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**Medication Use Improvement Committee**
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# Medications for Opioid Use Disorder Guideline

**SCOPE:** This Medications for Opioid Use Disorder (MOUD) Guideline is intended to offer prescribing assistance for providers, clients and the interested general public to increase the effectiveness and safety of MOUD in the ambulatory care setting. It is not intended to be comprehensive in scope. These recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual client.

**INTRODUCTION:** The American Society of Addiction Medicine (ASAM) defines opioid use disorder (OUD), also known as opioid addiction, as a "primary, chronic disease of brain reward, motivation, memory, and related circuitry." OUD requires ongoing attention to the affected physical, psychological, social and spiritual areas of an individual's life. Opioids are a group of drugs that include heroin and prescription pain relievers including morphine, hydrocodone, oxycodone, hydromorphone, methadone, fentanyl and others. In 2019, heroin use disorder affected 0.2% and pain reliever use disorder affected 0.5% of people 12 years and older in the US. Opioid use is associated with increased risk of death due to respiratory depression. In 2019, US opioid overdose death rates were 15.5 per 100,000 in the United States. This is a 500% increase in overdoses from 2000. In addition, opioid use is associated with increased risk of death due to injury from motor vehicle accidents and homicide. In San Francisco, opioid overdose deaths remained relatively stable from 2000-2016 despite an increase in the number of individuals injecting drugs, likely in part due to harm reductions strategies implemented by San Francisco residents and service providers. Despite these efforts, San Francisco saw an increase in opioid overdose deaths starting in 2018 with a rise in 2020 thought to be attributed to fentanyl and change in use patterns during the COVID-19 pandemic. Fentanyl is a synthetic opioid that is 50-100 times more potent than morphine, and it is increasingly found in illicit drug supplies, including non-opioid drugs. Fentanyl use disorder is also a growing concern in San Francisco and may necessitate the use of non-traditional dosing strategies in treatment (see Appendix 4 for more information).

Opioid exposure is common among adolescents and young adults. Family, friends, and prescriptions are the leading sources of opioids in youth who start misusing opioids. Earlier use of opioids increases the risk of developing an OUD.

Opioids are also associated with increased risk of multiple medical conditions. Opioids can lead to decreased gut motility and constipation. Taking opioids can lead to sexual dysfunction including erectile dysfunction in men and changes in menstruation in women. Syringe and paraphernalia sharing or unprotected sex in exchange for drugs can lead to multiple additional medical conditions such as: HIV, hepatitis C, hepatitis B, tetanus, botulism, and tuberculosis. Injecting contaminated drugs and/or non-sterile injection techniques can lead to infections of the skin, heart and bones. Injecting drugs can cause scarring of veins and swelling of extremities.

A range of interventions should be considered for all people with OUD, including assessment of withdrawal, management of detoxification, and long-term strategies to reduce the medical and

psychosocial harms of OUD. Retention in treatment is an important goal in order to address OUD as well as any co-occurring mental or physical conditions that may jeopardize a person's success in treatment.

Treatment with medications for OUD (MOUD) is recommended for those with moderate to severe OUD which reduces the risk of death from any cause as long as people take the medication. While medication remains the cornerstone for treating the withdrawal and cravings faced by those who are opioid dependent, non-medication supports and services may be helpful components in the comprehensive treatment of OUD. A range of treatment modalities should be considered, including, but not limited to, contingency management, cognitive behavioral therapy, intensive outpatient programs and residential treatment.

Racial and socioeconomic disparities hinder access to evidence-based treatment for OUD. Black/African American communities are experiencing dramatic increases in opioid use and overdose deaths nationally and in San Francisco. Effective interventions should be multifactorial and address community and system level factors. SAMHSA developed an issue brief in 2020 discussing the challenges of OUD prevention, treatment and recovery in Black/African American communities as well as strategies to address these challenges. Refer to "References and Further Reading" for more information.

The COVID-19 pandemic expanded the acceptability for the use of telehealth in the treatment of OUD. Telehealth has the potential to increase availability and treatment access by utilizing telecommunication modalities to deliver healthcare at a distance. SAMHSA developed a toolkit to guide providers on using telehealth in the treatment of OUD- see "References and Further Reading" section for a link to this toolkit. Changes to the regulation of opiate treatment programs (OTP) related to COVID-19 have also made it easier for clients to access methadone maintenance treatment.

**EVALUATION:** ASAM describes the comprehensive assessment and diagnosis of OUD that occurs during the initial phase of treatment as "a crucial aspect of client engagement and treatment planning." The initial task should include the identification of urgent or emergent medical or psychiatric crises that may require immediate attention and/or a transfer to a higher level of care. Thorough medical-psycho-social assessments should not delay or preclude initiating pharmacotherapy for opioid use disorder. If not completed before initiating treatment, assessments should be completed soon thereafter. The components of a comprehensive assessment are detailed below.

Medical History

- Review of systems, past diagnoses, pregnancy status, chronic conditions (HIV, viral or alcoholic hepatitis, diabetes, chronic pain conditions, thyroid, etc.), current medications and adherence, relevant family history and allergies
- Mental health status, screen for psychiatric disorders
- Sexual transmitted infections or diseases (STI/STD) risks/exposure (e.g., sharing needles, sex work, unprotected sex)
- Nicotine, alcohol and other substance use query, counseling on cessation if indicated
- Treatment history, pharmacotherapy history

Physical Examination

- Include signs of intoxication & withdrawal
- Include findings common with OUD or other substance use disorder

Diagnostics

- Labs: Hepatitis serologies, HIV, STIs, tuberculosis, pregnancy, complete blood count and liver function tests
- Urine drug screen

- Breathalyzer (as appropriate)
- Prescription Drug Monitoring Program (CURES in California)

**LEVEL OF CARE SELECTION:** Several factors should be considered when selecting level of care. This includes functional status indicators such as mental health conditions, co-occurring use disorders, housing and employment status, and community and family supports.

*Opiate Treatment Program (OTP)*: In the OTP, clients remain under daily management for MOUD with limited number of take-home doses expanding once clients' OUD is in remission. In addition, there is required counseling and urine drug screening. While the OTP has become synonymous with methadone, recent expansion of buprenorphine to the OTP setting expands medication options for treatment at this level of care. OTP-based buprenorphine or methadone is considered a higher level of care than office-based treatment (OBOT) by providing more structure and oversight. Buprenorphine and methadone provided in an OTP will not appear on CURES due to privacy requirements for substance abuse treatment programs. A benefit of OTP is that these clinics are generally open at earlier hours than primary care clinics and community pharmacies, therefore clients who require MOUD before work or during their lunch break may best be served by an OTP. Some OTPs offer directly observed therapy (DOT) of medications other than MOUD including alcohol use disorder MAT, psychiatric medications, HIV treatment medications, hepatitis C treatment medications and others. DOT may benefit clients who have difficulty with medication adherence.

