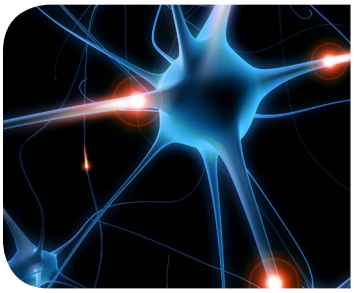


Prescribing Opioids for Chronic Non-Cancer Pain

Intermountain's Functional Restoration and Chronic Pain Development Team developed this care process model (CPM) to address the complexity of treating chronic pain patients with opioid medication. It should be used in conjunction with Intermountain's *Chronic Non-Cancer Pain Management CPM* and is not intended for patients < 18 years of age or those receiving treatment for cancer, palliative care, or end-of-life care. The recommendations outlined in the CPM are aligned with current Utah and CDC prescribing guidelines.

Key POINTS

Utah is ranked 4th in the U.S. for opioid-related deaths.[CDC2] The CDC recently reported that there is not enough evidence to support the benefits of long-term opioid therapy for chronic pain.[CDC] Therefore, **providers should manage patients conservatively. Opioids are not to be used as first-line or routine therapy for chronic pain.**

BEFORE PRESCRIBING

- **ASSESS** pain, function, and risks with the tools discussed in this CPM (***PEG***, ***SOAPP-R***, ***PHQ-9***, ***GAD-7***, ***MHI packets***, ***NIDA quick-screen***.) See page 7.
- **CHECK** the Utah Controlled Substance Database (CSD) or your local prescription drug monitoring program.
- **CONSULT or REFER,** if needed, to a pain specialist or for a substance use disorder evaluation (including medication-assisted therapy) for opioid use disorder.

WHEN PRESCRIBING

- **SET CRITERIA** for stopping or continuing opioid therapy when initiating therapy; as part of the discussion, document the criteria with a ***Controlled Substance Medication Management Agreement (MMA)***—see page 9.
- **TITRATE SLOWLY.** Use extra precautions when increasing a dose to ≥ 50 MME per day (using the morphine equivalency calculator)—see page 12. Daily dosages ≥ 90 MME per day are associated with significant risk, and rationale should be documented.
- **AVOID** concurrent prescriptions for benzodiazepines and sedative hypnotics.
- **MONITOR** for potential harms or misuse using the tools and guidance in this CPM (e.g., COMM, Opioid Red Flags checklist, Risk Assessment checklist, Urine drug screening).
- **CONSIDER** prescribing the rescue medication naloxone based on risk.
- **REFER** patient to chronic pain self-management education programs.
- **UPDATE** the *Chronic Pain Treatment Plan and Goals* in the patient record; note the diagnosis associated with opioid use on the problem list.

AFTER PRESCRIBING

- **SCHEDULE** follow-up visits based on dose, risk, and comorbidities.
- **COMPLETE** a comprehensive assessment at least annually, or more frequently, depending on risk. Include pain, function, side effects, and risk assessments.
- **PERFORM** a urine drug screen; review CSD records.
- **REVIEW** and update the MMA with the patient.

WHAT'S INSIDE?

TRACKING OUR PROGRESS

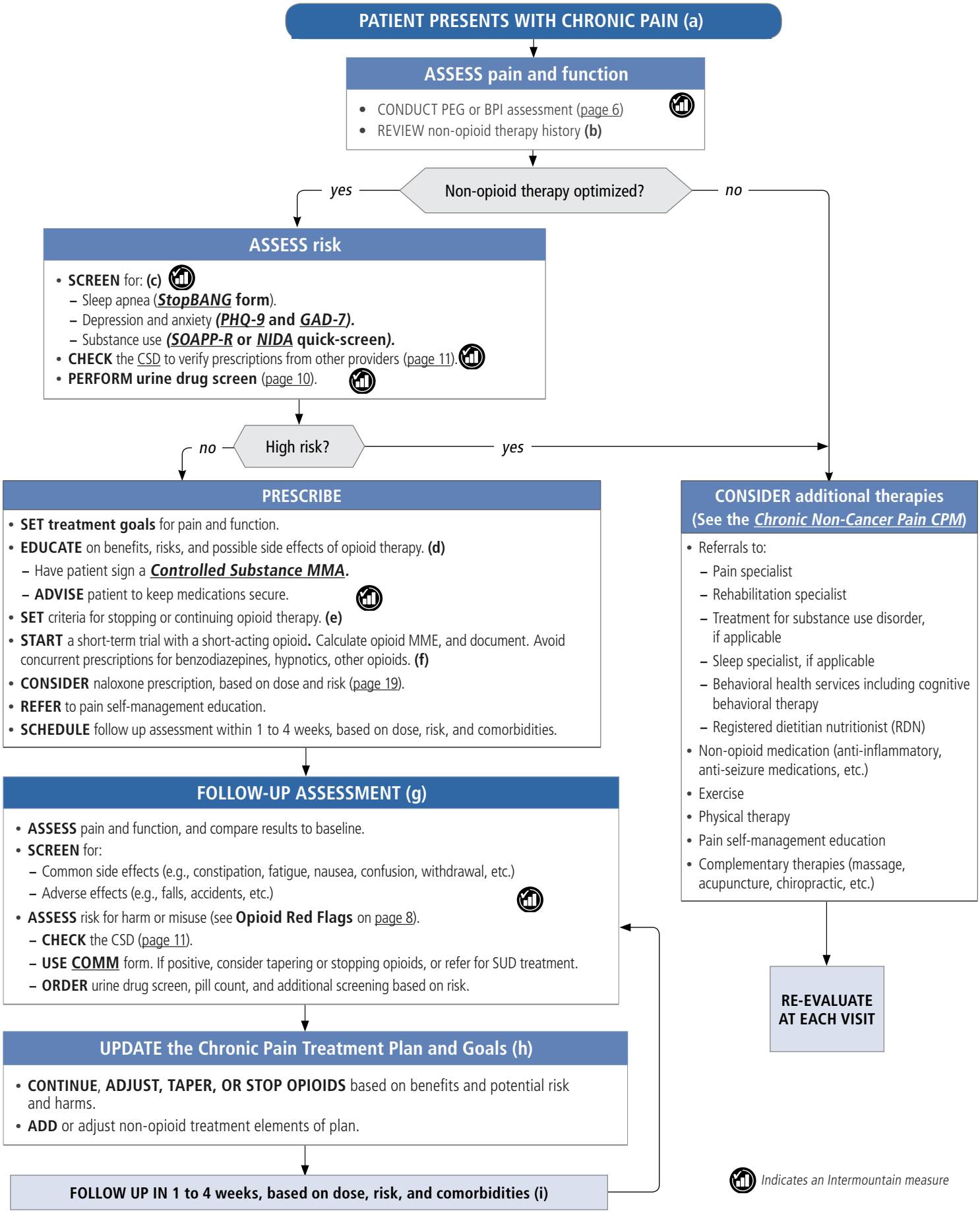
To determine system-wide benchmarks, the Functional Restoration / Chronic Pain Development team will monitor and evaluate the:

- Use of assessment tools
- Amount of morphine milligram equivalencies (MMEs) ordered
- Number of Controlled Substance MMAs
- Use of urine drug monitoring prior to opioid prescribing, and at least annually
- Number of naloxone prescriptions

Indicates an Intermountain measure

Intermountain® Healthcare

ALGORITHM 1: OPIOID THERAPY FOR CHRONIC PAIN: INITIAL



ALGORITHM 1 NOTES

(a) When to consider opioid therapy

Opioid therapy should only be initiated when ALL of the following criteria are met:

- Pain is moderate to severe, and adequate trials of other treatments and non-opioid analgesics have failed.
- The potential benefits outweigh the risks, and measurable treatment goals have been set.
- The patient is informed of the risks and benefits, and an MMA is signed.
- All medical records from referring providers are available, and drug tests are reviewed.

(b) Review of non-opioid therapy history

Review patient use of non-opioid therapies, including physical therapy, exercise, diet, complementary therapies, and procedures.

(c) Screening for sleep apnea, depression, and substance use disorder

Evaluate with sleep study if:

- The patient's ***STOP-BANG*** score is ≥ 5.
- Opioid dosage is greater than 50 MMEs (methadone > 20 mg per day).
- The patient or family observes abnormal breathing patterns during sleep.
- The patient reports hypersomnia or insomnia.
- Benzodiazepines or other hypnotics are part of the treatment plan.

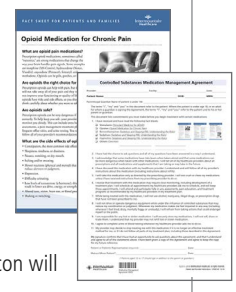
(*See the Obstructive Sleep Apnea CPM for more information.*)

Screen for depression or anxiety using the PHQ-9 or GAD-7 as these disorders often accompany chronic pain. (See table 1 on page 7.)

Discuss personal and family history of opioid use, substance use, misuse, and addiction. In patients with a known history of substance use, psychiatric illness, or aberrant drug-related behaviors, opioid therapy should only be considered with a highly-structured treatment plan that includes more frequent monitoring. Use the risk assessment tools on page 8 as a guide.

(d) Education and agreement

Intermountain's resources for informed consent are:



- ***Opioid Medication for Chronic Pain*** is a patient education fact sheet that explains safe opioid use and necessary risk monitoring.
- The ***Controlled Substance MMA*** includes specific agreements related to safety and monitoring. This agreement can be scanned as an image acquisition under *MMA* in the electronic health record. To view the MMA:
  - **In HELP2:** If a scanned image is present, an MMA icon will appear on the patient's record.
  - **In iCentra:** Once the image is scanned, it will appear under important patient notifications as a direct link to view the MMA.

(e) Set criteria for stopping opioid therapy[CDC]

Discontinue opioid therapy if:

- Adverse effects outweigh the benefits.
  - Adjust dose to reduce or eliminate adverse effects.
  - Consider changing medications or adding non-opioid medications.
- Patient demonstrates dangerous or illegal behaviors including misuse or diversion (see Opioid Red Flags on page 8).
- Pain is not relieved.

(f) Short-term opioid trial[CDC]

Use a brief trial with short-acting opioid medications as follows:

- Prescribe the lowest dose possible and titrate slowly to decrease the risk of adverse affects. **NOTE:** Utah Medicaid rules restrict initial short-acting opioid prescriptions to 7 days.
- Titrate opioid therapy incrementally until adequate pain relief is achieved and no serious harms or adverse effects are observed.
- Consider dose titration as generally complete after the first few weeks; dose adjustments may be needed periodically thereafter.

(g) Follow-up assessment

- **Adverse effects:** Check for common adverse events and side effects (page 18).
- **Pain assessment:** Consider trending the patient's answers to the 3 questions on the ***PEG assessment scale (PEG)*** or the severity score on the ***Brief Pain Inventory (BPI)*** (page 6).
- **Improvement in function:** Consider trending the patient's answers to the three questions on the **PEG** or to the interference score on the **BPI** (page 6).
- **Predicting risk of misuse, abuse, or harm:** (page 8)
  - Check the CSD (page 11).
  - Perform urine drug tests. (page 10).
  - Utilize the ***SOAPP–R*** for opioid-naive patients, ***COMM*** for patients currently taking opioids, and ***NIDA*** to check for at-risk substance use.
  - Evaluate patient's risk of opioid addiction or abuse before prescribing opioids. If any one method results in a high-risk evaluation, consider the patient at high risk. (See table 1 on page 7.)

