Inpatient Management of Opioid Use Disorder: **Buprenorphine**

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SHOUT SUPPORT FOR HOSPITAL OPIOID USE TREATMENT

This guideline applies to patients in inpatient medical settings. If any of the following points are different for pregnant patients, it is noted in each segment of the following document.

Goal of Treatment:

- COWS (Clinical Opioid Withdrawal Score – See Appendix A) of 5 or less for 24-36 hours
- Elimination of drug hunger or cravings
- No sedation or respiratory depression from medication
- If patient uses illicit opioids while on buprenorphine, they should not feel substantially intoxicated

Monitoring:

- COWS score is used to monitor a patient's response to buprenorphine, it can be done by a provider or RN
- COWS assessments should be done per protocol (See Appendix B) and should be documented after every check
- Each COWS must be reported to a supervising provider if performed by an RN
- Based on the COWS, the provider will decide if there will be a change in monitoring frequency
- ***Pregnancy Only***: Fetal monitoring beyond what is necessary for initial fetal evaluation is not necessary solely for methadone administration unless ordered by the provider.

Patients on outpatient buprenorphine or buprenorphine-naloxone:

1) Confirm dose by calling their pharmacy or checking the PDMP (in California this is https://cures.doj.ca.gov)
2) Determine whether the patient has been taking their medication as prescribed, and continue based on #3-6 below
3) Buprenorphine should typically be continued during acutely painful events, but buprenorphine alone will not control severe acute pain—see separate acute pain guidelines
4) Unless patient has severe alteration in mental status or intoxication, continue outpatient dose
5) If patient has missed outpatient dosing and has not used opioid agonists in the interim, provider may order patient's full outpatient dose
6) If patient has missed >1 day of buprenorphine AND has use opioid agonists in the interim, use clinical judgement to determine whether they are at risk for precipitated withdrawal. If, based on their period of time without buprenorphine, opioid use, and lack of current objective withdrawal you are concerned for precipitated withdrawal, please consider them a new induction and follow protocols in Appendix B.

For questions or concerns, please consider consulting the UCSF Clinician Consultation Center Substance Use Warmline at (855) 300-3595 Monday through Friday, between 10 a.m. and 6 p.m EST or https://tinyurl.com/yd4ymyx6

Patients considering buprenorphine induction:

1. Determine clinical indication for buprenorphine therapy:

Indication	Contraindications	Caution
❑ Opioid use disorder, with or without comorbid chronic pain ***and*** ❑ Desire for buprenorphine treatment to assist with cessation or reduction in use	❑ Allergy to buprenorphine ❑ Medically unstable and unable to tolerate mild withdrawal safely	❑ Severe psychiatric illness that limits ability to take daily medication, mania ❑ Acute pain requiring opioid agonist therapy ❑ EtOH or benzodiazepine use disorder ❑ Liver disease ❑ Use of methadone in the last week ❑ ***Pregnancy only:*** induction may occur at outpatient clinic or inpatient under obstetric team guidance **If the patient falls under the "caution" category, call the UCSF Substance Use Warmline (855.300.3595 or https://tinyurl.com/yd4ymyx6) or your local addiction specialists.**

2. Discuss options with patient and determine whether methadone or buprenorphine would be preferable (See Appendix C – Non-pregnancy Decision Guide; ***Pregnancy Only:*** See Appendix D – Pregnancy Only Decision guide). In the inpatient setting clinicians can legally order buprenorphine or methadone if the patient is admitted primarily for another medical reason, regardless of if they have an X license/DATA 2000 waiver. Additionally, prior to starting buprenorphine, ensure that someone in your hospital will be able to write a short prescription on discharge and that there are providers in the patient's area who are willing to prescribe buprenorphine after discharge for maintenance therapy.

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3. Prior to induction:

- Verify DSM 5 criteria for opioid use disorder
- Check baseline LFTs (rarely can cause hepatotoxicity), urine pregnancy test, check urine tox and CURES report for collateral information about substance use

  Pregnancy Only: also check baseline maternal vital signs, NST as indicated, and a urine tox (utox can only be performed after patient verbal consent)
- If a patient is experienced mixed alcohol and opioid withdrawal, be very cautious and consult with experts to determine which pathology predominate as the combination of benzodiazepines and opioids can be high risk
- Follow the attached flowsheet (appendix B) to ensure that the patient does not have fully activated opioid receptors, as this can lead to precipitated withdrawal from buprenorphine (very uncomfortable).