*Office-Based Opioid Treatment (OBOT)*: When considering buprenorphine for an office-based client, an assessment of psychosocial functioning is crucial and should include the client's capacity and ability to safely store medication, adhere with dosing instructions and an exploration of prior MOUD treatment history, if any. Given the safety profile of buprenorphine, it is reasonable to offer a trial of OBOT to almost all clients with OUD. Clients with moderate to severe ETOH and/or sedative use disorders may benefit from the higher level of care found in OTP. Loss of dispensed buprenorphine may indicate diversion or the presence of functional impairments that preclude participation in office-based treatment.

**MOUD PHARMACOTHERAPY SELECTION:** Three medications, methadone, buprenorphine and naltrexone, are approved by the US Food and Drug Administration. The effect of each medication is through effects on the mu-opioid receptor and each agent has demonstrated decreased time to relapse to non-prescribed opioids. Beyond this, the agents differ in their mechanism of action and respective treatment outcomes.

The two major medications available for the treatment of OUD are buprenorphine and methadone, which have both demonstrated to reduce all-cause mortality by 50%. Choice between these agents is based on client preference. Methadone, and possibly buprenorphine, are available in OTPs, while buprenorphine is available for OBOT. Additional considerations include past treatment experience with MOUD, level of motivation, their medical status and contraindications for each medication. For example, in a client with oxygen-dependent lung disease, buprenorphine may be a safer option. For a list of contraindications and cautions for each agent, see Appendix 1. For information on alternative buprenorphine induction protocols, see Appendix 4.

Buprenorphine and naltrexone are available as once-monthly long-acting injections. These medications must be obtained through a restricted distribution program and it should never be dispensed directly to a client. CBHS pharmacy can support providers in their use of this medication- see Appendix 3 for more information.

For relapse prevention in a client who has successfully completed opioid detoxification, extended-release naltrexone injection may be an effective choice. It is important to note that oral naltrexone pills are not

effective for OUD as evidence suggests they are no more effective than placebo. The main challenge to effective treatment with extended-release naltrexone injection is the long period of abstinence necessary to initiate the medication and limited effectiveness at retaining people in treatment.

**CO-OCCURRING MENTAL ILLNESS:** As complex brain diseases, substance use and psychiatric disorders share common genetic and environmental risk factors and brain pathways, contributing to the challenge of accurate assessment of either. However, the identification of co-occurring OUD and psychiatric conditions is crucial to developing appropriate interventions to address the complex interaction between both conditions. Inadequate or absence of treatment of the brain based diseases affecting the client may negatively impact the course and prognosis of recovery. Accordingly, a fundamental principle of effective OUD management emphasizes the need for comprehensive treatment of all conditions in these clients, who are likely to exhibit more severe, persistent and treatment resistant symptoms of their disorders.

In particular, ASAM recommends evaluating for co-occurring depression, anxiety, personality disorders and trauma in clients presenting with possible OUD. 42 Code of Federal Regulations (CFR) Part 2 confidentiality regulations protect and limit the disclosure of substance use-related health information by a substance use disorder program to a mental health program without the explicit and signed consent by the client for each disclosure made. Therefore, it is strongly recommended that providers of both substance use and mental health programs review and obtain the necessary consents for release of information between programs in order to ensure appropriate and timely coordination and access to necessary treatment.

Included in the initial comprehensive evaluation, immediate risks, such as suicidal or homicidal thoughts or behavior and/or acute psychosis or mania should be identified and managed appropriately. Clients should be assessed for psychiatric disorders, including a detailed mental status examination when starting on MOUD, and treated accordingly. Likewise, reassessment should occur after stabilization of MOUD to identify previously undiagnosed psychiatric disorders. It is also prudent clinical practice to consider the existence of undiagnosed psychiatric conditions in the client who repeatedly is unable to adhere with the established OUD management plan.

There is no contraindication to concurrent pharmacotherapy in clients with co-occurring psychiatric and OUD. Prescribers should remain aware of potential interactions between these medications. ASAM recommends the concurrent initiation of antidepressant and MOUD in clients that present with symptoms of depression, and the concurrent initiation of antipsychotics and MOUD in clients with a psychotic disorder, including the use of depot formulations as a strategy for increasing adherence. Clients with more severe psychiatric impairments may benefit from greater coordination between involved providers, or a referral for intensive case management. Clients with co-occurring OUD and psychiatric disorders should always be offered psychosocial support as a component of their long-term recovery.

**CO-OCCURRING OTHER DRUGS AND ALCOHOL:** OUD frequently co-occurs with alcohol and other substance use disorders. Using other substances with MOUD associated with poorer treatment outcomes. Treatment recommendations for clients who drink alcohol and/or take other drugs depends on the substance(s) used and the presence and severity of a use disorder.

MOUD should be initiated, not withheld, when a client is using other substances. There is no known adverse interaction between opioids and marijuana, tobacco, cocaine, methamphetamine or other non-CNS depressant substances.

Alcohol, benzodiazepines and other CNS depressants can have additive CNS depressants effects, but the risk of overdose and death is still lower with MOUD than without treatment. Methadone and

buprenorphine are safer than heroin and fentanyl. If naltrexone is chosen for relapse prevention, it may also help with treating co-occurring alcohol use disorder.

**CO-OCCURRING CHRONIC PAIN:** Chronic pain is very prevalent among clients on MOUD. General approaches to the management of co-occurring chronic pain include using nonpharmacological treatments and non-opioid treatments as first-line treatments. In clients where opioid-based treatments are used, both buprenorphine and methadone can be used for analgesic effects. The analgesic effects are shorter for both agents, therefore divided dosing can be beneficial.

**CO-OCCURRING HIV:** Injection drug use (IDU) is the second most common mode of HIV transmission in the United States. Maintaining adherence with antiretroviral therapy (ART) can be particularly challenging among active drug users as a consequence of the depression, anxiety and general social instability commonly associated with habitual use and/or withdrawal. Engagement in care and offering MOUD to clients who use opioids is crucial to reducing the harms associated with both untreated HIV and continued illicit opioid use. Directly observed therapy (DOT) can be a useful strategy for successful management of both HIV and OUD.