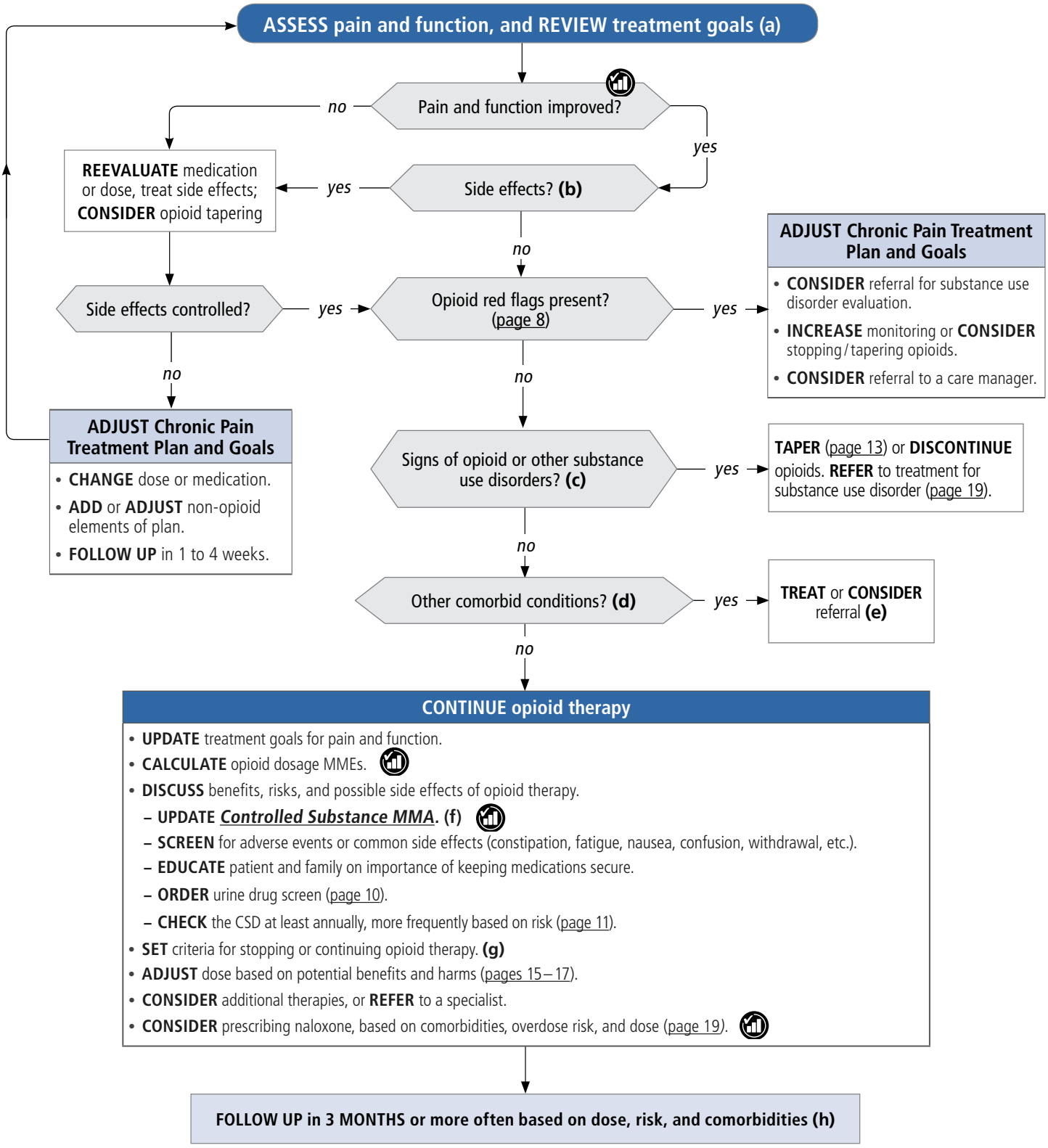
(h) Chronic pain treatment plan and goals

The *Chronic Pain Workflow* in iCentra allows providers to assess patients, document visits, and record treatment plans and goals. Accessed through the *Chronic Pain Management Workflow* component in iCentra, which can be added at the top of the ambulatory workflow page. (See table 1 on page 7.)

(i) Ongoing follow up and monitoring for new users

- The frequency of follow up should depend on the:
  - Dose
  - Patient's risk for opioid use disorder
  - Patient's pain condition, functional status, and level of pain
  - Results of urine drug screen and CSD check
- More frequent follow-up visits should be considered for higher-risk patients or if changing dose or medication.

ALGORITHM 2: OPIOID THERAPY FOR CHRONIC PAIN: ONGOING



Indicates an Intermountain measure

ALGORITHM 2 NOTES

(a) Assessing pain and function

- **Pain severity:** Consider trending the patient's answers to the three questions on the **PEG** scale or the severity score on the **BPI** (page 6).
- **Function:** Consider trending the patient's answers to the three questions on the **PEG** scale or the interference score on the **BPI** (page 6).

(b) Common side effects

- Constipation
- Nausea, vomiting, dry mouth
- Itching and/or sweating
- Difficulty urinating
- Sleepiness, tiredness, dizziness
- Slower mental and physical reactions
- Lower levels of testosterone
- Changes in appetite, vision, heart rate, or blood pressure
- Shaking, twitching

(c) Assessing risk of opioid or substance use disorder

Risk	Utah's Controlled Substance Database (page 11)	Urine drug screen (page 10)	SOAPP-R score (page 7)	NIDA score (page 7)	COMM score (page 7)
LOW RISK	Prescription history is consistent with patient's self-report; patient obtains prescriptions from a single provider.	Consistent with patient's self-report of current medications	< 10	No "yes" answers	< 9
MODERATE RISK	Patient obtains pain medication prescriptions from more than one prescriber or pharmacy; CSD history is consistent with patient's self-report	Consistent with patient's self-report of medications and other controlled substances such as benzodiazepenes	10 to 21	NA	NA
HIGH RISK (any ONE of these results)	Database shows pain medication prescriptions from more than one source AND prescription history is not consistent with patient's self-report.	NOT consistent with the patient's self-report OR indicates drugs of abuse	≥ 22	Any "yes" answer	≥ 9

(d) Other comorbid conditions

Comorbid conditions contributing to chronic pain include:

- Diabetes
- Cardiovascular disease
- Pulmonary disease, including COPD and asthma
- Obesity
- Other disabilities
- Psychosocial problems
- Childhood neglect, abuse, or trauma
- Mental health conditions, such as
  - Depression
  - Anxiety

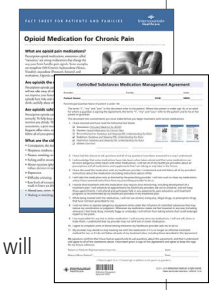
(e) Treat or consider referral

Consider:

- Pain self-management education
- Non-opioid medication
- Exercise and/or physical therapy
- Complementary therapies
- Referrals to:
  - Care management
  - Interventional specialist
  - Rehabilitation specialist
  - Substance abuse treatment, if applicable
  - Sleep specialist, if applicable
  - Behavioral health services, such as cognitive behavioral therapy
  - Registered dietitian nutritionist (RDN)

(f) Medication Management Agreement

Intermountain's resources for informed consent are the:



- ***Opioid Medication for Chronic Pain*** patient education fact sheet that explains safe opioid use and necessary risk monitoring.
- ***Controlled Substance MMA,*** which includes specific agreements related to safety and monitoring. It can be scanned as an image acquisition under *MMA* in the electronic health record. To view the MMA:
  - **In HELP2:** If a scanned image is present, an MMA icon will appear on the patient's record.
  - **In iCentra:** Once the image is scanned, it will appear under important patient notifications as a direct link to view the MMA

(g) When to discontinue opioid therapy

- **Reevaluate** opioid treatment if goals are not met or if function does not improve.
- **Discontinue** opioid therapy if:
  - Adverse effects outweigh the benefits.
  - Patient demonstrates dangerous or illegal behaviors including misuse or diversion (see **Opioid Red Flags** on page 8).
  - Pain is not relieved.

(h) Ongoing follow up and monitoring

- The frequency of follow up should depend on the:
  - Dose
  - Patient's risk for opioid addiction or abuse
  - Patient's pain condition, functional status, and level of pain
  - Results of urine drug screen and CSD check
- More frequent follow-up visits should be considered for higher-risk patients or if changing the dose or medication.

CLINICALLY MEANINGFUL IMPROVEMENT METRIC

A 30% improvement in pain and function is considered clinically meaningful and should be discussed with the patient during the MMA informed consent process.

PEG SCORING[KRE]

The PEG score is the average of the three individual item scores. To calculate the PEG score:

Q1 + Q2 + Q3 / 3 = _____

The final PEG score can mean very different things for different patients. Like most other screening instruments, it is most useful in tracking changes over time.

The PEG score should decrease over time after therapy has begun.

BPI VS PEG

The BPI is typically used in research settings and may be impractical for primary care providers. Hence, **Intermountain recommends the use of the PEG scale.**

PATIENT ASSESSMENT

Pain and function

Regular assessment of a patient's pain and function is essential to quality pain management. Continue opioids only as a careful decision by you and your patient when improvements in both pain and function outweigh the harms or adverse effects.[KRE] Discuss patient-centered goals and improvements in function (such as returning to work and recreational activities) and assess pain using validated instruments such as the ***PEG assessment scale*** or ***Brief Pain Inventory (BPI)***.

PEG assessment scale[KRE]

The PEG assessment scale is a three-item pain assessment tool located in iCentra:

- **P**ain average
- Interference with **E**njoyment of life
- Interference with **G**eneral activity

It comprises one intensity item and two interference items.

PEG Assessment Scale

Q1: What number from 0 – 10 best describes your pain in the past week?

0 1 2 3 4 5 6 7 8 9 10

No pain **Pain as bad as you can imagine**

Q2: What number from 0 – 10 describes how, during the past week, pain has interfered with your enjoyment of life?

0 1 2 3 4 5 6 7 8 9 10

Not at all **Complete interference**

Q3: What number from 0 – 10 describes how, during the past week, pain has interfered with your general activity?

0 1 2 3 4 5 6 7 8 9 10

Not at all **Complete interference**

Brief Pain Inventory (BPI)

The BPI includes two scales that assess pain intensity and pain-related functional impairment:

1. **BPI severity scale** (questions 1 – 6): Assesses the intensity of current pain and pain at its least, worst, and average during the past week on scales from 0 ("no pain") to 10 ("pain as bad as you can imagine")
2. **BPI interference scale** (questions 7 – 9): Assesses pain-related functional interference with seven items covering different domains (general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life) rated from 0 ("does not interfere") to 10 ("interferes completely")

Assessment tools in iCentra

The following forms can be used as **PowerForms** in iCentra. These forms are located under the **forms tab** in the ***Pain Management Workflow*** or in the **Ad Hoc forms** under **ambulatory >> pain management.**

TABLE 1. Assessment tools

Tool and description	When to use	
	Initial assessment	Treatment monitoring
Brief Pain Inventory (BPI)		
Patient-rated tool; measures the severity of pain and impact on function	√	√
Chronic Pain Treatment Plan and Goals		
Used to determine and document pain and function goals	√	√
Current Opioid Misuse Measure (COMM)		
Clinician tool; used to assess patients currently taking opioids		√
Generalized Anxiety Disorder 7-item (GAD-7) scale		
Patient-rated tool for assessing generalized anxiety disorder	√	√
Intermountain-Modified National Institute on Drug Abuse (NIDA) Quick Screen		
Determines current substance use (page 19)	√	√
MHI Baseline Patient Summary		
Helps identify and track mental health symptoms, impairment, and comorbidities that may otherwise be overlooked	√	√
Modified Oswestry Disability Index: Back		
Patient-rated tool; measures the degree of disability and the patient's ability to manage daily tasks.	√	√
Opioid Red Flags		
Identifies signs of opioid use, misuse, or diversion	√	√
Patient Exam: Lumbar Spine Evaluation		
Guides providers through patient exam	√	
Patient Self History: Back Pain		
Patient-rated tool; identifies type and source of back pain	√	
PEG pain score **(recommended chronic pain assessment tool located in iCentra)**		
Patient-rated tool; a three-item scale comprised of 1 intensity item and two interference items	√	√
PHQ-9 (Patient Health Questionnaire)		
Patient-rated tool that screens for the 9 symptoms of depression; can help evaluate and diagnose a major depressive episode and suicidal ideation	√	√
Screener and Opioid Assessment of Patients with Pain - Revised® (SOAPP-R®)		
For patients not currently taking opioids; identifies patient risk for opioid addiction or misuse; validated with chronic pain patients	√	√
STarT (Subgrouping for Targeted Treatment) Back Screening Tool		
A subgrouping tool that allocates patients into low-, medium-, or high-risk subgroups to guide decision making about treatment and referral	√	
STOP-BANG Questionnaire		
Screens for obstructive sleep apnea	√	√

SUGGESTED CLINICAL WORKFLOW

Pre-visit:

- Nurse or Medical Assistant
  - Prints Utah Controlled Substance Database report
  - Checks *Controlled Substance MMA* for last revision date
  - Determines date of patient's last urine drug screen

At visit:

- Nurse or Medical Assistant
  - Provides patient with assessment forms to complete
  - Enters the completed assessment forms into the patient's medical record
- Physician
  - Uses CPM assessment tools (checklists, etc.) to assess and document pain, function, risks, side effects (if present), etc.
  - Orders urine drug screen, if needed.
  - Updates MMA annually or more often for higher risk patients or if changing dose or medication
  - Refers to care manager for goal setting, education, and treatment coordination
  - Refers to other specialties
- Front Desk: Schedules follow up visits in accordance with the patient's treatment plan

NOTE: The iCentra Chronic Pain Workflow (CPW) gives providers an option for documenting encounters with patients with chronic pain. The CPW is comprised of multiple components that allow providers to assess patients, document visits, and record treatment plans in the ***Chronic Pain Treatment Plan and Goals***. The CPW is accessed through the *Pain Management Workflow* component in iCentra, which can be accessed at the top of the ambulatory workflow page. Click on the link above for further instructions.

