**Protocol for Initiating and Monitoring Buprenorphine/Naloxone (Suboxone®) for Opioid Use Disorder**

**BACKGROUND: Buprenorphine is an FDA approved treatment for Opioid Use Disorder (OUD). It is a high-affinity, partial agonist at the mu opioid receptor and suppresses opioid withdrawal and craving, reduces illicit opioid use and blocks exogenous opioid effects including respiratory depression. People with OUD are 50% less likely to die when they are being treated long term with methadone or buprenorphine. (National Academies Press, 2019).**

**As of April 2021, any physician or nurse practitioner can prescribe buprenorphine to up to 30 patients concurrently without additional training. Submit the Buprenorphine Waiver Notification of Intent to receive an X-waiver prior to prescribing. In order to provide this important treatment to more patients or for additional information on buprenorphine prescribing, please see these free waiver trainings: Physicians or RNPs. Keep a log of all current active patients (until the last day of their last prescription) and all buprenorphine prescriptions given.**

**CLINICAL SUPPORT/CONSULTATION**:

A. IMAT team 650-573-2735 (9 AM TO 9PM, 7 days a week) or by email.
B. BHRS Interface Team.
C. California National Clinician Consultation Center, UCSF MAT Warm Line: 844-326-2626 (24/7 clinical support).
D. CA Bridge Project Direct Line :1-415-643-3257 (24/7 clinical support).

**EXCLUSIONS: Pts who may not be appropriate for Suboxone or who may need additional monitoring include:**

A. Allergy to buprenorphine or naloxone.
B. Severe CNS depression, signs of intoxication (acute alcohol intoxication or delirium tremens), medically unstable.
C. Additional monitoring required for patients with current dependence on or misuse of high-dose benzodiazepines or other CNS depressants including high amounts of alcohol. Consult or refer for additional support.
D. Moderate to Severe Hepatic Impairment.
    - Patients with transaminase levels less than five times normal, including those with HepC, tolerate buprenorphine well. If LFTs are at or above five times normal, consider risks and benefits and monitor transaminases frequently.
    - Severe hepatic impairment (Child-Pugh Score 10-15)
        i. avoid combination product (naloxone)
        ii. consider 50% dose reduction (initial & titration doses) with the monoproduct.
        iii. monitor for signs of buprenorphine toxicity or overdose.
    - Moderate hepatic impairment (Child-Pugh Score 7-9)
        i. combination products not recommended.
        ii. use cautiously for maintenance treatment if initial induction is with the monoproduct.
        iii. monitor for signs of buprenorphine toxicity or overdose.

**EVALUATION:**

A. Complete a comprehensive evaluation for opioid use, alcohol and other substances to assess appropriateness of buprenorphine treatment. Other substance use is **not** a reason to exclude from treatment. However, patients with severe alcohol, benzodiazepine, or barbiturate use disorders will require additional monitoring. Other FDA Approved treatments for OUD also include methadone and naltrexone ER. Please see SAMHSA TIP 63 Medications for Opioid Use Disorder or ASAM National Practice Guideline for the Treatment of OUD 2020 for additional information.

B. Confirm diagnosis of OUD DSM5 Checklist.

C. Review CURES Prescription Drug Monitoring Program (PDMP) to detect unreported use of controlled substances.

D. All patients who have OUD, take high dose opioids for chronic pain, have overdosed on opioids, or have a period of abstinence (including incarceration), should receive naloxone (directly or by prescription) and training (video) or (handout) on how to use it. You can receive naloxone kits to provide directly to patients – request through your supervisor or IMAT Team.

E. Recommended Labs to order (do not wait for results to initiate treatment): urine drug screen (UDS) with expanded panel for opioids and single item drug screen for fentanyl, CMP, HBV, HBsAb, HCV, HIV, hepatitis panel, urine pregnancy test.

F. Identify and address co-occurring disorders.

G. Provide Patient Education:

- Provide attached Patient Education Sheet on Starting Buprenorphine/Naloxone (Suboxone) at Home.
- Review and document informed consent and controlled medication agreement.
- Provide instructions: Do NOT swallow. start with a moist mouth, avoid acidic drinks like coffee or fruit juice. Place film or tablet under the tongue and leave there for at least 15 minutes. Do not swallow or talk until fully dissolved.
- Review safe storage of medication (protected from theft/loss; locked away from children).
- Risks of concurrent alcohol, barbiturates, benzodiazepines.
- Alert provider if pregnant or planning pregnancy. Consult for additional guidance. (consider buprenorphine only formulation - Subutex).
- Any planned procedures that may require opiates for analgesia. Consult for additional guidance. (Lembke 2019).

H. Offer counseling & ancillary services (eg. relapse prevention therapy, CBT, Narcotics Anonymous; Medication-Assisted Recovery Anonymous (MARA); Dual Recovery Anonymous). Additional services are NOT required to prescribe buprenorphine.

- IMAT Case Management Support Line: 650-573-2735 (9am-9pm)
- Health Right 360 Outpatient Program: 650-348-6603
- Other Options

I. Writing the prescription: Buprenorphine/naloxone is Schedule 3, and can be called in, faxed in with an ink signature, written on a secure prescription pad, or sent electronically.

- Include your X-license number on the prescription.
- Suboxone comes in a film or tablet sublingual formulation – both can be split for dosing flexibility.
- Typical starting prescription is 7-10 days. (For example: suboxone 8mg/2mg sl bid #14 for 7 days).

