not fully reflect physical function. In addition to tracking function, it is important to promote improved function with efforts aimed at returning patients to work. [111] (See these tools in [Appendix A2, Tools for Tracking Pain and Function](#))
 - c. Discrepancies between the reported improvement in pain, reported level of function, and described work limitations; provide available details.
2. Document the patient's pain and function with the following frequency:
 - a. First three (3) months of opioid therapy following injury: **every visit**.
 - Establish baseline level of pain and function during the comprehensive exam preceding chronic opioid treatment (or at the beginning of the opioid trial)
 - b. From three months to one year after initiation of chronic opioid treatment: **monthly**.
 - c. For the duration of chronic opioid treatment: **quarterly**.

Rationale:

Most major guidelines reviewed recommend tracking the effectiveness of opioid treatment to improve pain and function. Use of validated instruments is the most consistent, scientifically reliable way to do so. Chronic opioid treatment for work-related injuries, the subject of this Guideline, aims to restore function and not just alleviate pain. If pain is considered the primary barrier to improved function, then chronic opioid treatment should lead to meaningful functional benefit in patients. In other words, a reduction in pain should correspond to increased function. In the absence of improved function, a decrease in pain intensity is not considered clinically meaningful improvement. (See [Section 3.3.7.2, Clinically Meaningful Improvement in Pain and Function](#))

⁸ <http://www.sf-36.org/tools/sf12.shtml>

The use of a combined brief instrument to measure both pain and pain interference with function is attractive because of the reliability and validity of several instruments, as well as their public availability, and the fact that this type of instrument would be the least burdensome and costly to administer across most practices. Extensive research shows the reliability, validity and responsiveness of these instruments to changes in pain severity. [112-114] The Graded Chronic Pain Scale (GCPS) and the PEG⁹ three-item scale both meet these criteria. [115] The West Haven-Yale Multidimensional Pain Inventory (WHYMPI) also performs well to assess clinical pain. [111]

The American Chronic Pain Association (ACPA) Quality of Life Ability Scale combines improved function across multiple categories such as work, home, and leisure activities, but this scale has not been validated. However, some providers find this type of inclusion of specific descriptors useful. [116]

3.3.7.2 Clinically Meaningful Improvement in Pain and Function

1. Document clinically meaningful (30% or more) improvement in pain and function or pain interference with function during the acute/subacute pain trial periods as well as during the trial of chronic opioid treatment, prior to initiating chronic opioid treatment. Continuing opioid treatment in the absence of this level of functional improvement is not medically necessary care. [61, 112, 113]
2. Please note that the need to document clinically meaningful improvement in pain and function does not apply to catastrophically injured patients during the recovery period. (See [Section 10, Opioid Use in Catastrophic Injuries](#))

Patients already on chronic opioid treatment may not experience a significant improvement in pain and function from one visit to the next while they are on “maintenance doses” of opioids. In these patients, worsening of pain and/or function following attempts to wean to a lower dose, rather than improved function on a maintenance dose, may be a more appropriate indicator of the effectiveness of the weaning attempt.

Rationale:

The existing guidelines and other evidence reviewed suggest that during chronic opioid treatment, many patients may report modest improvements in pain, but no improvement in function. Functional improvement is a basic tenet guiding the provision of care for injured workers. Clinically meaningful improvement in pain and function is a goal of opioid treatment in the worker population.

⁹ Selected items of the PEG assess average pain intensity (P), interference with enjoyment of life (E), and interference with general activity (G).

3.3.8. Opioid Titration and Dosing Threshold

Opioid titration refers to dose adjustments of opioid medications as required to adequately control pain and improve function. Opioid titration requires regular assessment of the patient's pain and (when used for work-related injuries) functional improvement, as well as the amount of medication used in a defined previous time period.

Decisions to increase opioids should be made jointly by both the provider and the patient. It is the responsibility of the provider to inform the patient that current evidence shows a dose-related increase in adverse events. Consultation with a pain specialist may be considered as clinically warranted.

The guidelines reviewed recommend increased clinical vigilance at daily doses ranging from 50–200 mg/day MED. [7, 54, 59, 60] However, it should be noted that all doses of opioids carry risks and that many deaths associated with opioids have occurred at much lower doses. Note that methadone requires particular attention and care in titration and dosing. (See [Section 8, Methadone](#))

1. Dosage threshold and increases

Providers and patients should recognize that opioid treatment, regardless of dose, carries risks. **For dosages above 80 mg/day MED,¹⁰ providers should be increasingly vigilant, as the known risk of adverse events increases while the evidence for increased benefit remains weak.** [77, 88, 89] In addition to the level of pain, functional improvement, and amount of medication used in a defined previous time period, providers should also document both of the following:

- a. A written patient treatment agreement acknowledging that the patient and provider recognize that there is no safe threshold and that the risk of adverse events is significantly higher at doses above 80 mg/day MED, while the benefit based on available data is unclear. [77, 88, 89] (See [Section 3.3.2, Patient Treatment Agreement and Informed Consent](#), and [Appendix B, Written Opioid Treatment Agreement \[Sample\]](#))
- b. The degree of documented meaningful improvement made by the patient and associated with clear-cut participation in formal return to work activities and/or evidence of independent functioning and self-management. (See [Section 3.3.7.2, Clinically Meaningful Improvement in Pain and Function](#))

¹⁰ To determine the MED dose of any opioid, providers should use an electronic dose calculator. The AMDG Guideline provides a calculator in two formats, web-based and in Excel. (<http://www.agencymeddirectors.wa.gov/opioiddosing.asp>) See also Appendix F3 for additional information on calculating the morphine equivalent dose. The table in Appendix F2 also provides MED dose equivalents for select opioids. See also Section 5, Documentation of Morphine Equivalents.

2. Frequency of visits during titration to a stable dose of opioids for chronic treatment:

- a. During titration, regular face-to-face visits should occur every two to four (2–4) weeks, with ongoing evaluation of progress against pain and toward functional goals, as well as potential side effects and adverse events.
- b. More frequent follow-up visits may occur if coexisting psychiatric problems, drug-behavior problems, or medical problems are suspected or documented, or when titrating doses above 80 mg/day MED, as the risk of adverse effects increases with increasing dose. [77, 88, 89]

3. Criteria for dosage increase:

For each increase in opioid dose among patients receiving chronic opioid treatment, providers must document all of the following:

- a. Agreement: Patient treatment agreement with informed consent regarding risk/benefit of increasing doses. (See [Section 3.3.2, Patient Treatment Agreement and Informed Consent](#), and [Appendix B, Written Opioid Treatment Agreement \[Sample\]](#))
- b. Analgesia: Assess meaningful improvement in level of pain (current, recent, trends, etc.). (See [Section 3.3.7, Monitoring Effectiveness of Chronic Opioid Treatment](#))
- c. Activity: Evaluate meaningful improvement in pain interference or function using validated instruments as well as quality of life. (See [Section 3.3.7, Monitoring Effectiveness of Chronic Opioid Treatment](#))
- d. Adverse events: Assess whether the medication is causing severe side effects. For instance, evidence of severe constipation during the current treatment episode is a clear contraindication for increasing the opioid dose. In the event of an overdose event, the provider should consider discontinuing opioid medication via tapering.
- e. Aberrant behavior: Evaluate for possible drug abuse-related behavior. No evidence should exist for a current substance use disorder. If the patient has had a history of opioid use disorder, the concurrence of an addiction specialist is required to continue opioid treatment as well as for dose escalation. (See [Section 3.3.5, Use of Tools to Monitor Patients on Chronic Opioid Treatment](#), and [Section 3.3.6, Use of Urine Drug Testing](#))

“Analgesia”, “Activity”, “Adverse events”, and “Aberrant behavior” assessments are also known as the “four As.” [117] The criteria prescribed here are a modification of the original criteria, tailored specifically to the California injured worker population.

4. Advise patients at each evaluation regarding responsible storage and disposal of opioid medications. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))
5. Caution patients about the potential adverse effects of opioid medications, including impacts on alertness, when engaging in personal activities. Chronic opioid use is not recommended for patients with safety-sensitive jobs, such as any position involving the operation of heavy equipment or motor vehicles. [82]
6. Due to lack of sufficient evidence to guide outpatient care, the routine prescription of naloxone to patients on chronic opioid treatment is not recommended. Naloxone is recommended in hospital-based and emergency department settings for the treatment of opioid overdose. Refer to the MTUS Chronic Pain Guidelines for more information.

Rationale:

A considerable body of medical evidence links increasing doses of chronic opioid treatment with increases in overdose-related morbidity and mortality and lack of efficacy of dose escalation. [77, 88, 89, 118] The recommendations above, along with the other recommendations in this Guideline, are aimed at reducing adverse events in California's injured workers.

The best data available to date, summarized above, suggest that risks of morbidity and mortality rise substantially at and above 100 mg/day MED. (See [Appendix E, Opioid Dose and Risk of Morbidity and Mortality](#)) These same studies demonstrate that the risk also rises within the dose range 50–100 mg/day MED. [77, 88, 89] However, none of the studies breaks down the risk within the 50–100 dose range to determine a more nuanced dose level above which risk increases. Based on a review of the best and most recently available scientific evidence to date, 80 mg/day MED has been identified in this Guideline as the dose at which increased vigilance should be exercised. [77, 88, 89]

Of note, other states such as Ohio¹¹ and Connecticut¹² have recently implemented guidelines with similar “thresholds.” [119, 120]

3.3.9. Maintenance of Chronic Opioid Treatment

Once a stable dose of opioid has been established (maintenance period), patients should have regular face-to-face visits with their provider (at least every three [3] months is recommended as good practice but alternate schedules may be considered if the need is documented). At these visits, the provider should monitor treatment goals, analgesia, activity (function), adverse effects, and aberrant behaviors.

¹¹ See Ohio's 2013 guideline, which recommends a threshold of 80mg/day
http://www.opioidprescribing.ohio.gov/PDF/OARRS/Print_Prescribing_Guidelinesfor%20.pdf

¹² See Connecticut's 2013 guideline, which recommends a threshold of 90mg/day MED:
<http://wcc.state.ct.us/download/acrobat/protocols.pdf>

1. Consider during chronic opioid treatment:
 - Patients who receive chronic maintenance doses of opioids should not meet criteria for tapering. (See [Section 4.1, Indications for Tapering Opioids](#))
 - Additional testing as may be deemed necessary to monitor and treat patients receiving chronic opioid treatment is considered part of a medically necessary treatment and monitoring program.
2. Document the “four A’s” at each visit during the maintenance phase of chronic opioid treatment. [121] (See [Section 3.3.8, Opioid Titration and Dosing Threshold](#)) If the patient fails to meet any of the following four criteria,¹³ the treatment should be reevaluated, including consideration of tapering. (See [Section 4, Tapering Opioids](#))
 - a. Analgesia: Meaningful improvement in level of pain.
 - b. Activity: Meaningful improvement in pain interference or function.
 - c. Adverse events: Whether the medication is causing severe side effects.
 - d. Aberrant behavior: Current substance use disorder or evidence of diversion. If the patient has had a history of opioid use disorder, the concurrence of an addiction specialist is required to continue opioid treatment as well as for dose escalation.
3. Conduct semiannual attempts to wean to lower than 80 mg/day MED in patients whose dose is above 80 mg/day MED, and who have been on that dose or higher for at least 180 days (i.e., six [6] months). [77, 88, 89]
 - Opioid medication should never be abruptly discontinued in any patient who has been treated for longer than two (2) weeks. In these patients, opioid doses should be reduced gradually as tolerated, while monitoring for symptoms of withdrawal or other adverse impact, including increase in pain, or decrease in function. (See [Section 4.2, Methods for Tapering Opioids](#))
 - Referral to a pain specialist may be considered.
4. Advise patients at each evaluation regarding responsible storage and disposal of opioid medications. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))
5. Recommend that patients on chronic opioid use not perform safety-sensitive jobs, such as operating heavy equipment and motor vehicles. [82] Caution patients about the potential adverse effects of opioid medications, including impacts on alertness, when engaging in personal activities.

¹³ For more discussion of these four terms, see [Section 3.3.8, Recommendations: Opioid Titration and Dosing Threshold](#).

Rationale:

The continued use of chronic opioid treatment in the injured worker should meet the statutory system goals of restoring the patient to full functional status, with the overall goal being improvement of pain, function, and return to work. No specific visit frequency applies to all patients. Select a frequency that allows close follow-up of the patient's adverse effects, pain status, and appropriate use of medication. [59]

3.3.10. Treating Breakthrough Pain (BTP)

Patients who are on opioid treatment for chronic pain and who experience an increase in pain, also known as breakthrough pain (BTP), should undergo a comprehensive assessment for the causative factors, including under-treatment of pain, abnormal sensitivity to pain attributed to opioid use, new pathology, drug diversion, dependency, addiction, abuse, and misuse.

Specific treatment should be based on the results of the assessment and should include, as appropriate to the individual case, education, cognitive behavioral therapy, exercise programs, and the addition of non-opioid medications such as NSAIDs and interventional techniques. (See [Section 3.2, Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment](#))

Rationale:

Research on breakthrough pain in cancer patients exists. However there is significant controversy regarding the nature of BTP in chronic noncancer pain and its optimal treatment. Systematic reviews recommend evaluation of the causes of episodic pain increase and thoughtful management utilizing the principles of chronic pain management. [122]

4. TAPERING OPIOIDS**4.1. Indications for Tapering Opioids**

Tapering, also known as weaning, refers to reducing the gradual reduction of the prescribed dose of opioids to the lowest dose effective in controlling pain and improving function. Opioid-naïve, acute-pain patients who have been treated for two (2) weeks or less can generally discontinue opioid treatment without the need to taper. Acute pain patients should discontinue use of opioids within two (2) weeks whenever possible.