*Methadone***:** Opioid-induced decreased gastric emptying may decrease the absorption of ARTs. The CYP450 2B6, 3A4 and 2D6 metabolism of methadone may interact with ARTs in any or all of the following ways: opioid withdrawal, methadone toxicity (including overdose) and decreased ART efficacy. Initial and first-line ARTs for the management of HIV include integrase strand transfer inhibitor (INSTI) based regimens, and include raltegravir, dolutegravir, and elvitegravir. There is no methadone dose adjustment recommendation for clients on concurrent INSTIs. While non-first-line agents, OUD MAT prescribers may encounter clients prescribed the non-nucleoside reverse transcriptase inhibitors (NNRTIs) efavirenz (EFV) and nevirapine (NVP), or the protease inhibitor (PI) agent lopinavir/ritonavir (LPV/r), all known to significantly decrease methadone levels. The clinical effects of decreased methadone levels are typically seen after seven days of the coadministration of EFV, NVP or LPVr and methadone. See "References and Further Readings" section for a link to a comprehensive list of methadone and ART interactions.

*Buprenorphine/naloxone***:** Buprenorphine is metabolized by CYP450 3A4, therefore there is a theoretical risk of buprenorphine toxicity with CYP450 3A4 inhibitors. However, there is little evidence that clinically significant interactions occur with the exception of the non-first-line agent PIs atazanavir (ATV) and ritonavir-boosted atazanavir (ATV/r). A small study and case reports showed increased sedation and buprenorphine concentration levels in the groups receiving coadministered ATV and ATV/r compared with buprenorphine alone. However, compared with methadone, buprenorphine has a much lower risk of respiratory depression. A significant advantage of buprenorphine is that primary care providers may prescribe buprenorphine in their clinic setting, enabling one provider to manage both primary care/HIV and OUD MAT in one visit.

*Naltrexone***:** Naltrexone is not metabolized via the CYP450 enzyme system and is not expected to interact with PIs or NNRTIs.

*Pre-exposure prophylaxis (PrEP)*: Individuals with OUD may benefit from PrEP. The Center for Disease Control (CDC) recommends that PrEP is offered to individuals without HIV who are at risk of acquiring HIV from sex or injection drug use. Those at risk include:

- Sexually active adults and adolescents
    - Anal or vaginal sex in the past 6 months **AND**
    - HIV positive sexual partner **OR**
    - Recent bacterial sexually transmitted infection **OR**

    - History of inconsistent or no condom use with sexual partner(s)
- Persons who inject drugs
    - HIV positive injecting partner **OR**
    - Shares drug preparation or injection equipment

Refer to "References and Further Reading" for a link to CDC's site with more information about PrEP as well as San Francisco AIDS foundation's site.

*Post-exposure Prophylaxis (PEP):* PEP is for HIV-negative people who may have been exposed to HIV during a single event. PEP is not a substitute for other effective HIV prevention methods, such as correct and consistent condom use, PrEP, or use of sterile injection equipment. PEP should be considered in the following scenarios:

- Sexual assault
- Needle sticks
- Shared injection equipment with someone of unknown HIV status
- Condom broke
- Anal sex without a condom with a person of unknown HIV status
- Anal sex without a condom with a person with a detectable HIV viral load (Note: people with undetectable viral loads do not transmit HIV)

Refer to "References and Further Reading for a link to CDC's site with more information about PEP. PEP is available for free in San Francisco through the San Francisco AIDS foundation.

**SPECIAL POPULATIONS:**

***Older Adults:*** Older adults are more susceptible to over sedation with buprenorphine and methadone. Therefore, doses may need to be titrated slower in order to prevent adverse effects. In addition, older adults may be taking more medications than the general population and the potential for drug interactions should be considered.

***Adolescents:*** Despite the known presence of OUD in youth, the evidence base and delivery systems for MOUD are sparse. Youth with OUD are less likely to obtain MOUD compared to adults. It is estimated that less than 2% of youth and young adults (13-22 years old) receive MOUD within 30-days of a nonfatal opioid-related overdose. Multiple clinical guidelines and medical organizations advocate and recommend increased availability and strong consideration of starting medications for youth with OUD. Treatment plans for treating OUD in youth should include harm reduction approaches, behavioral therapy referrals, and psychosocial interventions as well as consider the role for MOUD. Case management referrals can be beneficial in connecting youth with providers to help youth regularly attend appointments and support both youth and their families to navigate and link to community resources. Youth should be screened for other co-occurring psychiatric disorders and referred to behavioral services as necessary.

Buprenorphine is the only medication FDA indicated for OUD in youths for those under age 18. Current available buprenorphine literature with youth has focused on feasibility and efficacy. While there are no long-term buprenorphine studies with youth, we know that longer taper times are related to less opioid use, a higher percentage of opioid-negative urine tests, less injection drug use, and longer treatment retention compared to shorter tapers. Additionally, youth who receive a prescription for buprenorphine after an opioid overdose experience decreased opioid related and all-cause mortality. Like adult studies, detoxification only with either buprenorphine or methadone is not effective in promoting abstinence beyond initial stabilization - indicating that use of buprenorphine for maintenance is best. However, available data on retention and opioid abstinence rates with buprenorphine are lower for youth than adults. A suggested explanation is the unfamiliarity of adult programs in addressing youth's

developmental differences, challenges, and needs. As such, prescription of buprenorphine for maintenance by a provider or treatment program experienced with working with youth is optimal.

Methadone is not the preferred first-line medication for youth with OUD. Methadone treatment programs are typically not experienced in treating and addressing the needs of youth. Programs need a special federal waiver to treat clients younger than 18 with methadone.

Extended-release naltrexone injection is the least studied for the treatment of OUD in youth. A few case studies showed promise, but a subsequent randomized controlled trial of nearly 300 clients demonstrated poor retention in treatment (less than 2 months) with extended-release naltrexone injection. The risk of long-term use of naltrexone has not been established in youth, considering their ongoing brain development and maturation. However, naltrexone is considered well-tolerated among youth and children based on its use in modulating impulsivity and compulsivity (e.g., self-harming behaviors, binge eating, stereotypies) by pediatric psychiatrists and developmental pediatricians. Further, some youth and families may be more comfortable agreeing to an opioid antagonist rather than an agonist. Youth must be counseled on the loss of opioid tolerance with naltrexone and the risk of an opioid overdose if they return to use past amounts of opioids after stopping naltrexone.

***Pregnancy/Lactation:*** Pregnant individuals with active OUD should be treated with methadone or buprenorphine as the standard of care according to both ASAM and ACOG consensus opinions. Treatment should be initiated as early as possible during pregnancy to avoid the social, physical and legal destabilization and associated harms of illicit drug use. Individuals currently taking opioid agonist treatment who become pregnant should be encouraged to continue treatment during pregnancy. Data for the use of extended-release naltrexone in pregnancy are limited to small case series reporting normal birth outcomes, but experts remain concerned about the risk of treatment dropout seen with other groups, and the effects of opioid antagonism on the developing fetus are unclear.