OPIOID RED FLAGS

Opioid treatment can lead to potential abuse.
Be alert to when the patient:

- ☐ Appears sedated, confused, intoxicated, or exhibits withdrawal symptoms (below).
- ☐ Requests more frequent refills and with a sense of urgency. May claim that their medications were "lost."
- ☐ Travels to the clinic with others who each request controlled substance prescriptions on the same day.
- ☐ Resists changes in therapy despite clear evidence of adverse effects; wants to direct their own care.
- ☐ Implies or makes direct threats to the prescriber or staff.
- ☐ Refuses to sign a MMA or is non-compliant with the MMA.
- ☐ Alters, forges or rewrites prescriptions.
- ☐ Requests specific drug combinations.
- ☐ Repeatedly seeks medications from ED.
- ☐ Suffers overdose or frequent injuries and accidents.
- ☐ Shows signs of skin tracks or scars.
- ☐ Has a CSD report suggesting evidence of "doctor shopping" or use of multiple pharmacies to acquire controlled substance prescriptions; may "bad mouth" other physicians.
- ☐ Has urine drug screens inconsistent with prescribed medications or that show evidence of illegal substances.
- ☐ Has family and/or friends who report suspected diversion activities.

NOTE: Extra precautions should be taken to keep opioid medications secure when children and adolescents are present in the household.

OPIOID WITHDRAWAL

Symptoms of opioid withdrawal can occur any time a long-term prescription is curtailed or stopped. Symptoms can start any time after 6–30 hours of stopping opioids, depending on the dose and type of opioid.

Signs of withdrawal include:

- Agitation, anxiety, and/or insomnia
- Muscle cramps, runny nose, sweating, yawning, tearing, goose bumps
- Abdominal cramps and/or diarrhea
- Nausea and/or vomiting
- Dilated pupils

☑ Risk assessment *checklist*

Certain factors can increase the risk of harm or overdose. It is important to assess and follow up regularly.

1. ASSESS increased risk factors:

- ☐ Personal or family history of substance use disorder
- ☐ Use of illicit drugs
- ☐ Concurrent use of benzodiazepines, hypnotics, or sedatives
- ☐ High opioid dosage (≥ 50 MMEs/day)
- ☐ Obtaining opioids from multiple providers
- ☐ Pregnancy
- ☐ Age (< 18 years or > 65)
- ☐ Psychiatric diagnosis or psychosocial comorbidities including anxiety, depression, and childhood neglect, abuse, or trauma
- ☐ Renal or hepatic insufficiency
- ☐ COPD or other underlying respiratory or cardiovascular conditions
- ☐ Sleep apnea (STOP-BANG score ≥ 5.) →

STOP-BANG Assessment for sleep apnea

Snoring loudly
Tiredness/fatigue during the day
Observed apnea
Pressure (being treated for high BP)
Body mass index > 35
Age > 50 years
Neck size > 16" for a woman or 17" for a man
Gender — greater risk for males

2. MONITOR using urine drug testing for other prescription or illicit drugs, and CHECK the CSD.

3. DISCUSS potential **side effects**:

- ☐ **Nausea or constipation.** Routinely consider a bowel regimen before the development of constipation, especially in older individuals.
- ☐ **Sedation or alteration in mental status.** Discuss safety concerns, especially when changing doses or adding new medications.
- ☐ **Breathing interruptions during sleep.** Concurrent use of benzodiazapines increase risk of respiratory depression, especially in patients with sleep apnea who already have a higher risk for respiratory depression.
- ☐ **Taking or craving more opioids than prescribed or difficulty controlling use.** These are signs of possible opioid use disorder.

NOTE: Healthcare providers should be vigilant in looking for less-recognized effects including serotonin syndrome and hormonal disturbances in patients receiving opioids (see page 17).

4. OBSERVE. Look for early warning signs for overdose such as:

- Confusion, sedation, slurred speech, and abnormal gait (Consider further evaluation if present.)
- Changes in sleep
- Changes in anxiety and depression

(See page 18 for additional overdose risk factors.)

5. PREVENT. Prescribe naloxone for higher-risk patients (see page 19).

Controlled Substance Medication Management Agreement (MMA)

The MMA should be completed prior to prescribing opioids and is the recommended method to document the informed consent process. Treatment expectations are reviewed with patients and families to help keep patients safe.

Key benefits

The MMA allows providers and patients to start treatment with a mutual understanding by:

- Enhancing transparency
- Prompting discussion and engages patients in the decision-making process
- Helping to set functional goals and clarifies roles
- Documenting the patient's understanding and acceptance of risks and informed consent
- Helping avoid misunderstandings that may occur over time
- Providing a foundation for subsequent decisions, including medication changes, and setting criteria for treatment discontinuation

Key questions

When obtaining informed consent, a provider must be clearly understood by the patient. Use open-ended questions to facilitate teach-back and allow sufficient time for questions. Translators may be needed to help with the process. The following questions can assist with understanding:

- Does the patient understand the various treatment options?
- Has the patient been reasonably informed of the potential benefits and harms associated with the treatment options?
- Is the patient free to choose among those options, free from coercion by the healthcare provider, the patient's family, or others?
- Does the patient have the capacity to communicate his or her preferences?

Discussion points

- Share the responsibility between the patient and provider.
- Avoid punitive, stigmatizing, or dominating language.
- Do not set limitations based on the providers' convenience. There must be clear benefit to the patient.
- Do not use coercion.
- Do not insist on behaviors unrelated to actual use of medications.
- Do not use the term "fired" or threaten abandonment.


Opioid Medication for Chronic Pain

Controlled Substance Medication Management Agreement

Providers should review the MMA together with the *Opioid Medication for Chronic Pain* fact sheet as part of the informed consent process. When complete, the MMA must be entered into the patient's medical record.

RECOGNIZING AND MANAGING DIVERSION

If a patient reports taking opioids but there is no medication in the urine drug screen and/or if the Controlled Substance Database lists multiple prescribers, this might indicate the patient is seeking opioids for diversion or distribution. (Review **Opioid Red Flags** on page 8.)

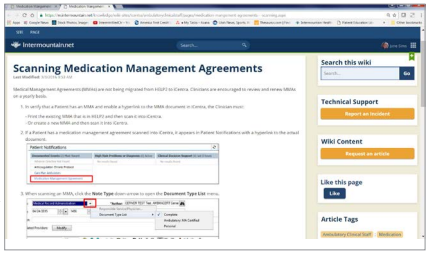
- **If you suspect a patient is diverting or distributing medication,** present the evidence and consequences to the patient. For example: "Based on x, y, and z, I think it's possible that you may be giving or selling your medications to other people. This is a crime that places the public and our children at risk."
- **If you suspect a patient is diverting or distributing a controlled substance, take action — start by seeking legal counsel.** See page 11 for contact information.

Providers should consider routine review of their DEA Registration report to view prescriptions written on their DEA number to ensure others are not prescribing under their DEA number.

RECORDING THE MMA IN ICENTRA

Controlled Substance MMAs have been migrated from HELP2 to iCentra. Follow these instructions on intermountain.net when you need to:

- Find out if a patient has an existing MMA
- Enter a new MMA into a patient's medical record
- Remove an MMA from a patient's medical record



MARIJUANA: KEY CONSIDERATIONS

Intermountain will continue to focus on marijuana's impact on health and well-being — and on our responsibility to educate and treat patients according to research-based recommendations.

When prescribing opioids, consider the following:

- Marijuana is a Schedule 1 drug; it's use is illegal according to Federal and Utah law.
- The use of marijuana by patients with chronic pain may put them at risk for opioid misuse.[MAN,IVE]
- The use of marijuana has its own risks including addiction, increased risk of anxiety and panic disorder, motor vehicle accidents, and cancer.[VOL]
- These risks may be difficult to predict due to the difficulty of controlling quantity, potency, and frequency of use.

For additional information on marijuana risks, see page 12 of the *Substance Use Disorder CPM.*

INTERPRETING QUANTITATIVE AND DEFINITIVE TEST RESULTS

The test report lists the presence or concentration of each analyte respective to cutoff concentration per each drug. Various factors can cause the lab report to be different than expected.

- **If prescribed medications are not detected,** possible explanations include medication diversion, medication non-adherence diluted urine, accelerated metabolism, or poor drug absorption (due to drug interactions, drug-metabolizing enzymes, or genetic variations).
- **If medications/substances are detected that were not prescribed,** possible explanations include unreported prescriptions, use of non-prescribed drugs, a false-positive due to a substance/medication that interferes with the test assay, or a medication error (ask the patient to bring their medication with them).
- **If the lab report shows results that are unexpected based on the prescription or patient report,** talk with the patient about the results. (See the Substance Use Disorders CPM for information on talking with patients about potential substance use issues.)

Urine drug testing

Urine drug testing should be used before starting opioid therapy and at least annually. Urine drug testing does not provide accurate information about **how much** or **what** *dose* of opioid or other drugs the patient took. Urine drug tests can be misinterpreted and some patients may feel they are stigmatized. Routine use of urine drug tests for all patients on opioids at the clinic may help patients feel less stigmatized.[CDC]

Drug testing panels

Drug testing panels designed specifically for monitoring patients enrolled in pain programs are recommended, as they are designed to include drugs and metabolites specific for pain management and for monitoring drug use. Providers should be familiar with the drugs included in urine drug testing panels used in their practice and should understand how to interpret results for these drugs.

General testing guidelines:

- **Plan for responding to unexpected results.** Providers should explain to patients that urine drug testing is intended to improve patient safety. Explain that the test may yield unexpected results (e.g., presence or absence of prescribed medication or illicit drugs not reported by the patient) and that the provider and the patient will talk about the test results together.
- **Ask patients about their use of prescribed or other drugs and whether or not the test may yield unexpected results.** This gives patients an opportunity to provide information about changes in their use of prescribed opioids or other drugs.
- **Discuss unexpected results with the local laboratory or toxicologist and with the patient.** Discussion can sometimes yield a candid explanation of why a particular substance is present or absent. For example, a patient may explain that the test is negative for prescribed opioids because he or she felt opioids were no longer helping and stopped taking them.

Understanding test results

There are two types of urine drug testing: **presumptive** and **definitive**.

Presumptive testing

Drug immunoassay screens that are performed either in a laboratory or point of service are considered presumptive. They require confirmatory testing by more specific analytical methods to determine which drugs and metabolites triggered the positive screen.

Presumptive tests are not recommended for patients in pain management programs because it is not possible to resolve prescription compliance, polypharmacy, or drug abuse due to the poor specificity and limited sensitivity of the immunoassays. Obligatory mass spectrometry-based confirmation testing is therefore required for accurate assessment.

Definitive testing

This testing aims to eliminate standard immunoassay screens by definitively measuring a large number of drugs and metabolites in a single test utilizing mass spectrometry. Because the patient is presumed to be positive for medication/substances, this workflow reduces costs and testing turnaround time while expanding the number of drugs and metabolites that are tested.[BAU] **These tests are recommended to monitor adherence to an MMA in patients who are prescribed opioids.** Definitive testing:

- Allows clinicians to monitor polypharmacy and illicit drug use, investigate further, and discuss the situation with the patient if results differ from the patient's self-report.
- Often includes a quantitative measurement panel for urine creatinine as a measure of sample integrity and to help normalize results for serial testing events.