Opioid medication should never be abruptly discontinued in any patient who has been treated for longer than two (2) weeks. In these patients, opioid doses should be reduced gradually as tolerated, while monitoring for symptoms of withdrawal or other adverse impact, including increase in pain, or decrease in function. Referral to a pain specialist may be considered to assist with the weaning process. (See [Section 6, Consultation with Specialists](#))

It is recommended that attempts be made to taper opioids to zero in patients who meet any of the criteria listed below. In situations where there may be clinical indications for tapering to a lower dose (rather than completely off opioids), clinical justification, such as worsened pain or function with even lower doses, should be documented. Patients who have been taking over 80 mg/day MED for over six (6) months and who are making their semiannual weaning attempt need only wean to below 80 mg/day MED. [77, 88, 89] (See [Section 3.3.9, Maintenance of Chronic Opioid Treatment](#))

1. Monitor for criteria for tapering, including the following (and document if any are present):
 - Patient expresses a desire to discontinue therapy.
 - Pain condition has resolved.
 - No documented improvement in pain *and* function (or patient claims a lack of effectiveness) following last increase in dose.
 - Patient does not adhere to the treatment plan (e.g., as detected through urine drug screening or CURES).
 - Illegal or dangerous activity including the following: diversion, prescription forgery, suicide attempt, involvement in a motor vehicle accident and/or arrest related to opioids, aggressive or threatening behavior in the clinic, surreptitious medication use, including use of non-prescribed prescription drugs.
 - Consumption of medication or substances that the patient has been advised not to take concomitantly (sedating medication, alcohol, benzodiazepines). Coordinate care with other providers who may be prescribing these medications.
 - Severe adverse effects or overdose events.
2. Advise patients being tapered off opioids regarding responsible of opioid medications. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))

Rationale:

The guidelines reviewed recommend tapering opioid doses when benefit is not demonstrated or there is likelihood of harm or misuse. Tapering, rather than abrupt cessation of medication, prevents withdrawal symptoms and provides the ability to monitor progress on changing treatment regimens in patients on high doses or who have been treated with opioids for extended periods. The guidelines reviewed universally agree that tapering should be considered when opioids have been ineffective, when serious adverse events have occurred, or when aberrant or illegal behaviors have occurred. [54, 56, 58, 60, 61]

4.2. *Methods for Tapering Opioids*

1. Complete a comprehensive assessment of the patient, including history of condition and treatment as well as comorbidities.
2. Provide to the patient and family oral and written instructions reflecting the tapering regimen chosen, including advice that the weaning process could take months.
3. Use a two-step algorithm method of tapering for all patients except those meeting Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria for substance use disorder [61]:
 - a. Step 1: Taper in outpatient setting using 10%–25% per week taper, with or without buprenorphine (Suboxone) support after opioid has ended. Patients should be periodically evaluated in an office setting, for example, every two to four (2–4) weeks. These cases may require pain medicine specialty and psychological support. Clonidine or other adjunctive agents may be used to provide further support.
 - b. Step 2: Patients who fail Step 1 may be referred to an addiction specialist or, if they are at higher risk, may be offered an inpatient detox, accompanied by a multidisciplinary pain program lasting up to four (4) weeks (20 full days or 160 hours), or the equivalent in part-time day sessions if required by the patient's other family and work responsibilities. The pain program may occur at the same time as the inpatient detox or in an outpatient setting right after the detox. Additionally, patients who have coexisting cardiorespiratory or other comorbid conditions that may make outpatient tapering dangerous should be tapered in an inpatient setting. Refer to MTUS Chronic Pain Guidelines for additional information.
4. Patients who meet the DSM-V criteria for substance use disorder should be treated by an addiction specialist, preferably concurrently with a pain medicine specialist. Treatment may include therapy in an inpatient multidisciplinary pain program or a dedicated inpatient substance abuse center. Maintenance therapy may be needed for six (6) months or longer, depending on circumstances. In this population, tapering down to zero may require several tapering periods that occur over several months.
5. **Never abandon** a patient for whom tapering is indicated. Patient abandonment is defined by the American Medical Association as “termination of a professional relationship between provider and patient at an unreasonable time and without giving the patient the chance to find an equally qualified replacement.” [123]
6. Advise patients being tapered off opioids regarding responsible storage and disposal of opioid medications. (See [Section 11, Responsible Storage and Disposal of Opioid Medications](#))

Rationale:

While the guidelines vary in their specific tapering regimens, they consistently recommend gradual, consistent tapers over a period of weeks to months and under careful supervision. [7, 56, 61, 124]

5. DOCUMENTATION OF MORPHINE EQUIVALENTS

The total opioid dose should be documented as morphine equivalent dose (MED) in mg/day at every patient visit. [6] Online dosing calculators may be used for this purpose. (See [Appendix F3, Morphine Equivalent Dose Calculation](#))

- Use an opioid dosing calculator to tracking the total morphine equivalent dose, along with pain and function, at patient visits. [60] Online dosing calculators permit calculation of prescribed opioids and should only be used to estimate the MED/day. (See [Appendix F3, Morphine Equivalent Dose Calculation](#))
- Do not use online dosing calculators to convert from one opioid *directly* to another, since the conversions are complex. Dosing thresholds for select opioids are presented in [Appendix F1, Dosing Thresholds for Selected Opioids](#), to facilitate conversion or rotation. To assure patient safety, it is recommended that the dose be reduced by 25–50% after calculating the appropriate conversion dose. As an added precaution, consultation with a practitioner who has relevant knowledge and experience (such as a pain specialist) may also be considered when converting from one opioid to another.

Rationale:

Several guidelines recommend using a dosing calculator to document dosage as mg/day MED at each visit, as well as consulting CURES. These practices allow the primary prescriber to know the exact dosing and ascertain compliance. [57, 60]

6. CONSULTATION WITH SPECIALISTS

The prescribing provider may find it useful to obtain consultation with specialist, including, but not limited to, those in pain medicine, psychiatry/behavioral medicine, and addiction medicine, at any time it is deemed necessary to assist with medical management during chronic opioid treatment. The purpose of such a consultation would be to assist with the complex issues related to the care of patients at all stages of pain.

Consultation may be considered medically necessary in the following situations, based on clinical assessment:

- At the acute or subacute phase, to help assess the risk-benefit ratio of using opioids to treat the pain of high-risk patients.
- To aid with a complex pain condition when there is a need for help with a diagnosis or verification of a diagnosis. (See [Section 3.1 Comprehensive Evaluation and Assessment of Patient](#))

- At the time of initiation or trial of chronic opioid treatment. (See [Section 3.3.3 Initiation of Chronic Opioid Treatment](#))
- To assist in the management of a patient with significant comorbidities.
- To assist with the assessment of risk-benefit ratio of chronic opioid treatment when the criteria for dose escalation are met and the prescribing provider requires additional assistance. (See [Section 3.3.8, Opioid Titration and Dosing Threshold](#))
- To assist with monitoring of adherence to the prescribed analgesic regimen. (See [Section 3.3.5, Use of Tools to Monitor Patients on Chronic Opioid Treatment](#))
- When the provider suspects development of significant tolerance to opioids, particularly at higher doses.
- To assist with the assessment and/or treatment of aberrant behavior or repeated, questionable UDTs. (See [Section 3.3.6, Use of Urine Drug Testing](#))
- To assist in converting from one opioid to another, as needed. (See [Section 5, Documentation of Morphine Equivalents](#))
- To assist with management of patients meeting DSM-V criteria for substance use disorder. (See [Section 4.2, Methods for Tapering Opioids](#))
- To assist with tapering or weaning regimens. (See [Section 3.3.9, Maintenance of Chronic Opioid Treatment](#), and [Section 4.2, Methods for Tapering Opioids](#))
- When clinical assessment indicates that psychiatric or behavioral factors may be impairing recovery and/or prolonging disability.

Rationale:

Primary care providers report greater confidence in appropriately managing complex patients and those on chronic opioid treatment when they have access to specialists with pain management expertise. [91]

7. CONCURRENT USE OF BENZODIAZEPINES AND OTHER SEDATIVE HYPNOTICS

Clinical practice should include all of the following:

1. Avoid introducing concomitant central nervous system (CNS) depressants to chronic opioid treatment regimens, including alcohol, benzodiazepines and non-benzodiazepine sedatives, such as carisoprodol (Soma). Throughout the time when they are on opioids (starting with their first prescription), patients should be counseled to avoid simultaneous use of opioids with non-opioid CNS depressants, including alcohol and sedatives. Coordinate care with other providers who may be prescribing these medications.

2. Prescribe central muscle relaxants such as baclofen or tizanidine with extreme caution for patients receiving chronic opioid treatment or other opioid regimens, and carefully monitor patient for side effects upon introduction of a new drug to a regimen or during periods of dose adjustment/escalation.
3. Counsel patient to stagger dosing to avoid excess sedation and potentially disastrous complications if, after careful consideration, the clinical decision is made to prescribe other sedatives or muscle relaxants to patients on chronic opioid treatment.

Rationale:

The available body of literature demonstrates that simultaneous use of opioids and sedating medications, particularly benzodiazepines, is associated with an increased risk of fatal overdose events. [32, 34, 125, 126]

8. METHADONE

1. The use of methadone is indicated for the following types of patients [127]:
 - Patients who have experienced inadequate pain control on previous opioid treatment regimens with dose-limiting side effects.
 - Patients experiencing confusion, hallucinations, or delirium on previous opioid treatment (often indicating opioid toxicity).
 - Patients at high risk for adverse effects to other opioids (e.g., those who have had previous anaphylaxis to morphine or COPD patients with history of CO₂ retention).
 - Patients with opioid intolerance.
2. Methadone is characterized by a narrow therapeutic window with complicated and variable pharmacokinetics and pharmacodynamics. As a result, only providers who have substantial experience with its use and risks and are prepared to conduct the necessary careful monitoring should initiate methadone treatment and do methadone titration. [54, 58]
3. Methadone is a last-line drug that should be started at low doses and titrated slowly. The recommended starting dose is indicated in [Appendix F1, Dosing Thresholds for Selected Opioids](#), with dose increases occurring no more frequently than weekly. In older patients or those with renal or hepatic comorbidities, less frequent dosing and more cautious dose titration are recommended. [54]
 - Extra caution is warranted in patients at risk for prolonged QTc interval, including those with structural cardiac disease, cardiac arrhythmias, or cardiac conduction abnormalities, and in patients taking another medication associated with QTc interval prolongation. [127] Providers should consider obtaining an electrocardiogram (ECG) to evaluate the QTc interval in patients treated with methadone, especially at higher doses (80 mg/day MED or greater).

[Appendix D, Select Black Box Warnings: Important Safety Information on Long-Acting Opioids](#), points out black box warnings on methadone, as well as other opioid medications.

Rationale:

The available literature indicates that methadone is an option when pain relief has not been obtained or intolerable side effects limit the use of other opioids. Because significant toxicity may occur with inappropriate dosing decisions, methadone should be used with caution. [61]

9. MANAGING PERI-OPERATIVE PAIN IN WORKERS ON CHRONIC OPIOID TREATMENT UNDERGOING ELECTIVE SURGERY

Chronic opioid treatment prior to surgery is a risk factor for prolongation of opioid use post-operatively. [128] In general, patients on chronic opioid treatment will report higher pain scores and manifest more anxiety than other patients. [128-130] They will also likely require higher opioid doses in the intra and post-operative period. Patients receiving chronic opioid treatment undergoing surgery also have more frequent and more deadly respiratory depressive episodes than opioid-naïve patients. [128] However, there is a paucity of data on best management practices for use of peri-operative opioids in these patients in whom elective surgery is planned.

Managing pain in workers on chronic opioid treatment who are undergoing elective surgeries presents unique challenges and requires a coordinated treatment plan for pain management prior to surgery. This requires a collaborative effort involving the surgeon, anesthesiologist, pain management specialist, attending provider and the worker.

Evidence is lacking regarding the advisability of tapering opioids in patients receiving chronic opioid treatment before elective surgery.

1. Before surgery (pre-operatively), the surgeon and attending provider should

- a. Have a coordinated treatment plan for managing surgical pain, including identifying the post-operative opioid prescriber.
- b. Obtain a pre-operative anesthesia consult one to two (1–2) weeks prior to surgery.
- c. Obtain consultation for special anesthesia care for patients on buprenorphine (Suboxone) at least two (2) weeks before surgery.
- d. Access CURES and review the patient's controlled substance history to get accurate information on opioid dose and concurrent medication use; discuss any apparent discrepancies with the patient.

- e. Prepare the patient for elective surgery by setting appropriate expectations for pain management. Patients need reassurance that their pain management needs will be met, and they need to know that their opioid use is expected to return to the pre-operative dose, or less, following surgery.
 - f. Avoid escalating opioid dose before surgery.
 - g. Advise patient not to take any benzodiazepines or sedative-hypnotics. Coordinate care with other providers who may be prescribing these medications
 - h. For opioid dose and pain management, as well as the advisability of pre-operative urine drug screening, consider a consult with a pain medicine specialist before surgery for patients on high-dose opioids or those who have comorbid mental health conditions or substance use disorder.
- 2. Day of surgery (intra-operatively), the anesthesiologist should**
- a. Use anti-inflammatory medications, acetaminophen, or both, if not contraindicated.
 - b. Continue pre-operative opioids to decrease the risk of withdrawal symptoms and use regional blocks, if appropriate.
 - c. Consider the use of other non-opioid analgesic adjuncts (e.g. gabapentin, ketamine or lidocaine) for opioid-sparing effects.
- 3. After surgery (post-operatively), the surgeon or hospitalist and attending provider should**
- a. Continue pre-operative opioids, with extra analgesia for acute pain via patient-controlled analgesia (PCA) while hospitalized.
 - b. Use care when transitioning from PCA to oral opioids. DO NOT perform a “straight” conversion from intravenous to oral opioids because of a lack of complete cross-tolerance.
 - c. Expect the patient to need more time than other patients to stabilize pain control after transitioning to oral opioids.
 - d. Do not prescribe long-acting or extended-release opioids for post-operative pain unless the patient was previously maintained on these drugs.
 - e. Avoid new sedative-hypnotics and benzodiazepines.

- f. Taper total opioids to pre-operative dose or lower by six (6) weeks, unless extenuating circumstances exist. Provide documentation to justify continued use of opioids at doses higher than pre-operative levels for up to 12 weeks.
- g. For appropriate post-operative pain management of patients on high dose opioids or those who have comorbid mental health or substance use disorder, consider consultation with an addiction or pain medicine specialist.

Rationale:

These recommendations are based on the available guidelines addressing pre-, peri-, and post-operative management of patients on chronic opioid treatment. They balance the need for pain control with the desire to decrease adverse effects and prevent post-operative dose escalation. [7, 61]

10. OPIOID USE IN CATASTROPHIC INJURIES

Catastrophic injuries in which significant recovery of physical function is not expected, such as severe burns, crush, or spinal cord injury, are exempt from many of the recommendations in this guideline. For example, clinically meaningful functional improvement may not occur following catastrophic injury.

For catastrophic injuries, chronic opioid treatment may be appropriate after the prescriber has documented all of the following:

1. A current signed treatment agreement. (See [Section 3.3.2, Patient Treatment Agreement and Informed Consent \[Sample\]](#))
2. Stable opioid dose at or below 80 mg/day MED.
3. When opioid dose is above 80 mg/day MED, a consultation with a pain specialist before further dose escalation.
4. Worker has no contraindication to the use of opioids:
 - a. No evidence of serious adverse outcomes from opioid use.
 - b. No aberrant behavior identified through CURES or urine drug screening. (See [Section 3.3.4, Use of CURES to Ensure Safe and Effective Opioid Use](#), and [Section 3.3.6, Use of Urine Drug Testing](#))
 - c. If any of the above conditions exist, provider must provide adequate justification of the need for chronic opioid treatment.

Rationale:

Adequate pain control helps the healing and recovery process and is of primary concern following catastrophic injuries. This need should be balanced with practices aimed at minimizing the adverse effects of unmitigated long-term opioid use.

11. RESPONSIBLE STORAGE AND DISPOSAL OF OPIOID MEDICATIONS

Patients should be counseled regarding responsible storage and disposal of opioid medications at the initial visit and reminded at every visit.