Opioid drug use during pregnancy is associated with increased risk of preeclampsia, miscarriage, premature delivery, fetal growth restriction and fetal death. Treatment with an opioid agonist during pregnancy is not associated with long-term effects on children. Neonatal opioid withdrawal syndrome (NOWS), where the infant experiences withdrawal if not treated, can occur with opioid agonist treatment during pregnancy. However, the risks of NOWS are much less substantial than untreated OUD.

Both methadone and buprenorphine can be used during pregnancy. Buprenorphine is associated with a shorter duration of NOWS, while methadone tends to lead to longer treatment retention. When using buprenorphine in pregnancy, the mono-product may be used to decrease exposure to the small amount of naloxone absorbed. However, there is currently no evidence to suggest that buprenorphine/naloxone carries additional risk compared to buprenorphine alone in pregnancy. When using methadone, a higher dose and/or split dosing may be needed in the second and third trimester. Client choice is an important factor in deciding between methadone and buprenorphine in pregnancy. Providers should also consider the availability of medication, as buprenorphine is more widely available in some settings than methadone.

Individuals can breastfeed when taking methadone or buprenorphine (either the mono-product or combination product) and this should be encouraged. Breastfeeding with these agents is associated with decreased NOWS. Insufficient research exists on the risks (if any) of naltrexone for breastfeeding infants. There is limited data indicating that naltrexone is minimally excreted into breast milk. The decision to continue breastfeeding while taking naltrexone should be based on a mother’s individual circumstances and preference.

The postpartum period can be a vulnerable time for individuals with opioid use disorder and research suggests that relapse and overdose is more likely to occur during this time compared to any other point during pregnancy.

See Local Resources for local resources for pregnant women.

***Individuals in the Criminal Justice System:*** All FDA approved medications for the treatment of OUD should be available to individuals receiving healthcare within the criminal justice system. Individuals entering the criminal justice system should not be subject to forced opioid withdrawal or detoxification. Clients should not be forced to transition from agonist (methadone or buprenorphine) to antagonist (naltrexone) treatment. Clients being treated for OUD at the time of entrance into the criminal justice system should continue their treatment. Clients with OUD who are not in treatment should be assessed and offered individualized pharmacotherapy and psychosocial treatment as appropriate. A client's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment of OUD, with appropriate medication management. Continuation of treatment after release results in a substantial reduction in all-cause and overdose mortality. Risk for relapse and overdose is particularly high in the weeks immediately following release from prison and jails. Clients being treated for OUD while in prison or jail should be stabilized on pharmacotherapy (methadone, buprenorphine or naltrexone) and connect to treatment after their release. Client care on reentry to the community should be individualized and coordinated with treatment providers in the community.

Naloxone kits should be available within correctional facilities. Individuals with OUD should receive a naloxone kit prior to release, and individuals and families should be educated in how to administer naloxone. Further, all staff within the criminal justice system should be well versed in administering naloxone and identifying signs of both opioid withdrawal and overdose.

***Liver impairment:*** The manufacturer of methadone does not provide guidance on dose adjustment in liver impairment. However, because methadone is metabolized by the liver, the half-life may be prolonged in moderate to severe liver impairment and dose reductions may be required.

Buprenorphine and naloxone can be used in mild liver impairment without dose adjustment. However, the half-life of buprenorphine and naloxone are prolonged in moderate and severe liver impairment. If the combination product is used, the prolongation is greater for naloxone than buprenorphine, potentially resulting in naloxone accumulation and precipitated withdrawal. Combination products with naloxone are contraindicated in severe liver impairment and should be used cautiously in moderate liver impairment. Instead, clients should be treated cautiously with mono-buprenorphine products.

Naltrexone can be used in mild to moderate liver impairment without dose adjustment. Naltrexone has not been studied in clients with severe liver impairment. Due to hepatotoxicity in studies with higher than recommended doses of naltrexone, it is recommended that naltrexone be avoided in severe liver impairment until studies have been completed in this population. One SAMSHA expert panel recommends avoiding naltrexone in clients with liver function tests greater than five times the upper limit of normal.

***Kidney impairment:*** Buprenorphine and methadone doses do not need to be adjusted in kidney impairment or dialysis. Naltrexone doses do not need to be adjusted in mild kidney impairment. Naltrexone long-acting injectable has not been studied in CrCl <50mL/min. Due to hepatotoxicity in studies with higher than recommended doses of naltrexone, it is recommend that naltrexone be avoided in moderate to severe kidney impairment.

**OPIOID OVERDOSE TREATMENT AND PREVENTION*:*** Naloxone is a mu-opioid receptor antagonist that reverses the effects of opioids. In California, anyone who is at risk for experiencing or witnessing an opioid overdose can be furnished take-home naloxone for bystander administration. As the drug supply becomes more saturated with fentanyl (and other novel synthetics), it is important to recognize that more than one dose of naloxone may be necessary, as might rescue breathing and CPR for trained individuals, if the drug is contaminated with other CNS depressants.

People with OUD, both not in treatment and in treatment, should be offered a take-home naloxone kit and provided education on reducing their risk of opioid overdose. Non-prescribed and street drugs can be contaminated with opioids. Therefore, anyone that takes these should be offered a take-home naloxone kit. The person's family and friends should be included in the education in order for them to be trained to identify and respond to an opioid overdose. For details on take-home naloxone, see the BHS Overdose Prevention and Naloxone guideline and the DPH Clearinghouse Naloxone Distribution Policy and Procedure. Providers may consider offering fentanyl test strips to clients who use drugs, now available via the DPH Naloxone Clearinghouse.

**OPIOID WITHDRAWAL AND MANAGEMENT:** The neurobiology of opioid withdrawal typically does not include the serious and life-threatening symptoms that may be common with prolonged and heavy alcohol or benzodiazepine use. However, it is crucial that clients are provided with a humane and tolerable withdrawal experience that preserves their dignity and safety. Failure to do so may lead to client relapse, overdose or abandonment of treatment, and may be experienced as a lack of empathy or concern for their well-being.

The symptoms of opioid withdrawal are experienced as the opposite of this class's pharmacologic effect (See Appendix 2 for review of opioid withdrawal symptoms). However, the onset, duration and intensity of the withdrawal is variable and dependent upon the particular agent used, the duration of use, and the degree of neuroadaptation. The severity of withdrawal experienced may also be influenced by numerous other factors, including conditions such as mood, anxiety, trauma, stress and tolerance.