Results are reported qualitatively (i.e., positive or negative) or quantitatively (typically in ng/mL).

Intermountain recommends the ARUP definitive test, *Pain Management Drug Panel by High-Resolution Time-of-Flight Mass Spectrometry and Enzyme Immunoassay, Urine (test code 2007479). 80100–QW.*

NOTE: Refer to each patient's insurance coverage regarding urine drug testing, as each policy provides specific guidance for coverage. Select Health *Policy #569: Urine Drug Testing in the Outpatient Setting* can be found through the Select Health website at https://intermountainphysician.org/selecthealth/Pages/home.aspx.

Utah Controlled Substance Database (CSD)

The CSD collects data on the dispensing of Schedule II–V drugs from all retail, outpatient hospital pharmacies, and in-state/out-of-state mail order pharmacies. The data are accessible by authorized individuals and may be used to identify potential cases of drug over-utilization, diversion, and over-prescribing of controlled substances throughout Utah. The Utah opioid prescribing guidelines recommend that providers **check the CSD before prescribing opioids, and recheck it quarterly** during chronic opioid therapy. **In addition, all physicians licensed to prescribe controlled substances must register to use the database, take a tutorial, and pass a test** that focuses on the database and the prescribing of controlled substances. (See **Regulatory Resources** on page 19.)

To access the CSD, go to csd.utah.gov. (Providers outside the state of Utah will need to check with your state's Prescription Data Monitoring Program for specific details.)

- **If you need a login, click the Create Account link and follow the steps** (see recommendation in sidebar at right). You'll need to provide personal contact info (including a reliable e-mail address), information for three security questions, and your DEA number. All fields must be filled in; otherwise background checks will be delayed and cannot be completed.
- **You can authorize three members of your clinic staff to check the database on your behalf.** To do this, give written notice to the Division of Occupational and Professional Licensing about the employee. After conducting a brief background check, the division will give the employee a password to the database.
- **Click the training link at the top of the database website to find the online tutorial** once you have logged in with your PIN.
- **After checking the CSD for information on a patient,** document that you checked the database.

NOTE: Utah healthcare providers licensed to prescribe controlled substances are required to participate in the online continuing education on Schedule II and III substances. In addition to this course, providers are required to complete the 30-minute CSD tutorial and examination every two years.

WHEN TO CONTACT INTERMOUNTAIN LEGAL COUNSEL

If you suspect a patient is diverting or distributing a controlled substance, seek legal counsel for help in evaluating the situation and deciding what to do. Intermountain-employed physicians can contact:

- Intermountain legal counsel directly at 801-442-3519
- The Intermountain Compliance Hotline at 800-442-4845 and ask to speak with Intermountain legal counsel

HOW TO SEARCH THE UTAH CSD

When searching patient names in the Utah CSD, it is possible to return multiple results on the same name or even no results on patient known to have one or more opioid prescriptions. This is because patients are sometimes prescribed medication under pseudonyms, nicknames, or initials (e.g., MJ for Mary Jane Brown). To optimize your search results, follow these steps:

1. Using the search function:
   Type in the first three letters of the patient's FIRST NAME and date of birth (DOB).
   (Example: Mar + 06/01/1967)
2. Note the name, addresses, and additional data of probable matches.
3. Perform a second search using the first three letters of the patient's LAST NAME and DOB.
   (Example: Bro + 06/01/1967)
4. Note and compare the additional data from the two searches. This will help you confirm that you are viewing the correct person's records under their known identities.
5. Sort the columns in either ascending or descending order to view the patient records chronologically before clicking on "PDF" and opening the records.
6. Search in other state databases.
   - Utah's CSD accesses information from 10 other states (including Idaho).
   - You will need both FIRST and LAST name plus the DOB.
   - Wyoming requires a faxed, written request. Turnaround usually runs from 10 to 60 minutes.

OPIOID MANAGEMENT PRIOR TO ELECTIVE SURGERY[CHO1]

Communication between the prescribing provider and the surgeon is essential for developing a coordinated treatment plan that includes a timeline for tapering opioids.

- Postoperative pain relief may be difficult to achieve after surgery and is best managed by a multi-modal approach.
- Care must be taken to manage the patient's expectations.
- Consider tapering high-dose opioids before surgery as this may be helpful for postoperative pain control and reducing risk of opioid-induced hyperalgesia.
- Once the patient presents for surgery, postoperative pain is best managed by keeping the patient on the same dose and adding break-through medications during immediate postoperative period.

Buprenorphine

It may prove difficult to provide adequate analgesia for patients who take buprenorphine and require surgery due to the unique pharmacological properties of this medication. Patient factors, including addiction / relapse history, pain history, and concern regarding anticipated procedure pain, should factor into decisions regarding the best strategy for perioperative analgesia management.

PRESCRIBING OPIOIDS

These guidelines follow the Utah prescribing guidelines and were developed with guidance from the 2016 CDC recommendations.

How to Calculate MMEs[CDC]

Calculating the total daily dose of opioids helps identify patients who may benefit from closer monitoring, reduction or tapering of opioids, prescribing of naloxone, or other measures to reduce overdose risk.

1. Determine the total daily amount of each opioid the patient takes (all sources).
2. Convert each to the appropriate MME. (Multiply the dose for each opioid by the conversion factor on the table at right.)
3. Add them together. (CDC guidelines recommend doses < 50 MME / day and cautions against prescribing doses > 90 MME / day due to increased risk. The rational for doses above that level should be clearly documented.)

TABLE 2. MME Conversion

Opioid	Conversion Factor
Morphine *(reference)*	1
Codeine	0.15
Hydrocodone	1
Oxycodone	1.5
Oxymorphone	3
Hydromorphone	4
Tapentadol	See ***CMS Guidelines*** for conversion information
Tramadol	

CAUTION:

Do not use the calculated dose in MMEs to determine dosage for converting one opioid to another. If converting to a different opioid, the new opioid should be 25 % to 50 % lower to avoid unintentional overdose caused by incomplete cross-tolerance and individual differences in opioid pharmacokinetics.

USE EXTRA CAUTION:

- The conversion factor for **methadone** increases at higher doses (see page 14). There is no reliable conversion factor when transitioning to methadone.
- **Fentanyl transdermal patches are dosed in mcg/hr instead of mg/day.** Absorption is affected by heat and other factors.

HOW TO USE THE TOTAL DAILY OPIOID DOSE IN CLINICAL PRACTICE

- When prescribing opioids at any dosage, **prescribe the lowest effective dose**.
- **Use extra precautions** when increasing dose to ≥ 50 MME per day, such as:
  - Monitoring and assessing pain and function more frequently
  - Discussing dose reduction or tapering and discontinuing opioids if benefits do not outweigh harms
  - Consider offering naloxone
- Avoid, or document the need for increasing dosage to ≥ 90 MME/day.

Extended-release and long-acting opioids

The use of extended-release (ER) and long-acting (LA) opioids may be appropriate for some patients with chronic pain. However, **there is no evidence that continuous, time-scheduled use of ER/LA opioids is more effective or safer than intermittent use of short-acting opioids.**[CDC,ARG]

ER/LA opioids include methadone, transdermal fentanyl, and extended-release versions of opioids such as:

- Oxycodone
- Hydrocodone
- Buprenorphine
- Tapentadol
- Oxymorphone
- Hydromorphone
- Morphine

These medications should only be used for opioid-tolerant patients and only when continuous, round-the-clock pain relief is necessary. Clinicians should neither initiate opioid treatment with ER/LA opioids nor prescribe ER/LA opioids for intermittent use or acute pain conditions. Combining short-acting opioids with ER/LA opioids is generally discouraged. There is no evidence that this practice improves pain control and may lead to dose escalation. In addition, many long-acting opioids remain very costly, despite generic availability.

Due to its unique risks, **methadone** should only be prescribed by physicians who are familiar with its pharmacokinetics and are prepared to closely monitor patients (see page 14). **Transdermal fentanyl** also has complex absorption and pharmacokinetic properties and should be used only by clinicians who are familiar with these properties and can closely monitor patients (**see below**).

When switching someone from short-acting to long-acting opioids (or vice versa), care should be taken to avoid unintentional overdose due to variable pharmacokinetics of these drugs. It is recommended that when making this change, the total daily morphine equivalency should be calculated and then the ER/LA formulation be started at a 25%–50% lower morphine equivalency (**see example at right**).

CONVERTING FROM A SHORT-ACTING TO A LONG-ACTING OPIOID

Current dose = 6 hydrocodone/acetaminophen immediate release 10–325 mg tablets per day

1 mg of hydrocodone = 1 mg of morphine

The MME is 60 mg per day.
Reduce by 25–50%.

New dose is 30–45 MME per day for a long-acting formulation. (e.g., 30–45 mg of a ER/LA morphine per day or 20–30 mg of an ER/LA oxycodone).

Fentanyl

Pharmaceutical **fentanyl** is a synthetic opioid pain reliever approved for treating severe pain. **Fentanyl is at least 50 to 100 times more potent than morphine.** It is not intended to treat postoperative pain or intermittent pain because of the high risk for respiratory depression. It is often diverted for illegal use.

Short-acting fentanyl (pills, nasal spray, lozenges) is usually only prescribed for advanced cancer pain. Transdermal fentanyl is sometimes prescribed for chronic pain. When prescribing transdermal fentanyl, start with the lowest possible dose (12–25 mcg/hr) and consider consultation with a pain management specialist.


Fentanyl (Duragesic): Safe use instructions

Provide the patient fact sheet, ***Fentanyl (Duragesic): Safe use instructions,*** that explains the safe use of fentanyl and necessary risk monitoring.

TAPERING OPIOIDS


Tapering Opioid Pain Medication

The Functional Restoration/Chronic Pain Development Team has developed a set of guidelines to assist providers with tapering patients' opioid pain medications. These guidelines address:

- When to consider tapering
- When to cut back and by what percentage
- How to approach patients who may be anxious about the process
- How to recognize the signs of withdrawal
- When to use methadone and buprenorphine

See the ***Tapering Opioid Pain Medication*** guideline.

ILLEGAL NARCOTICS

Heroin (diacetylmorphine) is a powerful Schedule I narcotic that is increasingly used as a substitute for, or in addition to, prescription opioid medications.

In Utah, heroin ranks as the third most-used illicit drug, behind methamphetamine and marijuana.[CEN1] People who are addicted to prescription opioids:

- Are 40 times more likely to also become addicted to heroin
- Often look for opioids or heroin on the street because they are less expensive or more accessible

Potent synthetic opioids, and sometimes other substances, are often found in counterfeit preparations of opioids obtained on the street and on the Internet. If there is any question that a patient may be using synthetic opioids, fentanyl, or fentanyl analogs, consider ordering special lab testing for these substances as they will not be detected in routine urine tests.

Testing for heroin use

Heroin rapidly metabolizes to morphine, which is what's usually detected on drug tests. More specific testing can detect the intermediate metabolite **6-mono-acetyl morphine,** which confirms that the morphine is from heroin instead of a prescription opioid.[NID]

For any positive test result, see Intermountain's ***Substance Use Disorder CPM,*** and refer as appropriate.

METHADONE AND QTC INTERVAL SCREENING[AAO, CHO1]

Methadone is associated with cardiac arrhythmia complications, specifically QT-prolongation and TdP. To avoid complications, prescribing physicians should:

- **Obtain a baseline ECG** for patients who are at risk for QTc prolongation.
- **Consider ordering a baseline ECG** on all patients who are starting methadone.
- **Not prescribe methadone** if QTc is greater than 500 ms, and monitor frequently if QTc is between 450 – 500 ms.
- **Repeat** the ECG in 2 – 4 weeks after initiating methadone if QTc is > 450 ms or if the patient has history of syncope.
- **Perform a follow-up ECG** if methadone dose reaches 40 mg/day and again at 100 mg / day.
- **Perform an ECG at any time** if new risk factors for QTc prolongation develop or the patient develops signs or symptoms suggesting arrhythmia.