  Pregnancy only: precipitated withdrawal can cause withdrawal symptoms in the fetus. Precipitated withdrawal is unlikely to occur if one of the following is true:
  - COWS score≥8 with some objective signs of opioid withdrawal
  - Patient who has been abstinent for a prolonged period, usually weeks (eg recently incarcerated, prolonged hospitalization without opioids)
- Consider adjunctive medications to help to control withdrawal symptoms, prior to starting and during induction. Of note, this will lower COWS scores therefore may prolong the induction.
  - Diphenhydramine 25-50 mg, PO three times daily prn insomnia/anxiety
  - Ondansetron 4 mg PO every 6 hours PRN nausea
  - Ibuprofen 400-800 mg, PO four times daily prn pain ***(Pregnancy Only****: Ibuprofen is contraindicated)*
  - Acetaminophen 650 mg PO 6 four times daily PRN pain
  - Loperamide 4mg PO x 1 initially, then 2mf prn each additional loose stool (NTE 16 mg/24 hours)
  - Clonidine 0.1 mg PO q4 hours prn w/d symptoms (NTE 2 doses/24 hours and include BP parameter)
  - DO NOT ORDER benzodiazepines as standard PRN adjunctive therapy.

4. Follow attached algorithm for dosing. MD or RN must evaluate before and 1 hour after each dose. Document each COWS score on the scoring sheet below and keep in patient chart. If sedation (Ramsey score ≥4) or RR<8 occurs, hold dosing. Total dose on the first day should not exceed 12 mg. On day two, start with day one total daily dose and give additional as needed per the algorithm. If precipitated withdrawal is suspected at any point, or if withdrawal symptoms are uncontrolled on the maximum daily dose, call the Substance Use Warmline (see item 3) or your local addiction specialist. Management usually involves repeating buprenorphine dose, or if patient is unstable giving full opioid agonist with strong affinity.

Discharge Planning

1) Call local buprenorphine prescriber (see SAMHSA database at https://tinyurl.com/mtyjtm5) to arrange appointment for patient after discharge. Ideally, this appointment will be within 3 days of discharge.
2) On discharge, provide enough buprenorphine to last until appointment at outpatient clinic. Of note, depending on pharmacy formularies inpatients may receive buprenorphine alone (Subutex), however buprenorphine-naloxone (Suboxone) should be dispensed on discharge to discourage diversion. Medi-Cal covers buprenorphine and buprenorphine-naloxone, with some other insurance providers a TAR may be necessary. Discharge prescription must be written by X licensed provider.
3) Skilled nursing facilities (SNFs) that are not classified as hospitals can only keep patients on buprenorphine if they have an outside provider—discuss these details with the SNF early in the process
4) Please prescribe naloxone in case of relapse and overdose, also consider PREP/PEP if indicated.

Other Dosing Considerations

- Product Selection:
  - The standard approach is to use sublingual films or tablets for treatment of opioid use disorder
  - In the hospital, either buprenorphine monoproduct or combination buprenorphine-naloxone may be used
  - On discharge, the combination buprenorphine-naloxone is recommended due to decreased diversion and does not have increased rates of side effects
  - Buprenorphine should be dosed sublingually and allowed to fully dissolve, not be swallowed. Up to 2 tablets can be administered sublingually at one time
  - ***Pregnancy Only***: In pregnancy, a provider must only prescribe buprenorphine and NOT the buprenorphine/naloxone combination medication
- Split Dosing:
  - Split dosing may be necessary for patient with acute or chronic severe pain
  - ***Pregnancy Only:*** As gestational age increases, plasma levels of buprenorphine change secondary to a decrease in half-life and an increase in clearance and volume of distribution. This generally occurs during the second and third trimester. As such, a provider may strongly consider splitting the daily buprenorphine dose to an AM and PM dose if the patient experiences withdrawal symptoms or cravings at night.

Breastfeeding Guidelines

Buprenorphine for opioid use disorder is not a contraindication for breastfeeding. Patients taking buprenorphine for opioid use disorder who are not currently abusing other substances and who wish to breastfeed should be encouraged to regardless of the buprenorphine dose. Current evidence shows that breastfeeding while on buprenorphine is beneficial to neonates with neonatal abstinence syndrome (NAS). Neonates receiving breast milk from these patients experience lower NAS scores, require less pharmacologic treatment such as morphine, and have shorter lengths of hospital stay.