Patients should be given the following specific advice:

1. Securely store the medications in bottles with child-resistant lids.
2. Do not share the medications with others.
3. Keep all opioid medications in a single location where a pet, child, teenage, or visitor would not easily have access to them.
4. Fold used fentanyl skin patches in half and then dispose of them safely.
5. Properly dispose of the medications when the pain has resolved:
 - a. Take all of the medication out of its container. Put the medication in a sealable container, such as a plastic bag or coffee can.
 - b. Mix the medication with an undesirable substance such as cat litter or used coffee grounds. **Do not** crush pills, tablets, or capsules.
 - c. Seal the container and be sure to put it in the trash, not in recycling bins.
 - d. Remove the label or completely cross out any personal information before putting an empty container in the recycling bin or trash. This will help protect your identity.
 - e. If you have questions about disposing of your medicine, ask your doctor, pharmacist, or call 1-888-INFO-FDA (1-888-463-6332).

Rationale:

Any medication can be extremely harmful when taken by someone other than the patient. It is essential that patients and caregivers be aware of safe storage and disposal methods.

APPENDICES

A. [Brief, Validated Tools](#)

A1. Tools to Screen for High-Risk Patients

- a. [Opioid Risk Tool \(ORT\)](#)
- b. [Cut down, Annoyed, Guilty, Eye-Opener \(CAGE-AID\)](#)
- c. [Two-ITEM Conjoint Screen \(TICS\)](#)
- d. [Patient Health Questionnaire \(PHQ\)](#)

A2. Tools for Tracking Pain and Function: Pain Interference Scales

- a. [Pain Numeric Rating Scale](#)
- b. [The PEG¹⁴ three-item scale](#)
- c. [Graded Chronic Pain Scale \(GCPS\)](#)
- d. [Brief Pain Inventory \(BPI\)](#)

B. [Sample of a Written Opioid Treatment Agreement \(Sample\)](#)

C. [Guidance on Conducting and Interpreting Urine Drug Testing \(UDT\)](#)

D. [Select Black Box Warnings](#)

E. [Opioid Dose and Risk of Morbidity and Mortality](#)

F. [Opioid Dose Calculations](#)

- F1. [Dosing Thresholds for Selected Opioids](#)
- F2. [Equianalgesic Dose Table for Converting Opioid Doses](#)
- F3. [Morphine Equivalent Dose \(MED\) Calculation](#)

G. [Chart: Summary of Screening Recommendations](#)

[Definition of Key Terms](#)

[Acronyms](#)

¹⁴ PEG = Selected items assess average pain intensity (P), interference with enjoyment of life (E), and interference with general activity (G).

Appendix A. Brief, Validated Tools

A1. Tools to Screen for High-Risk Patients

- a. [Opioid Risk Tool \(ORT\)](#)
- b. [Cut down, Annoyed, Guilty, Eye-opener \(CAGE-AID\)](#)
- c. [Two-ITEM Conjoint Survey \(TICS\)](#)
- d. [Patient Health Questionnaire \(PHQ\)](#)

A2. Tools for Tracking Pain and Function: Pain Interference Scales

- a. [Pain Numeric Rating Scale](#)
- b. [The PEG¹⁵ Three-Item Scale \(Short Survey\)](#)
- c. [Graded Chronic Pain Scale \(GCPS\) \(Longer Survey\)](#)
- d. [Brief Pain Inventory \(BPI\)](#)

¹⁵ PEG = Selected items assess average pain intensity (P), interference with enjoyment of life (E), and interference with general activity (G).

Appendix A1a. Opioid Risk Tool (ORT)¹⁶

Date _____

Patient Name _____

OPIOID RISK TOOL[®]

		Mark each box that applies	Item Score If Female	Item If Male
1. Family History of Substance Abuse	Alcohol	[]	1	3
	Illegal Drugs	[]	2	3
	Prescription Drugs	[]	4	4
2. Personal History of Substance	Alcohol	[]	3	3
	Illegal Drugs	[]	4	4
	Prescription Drugs	[]	5	5
3. Age (Mark box if 16–45)		[]	1	1
4. History of Preadolescent Sexual Abuse		[]	3	0
5. Psychological Disease	ADD, OCD	[]	2	2
	Bipolar, Schizophrenia			
6. Depression		[]	1	1
TOTAL		[]		

¹⁶ Source: Webster LR, Webster R. Predicting aberrant behaviors in Opioid-treated patients: preliminary validation of the Opioid risk tool. Pain Med. 2005;6(6):432

Tips on Administrating ORT:

Total Score Risk Category Low Risk 0–3 Moderate Risk 4–7 High Risk ≥ 8

If a psychologist administers the test (as opposed to having the patient complete the form independently), the results of the test are more likely to give an accurate prediction of aberrant drug-taking behavior. [131, 132]

DRAFT

Appendix A1b. CAGE-AID Questionnaire¹⁷

Patient Name _____ Date of Visit _____

When thinking about drug use, include illegal drug use and the use of prescription drug other than prescribed.

Questions:	YES	NO
1. Have you ever felt that you ought to cut down on your drinking or drug use?	<input type="checkbox"/>	<input type="checkbox"/>
2. Have people annoyed you by criticizing your drinking or drug use?	<input type="checkbox"/>	<input type="checkbox"/>
3. Have you ever felt bad or guilty about your drinking or drug use?	<input type="checkbox"/>	<input type="checkbox"/>
4. Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover?	<input type="checkbox"/>	<input type="checkbox"/>

Scoring

Regard one or more positive responses to the CAGE-AID as a positive screen.

Psychometric Properties

The CAGE-AID exhibited:	Sensitivity	Specificity
One or more Yes responses	0.79	0.77
Two or more Yes responses	0.70	0.85

(Brown 1995)

Appendix A1c. Two-Item Conjoint Screen (TICS) for Alcohol and Other Drug Problems¹⁸

¹⁷ To access this tool, visit <http://www.integration.samhsa.gov/images/res/CAGEAID.pdf>. Used with permission.

¹⁸ Source: <http://www.mirecc.va.gov/visn22/TICS.pdf>. Used by permission. (Brown 2001)

1. In the last year, have you ever drunk or used drugs more than you meant to?
2. Have you felt you wanted or needed to cut down on your drinking or drug use in the last year?

Scoring and interpretation

One or more affirmative response indicates a need for more in-depth assessment.

DRAFT

Appendix A1d. Patient Health Questionnaire-PHQ-9*

1. Over the last 2 weeks, how often have you been bothered by any of the following problems?

(Please circle your answer)

	Not at all	Several days	More than half the days	Nearly every day
a. Little interest or pleasure in doing things	0	1	2	3
b. Feeling down, depressed, or hopeless	0	1	2	3
c. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
d. Feeling tired or having little energy	0	1	2	3
e. Poor appetite or overeating	0	1	2	3
f. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
g. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
h. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
i. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

*PHQ-9 developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

Source: <http://www.agencymeddirectors.wa.gov/Files/depressionform.pdf> (WA AMDG 2010)

(continued)

2. If you indicated any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult
at all

Somewhat
difficult

Very
difficult

Extremely
difficulty

DRAFT

Appendix A1d. Patient Health Questionnaire-PHQ-9 (continued)

How to Score PHQ-9

Scoring Method for Diagnosis

Major Depressive Syndrome is suggested if:

- Of the 9 items, 5 or more are circled as at least "More than half the days"
- Either item 1a or 1b is positive, that is, at least "More than half the days"

Scoring Method for Planning and Monitoring Treatment

Minor Depressive Syndrome is suggested if:

- Of the 9 items, b, c, or d is circled as at least "More than half the days"
- Either item 1a or 1b is positive, that is, at least "More than half the days"

Question One

- To score the first question, tally each response by the number value of each response:
Not at all = 0
Several days = 1
More than half the days = 2
Nearly every day = 3
- Add the numbers together to total the score.

Question Two

In question two the patient responses can be one of four: not difficult at all, somewhat difficult, very difficult, extremely difficult. The last two responses suggest that the patient's functionality is impaired.

Appendix A1: Tools to Screen for High-Risk Patients

After treatment begins, the functional status is again measured to see if the patient is improving.

- Add the numbers together to total the score.
- Interpret the score by using the guide listed below

Score	Action
≤ 4	The score suggests the patient may not need depression treatment.
> 5– 14	Physician uses clinical judgment about treatment, based on patient's duration of symptoms and functional impairment.
≥ 15	Warrants treatment for depression, using antidepressant, psychotherapy and/or a combination of treatment

Appendix A2: Tools for Tracking Pain and Function: Pain Interference Scales

Appendix A2c. Graded Chronic Pain Scale (GCPS) (Longer Survey)²²

1. How would you rate your facial pain on a 0 to 10 scale at the present time, that is, right now, where 0 is “no pain” and 10 is “pain as bad as could be”?

No pain Pain as bad as could be
0 1 2 3 4 5 6 7 8 9 10

2. In the past six months, how intense was your worst pain, rated on a 0 to 10 scale where 0 is “no pain” and 10 is “pain as bad as could be”?

No pain Pain as bad as could be
0 1 2 3 4 5 6 7 8 9 10

3. In the past six months, on the average, how intense was your pain rated on a 0-10 scale where 0 is “no pain” and 10 is “pain as bad as could be”? (That is you usual pain at times you were experiencing pain.)

No pain Pain as bad as could be
0 1 2 3 4 5 6 7 8 9 10

4. In the past six months, how much has facial pain interfered with your daily activities rated on a 0 to 10 scale where 0 is “no interference” and 10 is “unable to carry on any activities”?

No interference Unable to carry on any activities
0 1 2 3 4 5 6 7 8 9 10

(continued)

²² Source: Von Korff M, Ormel J, Keefe FJ et al. Grading the severity of chronic pain. Pain 1992; 50:133-149. Used with permission.

Appendix A2: Tools for Tracking Pain and Function: Pain Interference Scales

5. In the past six months, how much has facial pain changed your ability to take part in recreational, social and family activities, where 0 is “no change” and 10 is “extreme change”?

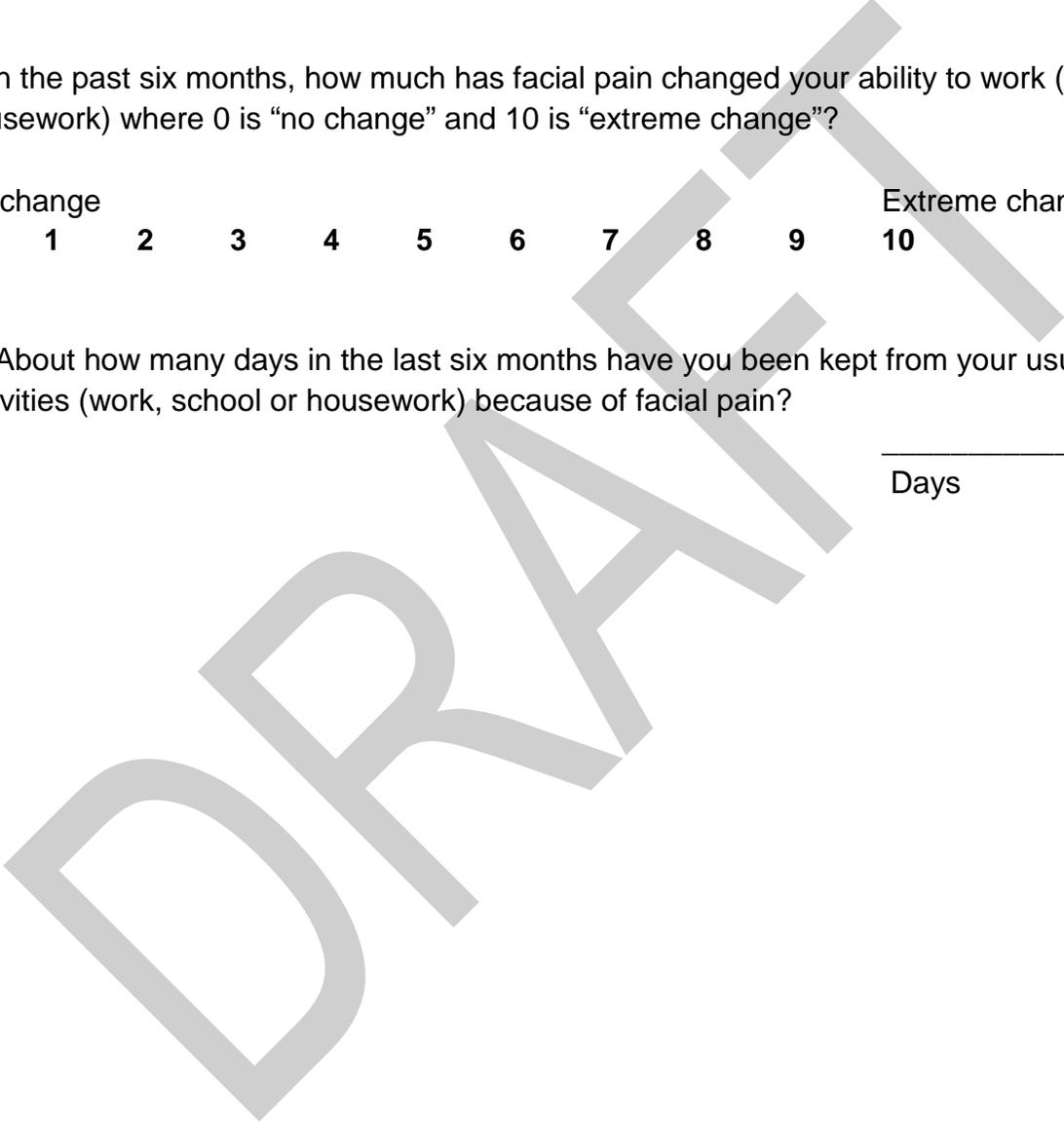
No change
0 1 2 3 4 5 6 7 8 9 10 Extreme change

6. In the past six months, how much has facial pain changed your ability to work (including housework) where 0 is “no change” and 10 is “extreme change”?

No change
0 1 2 3 4 5 6 7 8 9 10 Extreme change

7. About how many days in the last six months have you been kept from your usual activities (work, school or housework) because of facial pain?

_____ Days



Appendix A2: Tools for Tracking Pain and Function: Pain Interference Scales

Appendix A2c. Grading Chronic Pain Severity (continued)

Scoring Criteria for Grading Chronic Pain Severity

Characteristic Pain Intensity is a 0 to 100 score derived from Questions 1 through 3:

Mean (Pain Right Now, Worst Pain, Average Pain) X 10

Disability Score is a 0 to 100 score derived from Questions 4 through 6:

Mean (Daily Activities, Social Activities, Work Activities) X 10

Disability Points: Add the indicated points for Disability Days (Question 7) and for Disability Score.