In general, opioid withdrawal management alone is not recommended due to significant relapse rates and increased mortality, especially in those with moderate and severe OUD. However, it may be necessary to monitor inpatient or residential opioid withdrawal to ensure safety for individuals with severe or poorly managed co-occurring medical, psychiatric or cognitive conditions, and/or for individuals concurrently using other central nervous system (CNS) depressants. Facilitating linkage to appropriate long-term recovery support should occur as a treatment plan component. While opioid withdrawal management alone should not be considered adequate treatment, it may be included as the first of a series of step-wise interventions that include evaluation, stabilization and fostering readiness for and entry into treatment, as is the ASAM recommendation for all substance use disorders.

**LOCAL RESOURCES:**

| Program Name and Contact Information | Overview |
|---|---|
| ***12-Step Programs (NA, AA, Al-Anon, etc)***<br>Various dates, time and locations | A fellowship or society of men and women for whom drugs had become a major problem and who meet regularly to help each other stay clean.<br><br>Narcotics Anonymous (NA): http://sfna.org/<br><br>Alcoholics Anonymous (AA): http://www.aasf.org |
| ***BAART Market Street Clinic***<br>1111 Market St #1<br>San Francisco, CA 94103<br>Phone: (415) 863-3883<br>Business Hours:<br>M-F: 6am-2pm, 2:30-10pm<br>Sa-Su: 8am-12pm<br>Dispensing Hours:<br>M-F: 6am-1:30pm, 2:30-9:30pm<br>Sa-Su: 8am-12pm<br>Holidays: 8am-12pm | OTP with additional services including primary care and mental health. Clients may pay cash for services.<br><br>New client instructions: First-come, first-served. Early arrival recommended. |
| ***BAART Turk Street Clinic***<br>433 Turk St<br>San Francisco, CA 94102<br>Phone: (415) 928-7800<br>Business Hours:<br>M-F: 7am-3pm<br>Sa-Su: 8am-12pm<br>Dispensing Hours:<br>M-F: 7am-2:30pm<br>Sa-Su: 8am-12pm<br>Holidays: 9am-12pm | OTP with additional services including primary care, mental health and the Family Addiction Center for Education and Treatment (FACET) program. FACET is a program for pregnant to 2-year post-partum parents. Clients may pay cash for services.<br><br>New client instructions: First-come, first-served. Early arrival recommended. |
| ***Bayview Hunters Point Foundation***<br>1625 Carroll Ave.<br>San Francisco, CA 94124<br>Phone: (415) 822-8200 | OTP<br><br>New client instructions: Call intake coordinator, to make an appointment. |

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| Program Hours:<br>M-F: 6am-2pm<br>Sa-Su: 7am-10am<br>Holidays: 6:15am-10am<br>Dosing Hours:<br>M-F: 6:15am-11am | |
| ***CBHS Pharmacy***<br>1380 Howard St<br>San Francisco, CA 94103<br>Phone: (415) 255-3659<br>**Hours:** M-F: 9am-6:30pm<br>Sa-Su: 9am-4pm | Specializes in substance use and mental health disorders. Provides safe injection kits and naloxone furnishing without a prescription. Provides additional services for buprenorphine clients including daily dosing, urine drug screening, breathalyzers, and directly observed treatment (DOT) for buprenorphine, mental health, and alcohol use disorder maintenance medications. |
| ***Family Health Center Bridge Clinic***<br>995 Potrero Ave, Bldg 80<br>Phone: (415) 205-4665<br>**Hours**: M/W/F: 1-3pm for drop-in/in person<br>M-F: 1-5pm for telehealth | Diagnoses and treats OUD as well as other substance use disorders. Buprenorphine MOUD is provided. Provides care for individuals assigned to San Francisco Health Network (Healthy San Francisco, Healthy Workers, Medi-Cal, Medicare). They are also able to see individuals with private insurance (except Kaiser) for at least two appointments. |
| ***Fort Help***<br>915 Bryant St<br>San Francisco, CA 94103<br>Phone: (415) 777-9953<br>Hours of Operation: | OTP |
| ***Fort Help***<br>1101 Capp Street<br>San Francisco, CA 94110<br>Phone: (415) 821-1427 | OTP with additional services including primary care. |
| ***Harm Reduction Center***<br>117 6th Street (between Mission & Minna)<br>San Francisco, CA 94103<br>**Hours:**<br>M/Tu/Th/Fr: 11am-3pm, 3:30-7pm<br>W: 11am-3pm, 4-7pm<br>Saturday: temporarily closed | Safer substance use supplies, injection and syringe disposal equipment, overdose prevention training and supplies including naloxone, harm reduction counseling, HIV and STI testing, hepatitis C testing and treatment and other counseling services to people who use substances or who inject. Buprenorphine program is on hold during COVID. |
| ***HealthRight 360 Central Intake Office***<br>1563 Mission St<br>San Francisco, CA 94103 | Centralized access site for social model detox and residential treatment beds (no medical or medication management available on-site). Clients may self-present Mon-Fri to request detox and/or residential treatment. On weekends, the Daily Reporting Center (on-site) |

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| Phone: (415) 760-9263<br>**Hours:** M-F: 8:30am-1:30pm. Earlier arrival is always best.<br><br>**Weekends:** Saturday and Sunday, clients may present at the Daily Reporting Center at from 9am-1pm to request detox. | provides access and placement into detox when TAP is closed. This office works very closely with TAP and provides an alternative location for accessing healthRIGHT360 SUD services. |
| ***Homeless Prenatal Program***<br>2500 18th St.<br>San Francisco, CA 94110<br>Phone: (415) 546-6756 | Serves homeless and low-income families with children 17 years old or younger. Offers prenatal and parenting support, housing assistance, tax and benefits assistance, substance use services, domestic violence services, mental health services, and a variety of support groups and classes. Partners closely with the Women's Health Center and high-risk OB at SFGH. |
| ***Integrated Soft Tissue Injection Service (OASIS) Clinic***<br>San Francisco General Hospital, Main Building, 4th Floor, Suite 4C<br>1001 Potrero Avenue<br>San Francisco, CA 94110<br>Phone: (415) 206-3719<br>**Hours:** Mon, Wd-Fri: 8am-4:30pm (closed noon-1pm)<br>Sat: 8am-11am | Treats clients with fulminating or emergent soft tissue infections. Serves clients with previously untreated abscesses and cellulitis and offers treatment such as incision and drainage of abscesses and antibiotics prescriptions. ISIS clients are drop-in and seen on a first-come, first-served basis.<br><br>Clients with chronic wounds and previously treated abscesses are not appropriate for referral to the OASIS clinic. |
| ***Kaiser Chemical Dependency Recovery Program (CDRP)***<br>1201 Fillmore St<br>San Francisco, CA 94115<br>Phone: (415) 833-9400 | Offers day treatment, intensive outpatient treatment, co-dependent treatment, adolescent treatment and specialty groups for African-American, gay men and dually diagnosed. Call for appointments. |
| ***LifeRing***<br>Various dates, times and locations | A network of support groups for people who want to live free of alcohol and other addictive drugs.<br><br>http://liferingsf.org/ |
| ***Maternal Child and Adolescent Health (MCAH) Public Health Nurse Program***<br>Referrals: 415-920-3543<br>or dana.lazarovitz@sfdph.org | Provides urgent stabilization of pregnant and postpartum people in San Francisco. Public health nurses conduct home or field visits on a regular basis. |