OPIOID USE IN WORKER'S COMPENSATION

About 32 % of the U.S. workers' compensation population use opioids. However, there is little evidence to support the long-term use of opioids.[HEG] The 2014 American College of Occupational and Environmental Medicine guidelines cite the following:

- Surgical outcomes are worse when opioids are used preoperatively.
- Workers who receive more than a one-week supply of opioids or two or more opioid prescriptions soon after an injury have almost double the risk of disability at one year post-injury, compared with workers who do not receive opioids.
- Conservative initial therapies (e.g. acetaminophen or non-steroidal anti-inflammatory drugs) are recommended rather than opioids in almost all cases.
- Opioid-sparing treatments and lower doses of postoperative opioids are associated with better long-term functional outcomes.

Methadone

The pharmacokinetic and pharmacodynamic properties of methadone are complex and not well understood. **Only providers who understand methadone's unique risk profile and are prepared to educate and closely monitor their patients should consider prescribing methadone for pain.**[CDC] Providers should consult with a pain management specialist if considering methadone. Methadone represents only about 2 % of the opioids prescribed in the U.S., but has contributed to almost 5,000 deaths per year due to its long and variable half-life, which necessitates careful titration.[CDC] Key prescribing guidelines include the following:

- Methadone IS NOT an appropriate "first-choice" extended-release, long-acting opioid.
- Methadone IS NOT appropriate for acute pain, PRN use, breakthrough pain, or for patients with a variety of risk factors.[CHO2, MOD]
- Methadone IS an option for patients who do NOT have risk factors and who are:
  - On high doses of another opioid with opioid tolerance or opioid-induced hyperalgesia
  - Allergic to other opioids or are taking a CYP3A4 enzyme inducer or inhibitor (see page 17)

Dosing and titration

Many equianalgesic tables are inaccurate as they do not account for methadone's long half-life and repeated dosing. Rather than using a conversion table, consider the following:

- Regardless of the dosage of the previous opioid, begin with a starting methadone dose of 2.5 mg to 5 mg, 2 to 3 times per day. (Reduce dose for elderly or frail patients to 1 mg to 2 mg.)
- Reduce the original opioid by 30 % – 35 % before the first methadone dose. Gradually cross-taper the original opioid as methadone is increased. Make short-acting medication available for breakthrough pain, and warn patients NOT to take additional methadone for breakthrough pain.
- Increase the methadone dose by 20 % – 33%, no more frequently than weekly, at face-to-face visits.

In pregnancy...

Methadone doses may need to be increased or the dosing interval decreased when chronic doses are used during the second or third trimesters. To learn more about caring for pregnant patients who are using opioids, see Intermountain's ***Opioid Use in Pregnancy CPM.***

Enhanced monitoring

Assess the patient every 1 to 2 days when methadone is initiated or the dose is increased. Consider additional blood levels and ECG (see sidebar at left).

Utah state guidelines recommend that the physician be available 24 hours per day during titration of methadone.

The spouse or caregiver should be available to check patients at least twice daily and call physician for advice if problems occur. Educate the family or caregiver to:

- Be aware of potential drowsiness, and watch for respiratory depression.
- Know the signs and symptoms of opioid overdose.
- Call 911.
- Use naloxone if patient is unconscious or unable to be aroused.

If the patient does not have a full-time, live-in caregiver (such as a significant other or family member) consider following up in 1 to 2 days after any dose adjustment, or schedule phone appointments that (if missed) can trigger a safety check or EMS call.

Special populations

Consult the medication tables on pages 20–26 for specific information pertaining special-population dosing for each medication.

Patients with renal or hepatic impairment

Providers should use additional caution and increased monitoring to minimize risks of opioids prescribed for patients with renal or hepatic insufficiency.

Patients with sleep-disordered breathing

This category of patients includes those with sleep apnea, risk factors for sleep-disordered breathing, congestive heart failure, stroke, and obesity.

- Experts note that **careful monitoring and cautious dose titration** should be used if opioids are prescribed for patients with mild sleep-disordered breathing.
- **Avoid prescribing opioids** to patients with moderate or severe sleep-disordered breathing whenever possible to minimize risks for opioid overdose.
- If a patient is considered high-risk as a result of a STOP-BANG assessment, **obtain sleep study results before** prescribing.

Geriatric patients[CDC]

Inadequate pain treatment among geriatric patients has been documented. Pain management in this population can be challenging given increased risks of both non-opioid pharmacologic therapies and opioid therapy in this population. Geriatric patients are more likely to have renal impairment, decreased hepatic blood flow, increased susceptibility to the accumulation of opioids, and a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose.

Some older adults suffer from cognitive impairment, which can increase risk for medication errors and make opioid-related confusion more dangerous. Older adults are more likely than younger adults to experience comorbid medical conditions and more likely to receive multiple medications, making them more at risk for overdose and death.

Providers should use additional caution and increased monitoring (e.g., the MMA) to minimize risks of opioids prescribed for geriatric patients. To help reduce the risk of addiction, adverse effects, overdose, and diversion, use universal precautions such as:

- Prescribing exercise or bowel regimens to prevent constipation
- Assessing the patient's risk for falls
- Monitoring for cognitive impairment
- Educating the family / caregivers about adverse effects, risks and harms
- Prescribing naloxone

PREGNANCY AND BREASTFEEDING

Intermountain data suggest that **chronic use of opioids among pregnant women has resulted in more NICU admissions for neonatal abstinence syndrome and an increased length of stay for newborns.**

Providers and patients together should carefully weigh risks and benefits when making decisions about whether to initiate opioid therapy for chronic pain during pregnancy. Women who are pregnant or planning to become pregnant should be made aware of the possible risks, including:

- Neonatal Abstinence Syndrome (NAS)
- Neural tube defects
- Congenital heart defects
- Gastroschisis
- Stillbirth
- Poor fetal growth
- Preterm delivery

To care for pregnant patients, Intermountain's CPM, *Opioid Use in Pregnancy*, provides the following guidance:

- **Screen and educate every pregnant patient.**[ACO] Non-prescribed opioid use is common and often overlooked — even by patients. Obstetric care providers should screen using the *Intermountain-modified NIDA Quick Screen* flash card at every encounter or at least once every trimester of pregnancy.
- If the patient uses opioids, **coordinate management through team-based care** involving the patient's obstetric care provider, primary care physician, pain management specialist, and (if needed) a substance use disorder professional.

Breastfeeding women[CDC]

- Women taking opioid pain medications regularly (who do not have HIV) and are not using illicit drugs are generally encouraged to breastfeed.
- Prior to prescribing opioids, determine whether or not the patient is taking any other medication.
- During breastfeeding, avoid prescribing codeine per FDA recommendations. If needed, prescribe the lowest possible dose due to possible risk of newborn death.

See Intermountain's *Opioid Use in the Lactating Mother CPM*.

MEDICATION-ASSISTED THERAPY (MAT) FOR HEROIN OR PRESCRIPTION OPIOID ADDICTION

Research supports the use of methadone, buprenorphine (with or without naloxone), and/or naltrexone in the management of opioid use disorder as part of a comprehensive treatment plan.[KAM] Pharmacological agents include both agonist and antagonist medications. Buprenorphine is a partial agonist at the μ opioid receptor.

- Buprenorphine/naloxone (Suboxone) is preferred because if it is ground up and injected, the naloxone will precipitate withdrawal.
- Buprenorphine/naloxone can be used for short-term detox, but relapse rates are very high; it is best used as a maintenance medication.
- Office-based prescribing and retail pharmacy dispensing of buprenorphine/naloxone is permitted.

Studies report that MAT treatment is safe and effective for the mother and newborn and more effectively reduces neonatal abstinence syndrome severity vs. methadone.[ASA]

Federal and state regulations pertaining to use of these agents for treating opioid use disorder require:

- The treating physician to apply to SAMHSA for a waiver to the Controlled Substances Act.*
- Limits on the number of patients per prescriber
- A second DEA number for the prescriber

*In February 2017, NPs and PAs will also be able to apply for the waiver)

Patients with prior overdose

For patients who have experienced an opioid overdose, providers should seriously consider discontinuing opioids (refer to Intermountain's *Tapering Opioid Pain Medication* guideline.) Refer the patient to a behavioral health specialist for evaluation of possible suicidal thoughts and actions (see Intermoutain's *Suicide Prevention CPM*). If a decision is made to continue opioid treatment, the provider should:

- **Discuss and document the increased risks** for overdose with the patient (see page 18).
- **Incorporate strategies to mitigate risk** into the management plan, such as:[CDC]
  - Prescribing shorter-duration, lower-dose opioids
  - Increasing the frequency of urine drug screening
  - Engaging family members in monitoring
  - Educating the patient and family on opioid overdose and the use of naloxone
  - Prescribing naloxone (see page 19)
- **Look for coexisting use** of alcohol, benzodiazepines, or other hypnotics (e.g., zolpidem, zaleplon, and eszopiclone). **Do not coprescribe medications with these medications/substances.** Consult with the prescriber of those medications to discuss and formulate a treatment plan.
- **Evaluate for substance use disorder.** See Intermountain's *Substance Use Disorder CPM,* and refer as appropriate.

Patients with mental health conditions

Psychological distress augments the experience of pain and decreases function. Use validated instruments, such as the *Generalized Anxiety Disorder (GAD)-7* and the *Patient Health Questionnaire (PHQ)-9* or Intermountain's *MHI packet* to assess for mental health disorders, post-traumatic stress disorder, depression, and/or other comorbidities. These instruments may help providers improve overall pain treatment outcomes by ensuring contributing factors or other conditions are addressed.

- **Additional caution and increased monitoring is necessary** to lessen the increased risk for opioid use disorder among patients with mental health conditions (including depression, anxiety disorders, and PTSD) as well as increased risk for drug overdose, suicide, and opioid use disorder among patients with depression.[CEN2]
- **Opioid therapy should not be initiated during acute psychiatric instability or uncontrolled suicide risk.** Patients may be more impulsive and at risk for overdose. Providers should consider a consultation with a behavioral health specialist for any patient with a history of suicide attempt or significant psychiatric disorder. See Intermountain's *Suicide Prevention CPM*.
- **Avoid prescribing benzodiazepines** or other hypnotics (e.g., zolpidem, zaleplon, and eszopiclone) for anxiety disorders and other mental health conditions. The combination can exacerbate opioid-induced respiratory depression and increase risk for overdose. (See the FDA boxed warning.)
- **Consult with behavioral health specialists.** Treatment for depression can improve pain symptoms as well as depression and might decrease overdose risk. Consider that some psychiatric medications can cause added sedation and respiratory depression (such as quetiapine [Seroquel]). See Intermountain's *Management of Depression CPM*.
- For treatment of chronic pain in patients with depression, **strongly consider using tricyclic or serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants** for analgesic as well as antidepressant effects unless these medications are contraindicated.

CYP2D6 and CYP3A4 Inhibitors/Inducers

Most opioids are metabolized by cytochrome P450 (CYP450) 2D6 and/or 3A4. Opioid metabolism results in the production of active and inactive metabolites. Many drugs/substances (as well as one's genetics) can affect CYP2D6 and CYP3A4 activities, thereby affecting opioid metabolism and clinical effects.[FDA1] Inhibitors are defined as follows:

- A **strong inhibitor** is one that causes a >5-fold increase in the plasma AUC values or more than 80% decrease in clearance.
- A **moderate inhibitor** is one that causes a >2-fold increase in the plasma AUC values or 50–80% decrease in clearance.
- A **weak inhibitor** is one that causes a >1.25-fold but <2-fold increase in the plasma AUC values or 20–50% decrease in clearance.

Monitor patients with any CYP3A4 inhibitor or inducer who are taking these opioids. If the inhibitor/inducer changes, adjust the opioid dose cautiously and increase monitoring for efficacy and toxicity. The most common inhibitors/inducers are listed below. For all others, review the *Flockhart P450 Drug Interaction Table.*

TABLE 3. CYP2D6 and CYP3A4 inhibitors and inducers[IND]

CYP2D6 Strong inhibitors	CYP34A Strong inhibitors	CYP3A4 Inducers
• Buproprion • Fluoxetine • Paroxetine • Quinidine • Cinacalcet	• Clarithromycin • Itraconazole • Ketoconozole • Nefazodone • HIV antivirals: – Indanavir – Ritonavir – Nelfinavir – Saquinavir	• Barbituates (Phenobarbital) • Carbamazepine • Oxcarbazepine • Glucocorticoids • Modafinil • Phenytoin • Pioglitazone • Rifampin • St. John's Wort • HIV antivirals: – Efavirenz – Nevirapine

Drug-deterrent medications

Abuse-deterrent (AD) technologies were designed to prevent opioid use by unintended routes of administration. Formulations with AD properties target the known or expected routes of abuse, such as crushing in order to snort or dissolving in order to inject, for the specific opioid drug substance.