Disability Days (0–180 Days)		Disability Points Disability Score (0–100)	
0-6 Days	0 Points	0–29	0 Points
7–14 Days	1 Point	30–49	1 Point
15-30 Days	2 Points	50–69	2 Points
31+ Days	3 Points	70+	3 Points

Classification

Grade 0	No TMD pain in prior 6 months	
Grade 1		
Low Intensity	Characteristic Pain Intensity	<input type="checkbox"/> 50
Low Disability	< 3 Disability Points	
Grade II		
High Intensity	Characteristic Pain Intensity	<input type="checkbox"/> 50
Low Disability	< 3 Disability Points	
Grade III		
High Disability	3 to 4 Disability Points	
Moderately Limiting	(Regardless of Characteristic Pain Intensity)	
Grade IV		
High Disability	5 to 6 Disability Points	
Severely Limiting	(Regardless of Characteristic Pain Intensity)	

Appendix B. Written Opioid Treatment Agreement (Sample)

OPIOID TREATMENT AGREEMENT

Patient name (print): _____

Phone number where I may be reached within 24 hours: _____

Prescriber name (print): _____

Medical condition requiring opioid: _____

Planned opioid medication: _____

Name and phone of pharmacist: _____

I (patient) understand the following (initial each):

- _____ I understand this agreement applies to opioid medications. Common examples include, but are not limited to: oxycodone (e.g., Percocet), hydrocodone (e.g., Vicodin), hydromorphone (Dilaudid), morphine, fentanyl (e.g., Actiq), codeine (e.g., Tylenol with codeine), methadone, tramadol (e.g., Ultram), and buprenorphine (Suboxone).
- _____ I understand that opioids are prescribed to see if they increase my function, including my ability to work, perform household chores, or otherwise regain activities.
- _____ I understand that opioids are only one part of my treatment program.
- _____ I understand that opioids may slightly reduce pain levels. Opioids will **not** eliminate chronic pain and are unlikely to produce major improvements in pain.
- _____ I understand that opioid medications have all of the following reported adverse effects (see Table 1).
Many, but not all of these risks increase with higher doses.
- _____ I have had an opportunity to discuss these risks with my prescriber. I accept these risks.

Table 1. Adverse Opioid Effects by Organ System

System	Example(s) of Effect
Circulatory	Heart attack or sudden death
	Fainting on standing up
	Sudden death due to abnormal heart rhythm
Digestive	Nausea
	Constipation, bowel obstruction
	Stomach pain
Endocrine	Impotence or reduced sex drive, erectile dysfunction, and feminization in men
	Abnormal menstrual periods and infertility in women
	Osteoporosis, reduced muscle mass, reduced strength
	Fatigue, low blood pressure, electrolyte changes
Immune	If cancer is present, spread of tumor may hasten death
	Allergic reactions to medication: Rash, shortness of breath, itchy skin, edema
Nerves/ Psychiatric	Addiction
	Tolerance, requiring higher doses to achieve same effect of pain reduction
	Increased pain sensitivity
	Drowsiness , slower reaction time, unsafe operation of machinery, motor vehicle crashes
	Headache
	Outbursts, inappropriate behavior, violence, reduced impulse control
	Alterations in executive function, emotional response
	Reduced pleasure in eating, weight loss
	Problems thinking clearly, mistaken judgment, changed interactions with other people
	Depression, altered mood, suicidal thoughts
	Brain damage: slight to severe impairments if an overdose occurs
	Seizures
	Overdose, death
Reproductive	Birth defects, miscarriage
	Opioid withdrawal symptoms in newborn babies of mothers on opioids

Appendix B: Written Opioid Treatment Agreement (Sample)

Respiratory	Reduced ability to breath during sleep; could lead to death
	New or increased problems with obstructive sleep apnea; daytime sleepiness
	Pneumonia
	Worsening asthma and chronic obstructive pulmonary disease (COPD)
Urinary	Urinary retention
General	Reduced sense of balance, falls, fractures
	Physical dependence (defined below)

_____ Opioids will be initially prescribed to me on a trial basis. The primary goal of this treatment is to improve my ability to perform various functions, including return to work, household chores or other physical or mental activities. If significant demonstrable improvement in my functional capabilities does not result from this trial, my prescriber will likely end the trial.

Goal for improved function: _____

_____ Opioids may also be prescribed to make my pain more tolerable, but these medications may not cause the pain to disappear entirely.

_____ Drowsiness and slowed reflexes may be temporary or ongoing adverse effect of opioids, especially during dosage adjustments. If I am experiencing drowsiness while taking opioids, I agree not to drive a vehicle or perform other tasks that could involve danger to myself, family members, coworkers, or others.

_____ Increased motor vehicle crashes have been reported in many studies among those taking opioids on a chronic basis. Especially for this reason, workers performing safety sensitive jobs are frequently precluded by their employers from performing those jobs while taking opioids. If I am employed in a safety sensitive job, I will check with my employer to make sure this medication does not prevent me from working.

_____ Using opioids to treat chronic pain will result in the development of a **physical dependence** on this medication, and sudden decreases or discontinuation of the medication will lead to symptoms of opioid withdrawal. **Symptoms of withdrawal** may include nervousness, anxiety, difficulty sleeping, runny nose, yawning, large pupils, goose bumps, abdominal pain and cramping, diarrhea, vomiting, irritability, aches, and flu-like symptoms. I understand that symptoms of opioid withdrawal are uncomfortable but not physically life threatening. Withdrawal can be extremely difficult and last a long time.

_____ In order to reduce the severity of withdrawal symptoms, opioids may need to be slowly reduced, or tapered, to a lower dose under the direction of the prescriber.

Appendix B: Written Opioid Treatment Agreement (Sample)

_____ There is a risk that opioid addiction may occur. This most commonly occurs in, but is not limited to, patients with a personal or family history of other drug or alcohol abuse. If my prescriber of opioids believes I may be developing addiction, I should expect that I will be taken off opioids.

I agree to the following (initial each):

_____ I agree to take the medication, _____ (name) as prescribed. If problems arise, including adverse effects, I agree to promptly notify my prescriber.

_____ I agree to obtain opioids from **one** designated licensed prescriber.

_____ I understand that refills may be prescribed at in-person appointments (not over the phone, through the mail or by calling the pharmacist), depending on my doctor's evaluation. Refills are not guaranteed.

_____ I agree to obtain opioids from **one** designated licensed pharmacist or pharmacy. I agree to notify my provider immediately if I change pharmacies.

_____ By signing this agreement, I give consent to this provider to talk with the pharmacist, listed above, and to provide him/her with a copy of this agreement.

_____ I agree to take the following non-opioid medication(s) as prescribed for treatment of pain:

_____ I agree to **not** take more opioid medication than prescribed. I agree to **not** take doses of opioids more frequently than prescribed.

_____ I agree to have a working phone number where clinic staff can reach me within 24 hours. I agree to update the clinic anytime I move or change my phone number.

_____ I agree to let my other health care providers know that I am taking these pain medications and that I have a pain management agreement.

_____ I agree to attend and fully participate in all appointments, treatments, examinations, and consultations of my pain treatment which may be requested by my prescriber at any time.

_____ I agree to attend and fully participate in a regular exercise program if required. My specific exercise program is: _____.

_____ I agree to participate in fear avoidance belief training and/or cognitive behavior therapy, if prescribed.

_____ I will participate fully in any psychiatric or psychological assessments, if required.

_____ I agree to keep my scheduled appointments and/or cancel my appointment a minimum of 24 hours prior to the appointment.

Appendix B: Written Opioid Treatment Agreement (Sample)

_____ I understand that lack of improvements in function or a later loss of those functional benefit(s) are reasons or my prescriber to discontinue opioid medications.

_____ I agree that in the event of an emergency potentially requiring pain medication, I will notify the emergency room or other treatment facility of this agreement. I will ask that my designated prescriber be contacted and discuss the problem with the emergency room or other treating provider. I agree that no more than three (3) days of medications may be prescribed by the emergency room or other provider without this provider's approval. If a situation arises in which I have no alternative but to obtain my necessary prescription from another prescriber (e.g., out of the country), I will then immediately advise my prescriber that I obtained a prescription from another prescriber.

_____ I agree to keep the opioid medication in a safe and secure place. I will keep all medications from children.

_____ I understand that lost, damaged, or stolen medication will **not** be replaced.

_____ I agree to immediately report stolen opioid medication(s) to the police. My provider will also produce a police report if requested to do so.

_____ I agree not to share, sell, or in any way provide my medication to **any** other person.

_____ I agree to not use **any** other mood-modifying drugs, including alcohol (and marijuana regardless of its legal status in my state), unless agreed to by my prescriber. The moderate use of nicotine and caffeine are exceptions to this restriction.

_____ I agree to not use sedating over-the-counter medications, including diphenhydramine (e.g., Benadryl).

_____ Prior to taking any medication that has a warning label stating that it causes drowsiness or sleepiness, I agree to discuss the medication with my prescriber. This includes, but is not limited to, prescription drugs such as alprazolam (brand name Xanax, among others), valium (brand name Valium, among others), and triazolam (brand names Halcion, Rilamir)

_____ I agree to submit to unscheduled urine, blood, or saliva drug testing at my prescriber's request, to verify my compliance with the prescribed medication regimen.

_____ I agree that an abnormal urine, blood, or saliva test will likely result in an end to the treatment with opioids. This includes a finding of a substance not expected (e.g., marijuana and/or illicit drugs).

_____ I understand that, if applicable, my prescriber may check the California Controlled Substance Utilization Review and Evaluation System (CURES) at any time to check my compliance with the treatment plan.

_____ I agree to be seen by a specialist, such as a pain or addiction specialist, if requested by my provider.

Appendix B: Written Opioid Treatment Agreement (Sample)

_____ I hereby agree that my provider has the authority to discuss my pain and opioid management with other health care professionals and my family members and/or significant others when it is deemed medically necessary in the provider's judgment. I agree to involve family and/or significant others in periodic assessments of my progress.

I have read this document. I understand it and have had all my questions answered satisfactorily. I consent to the use of opioids to improve my daily functioning through controlling my pain. I understand that my treatment with opioids will be carried out as described above. I understand that ANY deviation(s) from the above agreement are grounds for my prescriber to stop prescribing opioids at any time.

Patient Signature

Date

Prescriber Signature

Date

This Opioid Treatment Agreement is adapted from ACOEM's Occupational Medicine Practice Guidelines, 3rd edition, Copyright © 2008–2014 by Reed Group, Ltd. Adapted with permission from Reed Group, Ltd., www.disabilityguidelines.com. All other rights reserved. Additional sources include the Southern Oregon Opioid Prescribing Guidelines, 2013 and the Washington State Agency Medical Director's Group (AMDG) Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain, 2010.

Appendix C. Guidance on Conducting and Interpreting Urine Drug Testing (UDT)

The following information is Recommendation 3 (R03) from the Canadian Guideline for Safe and Effective Use of Opioids for CNCP, which can be found at http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf. (Canada 2010)

R03 When using urine drug screening (UDS) to establish a baseline measure of risk or to monitor compliance, be aware of benefits and limitations, appropriate test ordering and interpretation, and have a plan to use results. (Grade C).

In the context of using opioids for treating CNCP, UDS can be used to as a tool for: 1) setting a baseline measure of substance use that may help assess risk for addiction, and 2) ongoing monitoring of the patient's compliance with opioids prescribed. However, opinions regarding UDS utility vary.

1. Types of Urine Drug Screening (UDS)²³

1.1 Point-of-care Testing

For point-of-care (POC) testing, the urine sample is collected and tested at the physician's office/clinic.

- POC test kits are available for purchase; urine dipsticks are required.
- Results are immediate, but it tends to be less sensitive and specific than laboratory tests.

1.2 Laboratory Testing

For laboratory testing, the urine sample is collected at physician's office/clinic and sent to a laboratory for testing.

There are two types of laboratory tests: immunoassay and chromatography:

- Province health plans vary in funding UDS; some provide immunoassays for classes of drugs (opioids, cocaine, benzodiazepines, cannabis) or one single drug at a time (e.g., oxycodone, methadone)
- Immunoassay detects drugs for a longer time than chromatography (5–7 days compared to 1–2 days) but does not distinguish between different types

²³ Please note that within the appendix, the term urine drug screening (UDS) is used in place of urine drug testing (UDT). The two are synonyms.

Appendix C: Guidance on Conducting and Interpreting Urine Drug Testing (UDT)

of opioids and often misses semi-synthetic or synthetic opioids such as oxycodone or meperidine.

- Chromatography is more expensive and requires specification of the drug(s) to be identified e.g., oxycodone, morphine, codeine, hydromorphone (alternatively can indicate: “full screen” or “broad spectrum screen”).

2. Clinical Usefulness of UDS

2.2 Baseline Measure of Risk

UDS can be helpful in establishing the reliability of a patient’s reported substance use.

Some clinicians believe that UDS should be used routinely to establish baseline information regardless how well the patient is known to the prescriber. They believe a universal approach will eventually “de-stigmatize” UDS and increase prescriber confidence in using opioids. Other clinicians point out that UDS, whether point-of-care or laboratory-completed, is costly, not available in all parts of Canada, and that routine use adds an unnecessary burden to the system. These clinicians believe that UDS should be used selectively with patients who may be at risk for misuse.

2.2 Monitoring for Compliance

During an opioid trial or after a patient is established on LTOT, UDS can be useful in detecting unauthorized drug use, noncompliance, and diversion (Adams 2001, Brown 2006). There is evidence that urine drug screening reduces substance use in LTOT patients (Manchikanti 2004, Manchikanti 2006.)

There is no compelling evidence to guide physicians on identifying CNCP patients who should have UDS or how often. In deciding whether to order a baseline UDS, and how often to use screening to monitor patients, consider:

- 2.2.1** patient’s risk for opioid misuse and addiction
- 2.2.2** aberrant drug-related behaviours
- 2.2.3** availability of UDS.

3. Conducting Urine Drug Screening

3.1 Prior to Ordering the Test

- 3.1.1 Take a detailed history of the patient's medication use for the preceding 7 days.
- 3.1.2 Inform patients that the UDS is not meant to "catch" or punish patients but to improve the safety and effectiveness of LTOT.
- 3.1.3 Tell the patient what results are expected from appropriate opioid use and ask the patient if anything else might show up. (This gives the patient the opportunity to inform the prescriber about changes in their use of the prescribed drug or illicit drug use).
If using a treatment agreement, add the requirement of UDS to the treatment agreement.

3.2 Sample Collection and Preventing Tampering

3.2.1. Sample Dilution

The most common and easiest form of tampering is diluting the urine sample with water. Supervised sample collection makes tampering more difficult, but is a costly use of staff time and patients may find it demeaning. Use supervision if the patient is known to have tampered with a sample.

3.2.2 Sample Temperature

The temperature of the sample can be used to detect tampering because water added to a sample usually varies from body temperature. Temperature-test strips can be used, but they are costly, and must be read within minutes because the sample cools rapidly.

3.2.3. Creatinine Level

A urine creatinine of less than 2–3 mmol/liter is non-physiologic and suggests dilution. Most laboratories can test creatinine level.

