



OHSU HEALTH

Use of Medication to Treat Opioid Use Disorder (Pregnant and Non-Pregnant Patients)

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Reviser (Title): Medication Safety Committee	Owner (Title): Clinical Knowledge and Therapeutics Executive Committee	

PURPOSE:

To clarify the use of medications (methadone, buprenorphine/naloxone, buprenorphine, naltrexone) for opioid withdrawal management or opioid maintenance therapy in patients with opioid use disorder who are hospitalized or seen in the emergency department.

PERSONS AFFECTED:

OHSU Healthcare Workforce administering, prescribing, and dispensing medications for opioid use disorders. This policy excludes patients on opioid agonist or partial agonist therapy for chronic pain.

DEFINITIONS:

1. Buprenorphine extended-release injection (Sublocade): An extended-release form for use as subcutaneous injection only. Following injection of the solution, a polymer is formed which releases buprenorphine via diffusion of the depot.
2. Buprenorphine/naloxone (Suboxone) (4:1 combination): sublingual tab or film and generic equivalents are schedule CIII prescription partial opioid-agonists indicated for treatment of moderate to severe opioid use disorder or opioid withdrawal and should be used as part of a complete treatment plan to include counseling and psychosocial support. Treatment should be initiated with guidance from physicians qualified under the Drug Addiction Treatment Act.
3. DATA 2000: Drug Addiction Treatment Act (DATA) of 2000. This program permits qualified physicians to treat opioid use disorders with schedules III-V opioids that are approved by the Food and Drug Administration (FDA) for that indication.
4. Extended release (ER) naltrexone (Vivitrol): An intramuscular extended release opioid antagonist indicated for the treatment of opioid use disorder. Opioid abstinence must be confirmed prior to administration of this medication. Naltrexone is currently contraindicated in pregnancy.
5. Methadone: a full opioid agonist medication that is typically given once daily as a liquid to treat opioid use disorder in patients with moderate to severe opioid use disorder. Methadone can only be administered in a hospital or a federally licensed opioid treatment program (OTP) unless it is prescribed for the use of pain.
6. Sublingual buprenorphine (Subutex): tablets and generic equivalents are partial opioid agonists indicated for the treatment of moderate to severe opioid use disorders or opioid withdrawal and subject to the same prescribing restrictions as buprenorphine/naloxone (Suboxone).

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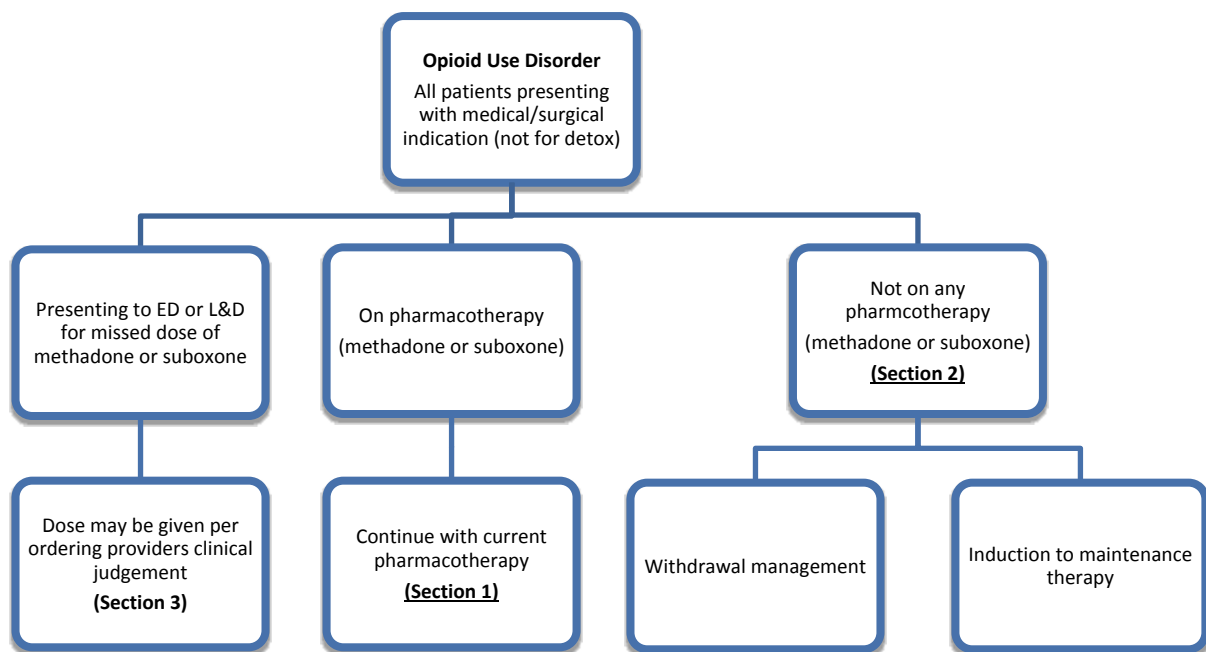
POLICY:

Opioid agonist (methadone) or partial-agonist therapy (buprenorphine/naloxone and buprenorphine) will only be administered or ordered for inpatient, emergency department (ED) and labor and delivery (L&D) patients under two circumstances.

1. To maintain the patient's current opioid use disorder maintenance treatment if the patient is admitted for a primary diagnosis or treatment condition other than opioid use disorder.
2. To initiate therapy - initiation and dose adjustments may be ordered by any provider in the inpatient, ED, and L&D setting for treatment of opioid withdrawal and/or opioid use disorder.

Extended release naltrexone can be administered during hospitalization regardless of hospitalization indication. However, this medication can only be prescribed after approval is granted by an addiction medicine consultant. Licensed Independent Practitioners may not prescribe opioid agonist therapy to treat opioid use disorder at discharge. Providers may only prescribe partial opioid agonist for opioid use disorder if they are DATA waived.

PROCEDURES:



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Section 1:

Continuation of opioid use disorder maintenance treatment during hospitalization:

- a. Prior to administration of the opioid agonist or partial-agonist therapy, the pharmacist or provider must ensure the opioid maintenance dose is confirmed with the licensed treatment program and document this information in the integrated healthcare record.
- b. In the event the patient's treatment center is closed or unable to be contacted, a dose may be ordered under the discretion of the provider. The patient's treatment center should be contacted as soon as possible for subsequent doses to be administered.
 - i. A single dose of methadone should not exceed 30 mg without treatment center confirmation. The total daily dose should not exceed 40 mg.
 - ii. Dose of buprenorphine/naloxone or buprenorphine can be confirmed via the patient's pharmacy or the state Prescription Drug Monitoring Program (PDMP) if DATA waiver physician is not available for confirmation.
- c. The admitting provider may order the maintenance dose for daily administration to the patient in the inpatient, ED, or L&D setting until the patient is discharged.
- d. Patient's own treatment medication may not be administered. Refer to, Use of Patient's Personal Medications policy.

Section 2:

Initiation of medications to treat opioid use disorder: **Admitted for a condition other than opioid use disorder**

- a. Any inpatient provider can order medications (methadone, buprenorphine/naloxone, buprenorphine) to treat opioid use disorder
- b. Addiction medicine consult is available if needed, but not required
- c. Patients do not need to be previously enrolled in an Opioid Treatment Program
- d. Providers may **not** prescribe opioid agonist to treat opioid use disorder after hospitalization. They may only prescribe partial agonists on discharge if they are DATA waived.
- e. If the patient wishes to continue agonist therapy, a prescribing community provider or an appropriate opioid treatment program should be identified before discharge
- f. Refer to **Appendix A** for methadone dosing guidance
- g. Refer to **Appendix B** for buprenorphine dosing guidance

Section 3:

Emergency Department and Labor and Delivery (L&D)

- a. Patients arriving in the ED only to request a missed dose of methadone, buprenorphine/naloxone or buprenorphine may receive a one-time administration under the discretion of the provider. A provider or pharmacist must contact the patient's licensed treatment program to verify dose prior to administration
- b. **Pregnant patients** prescribed methadone or buprenorphine maintenance therapy arriving in the ED or L&D only to request a dose of methadone or buprenorphine may be administered a one time dose of their confirmed medication to prevent opioid withdrawal, if clinically indicated and safe.
 - i. Clinical indication and safety is confirmed by the following

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1. The patient does not appear to be clinically intoxicated or sedated.
- ii. In the event the patient's treatment center is closed or unable to be contacted, a single dose may be ordered under the discretion of the provider. The patient's treatment center should be contacted as soon as possible for subsequent doses to be administered.
- c. Providers may **not** prescribe opioid agonist after hospitalization. DATA waived providers may prescribe partial-agonist therapy to treat opioid use disorder after hospitalization.