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| ***Needle Access***<br>Various dates, time and locations and hours | Injection drug users trade their used equipment for clean equipment. Also provides HIV and Hep C testing, vein care/safer injection education, naloxone distribution, and linkage to drug treatment and medical care.<br><br>Schedule: http://sfaf.org/client-services/syringe-access/site-schedule.html |
| ***OBIC- Office-based Buprenorphine Induction Clinic***<br>1380 Howard St, 2nd Floor<br>San Francisco, CA 94103<br>Phone: (415) 552 – 6242<br>Hours of Operation (appointments available and drop-ins welcome):<br>Mon/Tues/Thus/Fri: 8:30-11:30am, 1-6pm<br>Wed: 8:30-11:30am, 1-3pm<br>*Closed on major holidays* | OBIC provides medications and evidence-based treatments for substance use disorders in addition to treating other co-occurring mental health conditions. They aim to provide care for whomever walks in the door. They specialize in starting and stabilizing people on buprenorphine treatment for opioid use disorder including several methods of buprenorphine initiations and long-acting injectable buprenorphine. They also provide medications for other substance use disorders and counseling services. They support patients through the early phases of treatment for their substance use with the ultimate goal of connecting people to long-term, integrated care with community based primary care or mental health providers. They accept Medi-Cal, Medicare, Healthy Workers, Healthy SF, or uninsured patients. |
| ***Opiate Treatment Outpatient Program at Zuckerberg San Francisco General (ZSFG)***<br>1001 Potrero Ave.<br>Building 90 Ward 93<br>San Francisco, CA 94110<br>Phone: (415) 206-8412<br>Dosing Hours:<br>M-F: 6:45AM-11:00AM, 12:30-2:00PM<br>Sa-Su/Holidays: 7:30AM-11:30AM, 12:30PM-2:00PM | Opioid Treatment Program (OTP) on the ZSFG campus with special expertise in rapid methadone dose up-titration for clients using fentanyl, transitions from high dose methadone to buprenorphine, and additional services including on-site Hep C treatment and psychiatric care.<br><br>New client instructions: first-come, first-served. DPH providers may submit e-referral through Epic. For initiating treatment, arrive early. No ID or insurance coverage required.<br><br>After initiation, may transfer to a van at Newcomb & Newhall. |
| ***San Francisco Department of Public Health Treatment Bed Availability***<br>Site: https://findtreatment-sf.org/ | Online search tool to locate residential substance use disorder and mental health treatment beds. The site lists all programs along with their maximum capacity, current bed availability and contact information. It is updated daily. Programs are designed for Medi-Cal clients, although some of them may accept private insurance |
| ***Team Lily***<br>1001 Potrero Ave, Building 5, 5th Floor<br>San Francisco, CA 94110 | A Zuckerberg San Francisco General Hospital-based multidisciplinary care team providing person-centered, trauma-informed, wrap-around services to pregnant and postpartum people. They support pregnant people experiencing significant barriers to accessing clinic- |

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| Referrals: 415-802-7615<br>Rebecca.schwartz@ucsf.edu<br>Hours of Operation:<br>M-F: 9am-5pm<br>Drop-in hours on Thursdays | based prenatal care, primarily those experiencing homelessness, substance use disorders, incarceration, intimate partner violence, and/or mental illness. |
| ***Tenderloin Linkage Center***<br>1172 Market Street<br>San Francisco, CA 94102<br>Open 7 days a week, 8am-8pm | Part of San Francisco's Tenderloin Emergency Initiative. It is designed to provide a safe space for people to access health and human service resources. Methadone and buprenorphine services are available Monday-Thursday, 8-10am. Overdose prevention supplies available every day. Other services include free meals, showers, laundry, housing assessments, assistance with Medi-Cal and CalFresh applications, referrals and more. |
| ***Treatment Access Program (TAP)***<br>1380 Howard St, 1st Floor<br>San Francisco, CA 94103<br>Phone: (415) 503 – 4730<br>Hours of Operation: M-F 8am-5pm<br>*Accepts walk-in. Last client seen at 4:00pm* | The centralized site within SFDPH BHS that provides substance use disorders screening, assessment, level of care recommendations, and placement authorization for residential treatment at healthRIGHT360. Provide referrals to other SUD programs and provider consultation. |
| ***UCSF Youth Outpatient Substance Use Program (YoSUP)***<br>Pritzker Building - 675 18th Street, 3rd Floor, San Francisco, CA 94143<br>Phone: 415-353-2002<br>M-F 8am-5pm<br>https://youthsubstanceuse.ucsf.edu/ | Family-based program that provides comprehensive assessment and outpatient treatment for individuals up to age 25 with problematic substance use and substance use disorders. Composed of a multi-disciplinary team of medical professionals who specialize in the treatment of individuals who are struggling with substance use and other mental health conditions. YoSUP offers both in-person and telehealth appointments. Treatment with medications is available. Accepts all type of insurance except Kaiser and Anthem Medi-Cal. |
| ***UCSF Substance Use Warmline***<br>855-300-3595<br>Consultation is available Monday through Friday, between 9am and 8pm ET. Voicemail is available 24-hours a day | Free and confidential clinician-to-clinician telephone consultation focusing on substance use evaluation and management for primary care clinicians. Available clinicians are addiction medicine-certified physicians, clinical pharmacists, and nurses with special expertise in pharmacotherapy options for opioid use. This service is for healthcare providers only, not for clients or family members. |
| ***Veterans Affairs Medical Center Substance Abuse Programs***<br>4150 Clement St, Building 1<br>San Francisco, CA 94121<br>Phone: (415) 221-4810 ext. 22814 | OTP for veterans only. Treatment options include methadone, sublingual buprenorphine, extended-release buprenorphine injections and extended-release naltrexone.<br><br>New client instructions: Call beforehand to make an appointment. |