The fact that a product has FDA-approved labeling describing AD properties does not mean the product is impossible to abuse or that these properties necessarily prevent overdose and death. Because opioid medications must in the end be able to deliver the opioid to the patient, there may always be some potential for abuse of these products. In addition, abuse-deterrent technologies do not prevent unintentional overdose through oral intake.[FDA2]

Abuse-deterrent formulations are generally more expensive than non abuse-deterrent generic products. Additionally, some opioids may require step therapy or prior authorization before coverage by payer. Check with the patient's prescription insurance, Medicare, or Medicaid formulary for more specific information.

OPIOID ROTATION

Rotation refers to a switch among opioid medications in an effort to improve therapeutic response or reduce undesirable effects.

When to rotate

Opioid rotation may be considered when there is an apparent loss of analgesic effect for the current opioid. Rotating medication can help avoid dose escalation.[POP]

How to rotate

When rotating a patient on opioid therapy from one medication to another, use the **equianalgesic dose** to plan the dosage of the new medication. The equianalgesic dose is the opioid dose that produces an equal degree of analgesia. Morphine sulfate is usually the standard reference by which all other opioid analgesics are compared. To identify the lowest therapeutic dose of the new medication and plan the transition:

1. **Calculate the patient's current 24-hour opioid dose** (including both short- and long-acting medications).
2. **Convert the dose to its morphine milligram equivalent** using the table on page 12.
3. **Determine the dosing interval** by the formulation used (short acting vs. long acting).
4. **Reduce the calculated dose** of the new medication by approximately 25% to 50%.
5. **Determine the equivalency of the new medicine** based on the reduced dose.
6. **Cross-titrate,** slowly increasing the dose on the new medication while simultaneously decreasing the dose of the old medication.
7. **Consider prescribing a 1- to 3-day supply** of breakthrough pain medications.
8. **Reassess the strategy** in 3 to 5 days.

OPIOID OVERDOSE RISKS[CDC]

Patients most at risk for overdose include those who have overdosed on opioids before and/or are taking any medications as follows:

- High doses of opioid medicine
- Methadone
- Long-acting opioids
- Opioids for chronic pain management,
- Several different opioids on a rotating schedule
- More than one prescription opioid medicine
- A mix of opioids with alcohol or other drugs like benzodiazepines or other sedatives
- More opioids than prescribed or getting prescriptions filled early or at many different pharmacies
- Is the child of someone using opioids at home
- Using heroin
- Using opioids for non-medical reasons
- Using prescription opioid medicines and:
  - Smokes cigarettes
  - Has obstructive sleep apnea
  - Has lung, kidney, heart, or liver disease
  - Has HIV/AIDS
  - Is ≥65
  - Has dementia or Alzheimer's disease
- Living far from a hospital
- Recently released from a correctional facility or a substance abuse treatment center

Managing side effects

Opioid side effects, with prevention/management strategies, are listed below.

TABLE 4. Managing side effects

Side effect	Prevention/management notes
Most serious	
Respiratory depression	Screen for sleep apnea and avoid opioids if moderate-to-severe sleep apnea is present. Avoid prescribing opioids with sedatives, hypnotics, benzodiazepines, barbiturates, and alcohol. Educate and prescribe naloxone. (See page 15.)
Most common	
Constipation	Educate patients to increase fiber and fluids; start with a mild peristaltic stimulant (senna, dried plums, polyethylene glycol 3350) with a stool softener; increase dose if no BM in 48 hours. Second-line, more-expensive medications include a new category of constipation medications for opioid-induced constipation (naloxegol, lubiprostone, linaclotide). Despite availability, they are not considered first-line.
Nausea or vomiting	Consider prophylactic antiemetic therapy. Ondansetron (Zofran) is recommended because it does not interact with opioids. Use caution when prescribing ondansetron with drugs that cause serotonergic effects such as tramadol and tapentadol.
Itching	Reduce dose and increase frequency, change opioid, and/or consider a non-sedating antihistamine (e.g., cetirizine).
Less common	
Cognitive effects (such as sedation, confusion)	Reduce dose and/or change opioid; avoid sedatives.
Perceptual effects (e.g., hallucinations, depression)	Rule out other causes, and eliminate all nonessential CNS-acting medications (e.g., steroids). Reduce opioid dose, or switch opioid.
Sexual dysfunction	Rule out other causes. Reduce dose.
Serotonin syndrome	Avoid combining opioids (particularly tramadol) with medications that increase serotonin. (See box below.)
Hyperalgesia	Hyperalgesia, the result of a dysfunction of the nociceptive system, results in peripheral and/or central sensitization. Symptoms include widespread pain not consistent with physical findings and/or pain out of proportion to mild stimuli. Animal studies note a lower pain threshold after exposure to sustained opioids. Reduce the dose, taper the patient off opioid medication, or rotate the opioid.

LESS-RECOGNIZED HORMONAL AND SEROTONIN EFFECTS

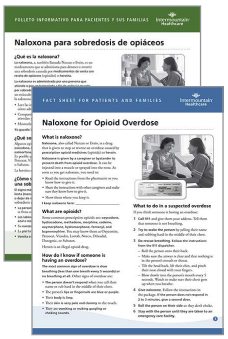
The US Food and Drug Administration (FDA) recently mandated opioid labeling changes to highlight several of the less-recognized effects including serotonin syndrome, adrenal gland suppression, and decreased sex hormone levels.

The FDA updated the labeling for all medications in the opioid drug class to include a statement about the risk for serotonin syndrome in the "Drug Interactions and Adverse Reactions" sections, adrenal insufficiency in the "Warnings and Precautions" section, and decreased sex hormone levels in the *Adverse Reactions* section.

The strength of evidence is greater for **serotonin syndrome** than for adrenal insufficiency. Further study is needed to define the scope and prevalence of these lesser-known adverse effects.

PREVENTING OVERDOSE DEATHS WITH NALOXONE

Utah law allows the prescribing of naloxone to anyone at risk for, or who may be in a position to assist someone at risk for, opioid overdose, even without a provider-patient relationship. (Utah Code Section 3, 26-55-101)


Naloxona para sobredosis de opiáceos

Naloxone for Opioid Overdose

Before prescribing:

- ☐ **Review** Intermountain's *Clinical Guideline for Prescribing Naloxone in the Outpatient Setting.*
- ☐ **Provide** patients and families with the *Naloxone for Opioid Overdose* fact sheet to help patients and their caregivers/family understand and identify risk factors.
- ☐ **Talk** with the patient and family. Educate the family on:
  - Opioid overdose risk
  - How to administer naloxone
  - The importance of keeping opioid medications secure
- ☐ **Find out** if there are children living in / visiting the home.

In Utah, *Pharmacy Collaborative Practice Agreements* (CPAs) allow patients to obtain naloxone in community pharmacies (including Intermountain Community Pharmacies) without a prescription from their provider. Contact the patient's local pharmacies to ask if they have a naloxone CPA in place.

TOLERANCE, DEPENDENCE, AND ADDICTION

It is important to distinguish addiction from tolerance, dependence, and pseudo-addiction, all of which can occur in the context of long-term opioid therapy. See the following definitions, established by the American Academy of Pain Medicine, American Pain Society, and the American Society of Addiction Medicine:[ASA]

- **Tolerance** is when the drug no longer has the same effect than it did initially. As a result, the patient must consume increasingly higher doses to achieve the same effect.
- **Physical dependence** is manifested by a drug-class specific withdrawal syndrome produced by cessation, dose reduction, decreasing blood level of the drug, and/or an antagonist.
- **Addiction** is a primary, chronic, neurobiological disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following:
  - Impaired control over drug use
  - Compulsive use
  - Continued use despite harm
  - Craving
- **Pseudo-addiction** is a term sometimes used to describe patient behaviors that may occur when pain is poorly-controlled. Patients with unrelieved pain may become focused on obtaining medications, may "clock watch," and may otherwise seem inappropriately "drug seeking." Even such behaviors as illicit drug use and deception can occur in the patient's efforts to obtain relief. Pseudo-addiction can be distinguished from true addiction in that the behaviors resolve when pain is effectively treated.

SUBSTANCE USE DISORDERS AND CHRONIC PAIN

Patients with chronic pain conditions present an additional challenge to providers when considering the risks of addiction or substance use disorder.

Providers should screen for substance use disorder (SUD), and monitor carefully during long-term opioid therapy.

If the patient is at high risk for SUD or is presenting with behaviors of abuse, diversion, or addiction, refer to a specialist for treatment. (See Intermountain's *Substance Use Disorders CPM* for more information.)

Medication management for a patient with an SUD and chronic pain should be supervised by a pain management provider.

RANDOM PILL COUNTS

Consider doing a random pill count for high-risk patients, especially if diversion is suspected. If you do a pill count, always count medications with the patient and have two persons in the room. Be sure to identify that the pills in the bottle are the same type and dose as identified on the label.

Examine patches to determine if they have been cut or scratched for possible diversion.

TABLE 5. SHORT-ACTING (Oral Dose) Opioid Medications[1,6,LEX]

Minimum dosing: For all medications, begin with the lowest possible dose.
Maximum dosing:[2] The maximum dose for all medications should not exceed 90 morphine milligram equivalents (MMEs) per day. (See page 12 for MME conversion table and additional cautions.)
Abuse-deterrent formulations may be more expensive; some long-acting opioids may require step therapy.

Medication	Lowest possible / Usual starting dose	50 MME Dose	90 MME Dose	Notes
codeine[3,4,5] • Used in combination with: – Acetaminophen (APAP) (Tylenol with Codeine #3 or Tylenol with Codeine #4) – Butalbital, aspirin,and caffeine (Fiorinal with Codeine) – Butalbital, acetaminophen, and caffeine (Fioricet with Codeine) • Alone	1 tablet every 6 hours (Tylenol with Codeine # 3)	333 mg / day	600 mg / day	• **Special populations.** Use with caution in the elderly or frail. • **Renal or hepatic impairment.** Initiate at lower doses or longer dosing intervals, and titrate carefully. • **Codeine alone is a weak analgesic;** more effective alternatives are available (including codeine combined with APAP). May cause more nausea and constipation than other opioids; 5 – 10 % of Caucasians lack enzyme (CYP2D6) to metabolize codeine to morphine; not the best choice for chronic use.
hydrocodone[3,4,5] • Used in combination with: – APAP (Norco, Vicodin) – Ibuprofen (Vicoprofen)	5 mg every 6 hours	50 mg / day	90 mg / day	• **Special populations**. Use with caution, and start at low end of initial dose range in elderly/frail patients. • **Renal or hepatic impairment.** Use lower initial dose for moderate impairment, and an even lower initial dose for severe impairment; use with caution, and monitor closely for respiratory and CNS depression.
hydromorphone **(Dilaudid)**	2 mg every 6 hours	12 mg / day	22 mg / day	• **Special populations**. Use with caution in elderly or debilitated patients. Risk of accumulation due to decreased clearance in patients with renal impairment. • **Renal or hepatic impairment.** Use lower initial dose for moderate impairment and an even lower initial dose for severe impairment; use with caution, and monitor closely for respiratory and CNS depression.
morphine **(MSIR)**	15 mg every 4 to 6 hours (Usually not used as first line oral therapy.)	50 mg / day	90 mg / day	• **Special populations.** Use with caution and reduce dose in elderly or debilitated patients. In **renal impairment**, avoid or start cautiously with lower doses, titrate more slowly, and carefully monitor for side effects, which may be delayed.

1 **All dosing based on tablets unless otherwise noted.** Consult with a pharmacist for liquid dosing equivalents.

2 **Minimum / maximum doses. Always begin with the lowest dose possible.** Ensure accurate diagnosis, and carefully weigh benefits (pain relief and function) against risk of increased dosage. If unclear, consult a pain management specialist. **Maximum dose should not exceed 90 MME** (see page 12).