Appendix A: Methadone Initiation Dosing Recommendations

Factors to remember about methadone:

1. Methadone is stored extensively in the liver and secondarily in other body tissues
2. Elimination half-life averages 24 – 36 hours at steady state and can range from 4 – 91 hours
3. Achieving steady-state serum methadone levels requires 4 – 5 days on average. A rule of thumb is that half of each day's dose remains in the body and is added to the next day's dose until steady state is achieved
4. There is a great deal of inter-patient variability in methadone metabolism and tolerance
5. Effects generally peak about 3 – 4 hours after the patient receives a dose

General dosing guidelines:

1. Recommended max daily doses
 - Day 1: Initial dose of 30 mg for most patients with an additional 10 mg after 3-4 hours if no sedation. May give additional full agonist opioids (e.g. oxycodone) if cravings and/or withdrawal symptoms persist. Consider lower doses if patients use prescription opioids or have risks for over-sedation (e.g. frail, advanced age, underlying respiratory conditions; see #5 below).
 - Day 2: 50 mg either as one single dose OR 40 mg once with an additional 10 mg after 3-4 hours if needed for continued withdrawal symptoms
 - Day 3: 60 mg either as one single dose or 50 mg once with an additional 10 mg after 3-4 hours if needed for continued withdrawal symptoms
 - Day 4+ : Hold at 60 mg once daily and increase by 5-10 mg every 3-5 days
 - Dose escalation can occur quicker if needed with guidance from IMPACT consult service
2. Full opioid agonist can be continued and increased if needed to manage cravings and/or withdrawal symptoms and if appropriate for patients clinical picture
3. Patients who are: taking low doses of opioids orally, who do not use opioids or heroin daily, and or who do not inject should be started on a dose of 10 – 20 mg of methadone daily
4. Patients with the following conditions should be started at lower doses (5 – 15 mg daily) and titrated slowly:
 - Respiratory disorder
 - Cor pulmonale
 - Morbid obesity
 - Sleep apnea
 - Kyphoscoliosis
 - Prolonged QT
 - Known arrhythmia
 - Recent MI
 - Family history of early cardiac death

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5. If the patient has missed methadone doses, do not automatically restart at last known dose. Remember that if the patient missed doses due to using, it is safer to restart than if they missed doses due to incarceration, in which case their tolerance will be lower. General rule of thumb:
 - If they have missed fewer than 3 doses, restart at last known dose
 - If they have missed 4 – 7 doses, decrease by 50%
 - If they have missed more than a week, restart at 40 mg or lower
6. Patients who are pregnant or recently post-partum may need higher doses and faster up-titration than non-pregnant/ post-partum patients. They may also need split dosing (meaning dosing twice daily instead of once daily) given metabolic changes in pregnancy.

Appendix B: Buprenorphine/naloxone (Suboxone) Initiation Dosing Recommendations

Factors to remember about buprenorphine:

1. Buprenorphine is a partial opioid agonist that has a high affinity for the mu opioid receptors. When it occupies the mu opioid receptor, it can decrease withdrawal symptoms and cravings without causing significant euphoria.
2. If buprenorphine is administered to an opioid dependent patient, it can displace full agonists from the mu receptor and trigger a precipitated withdrawal.
3. Opioid dependent patients who are undergoing traditional buprenorphine induction should be in moderate withdrawal (as measured by the Clinical Opioid Withdrawal Scale) before receiving buprenorphine to avoid precipitated withdrawal. This excludes patients for whom there is reasonable certainty no opioid has been ingested for >3 days, such as a patient who has been hospitalized for several days, in whom UDS shows no opioid, and who has prior history of withdrawal and high risk for relapse to opioid use at discharge. This also excludes patients who are starting buprenorphine via low dose induction. (see below)
4. Patients will generally begin to feel the effects of buprenorphine on cravings/withdrawal within 20 – 45 minutes of administration.