4. Interpreting Unexpected Results of UDS

UDS can assist clinical decision-making but should not be considered definitive. Two examples illustrate this: 1) a patient who is diverting prescribed opioids might take a small amount of the prescribed drug so the UDS will be positive; 2) for cocaine there is a relatively short window of detection, so binge cocaine use could be missed.

Appendix C: Guidance on Conducting and Interpreting Urine Drug Testing (UDT)

The table on the following page reviews some common unexpected results and provides a range of possible reasons and some potential actions. In some cases the physician may find it useful to review unexpected results with the laboratory or a physician experienced in interpreting UDS. Prescribers who are unfamiliar with using UDS should take steps to increase knowledge and skill by seeking out an appropriate educational resource or observership.

Interpreting Unexpected Results of Urine Drug Screens (Table B-3-1 in source document, Canada 2010)

	Unexpected Result	Possible Explanations	Actions for the Physician
1	UDS <i>negative</i> for prescribed opioid.	<ul style="list-style-type: none"> • False negative. • Noncompliance. • Diversion. 	<ul style="list-style-type: none"> • Repeat test using chromatography; specify the drug of interest (e.g. oxycodone often missed by immunoassay). • Take a detailed history of the patient's medication use for the preceding 7 days (e.g., could learn that patient ran out several days prior to test) • Ask patient if they've given the drug to others. • Monitor compliance with pill counts.
2	UDS <i>positive</i> for non-prescribed opioid or benzodiazepines.	<ul style="list-style-type: none"> • False positive. • Patient acquired opioids from other sources (double-doctoring, "street"). 	<ul style="list-style-type: none"> • Repeat UDS regularly. • Ask the patient if they accessed opioids from other sources. • Assess for opioid misuse/addiction. • Review/revise treatment agreement
3	UDS <i>positive</i> for illicit drugs (e.g., cocaine, cannabis).	<ul style="list-style-type: none"> • False positive. • Patient is occasional user or addicted to the illicit drug. • Cannabis is positive for patients taking dronabinol (Marinol[®]), THC: CBD Sativex[®]) or 	<ul style="list-style-type: none"> • Repeat UDS regularly. • Assess for abuse/addiction and refer for addiction treatment as appropriate • Ask about medical prescription of dronabinol, THC: CBD or medical marijuana access program.

Appendix C: Guidance on Conducting and Interpreting Urine Drug Testing (UDT)

	Unexpected Result	Possible Explanations	Actions for the Physician
4	Urine creatinine is lower than 2-3 mmol/liter.	<ul style="list-style-type: none"> • Patient added water to sample. 	<ul style="list-style-type: none"> • Repeat UDS • Consider supervised collection or temperature testing • Take a detailed history of the patient's medication use for the preceding 7 days • Review/revise treatment agreement.
5	Urine sample is cold.	<ul style="list-style-type: none"> • Delay in handling sample (urine cools within minutes). • Patient added water to sample. 	<ul style="list-style-type: none"> • Repeat UDS, consider supervised collection or temperature testing • Take a detailed history of the patient's medication use for the preceding 7 days • Review/revise treatment agreement.

Appendix C: Guidance on Conducting and Interpreting Urine Drug Testing (UDT)

The following table is from Appendix B of the Canadian Guideline for Safe and Effective Use of Opioids for CNCP, which can be found at

http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf.

(Canada 2010)

Urine Drug Screening (UDS) (Appendix B-3 in source document, Canada 2010)

Immunoassay versus Chromatography for Detection of Opioid Use

(Table B Appendix 3.1 in source document, Canada 2010)

Immunoassay	Chromatography
Does not distinguish between various opioids	Differentiates: codeine, morphine, oxycodone, hydrocodone, hydromorphone, heroin (monoacetylmorphine).
Will show false positives: Poppy seeds, quinolone antibiotics.	Does not react to poppy seeds.
Often misses semi-synthetic and synthetic opioids, e.g., oxycodone, methadone, fentanyl.	More accurate for semi-synthetic and synthetic opioids.

Appendix C: Guidance on Conducting and Interpreting Urine Drug Testing (UDT)

The following table is from Appendix B of the Canadian Guideline for Safe and Effective Use of Opioids for CNCP, which can be found at

http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf.

(Canada 2010)

Detection Times for Immunoassay and Chromatography

(Table B Appendix 3.2 in source document, Canada 2010)

Drug	Number of days drug is detectable	
	Immunoassay	Chromatography
Benzodiazepines (regular use)	<ul style="list-style-type: none"> • 20+ days for regular diazepam use. • Immunoassay does not distinguish different benzodiazepines. • Intermediate-acting benzodiazepines such as clonazepam are often undetected. 	Not usually used for benzodiazepines.
Cannabis	20+	Not used for cannabis.
Cocaine + metabolite	3–7	1–2
Codeine	2–5	1–2 (Codeine metabolized to morphine.)
Hydrocodone	2–5	1–2
Hydromorphone	2–5	1–2
Meperidine	1 (often missed)	1
Morphine	2–5	1–2: Morphine can be metabolized to hydromorphone
Oxycodone	Often missed	1–2

Source: Adapted from Brands 1998

Appendix C: Guidance on Conducting and Interpreting Urine Drug Testing (UDT)

The following chart is from the Appendix of the Canadian Guideline for Safe and Effective Use of Opioids for CNCP, which can be found in its entirety at

http://nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf.

(Canada 2010)

Example of Documenting Opioid Therapy

(Appendix B-7 in source document, Canada 2010)

Opioid Therapy Record Example

Date:	Jan 13 2008	Mar 23 2008	May 23 2008
Opioid type	Oxycodone	Oxycodone	
Opioid dose	20 tid	30 tid	
MEQ dose	90 mg	135	
Pain worst	8 →	6	
Pain least	3	3	
Pain average	6	5	
Pain right now	6 →	4	
BPI functional improvement	Sleep improved	Back to work	
Adverse effects	Nausea	Nausea continues	
Medical complications	nil	nil	
Compliance	UDS clear	No concerns	
Action	Increase to 30 tid	Keep this dose	
Other Comments			

Appendix D. Select Black Box Warnings: Important Safety Information on Long-Acting Opioids²⁴

[Fentanyl](#)

[Methadone](#)

Morphine Long-Acting Products:

[Avinza](#)

[Kadian](#)

[MS Contin](#)

[Oramorph SR](#)

[Oxycodone/Oxycontin](#)

[Zohydro](#)

Other Long-Acting Products:

[Oxymorphone](#)

[Buprenorphine \(Suboxone\)](#)

²⁴ Sources: <https://www.ncbi.nlm.nih.gov/books/NBK62343/> and <http://www.lni.wa.gov/ClaimsIns/Files/OMD/20120109MethadoneHealthAdvisory.pdf> (Oramorph)

FENTANYL**FOR USE IN OPIOID-TOLERANT PATIENTS ONLY**

DURAGESIC contains a high concentration of a potent Schedule II opioid agonist, fentanyl. Schedule II opioid substances which include fentanyl, hydromorphone, methadone, morphine, oxycodone, and oxymorphone have the highest potential for abuse and associated risk of fatal overdose due to respiratory depression. Fentanyl can be abused and is subject to criminal diversion. The high content of fentanyl in the patches (DURAGESIC) may be a particular target for abuse and diversion.

DURAGESIC is indicated for management of persistent, moderate to severe chronic pain that:

- requires continuous, around-the-clock opioid administration for an extended period of time,
- and cannot be managed by other means such as non-steroidal analgesics, opioid combination products, or immediate-release opioids

DURAGESIC should ONLY be used in patients who are already receiving opioid therapy, who have demonstrated opioid tolerance, and who require a total daily dose at least equivalent to DURAGESIC 25 mcg/h. Patients who are considered opioid-tolerant are those who have been taking, for a week or longer, at least 60 mg of morphine daily, or at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid.

Because serious or life-threatening hypoventilation could occur, DURAGESIC (fentanyl transdermal system) is contraindicated:*

- in patients who are not opioid-tolerant
- in the management of acute pain or in patients who require opioid analgesia for a short period of time
- in the management of post-operative pain, including use after out-patient or day surgeries (e.g., tonsillectomies)
- in the management of mild pain
- in the management of intermittent pain (e.g., use on an as needed basis [prn]) **(See CONTRAINDICATIONS for further information.)**

Since the peak fentanyl concentrations generally occur between 20 and 72 hours of treatment; prescribers should be aware that serious or life threatening hypoventilation may occur, even in opioid-tolerant patients, during the initial application period.

The concomitant use of DURAGESIC with all cytochrome P450 3A4 inhibitors (such as ritonavir, ketoconazole, itraconazole, troleandomycin, clarithromycin, nelfinavir, nefazodone, amiodarone, amprenavir, aprepitant, diltiazem, erythromycin, fluconazole, fosamprenavir, grapefruit juice, and verapamil) may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. Patients receiving DURAGESIC and any CYP3A4 inhibitor should be carefully monitored for an extended period of time and dosage adjustments should be made if warranted (see CLINICAL PHARMACOLOGY – Drug Interactions, WARNINGS, PRECAUTIONS, and DOSAGE AND ADMINISTRATION for further information).

The safety of DURAGESIC has not been established in children under 2 years of age. DURAGESIC should be administered to children only if they are opioid-tolerant and 2 years of age or older (see PRECAUTIONS Pediatric Use).

DURAGESIC is ONLY for use in patients who are already tolerant to opioid therapy of comparable potency. Use in non-opioid tolerant patients may lead to fatal respiratory depression. Overestimating the DURAGESIC dose when converting patients from another opioid medication can result in fatal overdose with the first dose (see DOSAGE And ADMINISTRATION – Initial DURAGESIC Dose Selection). Due to the mean half-life of approximately 20-27 hours, patients who are thought to have had a serious adverse event, including overdose, will require monitoring and treatment for at least 24 hours.

DURAGESIC can be abused in a manner similar to other opioid agonists, legal or illicit. This risk should be considered when administering, prescribing, or dispensing DURAGESIC in situations where the healthcare professional is concerned about increased risk of misuse, abuse, or diversion.

Persons at increased risk for opioid abuse include those with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse, abuse, and addiction. Patients at increased risk of opioid abuse may still be appropriately treated with

modified-release opioid formulations; however, these patients will require intensive monitoring for signs of misuse, abuse, or addiction.

DURAGESIC patches are intended for transdermal use (on intact skin) only. Do not use a DURAGESIC patch if the pouch seal is broken or the patch is cut, damaged, or changed in any way.

Avoid exposing the DURAGESIC application site and surrounding area to direct external heat sources, such as heating pads or electric blankets, heat or tanning lamps, saunas, hot tubs, and heated water beds, while wearing the system. Avoid taking hot baths or sunbathing. There is a potential for temperature-dependent increases in fentanyl released from the system resulting in possible overdose and death. Patients wearing DURAGESIC systems who develop fever or increased core body temperature due to strenuous exertion should be monitored for opioid side effects and the DURAGESIC dose should be adjusted if necessary.

* In addition, fentanyl is not recommended for treatment of musculoskeletal pain.

METHADONE

Deaths, cardiac and respiratory, have been reported during initiation and conversion of pain patients to methadone treatment from treatment with other opioid agonists. It is critical to understand the pharmacokinetics of methadone when converting patients from other opioids (see DOSAGE AND ADMINISTRATION). Particular vigilance is necessary during treatment initiation, during conversion from one opioid to another, and during dose titration.

Respiratory depression is the chief hazard associated with methadone hydrochloride administration. Methadone's peak respiratory depressant effects typically occur later, and persist longer than its peak analgesic effects, particularly in the early dosing period. These characteristics can contribute to cases of iatrogenic overdose, particularly during treatment initiation and dose titration.

In addition, cases of QT interval prolongation and serious arrhythmia (torsades de pointes) have been observed during treatment with methadone. Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction.

Methadone treatment for analgesic therapy in patients with acute or chronic pain should only be initiated if the potential analgesic or palliative care benefit of treatment with methadone is considered and outweighs the risks.

MORPHINE LONG-ACTING PRODUCTS: AVINZA

AVINZA capsules are a modified-release formulation of morphine sulfate indicated for once daily administration for the relief of moderate to severe pain requiring continuous, around-the-clock opioid therapy for an extended period of time.

AVINZA CAPSULES ARE TO BE SWALLOWED WHOLE OR THE CONTENTS OF THE CAPSULES SPRINKLED ON APPLE SAUCE. THE CAPSULE BEADS ARE NOT TO BE CHEWED, CRUSHED, OR DISSOLVED DUE TO THE RISK OF RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF MORPHINE.

PATIENTS MUST NOT CONSUME ALCOHOLIC BEVERAGES WHILE ON AVINZA THERAPY. ADDITIONALLY, PATIENTS MUST NOT USE PRESCRIPTION OR NON-PRESCRIPTION MEDICATIONS CONTAINING ALCOHOL WHILE ON AVINZA THERAPY. CONSUMPTION OF ALCOHOL WHILE TAKING AVINZA MAY RESULT IN THE RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF MORPHINE.

MORPHINE LONG-ACTING PRODUCTS: KADIAN

KADIAN contains morphine sulfate, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. KADIAN can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing KADIAN in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse or diversion.

KADIAN capsules are an extended-release oral formulation of morphine sulfate indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.

KADIAN capsules are NOT for use as a prn analgesic.

KADIAN 100 mg and 200 mg Capsules ARE FOR USE IN OPIOID PATIENTS ONLY. Ingestion of these capsules or of the pellets within the capsules may cause fatal respiratory depression when administered to patients not already tolerant to high doses of opioids. KADIAN CAPSULES ARE TO BE SWALLOWED WHOLE OR THE CONTENTS OF THE CAPSULES SPRINKLED ON APPLE SAUCE. THE PELLETS IN THE CAPSULES ARE NOT TO BE CHEWED, CRUSHED, OR DISSOLVED DUE TO THE RISK OF RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF MORPHINE.

MORPHINE LONG-ACTING PRODUCT: MS Contin

MS CONTIN contains morphine sulfate, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics.

Morphine can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing MS CONTIN in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

MS CONTIN Tablets are a controlled-release oral formulation of morphine sulfate indicated for the management of moderate to severe pain when a continuous, around-the clock opioid analgesic is needed for an extended period of time.

MS CONTIN Tablets are NOT intended for use as a prn analgesic.

MS CONTIN 100 and 200 mg Tablets ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. These tablet strengths may cause fatal respiratory depression when administered to patients not previously exposed to opioids.

MS CONTIN TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, DISSOLVED, OR CRUSHED. TAKING BROKEN, CHEWED, DISSOLVED, OR CRUSHED MS CONTIN TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF MORPHINE.

MORPHINE LONG-ACTING PRODUCTS: ORAMORPH SR

Oramorph SR (morphine sulfate) Sustained Release Tablets are indicated for the relief of pain in adult patients who require opioid analgesics for more than a few days.

Oramorph SR is a sustained release dosage form. Patients must be instructed to swallow the tablet whole; the tablet should not be broken in half, nor should it be crushed or chewed.