J. Opioid dependent clients should have mild-moderate symptoms of withdrawal prior to starting buprenorphine. Use an opioid withdrawal scale to determine at least mild withdrawal. The higher the score, the easier the initiation. (Buprenorphine Quick Start Guide)
Clinical Opioid Withdrawal Scale (COWS):
Subjective Opioid Withdrawal Scale (SOWS):

- SHORT-ACTING OPIOIDS (such as heroin, oxycontin, percocet, vicodin): the last dose should be at least 12 hours prior to first dose of buprenorphine.
- LONG-ACTING OPIOIDS (such as methadone, fentanyl): the last dose should be at least 36-48 hours prior to first dose of buprenorphine. *Precipitated withdrawal is more common in these patients

(regardless of COWS/SOWS scores). Consider consultation as there are now more nuanced strategies (micro-dosing; macro-dosing) that can improve outcomes in these clinically challenging situations (ex: Moe et al 2020).Consider methadone.

**DOSING:**

**A. Day 1:** Max first day dose is 16mg (FDA guidelines recommend max dose of 8mg on day one. Clinical practice supports max dose of 16mg; fentanyl may require up to 24-32 mg, but this should occur in the ED not a home or clinic start).

- If not currently physically dependent, start with 2 mg and repeat x1 if needed.
- Mild to moderate OUD, start with 2 mg. Reassess symptoms. May repeat 2-4mg after 30 min to 2 hours if withdrawal/cravings not yet controlled.
- Severe OUD (with short-acting opioid), start with 4mg. Reassess symptoms. May repeat 2-4mg every 30 minutes to 2 hrs if withdrawal/cravings not yet controlled.
- Severe OUD (with long-acting opioid): Consider consultation as there are now more nuanced strategies (micro-dosing; macro-dosing) that can improve outcomes in these clinically challenging situations. (ex: Moe et al 2020).
- If precipitated withdrawal, reduce the repeat dose to 2 mg Q 30min until resolved.
- **Consider prn medications to help with withdrawal symptoms:**
  - Ondansetron 4-8mg (OR Prochlorperazine 10mg) three times daily for nausea/vomiting.
  - Clonidine 0.1mg two to three times daily for agitation (caution hypotension).
  - Hydroxyzine (or Trazodone) 25-50mg at bedtime for insomnia.
  - NDSAIDS
  - Loperamide 2 mg prn after each additional loose stool. NTE 16 MG/24 Hours

B. **Day 2:** Max Day 2 dose is 24mg (16mg per FDA).

- If patient wakes up with no or some withdrawal, start with total dose taken on Day 1
- If patient wakes up with excess sedation or nausea, reduce dose by 2-4 mg
- Reassess every 30min to 2 hours, if withdrawal symptoms, add additional 2-4 mg.

C. **Day 3:** Max Day 3 dose is 24mg (16mg per FDA).

- Same instructions as on Day 2.

**MAINTENANCE: It is recommended that patients are seen approximately weekly until stabilized and then monthly for ongoing care. Stable patients can be seen every 2-3 months.**

**A.** Dosing

- Continue dose on which patient has stabilized. Buprenorphine withdrawal protocols (without maintenance) are not recommended with a very few exceptions. Please consult if considering this.
- Typical maintenance range: Buprenorphine/naloxone 4mg/1mg to 24mg/6mg SL or buccal once daily.
- 16mg daily has shown better patient retention in treatment than lower doses.
- Higher doses often needed at beginning and can be gently reduced over time.
- Once daily dosing is appropriate for most OUD. If the patient has concurrent pain consider splitting dose into BID, or TID. There is no ceiling effect for analgesia.
- Consider injectable buprenorphine (Sublocade) or observed daily dosing at an opioid treatment program if concerns of diversion or adherence. Consult for additional information or to coordinate.

B. Check LFTs semi-annually to annually. Learn More.

- Consider consultation in moderate to severe hepatic impairment. Please see exclusions section above.

A. Check Urine Tox Screen, including fentanyl and buprenorphine screens: as needed (every 1-2 visit during initiation phase, every 1-2 months or as needed when stable).

- Do not stop buprenorphine, if UDS positive for methamphetamine, opioids, or other substances. Adapt treatment plan. Consider consultation with any questions.

- Consider dose reduction if on concurrent sedative hypnotics.
- Clients who misuse high-dose benzodiazepines or other CNS depressants* may need additional monitoring.
- Buprenorphine and Norbuprenorphine (metabolite) levels:
    - Urine buprenorphine: test periodically to assess adherence.
    - Norbuprenorphine should be present, usually higher than buprenorphine.
    - Buprenorphine with little or no metabolite indicates tampered urine sample by adding buprenorphine.
    - No guidelines about correlation with dosing, how much consistency to expect (multifactorial: timing of UDS, whether taking in divided doses, individual metabolism, pregnancy etc.)

DURATION/TERMINATION:

A. Long term maintenance is standard of care. OUD is in remission when successfully treated with MAT. Continue treatment indefinitely, as long as client is benefitting.
B. Consider transition to injectable buprenorphine (Sublocade).
C. When discontinued, regardless of cause, relapse rates are consistently over 50% (Bentzley 2015)
D. If patient strongly prefers to discontinue, discuss risks associated with relapse including heightened overdose risk. Taper very slowly with close monitoring. (Ling 2009) There are rapid taper protocols. Seek consultation.
    - Continue psychosocial services and frequently assess opioid and other drug use throughout the taper and afterwards.
    - Establish a plan to immediately resume buprenorphine if client experiences cravings or relapses.
E. Buprenorphine should be continued through the perioperative period. (Lembke 2019). Consult for additional guidance.

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