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| Business Hours:<br>M-F: 7am-3pm<br>Dosing Hours:<br>M-F: 7am-12pm | |
| ***Westside Methadone Detoxification & Maintenance Programs***<br>1301 Pierce St (at Ellis St)<br>San Francisco, CA 94115<br>Phone: (415) 563-8200<br>Business Hours:<br>M-F: 7am-3:30pm<br>Dosing Hours:<br>M-F: 7am-10:45am & 12pm-1:45pm<br>Sa-Su/Holidays: 8am-11am<br>*Walk-ins accepted, calling beforehand is recommended to ensure MD availability.*<br>*Photo ID required.* | OTP<br><br>New client instructions: Walk-ins accepted, calling beforehand is recommended to ensure MD availability.<br>Photo ID required. |
| ***Women's Health Center 5M (Includes high-risk OB)***<br>San Francisco General Hospital, Main Hospital, Ward 5M<br>1001 Potrero Avenue<br>San Francisco, CA 94110<br>Phone for Appointments: (415) 206 – 3409 | Obstetrics and gynecology practice that includes prenatal care, including managing high-risk pregnancies. Clients have access to mental health and psychiatric support. Partners closely with Homeless Prenatal Program. |

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## APPENDIX 1: MEDICATION TABLES

### TABLE 1: MEDICATIONS FOR OPIOID USE DISORDER

| Medication | Mechanism of Action | Dose & Administration | Contra-indications | Adverse Effects | Comments |
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| **Buprenorphine**<br><br>**Buprenorphine injection** | Partial μ opioid agonist which reduces opioid withdrawal symptoms and cravings. The high binding affinity for the μ opioid receptor blocks the effects of other opioids. | *Clients should be in mild to moderate opioid withdrawal (COWS >10) when initiating buprenorphine to prevent precipitated withdrawal*<br><br>**Sublingual/buccal:** Induction 2-4mg q2h prn opioid withdrawal symptoms up to 8mg on Day 1. Then increase in 4-8mg increments to a maintenance dose of 12-16mg per day. Max 32mg per day. To avoid precipitated withdrawal among people on fentanyl or methadone, clinicians offer low-dose buprenorphine inductions (with film or patches) with overlap of full agonist opioid.<br><br>A maintenance dose is established when a client no longer experiences opioid cravings or opioid withdrawal.<br><br>**Injection:** Recommended dose is 2 | Use of opioid antagonists | Sedation, constipation, nausea, vomiting, diaphoresis, headache | Buprenorphine was the first opioid agonist treatment available in an office-based setting. Buprenorphine can be prescribed for OUD treatment by a physician, nurse practitioner or physician assistant that has a DATA 2000 waiver, also known as a "DEA X" number. There are no regulations for treatment inclusion or exclusion. DATA 2000 waiver trainings can be found at: https://www.buppractice.com/.<br><br>Partial μ opioid agonist leads to ceiling effect for respiratory depression and improved safety profile. However, when combined with additional CNS depressants the ceiling effect is mitigated and respiratory depression effects are similar to a full μ opioid agonist.<br><br>In addition to treating opioid withdrawal and cravings, maintenance treatment with buprenorphine is associated with increased treatment retention compared to detoxification.<br><br>Buprenorphine binds with high affinity to the mu opioid receptor and can displace full opioid agonists leading to precipitated withdrawal. Therefore, people should be in mild withdrawal with objective symptoms prior to starting buprenorphine.<br><br>Buprenorphine can be prescribed in a co-formulated product with naloxone as an IV abuse deterrent. Naloxone is not absorbed at clinically relevant amounts sublingually or buccally (see Hepatic Impairment for exceptions). If the co-formulated |

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| | | monthly initial doses of 300mg followed by 100mg monthly maintenance dose. Increasing the maintenance dose to 300mg may be considered when benefits outweigh risks. Healthcare settings and pharmacies that dispense injection must be enrolled in REMS program.<br><br>*Renal impairment:* no adjustment<br><br>*Hepatic impairment:* Buprenorphine: decrease dose by 50% in severe impairment.<br><br>Naloxone: avoid naloxone containing products in severe (and possibly moderate) impairment | | | product is injected by an opioid physically dependent person precipitated withdrawal can occur.<br><br>In January 2022, FDA issued a warning about the potential for dental problems in buprenorphine products that dissolve in the mouth. They recommend swishing with a large sip of water after the medication dissolved and recommend regular dental check-ups while on buprenorphine. Several professional societies called for FDA to retract this warning, stating that the FDA's findings are not based on solid research evidence and can lead to potentially harmful, stigmatizing effects that may further limit access to buprenorphine. BHS supports reducing barriers and stigma to buprenorphine access.<br><br>***Injection:*** Indicated for people who have initiated treatment with a buprenorphine containing product delivering the equivalent of 8-24mg of buprenorphine for a minimum of 7 days.<br><br>***Drug Interactions:*** Metabolized by CYP3A4<br><br>***Monitoring:*** Check LFTs prior to initiation and monitor periodically while on treatment. Attend regular dental check ups. |
| **Methadone** | Full μ opioid agonist which reduces opioid withdrawal symptoms and cravings. The high binding affinity for the μ opioid receptor blocks the | *Only available from a Narcotic Treatment Program when treating OUD.*<br><br>**Oral:** 10-30mg PO daily titrated every 5 days to a maintenance dose of 60 – 120mg daily. | Contraindications: Paralytic ileus, documented Torsade de pointes (Tdp) on methadone, use of opioids antagonists | Sedation, constipation, nausea, vomiting, diaphoresis, QTc prolongation, Tdp, respiratory depression | The use of methadone for the treatment of OUD is restricted to licensed Opioid Treatment Programs (OTP).<br><br>In addition to reducing withdrawal and cravings, methadone for OUD improves treatment retention, reduces mortality of OUD, reduces criminal behavior associated with opioid use and decreases high risk behaviors associated with opioid use. |