PATIENT NAME:	DATE OF ASSESSMENT:
PATIENT DATE OF BIRTH:	MEDICAL RECORD NUMBER:

Clinical Opioid Withdrawal Score (COWS)

For each item, write in the number that best describes the patient's signs or symptom. Rate only the apparent relationship to opiate withdrawal. *For example: If heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.*

Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc.	*Time:*	*Time:*	*Time:*	*Time:*
Resting Pulse Rate: Record beats per minute *after patient is sitting or lying down for one minute* • 0 - pulse rate 80 or below • 1 - pulse rate 81–100 • 2 - pulse rate 101–120 • 4 - pulse rate greater than 120				
Sweating: *Over past ½ hour not accounted for by room temperature or activity* • 0 - no chills or flushing • 1 - subjective chills or flushing • 2 - flushed or observable moistness on face • 3 - beads of sweat on brow or face • 4 - sweat streaming off face				
Restlessness: *Observation during assessment* • 0 - able to sit still • 1 - reports difficulty sitting still, but is able to do so • 3 - frequent shifting or extraneous movement of legs/arms • 5 - unable to sit still for more than a few seconds				
Pupil size • 0 - pupils pinned or normal size for light • 1 - pupils possibly larger than normal for light • 2 - pupils moderately dilated • 5 - pupils dilated that only rim of the iris is visible				
Bone or joint aches: *If patient was having pain previously, only the additional component attributed to opiate withdrawal is scored* • 0 - not present • 1 - mild/diffuse discomfort • 2 - patient reports severe diffuse aching of joints/muscles • 4 - patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing: *Not accounted for by cold symptoms or allergy* • 0 - none present • 1 - nasal stuffiness or unusually moist eyes • 2 - nose running or tearing • 4 - nose constantly running or tears streaming down cheeks				
GI upset: *Over last ½ hour* • 0 - no GI symptoms • 1 - stomach cramps • 2 - nausea or loose stool • 3 - vomiting or diarrhea • 5 - multiple episodes of diarrhea or vomiting				
Tremor: *Observation of outstretched hands* • 0 - no tremor • 1 - tremor can be felt, but not observed • 2 - slight tremor observable • 4 - gross tremor or muscle twitching				
Yawning: *Observation during assessment* • 0 - no yawning • 1 - yawning once or twice during assessment • 2 - yawning three or more times during assessment • 4 - yawning several times/minute				
Anxiety or irritability • 0 - none • 1 - patient reports increasing irritability or anxiousness • 2 - patient obviously irritable or anxious • 4 - patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin • 0 - skin is smooth • 3 - piloerrection of skin can be felt or hairs standing up on arms • 5 - prominent piloerrection				
5—12 = mild; *13—24 = moderate;* *25—36 = moderately severe;* *> 36 = severe withdrawal* **TOTAL** OBSERVER INITIALS				