General Dosing Guidelines

1. Buprenorphine and naloxone (Suboxone) dosing is based of buprenorphine dose
2. In general, the maximum daily dose on day one is 8 – 12 mg, but it may be higher with IMPACT guidance
3. Low dose induction
 - a. Full opioid agonist therapy continues and dose of buprenorphine is escalated gradually every day. This dosing strategy does not require the patient to be in withdrawal
 - b. (GEN: BUPRENORPHINE- NALOXONE: MICRO-INDUCTION)
4. Traditional induction:
 - a. Opioid dependent patients should be in moderate withdrawal (as measured by the Clinical Opioid Withdrawal Scale) before receiving buprenorphine in order to avoid precipitated withdrawal. This excludes patients for whom there is reasonable certainty no opioid has been ingested for >3 days, such as a patient who has been hospitalized for several days, in whom UDS shows no opioid, and who has prior history of withdrawal and high risk for relapse to opioid use at discharge
 - b. Buprenorphine is offered every 1-2 hours until the maximum dose for the day has been reached, or the patient reports no further cravings or withdrawal
 - c. (GEN: BUPRENORPHINE-NALOXONE: INITIATION)

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- d. There is an order set in EPIC that attaches the Clinical Opioid Withdrawal Scale (COWS), to supportive medications and to dosing for induction
5. For patients who report illicit fentanyl use, there is emerging evidence that patients are at high risk for precipitated withdrawal if buprenorphine is administered within 48 hours of last use. Teams may want to delay first buprenorphine dose, treat with adjunctive medications (including full agonist opioids in first 24-36 hours), and counsel patients re risk for precipitated withdrawal. Teams can also consider IMPACT consult for support.

Appendix C: Supportive Care Medications

Can be quickly ordered via Panel titled "Opioid Withdrawal Supportive Medications" in order section of Epic

Medication	Dose and frequency
Clonidine	0.1-0.2 mg PO three times daily as needed, sweating/agitation. Hold for sedation/dizziness
Tizanidine	2-4 mg PO every 6 hours as needed, muscle spasms
Hydroxyzine	25-50 mg PO every 4 hours as needed, anxiety
Ondansetron	4 mg PO every 8 hours as needed, nausea/vomiting
Hyoscyamine	0.125 mg PO every 6 hours as needed, abdominal cramping
loperamide	4 mg PO four times daily as needed, diarrhea

RELEVANT REFERENCES:

- Drug Enforcement Administration §1306.07 and §1301.28
- Drug Enforcement Administration: Drug Addiction Treatment Act 2000
- Substance Abuse and Mental Health Services Administration FAQ on buprenorphine: <http://buprenorphine.samhsa.gov/faq.html#A14>
- <https://www.samhsa.gov/programs-campaigns/medication-assisted-treatment/legislation-regulations-guidelines/special>
- Kleinman RA, Wakeman SE. Treating Opioid Withdrawal in the Hospital: A Role for Short-Acting Opioids [published online ahead of print, 2021 Nov 23]. *Ann Intern Med.* 2021;10.7326/M21-3968. doi:10.7326/M21-3968
- Varshneya NB, Thakrar AP, Hobelmann JG, Dunn KE, Huhn AS. Evidence of Buprenorphine-precipitated Withdrawal in Persons Who Use Fentanyl [published online ahead of print, 2021 Nov 23]. *J Addict Med.* 2021;10.1097/ADM.0000000000000922. doi:10.1097/ADM.0000000000000922

RELATED DOCUMENTS/EXTERNAL LINKS:

Use of Patient's Personal Medications

APPROVING COMMITTEE(S):

Medication Safety Committee

Clinical Knowledge and Therapeutics Executive Committee

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REVISION HISTORY

Revision History Table

Document Number and Revision Level	Final Approval by	Date	Brief description of change/revision
HC-CKT-119-POL Rev. 120618	Clinical Knowledge and Therapeutics Executive Committee	2/26/20	<ul style="list-style-type: none">• Transfer to new policy/guideline template
HC-CKT-119-POL Rev. 022422	Clinical Knowledge and Therapeutics Executive Committee	2/24/22	<ul style="list-style-type: none">• Updates based on new literature

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