3 **Affected by medications that inhibit CYP2D6** and medications that induce or inhibit CYP3A4 (page 17).

4 **For APAP-containing products.** Use the lowest possible dose and shortest duration in hepatic impairment. In renal impairment, do not use more frequently than every 6 hours (moderate impairment) or 8 hours (severe impairment). Counsel patients to avoid OTC products containing APAP.

5 **For ibuprofen-containing products**. Avoid use in advanced renal disease. Counsel patients to avoid OTC products containing ibuprofen, naproxen, and aspirin.

6 **Meperidine.** Meperidine is intentionally excluded from this table as it is not recommended.

TABLE 5. SHORT-ACTING (Oral Dose) Opioid Medications[1,6,LEX], *continued*

Minimum dosing: For all medications, begin with the lowest possible dose.
Maximum dosing:[2] The maximum dose for all medications should not exceed 90 morphine milligram equivalents (MMEs) per day. (See page 12 for MME conversion table and additional cautions.)
Abuse-deterrent formulations may be more expensive; some long-acting opioids may require step therapy.

Medication	Lowest possible / Usual starting dose	50 MME Dose	90 MME Dose	Notes
oxycodone IR[3,4,5] • Used in combination with: – APAP (Percocet) – Aspirin (Roxiprin) – Ibuprofen (Combunox) • Alone (Roxicodone)	5 mg every 6 to 8 hours	33 mg / day	60 mg / day	• **Special populations.** Reduce dose for elderly or debilitated patients. • **For oxycodone (alone).** Initiate at the lowest dosage. Use caution in renal impairment; in hepatic impairment initiate at 33 % – 50 % of the usual dosage and titrate carefully. • **Use with caution** in hepatic or renal dysfunction.
oxymorphone **(Opana IR)**	5 mg every 6 hours	17 mg / day	30 mg / day	• Instruct patients not to consume alcoholic beverages or use prescription or nonprescription products that contain alcohol while taking oxymorphone.
tapentadol **(Nucynta)**	50 mg every 6 hours	See CDC guidelines and / or CMS guidelines for conversion information.		• **Renal impairment:** Not recommended in patients with CrCl < 30 mL / minute • **Hepatic impairment:** Not recommended in severe impairment (Child – Pugh Class C) • Helpful for patients prone to nausea and vomiting with other opioids. • Prescribe with caution in patients taking SSRIs or tricyclic antidepressants.
tramadol[3,4] • Used in combination with acetaminophen APAP (Ultracet) • Alone (Ultram)	50 mg every 6 hours	See CMS guidelines for conversion information.		• **Special populations.** For elderly patients, do not exceed 300 mg / daily in divided doses; initiate at lowest dose possible. Use with caution in debilitated patients due to greater risk for respiratory depression, even at therapeutic doses. For patients with renal dysfunction, use 12-hour dosing, and do not exceed 200 mg / day. • **Tramadol can increase seizure risk,** especially in patients taking SSRIs, tricyclics, MAOIs, neuroleptics, or other drugs that decrease seizure threshold in patients with epilepsy or seizure risk; in those taking > 400 mg / day. • Poses higher risk of serotonin syndrome than other opioids; see page 17.

1 **All dosing based on tablets unless otherwise noted.** Consult with a pharmacist for liquid dosing equivalents.

2 **Minimum / maximum doses. Always begin with the lowest dose possible.** Ensure accurate diagnosis, and carefully weigh benefits (pain relief and function) against risk of increased dosage. If unclear, consult a pain management specialist. **Maximum dose should not exceed 90 MME** (see page 12).

3 **Affected by medications that inhibit CYP2D6** and medications that induce or inhibit CYP3A4 (page 17).

4 **For APAP-containing products.** Use the lowest possible dose and shortest duration in hepatic impairment. In renal impairment, do not use more frequently than every 6 hours (moderate impairment) or 8 hours (severe impairment). Counsel patients to avoid OTC products containing APAP.

5 **For ibuprofen-containing products**. Avoid use in advanced renal disease. Counsel patients to avoid OTC products containing ibuprofen, naproxen, and aspirin.

6 **Meperidine.** Meperidine is intentionally excluded from this table as it is not recommended.

TABLE 6. LONG-ACTING Opioid Medications[1,LEX]

Minimum dosing: For all medications, begin with the lowest possible dose.
Maximum dosing:[2] The maximum dose for all medications should not exceed 90 morphine milligram equivalents (MMEs) per day.
See page 12 for MME conversion table and additional cautions.

Medication	50 MME Dose	90 MME Dose	Notes
buprenorphine transdermal system[4] (Butrans)	See CMS guidelines for conversion information.		• **Dosing.** May be used in opioid-naïve patients at initial dose of 5 mcg/hour. Doses exceeding the maximum of 20 mcg/hr have shown QT prolongation in clinical trials. • **Titration.** Should occur on an individualized basis. Wait at least 3 days before increasing dose of buprenorphine. • **Conversion.** Buprenorphine conversion has the potential to precipitate withdrawal in patients who are already on opioids. Before conversion, taper total daily dose for up to 7 days to no more than 30 mg per day morphine (or equianalgesic dose). • **Application.** If adhesion is an issue, patch edges may be taped with first aid tape. Avoid external heat sources on application site.
buprenorphine buccal[4] (Butrans)	See CMS guidelines for conversion information.		• **Titration.** Taper current opioid to no more than 30 mg oral MME daily before initiating. Base initial dose on daily opioid dose prior to taper; additional short-acting analgesics may be needed during taper. Titrate in increments of 150 mcg every 12 hours, no more frequently than every 4 days; additional short-acting analgesics may be needed during titration. • **Special populations.** Use reduced dose in elderly or debilitated patients. Use with caution in renal impairment. For moderate hepatic impairment (Child-Pugh Class C), use with caution and monitor carefully, For severe hepatic impairment, reduce starting dose and reduce titration dose by 50 %. • **Administration.** Educate patient not to chew, swallow, touch, or move film after placement. Liquids and food can be consumed after film dissolves. Film should not be cut or torn. Avoid applying to areas of the mouth with any open sores or lesions.
fentanyl transdermal system[3,4] (Duragesic)	See CMS guidelines for conversion information. Fentanyl is provided in multiple dosage forms and absorption/bioavailability vary.		• **Dosing.** Use only in opioid-tolerant patients who have been taking >60 mg/day morphine (or equianalgesic dose) for at least 1 week. • **Titration:** Base increments on supplemental opioid doses with ratio of 25 mcg/hr fentanyl for every 90 mg/day of morphine equivalent. Wait at least 3 days after starting dose, then increase no more often than every 6 days. Half-life continues 17 hours after removal; steady state is reached after two 72-hour applications. • **Special populations.** Use with caution in elderly or frail patients. Use caution in hepatic or renal dysfunction. Reduce dose and monitor for adverse effects in patients with fever. Helpful for patients prone to constipation, with GI absorption problems, or intestinal resection. • **Application site:** Avoid external heat sources on application site. Use tegaderm over the patch to help fix it in place.

1 **All dosing based on tablets unless otherwise noted.** Consult with a pharmacist for liquid dosing equivalents.

2 **Minimum/maximum doses. Always begin with the lowest dose possible.** Ensure accurate diagnosis and carefully weigh benefits (pain relief and function) against risk of increased dosage. If unclear, consult a pain management specialist. **Maximum dose should not exceed 90 MME** (see page 12).

3 **Affected by meds that inhibit CYP2D6** and medications that induce or inhibit CYP3A4 (see page 17).

4 **Step therapy required:** SelectHealth requires step therapy for this medication. (For Butrans, Embeda, Exalgo, Kadian, Opana ER, and OxyContin ER capsules or tablets, two other long-acting opioids must be tried first. For Avinza, one other long-acting opioid must be tried first.)

5 **Opioid tolerance.** The FDA describes opioid tolerance as patients who are taking, for one week or longer, 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 any other opioid.

6 **Swallow tablets whole.** Crushing, chewing, or dissolving can cause a potentially fatal dose. Educate patients to abstain from alcoholic beverages or alcohol-containing products to be consistent with the MMA.

TABLE 6. LONG-ACTING Opioid Medications[1,LEX], *continued*

Minimum dosing: For all medications, begin with the lowest possible dose.
Maximum dosing[2]: The maximum dose for all medications should not exceed 90 morphine milligram equivalents (MMEs) per day.
See page 12 for MME conversion table and additional cautions.

Medication	50 MME Dose	90 MME Dose	Notes
hydrocodone ER[3,5] (Hysingla ER, Zohydro ER)	50 mg / day	90 mg / day	• **Dosing.** Discontinue all other, around-the-clock opioids when hydrocodone ER is initiated. • **Titration.** May increase Hysingla ER by 10 to 20 mg every 3 to 5 days and Zohydro ER by 10 mg every 12 hours every 3 to 7 days. • **Conversion.** When converting from other oral hydrocodone formulations, initiate Hysingla ER at the same total daily dose once daily; initiate Zohydro ER at the same total daily dose, divided in half, as equal doses every 12 hours. When converting from other opioids, consult prescribing information for guidance. • **Special populations**. In renal impairment, monitor closely. Initiate Zohydro ER at a low dose. In moderate-to-severe impairment or end-stage renal disease, start with 50 % of the initial Hysingla ER dose. In severe hepatic impairment, monitor closely. Initiate Zohydro ER 10 mg every 12 hours; initiate Hysingla ER at 50 % of the initial dose.
hydromorphone ER[4,5,6] (Exalgo)	12 mg / day	22 mg / day	• **Dosing.** For opioid-tolerant patients only. Only prescribe after discontinuation of all other extended-release opioids and around-the-clock opioids. • **Titration.** May increase by 4 mg to 8 mg every 3 to 4 days as needed. • **Conversion.** When converting from hydromorphone immediate release, initiate at the same total daily dose every 24 hours. When converting from other opioids, consult prescribing information for guidance. • **Special populations.** Reduce initial dose in elderly / frail patients. Avoid in severe hepatic impairment. In moderate impairment, initiate with 25 % of the usual starting dose. In severe renal impairment, initiate with 25 % of the usual starting dose and 50 % of the starting dose in moderate impairment.
methadone[3,5] See page 14 for specific guidance on methadone prescribing.	See CDC Guidelines for conversion information; there are four different conversion factors for this medication.		• **Dosing.** Mismatch of long half-life with shorter duration of analgesia can be life-threatening. Methadone should only be prescribed by experienced providers who are both familiar with its risks and appropriate use and prepared to conduct necessary and careful monitoring (see page 14). • **Special populations.** Use caution with elderly or debilitated patients; reduce dosage and consider inpatient monitoring during initial titration. Avoid in patients with cardiac conditions and/or patients using medications that can prolong QT interval. Avoid in patients with sleep-disordered breathing.

1 **All dosing based on tablets unless otherwise noted.** Consult with pharmacist for liquid dosing equivalents.

2 **Minimum / maximum doses. Always begin with the lowest dose possible.** Ensure accurate diagnosis and carefully weigh benefits (pain relief and function) against risk of increased dosage. If unclear, consult a pain management specialist. **Maximum dose should not exceed 90 MME** (see page 12).

3 **Affected by meds that inhibit CYP2D6** and medications that induce or inhibit CYP3A4 (see page 17).

4 **Step therapy required:** SelectHealth requires step therapy for this medication. (For Butrans, Embeda, Exalgo, Kadian, Opana ER, and OxyContin ER capsules or tablets, two other long-acting opioids must be tried first. For Avinza, one other long-acting opioid must be tried first.)

5 **Opioid tolerance.** The FDA describes opioid tolerance as patients who are taking, for one week or longer, 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 any other opioid.

6 **Swallow tablets whole.** Crushing, chewing, or dissolving can cause a potentially fatal dose. Educate patients to abstain from alcoholic beverages or alcohol-containing products to be consistent with the MMA.

TABLE 6. LONG-ACTING Opioid Medications[1,LEX], *continued*

Minimum dosing: For all medications, begin with the lowest possible dose.
Maximum dosing:[2] The maximum dose for all medications should not exceed 90 morphine milligram equivalents (MMEs) per day.
See page 12 for MME conversion table and additional cautions.

