### 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. **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.
2. **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.
3. **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.
4. **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).
5. **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.
6. **Buprenorphine extended-release injection (Sublocade)**: An intramuscular 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.
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 waivered.

PROCEDURES:

Section 1:

Continuation of opioid use disorder maintenance treatment during hospitalization:

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.

a. 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.

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Englander et al, Journal of Addiction Medicine, 2019
I. A single dose of methadone should not exceed 30 mg without treatment center confirmation.

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.

b. 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.

c. 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 waivered.
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 Attachment A for methadone dosing guidance
g. Refer to Attachment 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
      1. Clinical Opioid withdrawal scale (COWS) > 5
      2. Urine drug test results show negative benzodiazepine and negative alcohol
      3. 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 waivered providers may prescribe partial-agonist therapy to treat opioid use disorder after hospitalization.
Attachment 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. A max dose 30 mg single dose on day one
   - May provide an additional 10 mg dose if needed to equal a total of 40 mg on day one
2. Patients injecting more than 1.5 grams heroin/day and without other risk factors should generally start on 30–40 mg daily to attenuate withdrawal symptoms. If the patient still feels withdrawal symptoms 3–4 hours after a dose of 30 mg, it is generally safe and recommended to provide another 10 mg
3. Patients who are: taking 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
5. Once on 50 mg, generally stay at 50 mg daily x 5–7 days, then increase by 5–10 mg every 5–7 days
6. 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 30 mg or lower
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 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
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
3. Patients who are dependent on oral pain pills should generally start with a 2 mg dose. Patients injecting heroin or snorting/injecting pills may start with 4 mg
4. Continue to offer buprenorphine every 1-2 hours until the maximum dose for the day has been reached, or the patient reports no further cravings or withdrawal
5. There is an order set in EPIC that attaches the Clinical Opioid Withdrawal Scale (COWS), to supportive medications and to dosing for induction (GEN: BUPRENORPHINE-NALOXONE: INITIATION)

Attachment C: Supportive Care Medications

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

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Englander et al, Journal of Addiction Medicine, 2019
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

RELATED DOCUMENTS/EXTERNAL LINKS:

Use of Patient’s Personal Medications

TITLE, POLICY OWNER:

Department of Pharmacy Services

APPROVING COMMITTEE(S):

Medication Safety Committee

FINAL APPROVAL:

Pharmacy and Therapeutics Committee