The sustained release of morphine from Oramorph SR should be taken into consideration in the event of adverse reactions or overdose. Serious adverse reactions caused by morphine, which can be fatal, include **respiratory depression, circulatory depression, apnea, shock, and cardiac arrest.**

Oramorph SR should be used with extreme caution in any patient who may have decreased respiratory reserve. Respiratory depression is the chief hazard of all morphine preparations. Oramorph SR is contraindicated in patients with respiratory depression in the absence of resuscitative equipment, in patients with acute or severe bronchial asthma and in patients with known hypersensitivity to morphine.

Oramorph SR is also contraindicated in any patient who has or is suspected of having a paralytic ileus.

Morphine sulfate is a Schedule II controlled substance. Morphine is the most commonly cited prototype for narcotic substances that possess an addiction-forming or addiction-sustaining liability. A patient may be at risk for developing dependence to morphine if used improperly or for overly long periods of time. Oramorph SR should be used with caution in individuals with a prior history of substance abuse or dependence.

Oramorph SR should be used with extreme caution in patients with increased intracranial pressure or those with a head injury.

The clearance of morphine or its metabolites may be reduced in patients with hepatic or renal dysfunction. Pharmacodynamic changes in these patients should be considered when adjusting the dose and dosing intervals.

The depressant effects of morphine are potentiated by the presence of other CNS depressants such as alcohol, sedatives, antihistamines, or psychotropic drugs. Opioid receptor agonist/antagonist analgesics should NOT be administered to patients who have received or are receiving a course of therapy with a pure opioid agonist analgesic.

There has been no systematic evaluation of Oramorph SR as an initial opioid analgesic in the management of pain. Because it may be more difficult to titrate a patient using a sustained-release morphine, it is ordinarily advisable to begin treatment using an immediate release formulation.

OXYCODONE/OXYCONTIN

IMPORTANCE OF PROPER PATIENT SELECTION AND POTENTIAL FOR ABUSE
OxyContin[®] contains [oxycodone](#) which is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to [morphine](#).

OxyContin[®] can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OxyContin[®] in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

OxyContin[®] is a controlled-release oral formulation of [oxycodone](#) hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. OxyContin[®] is not intended for use on an as-needed basis.

Patients considered opioid tolerant are those who are taking at least 60 mg oral [morphine](#)/day, 25 mcg transdermal [fentanyl](#)/hour, 30 mg oral [oxycodone](#)/day, 8 mg oral [hydromorphone](#)/day, 25 mg oral [oxymorphone](#)/day, or an equianalgesic dose of another opioid for one week or longer. OxyContin[®] 60 mg and 80 mg tablets, a single dose greater than 40 mg, or a total daily dose greater than 80 mg are only for use in opioid-tolerant patients, as they may cause fatal respiratory depression when administered to patients who are not tolerant to the respiratory-depressant or sedating effects of opioids. Persons at increased risk for opioid abuse include those with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse, abuse and addiction.

OxyContin[®] must be swallowed whole and must not be cut, broken, chewed, crushed,

or dissolved. Taking cut, broken, chewed, crushed or dissolved OxyContin tablets leads to rapid release and absorption of a potentially fatal dose of [oxycodone](#).

The concomitant use of OxyContin[®] with all cytochrome P450 3A4 inhibitors such as macrolide antibiotics (e.g., [erythromycin](#)), azole-antifungal agents (e.g., [ketoconazole](#)), and protease inhibitors (e.g., [ritonavir](#)) may result in an increase in [oxycodone plasma](#) concentrations, which could increase or prolong adverse effects and may cause potentially fatal respiratory depression. Patients receiving OxyContin[®] and a CYP3A4 inhibitor should be carefully monitored for an extended period of time and dosage adjustments should be made if warranted.

OTHER LONG-ACTING OPIOID PRODUCTS: OXYMORPHONE

POTENTIAL FOR ABUSE, IMPORTANCE OF PROPER PATIENT SELECTION AND LIMITATIONS OF USE

Potential for Abuse

OPANA ER[®] contains [oxymorphone](#), which is a [morphine](#)-like opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics.

[Oxymorphone](#) can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OPANA ER[®] in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

Proper Patient Selection

OPANA ER[®] is an extended-release oral formulation of [oxymorphone](#) indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.

Limitations of Use

OPANA ER[®] is NOT intended for use as an as needed analgesic.

OPANA ER[®] TABLETS are to be swallowed whole and are not to be broken, chewed, dissolved, or crushed. Taking broken, chewed, dissolved, or crushed OPANA ER[®] TABLETS leads to rapid release and absorption of a potentially fatal dose of [oxymorphone](#).

Patients must not consume alcoholic beverages, or prescription or non-prescription medications containing alcohol, while on OPANA ER[®] therapy. The co-ingestion of alcohol with OPANA ER[®] may result in increased [plasma](#) levels and a potentially fatal overdose of [oxymorphone](#).

OTHER LONG-ACTING OPIOID PRODUCTS: BUPRENORPHINE (SUBOXONE)**POTENTIAL FOR ABUSE and IMPORTANCE OF PROPER PATIENT SELECTION, POTENTIAL FOR ABUSE, AND LIMITATIONS OF USE**

Proper Patient Selection Butrans™ is a transdermal formulation of [buprenorphine](#) indicated for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time.

Potential for Abuse Butrans™ contains [buprenorphine](#) which is a mu opioid partial agonist and a Schedule III controlled substance. Butrans™ can be abused in a manner similar to other opioid agonists, legal or illicit. Consider the abuse potential when prescribing or dispensing Butrans™ in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

Persons at increased risk for opioid abuse include those with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). Assess patients for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. Routinely monitor all patients receiving opioids for signs of misuse, abuse and addiction.

Limitations of Use Do not exceed a dose of one 20 mcg/hour Butrans™ system due to the risk of QTc interval prolongation. Avoid exposing the Butrans application site and surrounding area to direct external heat sources. Temperature-dependent increases in [buprenorphine](#) release from the system may result in overdose and death.

OTHER LONG-ACTING OPIOID PRODUCTS: ZOHYDRO

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL EXPOSURE; NEONATAL OPIOID WITHDRAWAL SYNDROME; and INTERACTION WITH ALCOHOL [See full](#)

[prescribing information for complete boxed warning.](#)

- Zohydro ER exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk before prescribing, and monitor regularly for development of these behaviors or conditions.
- Serious, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Instruct patients to swallow Zohydro ER whole to avoid exposure to a potentially fatal dose of hydrocodone.

- Accidental consumption of Zohydro ER, especially in children, can result in fatal overdose of hydrocodone.
- For patients who require opioid therapy while pregnant, be aware that infants may require treatment for neonatal opioid withdrawal syndrome. Prolonged use during pregnancy can result in life-threatening neonatal opioid withdrawal syndrome.
- Instruct patients not to consume alcohol or any products containing alcohol while taking Zohydro ER because co-ingestion can result in fatal plasma hydrocodone levels.

Appendix E. Opioid Dose and Risk of Morbidity and Mortality

	Population, N	Health effect measured	Risk measure (95% confidence interval)	Dose range at which risk observed	Other risks observed
Dunn et al. 2010	9940 patients treated with opioids for chronic noncancer pain followed for a mean 42 months (range < 1 to 119 months)	Opioid-related overdose events	(Hazard ratio for overdose events)		Patients receiving sedative-hypnotics concurrently at increased risk
			8.87 (3.99–19.72)	>100 mg/day MED	
			3.73 (1.47–9.50)	50-<100 mg/day MED	
			1.44 (0.57–3.62)	20-<50 mg/day MED	
			1.0 (Reference)	1–20 mg/ day MED	
Bohnert et al. 2011	155,434 VA patients who received opioids for pain followed for up to 4 years	Opioid-related mortality	(Hazard ratio for mortality)		0.04% overall risk of opioid overdose
			1.9 (1.33-2.67)	20-50mg/day MED	
			4.6 (3.18-6.74)	50-100 mg/day MED	
			7.18 (4.85-10.65)	> 100 mg/day MED	
			1 (Reference)	20 mg/ day MED	
Gomes et al. 2011	607,156 patients treated with opioids for noncancer pain	Opioid-related mortality	(Odds Ratio for mortality)		“Attenuated but significant risk” for doses 50–199mg/day MED
			1.3 (0.94-1.84)	20-49 mg/day MED	
			1.92 (1.30-2.85)	50-99 mg/day MED	
			2.04 (1.28-3.24)	100-199 mg/day MED	
			2.88 (1.79-4.63)	>200 mg/day MED	

Appendix F. Opioid Dose Calculations

F1. [Dosing Thresholds for Selected Opioids](#)

F2. [Equianalgesic Dose Table for Converting Opioid Doses](#)

F3. [Morphine Equivalent Dose \(MED\) Calculation](#)

DRAFT

Appendix F1. Dosing Thresholds for Selected Opioids

Opioid	Recommended dose threshold for pain consult (not equianalgesic)	Recommended starting dose for opioid-naïve patients (not equianalgesic)	Considerations
Codeine	533 mg per 24 hours	30mg q 4–6 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See acetaminophen warning on the next page.
Fentanyl Transdermal	33 mcg/hour (q 72 hours)		Use only in opioid tolerant patients who have been taking ≥ 60mg MED daily for a week or longer
Hydrocodone	80 mg per 24 hours	5-10mg q 4–6 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See acetaminophen warning on the next page.
Hydromorphone	20 mg per 24 hours	2 mg q 4–6 hours	
Methadone	11 mg per 24 hours	2.5-5 mg BID – TID	Methadone is difficult to titrate due to its half-life variability. It may take a long time to reach a stable level in the body. Methadone dose should not be increased more frequently than every 7 days. Do not use as PRN or combine with other long-acting (LA) opioids.
Morphine	80 mg per 24 hours	Immediate-release: 10 mg q 4 hours Sustained-release: 15 mg q 12 hours	Adjust dose for renal impairment.
Oxycodone	53 mg per 24 hours	Immediate-release: 5 mg q 4–6 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See acetaminophen warning on the next page.
Oxymorphone	27 mg per 24 hours	Immediate-release: 5–10 mg q 4–6 hours Sustained Release: 10 mg q 12 hours	Use with extreme caution due to potential fatal interaction with alcohol or medications containing alcohol.

See [Section 8, Methadone](#), for more details and for warnings against prescribing methadone to certain patient subgroups.

(continued)

Acetaminophen warning with combination products

Hepatotoxicity can result from prolonged use or doses in excess of recommended maximum total daily dose of acetaminophen including over-the-counter products.

Short-term use (<10 days) – 4000 mg/day

Long-term use – 2500mg/day

Key considerations in dosing long acting opioids

Monitoring for adequate analgesia and use of “rescue” medications (at least until the long-acting opioid dose is stabilized). All new dosage calculations should include consideration for concurrent utilization of short-acting opioids.

If the patient is more debilitated, frail and/or has significant metabolic impairments (e.g. renal or hepatic dysfunction), consider starting at the lower end of the conversion dose range.

Always monitor for adverse effects (nausea, constipation, oversedation, itching, etc.)

Adapted for California with permission from Washington State Agency Medical Directors Group Interagency (AMDG) Guideline on Opioid Dosing for Chronic Non-cancer Pain, 2010. (WA AMDG 2010)

Appendix F2. Equianalgesic Dose Table for Converting Opioid Doses²⁵

All conversions between opioids are estimates generally based on equianalgesic dosing or ED. Patient variability in response to these EDs can be large, due primarily to genetic factors and incomplete cross-tolerance. **It is recommended that, after calculating the appropriate conversion dose, it be reduced by 25–50% to assure patient safety.**

Opioid	Morphine Equivalent Dose (MED) Factor	Approximate Equianalgesic Dose (oral & transdermal)*
Morphine (reference)	1	30mg
Codeine	0.15	200mg
Fentanyl transdermal	2.4	12.5mcg/hr
Hydrocodone	1	30mg
Hydromorphone	4	7.5mg
Methadone	7.5	Chronic: 4mg [†]
Oxycodone	1.5	20mg
Oxymorphone	3	10mg

*Adapted from VA 2003 & FDA labeling

[†]Equianalgesic dosing ratios between methadone and other opioids are complex, thus requiring slow, cautious conversion (Ayonrinde 2000)

²⁵ From the Washington State Agency Medical Directors Group Interagency (AMDG) Guideline on Opioid Dosing for Chronic Non-cancer Pain, 2010. (WA AMDG 2010). Used with permission. Notes below table come from the source table.

Appendix F3. Morphine Equivalent Dose (MED) Calculation²⁶

For patients taking more than one opioid, the morphine equivalent doses of the different opioids must be added together to determine the cumulative dose (see the table in [Appendix F1, Dosing Thresholds for Selected Opioids](#), for MEDs of selected medications). For example, if a patient takes six hydrocodone 5mg / acetaminophen 500mg and two 20mg oxycodone extended release tablets per day, the cumulative dose of opioids in morphine equivalents may be calculated as follows:

- Hydrocodone 5mg x 6 tablets per day = 30mg per day.
Hydrocodone 30mg = 30mg morphine equivalents (MED)
- Oxycodone 20mg x 2 tablets per day = 40mg per day.
20mg oxycodone = 30mg morphine so 40mg oxycodone = 60mg MED
- Cumulative dose is 30mg MED + 60mg MED = 90mg MED per day.

An electronic opioid dose calculator is available in two formats (web-based and Excel) at this web page:

<http://www.agencymeddirectors.wa.gov/opioiddosing.asp>

²⁶ Source: Washington State Agency Medical Directors Group Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain, 2010. Used with permission.

Appendix G. Summary of Screening and Monitoring Recommendations

Screening and Monitoring for Safe Opioid Prescribing								
		Acute Pain (1st month after onset of pain)		Subacute Pain (1–3 months)		Chronic Pain (> 3 months)		
	Pre-Operatively in Workers on Chronic Opioid Treatment	Prior to First Opioid Prescription	Week 4	Just Prior to Opioid Trial	During Opioid Trial	Titration	Maintenance	Any Unscheduled Visit for Opioids (E.R.)
Consult CURES	✓ Every visit ¹							
Use Screening Tools to Identify High-Risk Patients ²				✓				
Use Screening Tools to Identify Current Misuse/Abuse of Opioids ³					✓	As needed		
Administer UDT at POC				✓	As needed	Randomly at least 2x/year for all patients, and up to 4x/year for high-risk patients		✓
Treatment Agreement				✓	Modify agreement as needed			
Track Pain and Function	Every visit			Every visit Establish baseline levels at start of trial	Monthly during first year (after the 3 rd month) and quarterly after first year (need 30% improvement in both pain and function to continue treatment)			
Determine and Document Current MED Dose ⁴	✓ Every visit (Make semi-annual weaning attempts for patients on >80 mg/day MED for over 6 months to reduce dosage to < 80 mg/day MED)							

Table adapted with permission from Washington State Agency Medical Directors Group Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain, 2010

¹ See Sections 1.2 and 1.3 for for providers treating patients with moderate to severe pain in emergency departments, urgent care clinics and other clinical settings.