Medication	50 MME Dose	90 MME Dose	Notes
morphine[4,5,6] • ER (Avinza, Kadian—capsules; MS Contin—tablet) • In combination with naltrexone core (Embeda)	50 mg / day	90 mg / day	• **Titration.** For Avinza, increase by as much as 30 mg daily, every 3 to 4 days; adjust Kadian, MS Contin, or Embeda every 1 to 2 days. • **Conversion.** When converting from morphine immediate release, initiate at the same total daily dose: For Avinza, every 24 hours; for Kadian, once daily or in 2 divided doses every 12 hours; for MS Contin, in 2 divided doses every 12 hours or in 3 divided doses every 8 hours. When converting from other opioids, consult prescribing information for guidance. • **Special populations.** Use caution with elderly or debilitated patients. Dose adjustment may be necessary in moderate to severe hepatic impairment and cirrhosis. In renal impairment, avoid or start cautiously with lower doses, titrate more slowly, and carefully monitor for side effects that may be delayed. • **Administration.** CR tablets must be swallowed whole. Kadian and Avinza capsules can be opened and sprinkled on applesauce and eaten immediately without chewing. Ensure all pellets have been swallowed by rinsing mouth.
oxycodone ER[3,4,5,6] • (Oxycontin) tablet • (Xtampza) capsule	33 mg / day	60 mg / day	• **Titration:** Adjust in increments (tablets 25 %, capsules 25 % to 50 %) no more frequently than every 1 to 2 days; rescue medications may be needed during titration. • **Special populations.** In renal or hepatic impairment, initiate at 33 % to 55 % of the calculated recommended dose; consider alternative if dose is less than the smallest available dosage form. • **Administration.** Tablets must be swallowed whole. Capsules be opened and the contents sprinkled on soft foods or into a cup for administration directly into the mouth. Ensure all pellets have been swallowed by rinsing mouth.
oxymorphone[4,5,6] (Opana ER)	17 mg / day	30 mg / day	• **Titration:** Increase by increments of 5—10 mg every 12 hours, every 3 to 7 days. • **Special populations.** Use caution and reduce dosage with elderly patients. Avoid in hepatic dysfunction. For renal impairment, start at the lowest dose and titrate slowly while monitoring side effects. • **Administration.** Administer on an empty stomach; must be swallowed whole.

1 **All dosing based on tablets unless otherwise noted.** Consult with pharmacist for liquid dosing equivalents.

2 **Minimum / maximum doses. Always begin with the lowest dose possible.** Ensure accurate diagnosis and carefully weigh benefits (pain relief and function) against risk of increased dosage. If unclear, consult a pain management specialist. **Maximum dose should not exceed 90 MME** (see page 12).

3 **Affected by meds that inhibit CYP2D6** and medications that induce or inhibit CYP3A4 (see page 17).

4 **Step therapy required:** SelectHealth requires step therapy for this medication. (For Butrans, Embeda, Exalgo, Kadian, Opana ER, and OxyContin ER capsules or tablets, two other long-acting opioids must be tried first. For Avinza, one other long-acting opioid must be tried first.)

5 **Opioid tolerance.** The FDA describes opioid tolerance as patients who are taking, for one week or longer, 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 any other opioid.

6 **Swallow tablets whole.** Crushing, chewing, or dissolving can cause a potentially fatal dose. Educate patients to abstain from alcoholic beverages or alcohol-containing products to be consistent with the MMA.

TABLE 6. LONG-ACTING Opioid Medications[1,LEX], *continued*

Minimum dosing: For all medications, begin with the lowest possible dose.
Maximum dosing:[2] The maximum dose for all medications should not exceed 90 morphine milligram equivalents (MMEs) per day.
See page 12 for MME conversion table and additional cautions.

Medication	50 MME Dose	90 MME Dose	Notes
tapentadol ER[4,5] (Nucynta ER)	See CDC guidelines and/or CMS guidelines for conversion information.		• **Dosing.** Discontinue all other around-the-clock opioids when tapentadol ER is initiated. In opioid-tolerant patients[5], begin with a dose that is 50% of the estimated daily tapentadol requirement; use 2 equal doses every 12 hours with immediate-release medications to supplement (if needed). • **Titration.** Titrate in increments of 50 mg no more frequently than twice daily every 3 days. • **Conversion.** When converting from tapentadol immediate release, initiate at the same total daily dose, divided in half, as equal doses every 12 hours. • **Special populations.** For renal impairment, not recommended in patients with CrCl < 30 mL/minute. For moderate hepatic impairment (Child-Pugh Class B), start with an initial dose of 50 mg every 24 hours or longer with a maximum of 100 mg once daily. Use is not recommended in severe impairment (Child-Pugh Class C).
tramadol ER[3] (Ultram ER)	See CMS guidelines for conversion information.		• **Dosing.** Tramadol can increase seizure risk, especially in patients taking SSRIs, tricyclic antidepressants, MAOIs, neuroleptics, or other drugs that decrease seizure threshold and in patients with epilepsy or seizure risk factors. • **Special populations.** Start at low end of dosing range, and use the lowest effective dose in elderly patients. Use with caution in mild or moderate renal or hepatic impairment. Avoid in severe renal or hepatic impairment.

1 **All dosing based on tablets unless otherwise noted.** Consult with pharmacist for liquid dosing equivalents.

2 **Minimum/maximum doses. Always begin with the lowest dose possible.** Ensure accurate diagnosis and carefully weigh benefits (pain relief and function) against risk of increased dosage. If unclear, consult a pain management specialist. **Maximum dose should not exceed 90 MME** (see page 12).

3 **Affected by meds that inhibit CYP2D6** and medications that induce or inhibit CYP3A4 (see page 17).

4 **Step therapy required:** SelectHealth requires step therapy for this medication. (For Butrans, Embeda, Exalgo, Kadian, Opana ER, and OxyContin ER capsules or tablets, two other long-acting opioids must be tried first. For Avinza, one other long-acting opioid must be tried first.)

5 **Opioid tolerance.** The FDA describes opioid tolerance as patients who are taking, for one week or longer, 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 any other opioid.

6 **Swallow tablets whole.** Crushing, chewing, or dissolving can cause a potentially fatal dose. Educate patients to abstain from alcoholic beverages or alcohol-containing products to be consistent with the MMA.

PATIENT EDUCATION

Written materials can support your efforts to educate patients and engage them to change behavior, but don't replace direct, personal contact with patients in the clinic. **Table 7 below identifies Intermountain materials recommended for supporting opioid prescribing in primary care.** To access these materials:

- **Log in to** intermountainphysician.net**.** Search for the patient education library under A-Z. Then, search the item number and title in the appropriate area.
- **Use the iprintstore.org**, Intermountain's Online Library and Print Store, for one-stop access and ordering for all Intermountain materials (fact sheets, booklets, trackers, etc.): iprintstore.org. If you need any assistance, email printservices@imail.org.
- **For providers using iCentra**, search for Intermountain items in the patient education module.

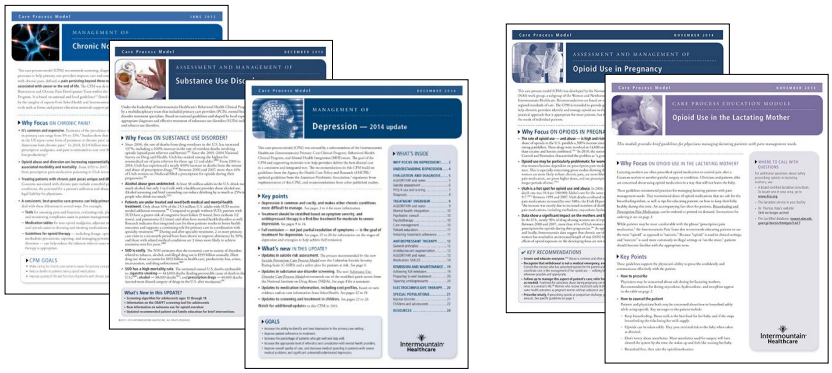
Table 7: Recommended patient and family education

Intermountain Education item	When to give or use as a decision aid
Managing Chronic Pain handbook (PM008)	Upon diagnosis. Use as a decision aid when creating a treatment plan.
Opioid Medication for Chronic Pain (FS052)	When first prescribing. Review when updating the patient's MMA.
Prescription Opioids: What you need to know (FS433)	When first prescribing.
Medication Side Effects (FS400)	When first prescribing.
Leftover Medications: How to Dispose of Them Safely (FS194)	When first prescribing.
Naloxone for Opioid Overdose (FS474)	Decision aid when discussing with patient.
Sedatives and Sleeping Pills: Understanding the Risks (FS432)	Decision aid when discussing with patient.
Buprenorphine for Opioid Use Disorder (FS462)	Decision aid when discussing with patient.
Fentanyl (Duragesic): Safe use instructions (FS339)	Decision aid when discussing with patient.
Stimulant Medicine for ADHD (FS461)	Decision aid when discussing with patient.
Cutting Back on Opioid Pain Medication (FS454)	Decision aid when discussing with patient.
Addiction (FS278)	When addiction suspected in patient and/or family member; decision aid.
Prescription Pain Medication in Pregnancy (FS395)	When first prescribing or when patient who is on opioids receives a pregnancy diagnosis.
Breastfeeding and Prescription Pain Medication (FS073)	When first prescribing or when patient who is on opioids receives a pregnancy diagnosis.
Substance Use During Pregnancy (FS355)	If pregnant patient scores positive on NIDA.
Opioid Medicines in the Emergency Department (FS490)	In Emergency Department to explain prescribing guidelines.

PROVIDER RESOURCES

Related Care Process Models (CPMs)

- *Management of Chronic Non-cancer Pain CPM*
- *Substance Use Disorder (SUD) CPM*
- *Management of Depression CPM*
- *Opioid Use in Pregnancy CPM*
- *Opioid Use in the Lactating Mother CPM*

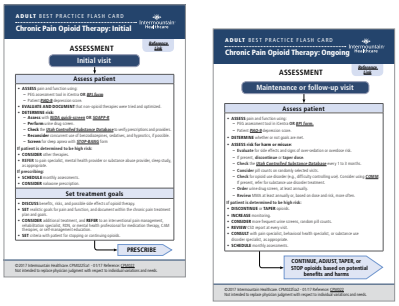


To access Intermountain materials, go to:

- IntermountainPhysician.org/ClinicalPrograms (and select from the A-Z topic list).
- Intermountain's iprintstore.org.

Best Practice Flash Cards

- *Chronic Pain Opioid Therapy: Initial*
- *Chronic Pain Opioid Therapy: Ongoing*



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AAO American Association for the Treatment of Opioid Dependence, Inc. QTc interval screening: AATOD policy and guidance statement. 2012. http://www.aatod.org/OLD_SITE/qtc.html. Accessed 12/9/16.

ACO ACOG Committee on Health Care for Underserved Women; American Society of Addiction Medicine. ACOG committee opinion No. 524: Opioid abuse, dependence, and addiction in pregnancy. *Obstet Gynecol.* 2012;119(5):1070-1076.

ARG Argoff CE, Silvershein DI. A comparison of long- and short-acting opioids for the treatment of chronic non-cancer pain: Tailoring therapy needs to meet patient needs. *Mayo Clin Proc.* 2009;84:602-612.

ASA Mee-Lee D, ed. *The ASAM criteria: Treatment criteria for addictive, substance-related, and co-occurring conditions.* Chevy Chase, MD: American Society of Addiction Medicine; 2013.

BAT Bateman BT, Choudhry NK. Limiting the duration of opioid prescriptions: Balancing excessive prescribing and the effective treatment of pain. *JAMA Internal Medicine.* 2016;5:583-584.

CDC1 Centers for Disease Control and Prevention. *CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016.* CDC. https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm. Updated March, 2016. Accessed January 21, 2017.

REGULATORY RESOURCES

The following are links to Utah and Federal regulations and guidelines that can provide additional direction for providers concerning opioid prescribing:

- 2016 Utah Legislative Bills
- Utah Controlled Substance Act - Rule #R156-37
- CDC Guidelines for Prescribing Opioids for Chronic Pain
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This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to Dr. Joel Porter, Intermountain Healthcare. Joel.Porter@imail.org