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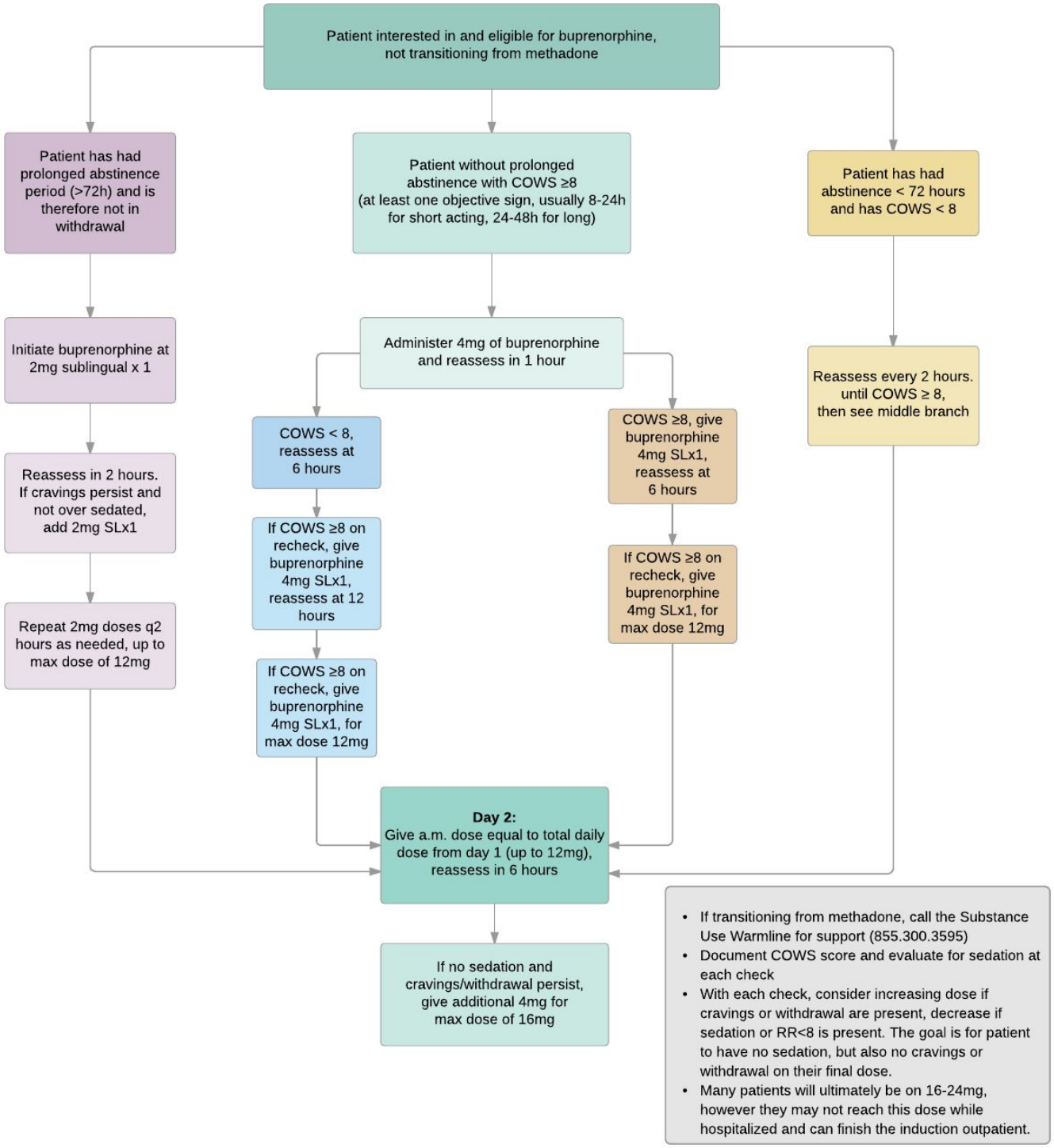
Appendix B - Buprenorphine Induction Algorithm



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Appendix C – Non-Pregnancy Decision Guide

	Methadone	Buprenorphine
Mechanism	Full opioid agonist	Partial opioid agonist, usually paired with naloxone (opioid antagonist)
Patients for whom should use caution or avoid	Allergy, severe liver disease, QTc prolongation, drug-drug interactions, high risk job	Allergy, severe liver disease, heavy EtOH or benzo, need for acute opioids, recent methadone
Risk of withdrawal when starting medication	None	Some, if not in withdrawal prior to starting may have precipitated withdrawal
Side effects/risks	Hypogonadism, Torsades, constipation, sweating	GI upset, constipation, headache, insomnia
Sedation/respiratory depression	At high doses in non-tolerant patients or slow metabolizers has potential for sedation, worse in combination with some medications	Ceiling effect for respiratory depression therefore less risky (unless concurrent use of sedating drugs, e.g., alcohol/benzodiazepines)
Overdose risk from opioid replacement	Low-moderate, higher when initiating treatment or in combo with other medications	Low, increased by concurrent sedating medications
Retention in treatment	Higher in methadone[1], with possible contribution from increased structure of programs	May be slightly lower than methadone, retention improves at doses over 16mg
Visit frequency	Daily visits to maintenance treatment program, take-homes may be allowed if stable for long term. This structure helps some patients, some dislike it.	Can range from daily to monthly depending on patient treatment needs, may be provided in primary care setting. Also available in some methadone clinics, increasing structure and decreasing diversion risk.
Diversion potential	Low for directly observed therapy (DOT), high for take home	Low for DOT, moderate for take-homes, reduced by co-formulation with naloxone
Who can prescribe after discharge?	Opioid treatment program only	Any physician, NP, or PA who has been trained and possesses DATA2000 waivers (aka X-number)
Mortality	Both options substantially decrease all-cause mortality over no treatment, methadone may have higher mortality but may be confounded[2]	Both options substantially decrease all-cause mortality over no treatment, buprenorphine may have lower mortality but may be confounded