² Use validated screening tools (ORT or SOAPP-R for risk of drug misuse, PHQ-9 for depression, and CAGE-AID or TICS for risk of alcohol misuse)

³ Use validated screening tools (POMI or COMM)

⁴ Use an online dose calculator such as <http://www.agencymeddirectors.wa.gov/Files/DosingCalc.xls>

DEFINITION OF KEY TERMS

Addiction:

A chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences. [58]

Note: The term “addiction” is not a specific diagnosis in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5).

Substance Use Disorder:

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.

10. Tolerance, as defined by either of the following:

- a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
- b. A markedly diminished effect with continued use of the same amount of an opioid.

Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.

11. Withdrawal, as manifested by either of the following:

- a. The characteristic opioid withdrawal syndrome
- b. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.” [133]

Note: The DSM-V definition no longer makes a distinction between substance abuse and substance dependence. Both of these conditions are now included within Substance Abuse Disorder, which can be measured on a continuum from mild to severe. [133, 134]

Opioid Withdrawal:

Opioid withdrawal is distinct from opioid use disorder and does not necessarily occur in the presence of the drug-seeking behavior associated with opioid use disorder. Opioid withdrawal may occur in any individual after cessation of repeated use of an opioid, whether in the setting of medical management of pain, during opioid agonist therapy for opioid use disorder, in the context of private recreational use, or following attempts to self-treat symptoms of mental disorders with opioids. [133]

Signs and symptoms may include:

1. Dysphoric mood.
2. Nausea or vomiting.
3. Muscle aches.
4. Lacrimation or rhinorrhea.
5. Pupillary dilation, piloerection, or sweating.
6. Diarrhea.
7. Yawning.
8. Fever.
9. Insomnia.

Physical dependence:

Physical dependence is not equivalent to dependence or addiction, and may occur with the regular (daily or almost daily) use of any substance, legal or illegal, even when taken as prescribed. It occurs because the body naturally adapts to regular exposure to a substance (e.g., caffeine or a prescription drug). When that substance is taken away, symptoms can emerge while the body re-adjusts to the loss of the substance. Physical dependence can lead to craving the drug to relieve the withdrawal symptoms. Drug dependence and addiction refer to substance use disorders, which may include physical dependence but must also meet additional criteria. [134]

Tolerance:

A condition in which higher doses of a drug are required to produce the same effect achieved during initial use; often associated with physical dependence. [134]

ACRONYMS

BTP	Break-Through Pain
CAGE-AID	Cut down, Annoyed, Guilty, Eye-opener-Adapted to Include Drugs
CNS	Central Nervous System
COMM	Current Opioid Misuse Measure
COPD	Chronic Obstructive Pulmonary Disease
CURES	Controlled Substance Utilization Review and Evaluation System
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
DWC	Division of Workers' Compensation
ECG	Electrocardiogram
GC/MS	Gas Chromatography/Mass Spectrometry
GCPS	Graded Chronic Pain Scale
LC/MS	Liquid Chromatography/Mass Spectrometry
MED	Morphine Equivalent Dose
MTUS	Medical Treatment Utilization Schedule
NSAID	Nonsteroidal Anti-Inflammatory drug
ORT	Opioid Risk Tool
PCA	Patient-Controlled Analgesia
PDMP	Prescription Drug Monitoring Program
PEG	Average Pain Intensity (P), Interference with Enjoyment of Life (E), and Interference with General Activity (G).
PHQ-9	Patient Health Questionnaire, Ninth Edition
PMQ	Patient Medication Questionnaire
POC	Point of Collection
POMI	Prescription Opioid Misuse Index

PTSD	Post-Traumatic Stress Disorder
RCT	Randomized Controlled Trial
SIMP	Structured Intensive Multidisciplinary Program
SOAPP-R	Screener and Opioid Assessment for Patients with Pain-Revised
TICS	Two-Item Conjoint Screen
UDS	Urine Drug Screen (same as urine drug test)
UDT	Urine Drug Test (same as urine drug screen)
WHYMPI	West Haven-Yale Multidimensional Pain Inventory

REFERENCES

1. Cheadle, A., et al., *Factors influencing the duration of work-related disability: a population-based study of Washington State workers' compensation*. Am J Public Health, 1994. **84**(2): p. 190-6.
2. Institute of Medicine-National Academy of Sciences, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research*. June 2011.
3. Noble, M., et al., *Long-term opioid management for chronic noncancer pain*. Cochrane Database Syst Rev, 2010(1): p. CD006605.
4. Frank, J., et al., *Preventing disability from work-related low-back pain. New evidence gives new hope--if we can just get all the players onside*. CMAJ, 1998. **158**(12): p. 1625-31.
5. Wickizer, T.M., et al., *Improving quality, preventing disability and reducing costs in workers' compensation healthcare: a population-based intervention study*. Med Care, 2011. **49**(12): p. 1105-11.
6. Bernacki, E.J. and S.P. Tsai, *Ten years' experience using an integrated workers' compensation management system to control workers' compensation costs*. J Occup Environ Med, 2003. **45**(5): p. 508-16.
7. Opioids Guideline. ACOEM Occupational Medicine Practice Guidelines-part of Reed Group® DisabilityGuidelines™. 2014, Copyright 2008-2014 Reed Group, Ltd., www.DisabilityGuidelines.com. All rights reserved.
8. Franceschi, F., et al., *Use of oxycodone in polytrauma patients: the "Gemelli" experience*. Eur Rev Med Pharmacol Sci, 2008. **12**(2): p. 123-6.
9. Gaskell, H., et al., *Single dose oral oxycodone and oxycodone plus paracetamol (acetaminophen) for acute postoperative pain in adults*. Cochrane Database Syst Rev, 2009(3): p. CD002763.
Evidence Level 1a.
10. Kelley, N.E. and D.E. Tepper, *Rescue therapy for acute migraine, part 3: opioids, NSAIDs, steroids, and post-discharge medications*. Headache, 2012. **52**(3): p. 467-82.
11. Moore, R.A., et al., *Single dose oral analgesics for acute postoperative pain in adults*. Cochrane Database Syst Rev, 2011(9): p. CD008659.
12. Toms, L., et al., *Single dose oral paracetamol (acetaminophen) with codeine for postoperative pain in adults*. Cochrane Database Syst Rev, 2009(1): p. CD001547.
Evidence Level 1a.
13. Brown, F.L., Jr., et al., *Comparison of diflunisal and acetaminophen with codeine in the treatment of initial or recurrent acute low back strain*. Clin Ther, 1986. **9 Suppl C**: p. 52-8.

References

14. Clark, E., et al., *A randomized, controlled trial of acetaminophen, ibuprofen, and codeine for acute pain relief in children with musculoskeletal trauma*. *Pediatrics*, 2007. **119**(3): p. 460-7.
 15. Ekman, E.F., et al., *The COX-2 specific inhibitor Valdecoxib versus tramadol in acute ankle sprain: a multicenter randomized, controlled trial*. *Am J Sports Med*, 2006. **34**(6): p. 945-55.
 16. Innes, G.D., et al., *Ketorolac versus acetaminophen-codeine in the emergency department treatment of acute low back pain*. *J Emerg Med*, 1998. **16**(4): p. 549-56.
 17. Li, C., et al., *Analgesic efficacy and tolerability of flupirtine vs. tramadol in patients with subacute low back pain: a double-blind multicentre trial**. *Curr Med Res Opin*, 2008. **24**(12): p. 3523-30.
 18. Lovell, S.J., et al., *Comparison of valdecoxib and an oxycodone-acetaminophen combination for acute musculoskeletal pain in the emergency department: a randomized controlled trial*. *Acad Emerg Med*, 2004. **11**(12): p. 1278-82.
 19. Veenema, K.R., N. Leahey, and S. Schneider, *Ketorolac versus meperidine: ED treatment of severe musculoskeletal low back pain*. *Am J Emerg Med*, 2000. **18**(4): p. 404-7.
 20. Blondell, R.D., M. Azadfar, and A.M. Wisniewski, *Pharmacologic therapy for acute pain*. *Am Fam Physician*, 2013. **87**(11): p. 766-72.
- Evidence Level 5.**
21. Furlan, A.D., et al., *Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects*. *CMAJ*, 2006. **174**(11): p. 1589-94.
 22. Kalso, E., et al., *Opioids in chronic non-cancer pain: systematic review of efficacy and safety*. *Pain*, 2004. **112**(3): p. 372-80.
 23. Papaleontiou, M., et al., *Outcomes associated with opioid use in the treatment of chronic noncancer pain in older adults: a systematic review and meta-analysis*. *J Am Geriatr Soc*, 2010. **58**(7): p. 1353-69.
 24. Furlan, A., et al., *A comparison between enriched and nonenriched enrollment randomized withdrawal trials of opioids for chronic noncancer pain*. *Pain Res Manag*, 2011. **16**(5): p. 337-51.
 25. White, A.P., et al., *Pharmacologic management of chronic low back pain: synthesis of the evidence*. *Spine (Phila Pa 1976)*, 2011. **36**(21 Suppl): p. S131-43.
 26. Nuckols, T.K., Diamant A.L., *Report to the California Department of Industrial Relations and the California Commission on Health and Safety and Workers' Compensation. Identifying risky opioid prescribing practices*. 2012.
 27. Chou, R., *Pharmacological management of low back pain*. *Drugs*, 2010. **70**(4): p. 387-402.
 28. DIR-Division of Workers' Compensation, *DWC Chronic Pain Medical Treatment Guideline*. 2009.
 29. Niwa, Y. and A. Haji, *M3-receptor activation counteracts opioid-mediated apneusis, but the apneusis per se is not necessarily related to an impaired M3 mechanism in rats*. *Life Sci*, 2011. **89**(19-20): p. 685-90.

References

30. Boyer, E.W., *Management of opioid analgesic overdose*. N Engl J Med, 2012. **367**(2): p. 146-55.
31. Centers for Disease Control and Prevention (CDC), *Policy Impact: Prescription Painkiller Overdoses*. 2011.
32. Warner, M., et al., *Drug poisoning deaths in the United States, 1980-2008*. NCHS Data Brief, 2011(81): p. 1-8.
Evidence Level 4.
33. Fulton-Kehoe, D., et al., *Opioid poisonings and opioid adverse effects in workers in Washington State*. Am J Ind Med, 2013. **56**(12): p. 1452-62.
Evidence Level 4.
34. Warner, M., L.H. Chen, and D.M. Makuc, *Increase in fatal poisonings involving opioid analgesics in the United States, 1999-2006*. NCHS Data Brief, 2009(22): p. 1-8.
Evidence Level 4.
35. Fishbain, D.A., et al., *Do opioids induce hyperalgesia in humans? An evidence-based structured review*. Pain Med, 2009. **10**(5): p. 829-39.
36. Chu, L.F., et al., *The endogenous opioid system is not involved in modulation of opioid-induced hyperalgesia*. J Pain, 2011. **12**(1): p. 108-15.
37. Elliott, J.A., et al., *Non-analgesic effects of opioids: opioids and the endocrine system*. Curr Pharm Des, 2012. **18**(37): p. 6070-8.
38. Katz, N.P., H.G. Birnbaum, and A. Castor, *Volume of prescription opioids used nonmedically in the United States*. J Pain Palliat Care Pharmacother, 2010. **24**(2): p. 141-4.
39. U.S. Dept of Health and Human Services-Substance Abuse and Mental Health Services Administration (SAMHSA), *Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings*. 2011.
40. U.S. Dept. of Health and Human Services, *Results from the 2005 National Survey on Drug Use and Health: National Findings*. 2006.
41. Minozzi, S., L. Amato, and M. Davoli, *Development of dependence following treatment with opioid analgesics for pain relief: a systematic review*. Addiction, 2013. **108**(4): p. 688-98.
42. Juurlink, D.N. and I.A. Dhalla, *Dependence and addiction during chronic opioid therapy*. J Med Toxicol, 2012. **8**(4): p. 393-9.
43. Boscarino, J.A., et al., *Prevalence of prescription opioid-use disorder among chronic pain patients: comparison of the DSM-5 vs. DSM-4 diagnostic criteria*. J Addict Dis, 2011. **30**(3): p. 185-94.
44. Grattan, A., et al., *Depression and prescription opioid misuse among chronic opioid therapy recipients with no history of substance abuse*. Ann Fam Med, 2012. **10**(4): p. 304-11.
Evidence Level 4.
45. Martins, S.S., et al., *Mood and anxiety disorders and their association with non-medical prescription opioid use and prescription opioid-use disorder: longitudinal evidence from the National Epidemiologic Study on Alcohol and Related*

- Conditions*. Psychol Med, 2012. **42**(6): p. 1261-72.
- Evidence Level 4.**
46. Outcalt, S.D., et al., *Health Care Utilization Among Veterans with Pain and Post-traumatic Stress Symptoms*. Pain Med, 2013: p.
- Evidence Level 2.**
47. Kenan, K., K. Mack, and L. Paulozzi, *Trends in prescriptions for oxycodone and other commonly used opioids in the United States, 2000-2010*. Open Med, 2012. **6**(2): p. e41-7.
48. Drug Enforcement Administration, *Hydrocone*. 2013.
49. Policy., W.H.O.o.N.D.C., *Epidemic: Responding to America's Prescription Drug Abuse Crisis*. 2011.
50. Chou, R., et al., *Medications for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline*. Ann Intern Med, 2007. **147**(7): p. 505-14.
51. Chou, R., et al., *Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline*. Ann Intern Med, 2007. **147**(7): p. 492-504.
- Evidence Level 5.**
52. Harber, P., et al., *Selection of workers' compensation treatment guidelines: California experience*. J Occup Environ Med, 2008. **50**(11): p. 1282-92.
53. Opioids Guideline. ACOEM Occupational Medicine Practice Guidelines-part of Reed Group® DisabilityGuidelines™. Copyright 2008-2011 Reed Group, Ltd., www.DisabilityGuidelines.com. All rights reserved.
54. Chou, R., et al., *American Pain Society-American Academy of Pain Medicine (APS/AAPM). Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain* J Pain, 2009. **10**(2): p. 113-30.
55. Manchikanti, L., et al., *American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2--guidance*. Pain Physician, 2012. **15**(3 Suppl): p. S67-116.
56. Canadian Guideline for Safe and Effective Use of Opioids for Chronic Noncancer Pain, *National Opioid Use Guideline Group (NOUGG)*. April 30 2010.
57. Work Loss Data Institute, *ODG Evidence-Based Medical Treatment and Return-to-Work Guidelines (Official Disability Guidelines). Chronic Pain Chapter (updated 4/6/13)*. 2015.
58. Utah Department of Health, *Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain*. 2009.
59. U.S. Veteran Affairs Administration, *Clinical Practice Guideline: Management of Opioid Therapy for Chronic Pain*. 2010.
60. Washington State Agency Medical Directors' Group (AMDG), *Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain: An educational aid to improve care and safety with opioid therapy*. 2010.
61. Washington State Department of Labor & Industries. Washington Agency Medical Directors' Group, *Guideline for Prescribing Opioids to Treat Pain in Injured Workers*. July 1, 2013.

References

62. National Center for Complementary and Integrative Health (NCCIH), *Chronic Pain and Complementary Health Approaches: What You Need to Know*. September 2010.
63. Mills, K.L., et al., *The costs and outcomes of treatment for opioid dependence associated with posttraumatic stress disorder*. *Psychiatr Serv*, 2005. **56**(8): p. 940-5.
Evidence Level 1b.
64. Centers for Disease Control and Prevention (CDC), *Unintentional Deaths from Drug Poisoning by Urbanization of Area - New Mexico, 1994-2003*. 2005. p. 870-3.
65. Nyhlen, A., et al., *Substance abuse and psychiatric co-morbidity as predictors of premature mortality in Swedish drug abusers: a prospective longitudinal study 1970-2006*. *BMC Psychiatry*, 2011. **11**: p. 122.
Evidence Level 1b.
66. Paulozzi, L.J., et al., *A comparison of drug overdose deaths involving methadone and other opioid analgesics in West Virginia*. *Addiction*, 2009. **104**(9): p. 1541-8.
Evidence Level 4.
67. Seal, K.H., et al., *Association of mental health disorders with prescription opioids and high-risk opioid use in US veterans of Iraq and Afghanistan*. *JAMA*, 2012. **307**(9): p. 940-7.
Evidence Level 4.
68. Shah, N.G., et al., *Unintentional drug overdose death trends in New Mexico, USA, 1990-2005: combinations of heroin, cocaine, prescription opioids and alcohol*. *Addiction*, 2008. **103**(1): p. 126-36.
Evidence Level 4.
69. Toblin, R.L., et al., *Mental illness and psychotropic drug use among prescription drug overdose deaths: a medical examiner chart review*. *J Clin Psychiatry*, 2010. **71**(4): p. 491-6.
Evidence Level 4.
70. Webster, L.R., et al., *An analysis of the root causes for opioid-related overdose deaths in the United States*. *Pain Med*, 2011. **12 Suppl 2**: p. S26-35.
Evidence Level 5.
71. Wunsch, M.J., et al., *Opioid deaths in rural Virginia: a description of the high prevalence of accidental fatalities involving prescribed medications*. *Am J Addict*, 2009. **18**(1): p. 5-14.
Evidence Level 4.
72. Wysowski, D.K., L.A. Governale, and J. Swann, *Trends in outpatient prescription drug use and related costs in the US: 1998-2003*. *Pharmacoeconomics*, 2006. **24**(3): p. 233-6.
Evidence Level 4.
73. Hall, A.J., et al., *Patterns of abuse among unintentional pharmaceutical overdose fatalities*. *JAMA*, 2008. **300**(22): p. 2613-20.
Evidence Level 4.

References

74. Hadidi, M.S., et al., *Current trends in drug abuse associated fatalities - Jordan, 2000-2004*. *Forensic Sci Int*, 2009. **186**(1-3): p. 44-7.
Evidence Level 4.
75. Goodridge, D., et al., *Factors associated with opioid dispensation for patients with COPD and lung cancer in the last year of life: A retrospective analysis*. *Int J Chron Obstruct Pulmon Dis*, 2010. **5**: p. 99-105.
Evidence Level 4.
76. Fareed, A., et al., *High dose versus moderate dose methadone maintenance: is there a better outcome?* *J Addict Dis*, 2009. **28**(4): p. 399-405.
Evidence Level 4.
77. Dunn, K.M., et al., *Opioid prescriptions for chronic pain and overdose: a cohort study*. *Ann Intern Med*, 2010. **152**(2): p. 85-92.
Evidence Level 4.
78. Deyo, R.A., et al., *Opioids for back pain patients: primary care prescribing patterns and use of services*. *J Am Board Fam Med*, 2011. **24**(6): p. 717-27.
Evidence Level 4.
79. Dean, M., *Opioids in renal failure and dialysis patients*. *J Pain Symptom Manage*, 2004. **28**(5): p. 497-504.
Evidence Level 5.
80. Cheng, M., et al., *Comparison of opioid-related deaths by work-related injury*. *Am J Ind Med*, 2013. **56**(3): p. 308-16.
Evidence Level 4.
81. Haack, M., et al., *Pain sensitivity and modulation in primary insomnia*. *Eur J Pain*, 2012. **16**(4): p. 522-33.
Evidence Level 3.
82. Hegmann, K.T., et al., *ACOEM practice guidelines: opioids and safety-sensitive work*. *J Occup Environ Med*, 2014. **56**(7): p. e46-53.
83. *Code of Federal Regulations (CFR) in Title 21. Controlled Substances Act.*, U.S.F.a.D.A.
URL:<http://www.fda.gov/regulatoryinformation/legislation/ucm148726.htm>, Editor.
84. *Code of Federal Regulations (CFR), in Title 21, Controlled Substances Act*, U.S.F.a.D.A.
URL:<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=1305>, Editor.
85. Cifuentes, M., et al., *The course of opioid prescribing for a new episode of disabling low back pain: opioid features and dose escalation*. *Pain*, 2010. **151**(1): p. 22-9.
Evidence Level 4.
86. Dersh, J., et al., *Prescription opioid dependence is associated with poorer outcomes in disabling spinal disorders*. *Spine (Phila Pa 1976)*, 2008. **33**(20): p. 2219-27.
Evidence Level 3.

References

87. Volinn, E., J.D. Fargo, and P.G. Fine, *Opioid therapy for nonspecific low back pain and the outcome of chronic work loss*. *Pain*, 2009. **142**(3): p. 194-201.
Evidence Level 3.
88. Bohnert, A.S., et al., *Association between opioid prescribing patterns and opioid overdose-related deaths*. *JAMA*, 2011. **305**(13): p. 1315-21.
Evidence Level 2.
89. Gomes, T., et al., *Opioid dose and drug-related mortality in patients with nonmalignant pain*. *Arch Intern Med*, 2011. **171**(7): p. 686-91.
Evidence Level 3.
90. Cifuentes, M., R. Powell, and B. Webster, *Shorter time between opioid prescriptions associated with reduced work disability among acute low back pain opioid users*. *J Occup Environ Med*, 2012. **54**(4): p. 491-6.
Evidence Level 4.
91. Franklin, G.M., et al., *Changes in opioid prescribing for chronic pain in Washington State*. *J Am Board Fam Med*, 2013. **26**(4): p. 394-400.
Evidence Level 4.
92. Moore, B.C., C.J. Easton, and T.J. McMahon, *Drug abuse and intimate partner violence: a comparative study of opioid-dependent fathers*. *Am J Orthopsychiatry*, 2011. **81**(2): p. 218-27.
Evidence Level 3.
93. Butler, S.F., et al., *Validation of the revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R)*. *J Pain*, 2008. **9**(4): p. 360-72.
Evidence Level 1c.
94. Racoosin, J.A., et al., *New evidence about an old drug--risk with codeine after adenotonsillectomy*. *N Engl J Med*, 2013. **368**(23): p. 2155-7.
Evidence Level 5.
95. Johnson, E.M., et al., *Unintentional prescription opioid-related overdose deaths: description of decedents by next of kin or best contact, Utah, 2008-2009*. *J Gen Intern Med*, 2013. **28**(4): p. 522-9.
Evidence Level 3.
96. Wasan, A.D., et al., *Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain*. *Clin J Pain*, 2007. **23**(4): p. 307-15.
Evidence Level 4.
97. Federation of State Medical Boards, *Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain (FSMB)*. 2013.
98. Karlsson, J., et al., *Is buprenorphine transdermal patch equally safe and effective in younger and elderly patients with osteoarthritis-related pain? Results of an age-group controlled study*. *Curr Med Res Opin*, 2014. **30**(4): p. 575-87.
Evidence Level 4.
99. Naing, C., et al., *Safety and efficacy of transdermal buprenorphine for the relief of cancer pain*. *J Cancer Res Clin Oncol*, 2013. **139**(12): p. 1963-70.
Evidence Level 1a.

References

100. Tao, X.G., et al., *Natural history of opioid dosage escalation post-injury: a cohort study of injured workers in the State of Louisiana*. J Occup Environ Med, 2012. **54**(4): p. 439-44.
Evidence Level 1c.
101. Neven, D.E., et al., *The development of the Washington State emergency department opioid prescribing guidelines*. J Med Toxicol, 2012. **8**(4): p. 353-9.
Evidence Level 5.
102. Juurlink, D.N., I.A. Dhalla, and L.S. Nelson, *Improving opioid prescribing: the New York City recommendations*. JAMA, 2013. **309**(9): p. 879-80.
Evidence Level 5.
103. Butler, S.F., et al., *Cross validation of the current opioid misuse measure to monitor chronic pain patients on opioid therapy*. Clin J Pain, 2010. **26**(9): p. 770-6.
Evidence Level 4.
104. Knisely, J.S., et al., *Prescription Opioid Misuse Index: a brief questionnaire to assess misuse*. J Subst Abuse Treat, 2008. **35**(4): p. 380-6.
Evidence Level 1c.
105. Butler, S.F., et al., *Development and validation of the Current Opioid Misuse Measure*. Pain, 2007. **130**(1-2): p. 144-56.
Evidence Level 1c.
106. Kahan, M., et al., *Canadian guideline for safe and effective use of opioids for chronic noncancer pain: clinical summary for family physicians. Part 1: general population*. Can Fam Physician, 2011. **57**(11): p. 1257-66, e407-18.
Evidence Level 5.
107. U.S. Department of Transportation. *Medical Review Officers*. Accessed 04/04/2014]; Available from: <http://www.dot.gov/odapc/mro>.
108. Manchikanti, L., et al., *Comparative evaluation of the accuracy of benzodiazepine testing in chronic pain patients utilizing immunoassay with liquid chromatography tandem mass spectrometry (LC/MS/MS) of urine drug testing*. Pain Physician, 2011. **14**(3): p. 259-70.
Evidence Level 2.
109. Manchikanti, L., et al., *Comparative evaluation of the accuracy of immunoassay with liquid chromatography tandem mass spectrometry (LC/MS/MS) of urine drug testing (UDT) opioids and illicit drugs in chronic pain patients*. Pain Physician, 2011. **14**(2): p. 175-87.
Evidence Level 1c.
110. Mikel, C., et al., *Therapeutic monitoring of benzodiazepines in the management of pain: current limitations of point of care immunoassays suggest testing by mass spectrometry to assure accuracy and improve patient safety*. Clin Chim Acta, 2012. **413**(15-16): p. 1199-202.
Evidence Level 1c.
111. Kerns, R.D., D.C. Turk, and T.E. Rudy, *The West Haven-Yale Multidimensional Pain Inventory (WHYMPI)*. Pain, 1985. **23**(4): p. 345-56.
Evidence Level 1b.

References

112. Dworkin, R.H., et al., *Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations*. J Pain, 2008. **9**(2): p. 105-21.
Evidence Level 5.
113. Ostelo, R.W., et al., *Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change*. Spine (Phila Pa 1976), 2008. **33**(1): p. 90-4.
Evidence Level 5.
114. Von Korff, M., et al., *Grading the severity of chronic pain*. Pain, 1992. **50**(2): p. 133-49.
Evidence Level 1b.
115. Krebs, E.E., et al., *Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference*. J Gen Intern Med, 2009. **24**(6): p. 733-8.
Evidence Level 1c.
116. American Chronic Pain Association (ACPA), *Living with Arthritis Ability Chart*. 2012.
Evidence Level 5.
117. Passik S, H.H., Rzetelny A, Pesce A, Mikel C, Kirsh K. . *Trends in Drug and Illicit Use from Urine Drug Testing from Addiction Treatment Clients. Proceedings of the International Conference on Opioids*. 2013. Boston, MA.
Evidence Level 5.
118. Naliboff, B.D., et al., *A randomized trial of 2 prescription strategies for opioid treatment of chronic nonmalignant pain*. J Pain, 2011. **12**(2): p. 288-96.
Evidence Level 1b.
119. State of Connecticut Workers' Compensation, *Medical Protocols: Introduction*. 2014.
120. State Medical Board of Ohio (SMBO), *Guidelines for Prescribing Opioids for the Treatment of Chronic, Non-Terminal Pain 80 mg of a Morphine Equivalent Daily Dose (MED) " Trigger Point"*. 2013.
121. Trescot, A.M., et al., *Opioid guidelines in the management of chronic non-cancer pain*. Pain Physician, 2006. **9**(1): p. 1-39.
Evidence Level 5.
122. Manchikanti, L., et al., *Breakthrough pain in chronic non-cancer pain: fact, fiction, or abuse*. Pain Physician, 2011. **14**(2): p. E103-17.
Evidence Level 5.
123. Alspaugh, D.W., *Desertion, Abandonment, and Neglect of Patient*. . JAMA 1967. **199**(8): p. 245–246.
Evidence Level 5.
124. Chou, R., et al., *Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors: a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline*. J Pain, 2009. **10**(2): p. 131-46.
Evidence Level 5.

References

125. Almeida, J.C. and E.W. Grimsley, *Coma from the health food store: interaction between kava and alprazolam*. *Ann Intern Med*, 1996. **125**(11): p. 940-1.
Evidence Level 4.
126. Bramness, J.G. and H. Kornor, *Benzodiazepine prescription for patients in opioid maintenance treatment in Norway*. *Drug Alcohol Depend*, 2007. **90**(2-3): p. 203-9.
Evidence Level 4.
127. College of Physicians and Surgeons of British Columbia (CPSBC), *Recommendations for the Use of Methadone for Pain*. 2010: Vancouver, BC.
Evidence Level 5.
128. Rapp, S.E., L.B. Ready, and M.L. Nessly, *Acute pain management in patients with prior opioid consumption: a case-controlled retrospective review*. *Pain*, 1995. **61**(2): p. 195-201.
Evidence Level 2.
129. Carroll, I., et al., *A pilot cohort study of the determinants of longitudinal opioid use after surgery*. *Anesth Analg*, 2012. **115**(3): p. 694-702.
Evidence Level 1b.
130. Theunissen, M., et al., *Preoperative anxiety and catastrophizing: a systematic review and meta-analysis of the association with chronic postsurgical pain*. *Clin J Pain*, 2012. **28**(9): p. 819-41.
Evidence Level 4.
131. Jones, T. and S.D. Passik, *A comparison of methods of administering the opioid risk tool*. *J Opioid Manag*, 2011. **7**(5): p. 347-51.
Evidence Level 1c.
132. Jones, T., et al., *A comparison of various risk screening methods in predicting discharge from opioid treatment*. *Clin J Pain*, 2012. **28**(2): p. 93-100.
Evidence Level 1c.
133. American Psychiatric Association (APA), *Substance use disorder*, in *Diagnostic and statistical manual of mental disorders*. 2013: Washington, D.C.
134. National Institute on Drug Abuse (NIDA), *Drugs, Brains, and Behavior: The Science of Addiction*. July 2014.