Some patients may decline buprenorphine or methadone, but still be interested in medication assisted treatment. In these cases, one option is naltrexone, however it has been shown to have very high drop-out rates so is not considered first line[3]. Naltrexone can only be started after a patient has completely withdrawn from opioids—roughly 5-7 day for short acting and 7-10 days for long acting. One option is to give naloxone as a trial before administering naltrexone, to make sure the patient doesn't experience precipitated withdrawal. Dosing usually begins with 25mg on the first day, and is then increased to 50 mg daily. For IM formulation, the dose is usually 380 mg q4 weeks. The most common side effects are nausea, vomiting, and headache

[1] McLellan A, Arndt I, Metzger D, Woody G, O'Brien C. Treatment Retention among Patients Randomized to Buprenorphine/Naloxone Compared to Methadone in a Multi-Site Trial. Addiction . 2014; 109(1): 79–87.

[2] Sordo L, Barrio G, Bravo M, Indave B, Degenhardt L, Wiessig L, Ferri M, Pastor-Barriuso R. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ. 2017:357:j1550

[3] Minozzi S, Amato Le Vecchi S, Davoli M, Kirchmayer, U, Verster A. Oral naltrexone maintenance treatment for opioid dependence. Cochrane Database of Systematic Reviews: Reviews. 2011.

Appendix D– Pregnancy Decision Guide

	Methadone	Buprenorphine
Mechanism	Full opioid agonist	Partial opioid agonist, usually paired with naloxone (opioid antagonist)
Patients for whom should use caution or avoid	Allergy, severe liver disease, QTc prolongation, drug-drug interactions, high risk job	Allergy, severe liver disease, heavy EtOH or benzo, need for acute opioids, recent methadone
Risk of withdrawal when starting medication	None	Some, if not in withdrawal prior to starting may have precipitated withdrawal
Side effects/risks	Hypogonadism, Torsades, constipation, sweating	GI upset, constipation, headache, insomnia
Sedation/respiratory depression	At high doses in non-tolerant patients or slow metabolizers has potential for sedation, worse in combination with some medications	Ceiling effect for respiratory depression therefore less risky (unless concurrent use of sedating drugs, e.g., alcohol/benzodiazepines)
Overdose risk from opioid replacement	Low-moderate, higher when initiating treatment or in combo with other medications	Low, increased by concurrent sedating medications
Retention in treatment[4]	Higher in methadone (88% in the MOTHER study), with possible contribution from increased structure of programs	Slightly lower than methadone (67% in the MOTHER study, with most drop outs during induction)
Visit frequency	Daily visits to maintenance treatment program, take-homes may be allowed if stable for long term. This structure helps some patients, some dislike it.	Can range from daily to monthly depending on patient treatment needs, may be provided in primary care setting. Also available in some methadone clinics, increasing structure and decreasing diversion risk.
Diversion potential	Low for directly observed therapy (DOT), high for take home	Low for DOT, moderate for take-homes, reduced by co-formulation with naloxone
Who can prescribe after discharge?	Opioid treatment program only	Any physician, NP, or PA who has been trained and possesses DATA2000 waivers (aka X-number)
Mortality	Both options substantially decrease all-cause mortality over no treatment, methadone may have higher mortality but may be confounded[5]	Both options substantially decrease all-cause mortality over no treatment, buprenorphine may have lower mortality but may be confounded
Neonatal Outcomes[6]	Reduced preterm birth and low birth weight rates Higher doses do NOT correlate with more NAS NAS is 75% - in MOTHER study: 17.5 day average length of hospitalization 10.4 mg morphine required during hospitalization	Reduced preterm birth and low birth weight rates Later average gestational age and higher average birth weight than methadone Higher doses do NOT correlate with more NAS NAS less severe than for methadone – in MOTHER study: 10 day average length of hospitalization 1.1 mg morphine required during hospitalization

Naltrexone is not a good option in pregnancy due to safety concerns

[4] Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. N Engl J Med. 2010;363(24):2320-31.
[5] Sordo L, Barrio G, Bravo M, Indave B, Degenhardt L, Wiessig L, Ferri M, Pastor-Barriuso R. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ. 2017:357:j1550
[6] Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. N Engl J Med. 2010;363(24):2320-31.