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| | effects of other opioids. | A maintenance dose is established when a client no longer experiences opioid cravings or opioid withdrawal. Of note, higher doses are expected among people who use fentanyl. Further, women who are pregnant or those deemed to be rapid metabolizers may need split dosing.<br><br>*Hepatic impairment:* no adjustments providers in package insert<br><br>*Renal impairment:* CrCl ≥10mL/min: no dose adjustment. CrCL <10mL/min: use 50-75% of normal dose | Caution: decompensated liver disease, severe apnea, severe asthma, severe COPD, sedative-hypnotic or CNS depressant abuse, familial QTc prolongation or QTc prolongation >450 msec, concomitant use of medications that prolong the QTc interval | | Methadone has a long half-life resulting in a steady-state serum levels 3-5 days after dose adjustments, therefore doses are titrated slowly to reduce toxicity.<br><br>OTP's have additional confidentiality requirements under Code of Federal Regulations 42, therefore methadone will not be present on CURES.<br><br>***Drug Interactions:*** Multiple drug interactions, primarily metabolized by CYP3A4, followed by CYP2B6 and CYP2C19 and, to a lesser degree by CYP2C9 and CYP2D6. Examples of medications increase methadone serum levels by CYP3A4 inhibition include: azole antifungals, macrolides, fluoroquinolones and some antidepressants<br><br>Medications to avoid with methadone include efavirenz, ketoconazole, rifampin<br><br>***Monitoring:*** Check LFTs prior to initiation and monitor periodically while on treatment<br><br>EKG monitoring practices are variable in terms of timing and dose. Expert consensus from the American Society of Addition Medicine (ASAM) recommends EKG in clients on methadone doses >120mg per day, clients with a history of QTc prolongation and in clients taking medications that prolong the QTc interval |
| **Naltrexone long acting injection** | μ opioid antagonist which may block the effects of opioids | **Injection:** 380mg IM monthly<br><br>Clients must be opioid free for 7-14 days before starting naltrexone, duration of opioid abstinence will depend on half-life of opioids used. Consider naloxone | Decompensated cirrhosis as manifested by AST/ALT > 5x ULN, INR >1.5, ascites, esophageal varices, hepatorenal syndrome, | Nausea, headache, anxiety, sedation.<br><br>Warnings of hepatotoxic effects are derived from studies using | Naltrexone that has no required certifications to prescribe or requirements for treatment setting.<br><br>Does not treating opioid cravings.<br><br>A person must be opioid free 7-10 days prior to initiating naltrexone to avoid precipitated withdrawal.<br><br>Long acting injection may improve adherence however is cost prohibitive and has limited |

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| | | challenge to assess for opioid withdrawal. | spontaneous bacterial peritonitis, encephalopathy<br><br>Pregnancy: Use is not recommended | oral dosages up to 300mg/day for obesity and dementia. No reports of hepatotoxicity at FDA recommended dose. | availability as an outpatient drug benefit through Medi-Cal.<br><br>***Monitoring:*** Check LFTs and INR prior to initiation and monitor LFTs periodically while on treatment (annually unless signs or symptoms of hepatitis develop). |

**TABLE 2: MEDICATIONS FOR PRECIPITATED WITHDRAWAL**

| Medication | Target withdrawal symptom | Dose & Administration | Adverse Effects | Comments |
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| Acetaminophen | Myalgias | **Oral**: 325mg q6 hours | Nausea, loss of appetite | |
| Baclofen | Muscle cramps | **Oral:** 5-10 mg up to three times daily as needed | Drowsiness, nausea/vomiting, confusion, dizziness, hypotonia, asthenia | Use with caution with other CNS depressants as they may have additive effects with baclofen |
| Clonidine | Restlessness, sweating, anxiety | **Oral:** 0.1 to 0.2 mg (patients >90 kg may receive up to 0.3 mg); may repeat every 45 to 60 minutes if needed, up to a total of 4 doses until symptoms resolve, provided blood pressure and heart rate remain stable; maximum dose: 1.2 mg/day | Bradycardia, hypotension, dry mouth, dizziness, headache | Check blood pressure and watch out for hypotension when using |
| Hydroxyzine | Anxiety, insomnia | **Oral:** 25mg q6 hours as needed | Somnolence, dry mouth | |
| Ibuprofen | Myalgias | **Oral:** 400mg four times/day | Stomach upset | Take with food |
| Lofexidine | Restlessness, sweating, anxiety | **Oral:** 0.54-0.72 mg q5-6 hours during the period of peak withdrawal symptoms (generally the first 5 to 7 days following last use of opioid) with | Orthostatic hypotension, bradycardia, hypotension, dizziness, | Limited efficacy seen in clinical trials<br><br>***Drug Interactions:*** |

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| | | dosing guided by symptoms and side effects. Max dose is 2.88mg/day. When discontinuing treatment, taper lofexidine by 1 tablet every 1-2 days. Adjust dose for renal and hepatic impairment (see package insert). | somnolence, sedation, dry mouth | **Methadone**: Concern for QT prolongation. ECG monitoring is recommended when used concomitantly. **Oral naltrexone:** Comcomitant use may reduce efficacy of oral naltrexone. **CYP2D6 Inhibitors:** Monitor for symptoms of orthostasis and bradycardia with concomitant use.<br><br>***Monitoring:*** Monitor vital signs before dosing and advise clients on how to minimize risk of hypotension, bradycardia and syncope. Monitor ECG in clients at risk for QT prolongation. |
| Loperamide | Diarrhea | **Oral:** 4mg then 2mg four times/day | Dizziness, constipation, stomach upset | |
| Ondansetron | Nausea | **Oral:** 8mg BID for anticipated length of withdrawal | Constipation, fatigue, headache, malaise | Check QTc in individuals with risk factors for arrhythmias |
| Trazodone | Insomnia | **Oral**: 50-100mg at bedtime | Dry mouth, dizziness, fatigue, blurred vision, next-day somnolence | |

**APPENDIX 2: CLINICAL OPIATE WITHDRAWAL SCALE (COWS)**

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name: _____ Date and Time_____/_____/_____:_____

Reason for this assessment:_____

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|---|---|
| **Resting Pulse Rate:** _____beats/minute<br>*Measured after patient is sitting or lying for one minute*<br>0 pulse rate 80 or below<br>1 pulse rate 81-100<br>2 pulse rate 101-120<br>4 pulse rate greater than 120 | **GI Upset:** *Over last 1/2hour*<br>0 no GI symptoms<br>1 stomach cramps<br>2 nausea or loose stool<br>3 vomiting or diarrhea<br>5 multiple episodes of diarrhea or vomiting |
| **Sweating:** *Over past 1/2hour not accounted for by room temperature or patient activity.*<br>0 no report of chills or flushing<br>1 subjective report of chills or flushing<br>2 flushed or observable moistness on face<br>3 beads of sweat on brow or face<br>4 sweat streaming off face | **Tremor:** *Observation of outstretched hands*<br>0 no tremor<br>1 tremor can be felt, but not observed<br>2 slight tremor observable<br>4 gross tremor or muscle twitching |
| **Restlessness**: *Observation during assessment*<br>0 able to sit still<br>1 reports difficulty sitting still, but is able to do so<br>3 frequent shifting or extraneous movements of legs/arms<br>5 unable to sit still for more than a few seconds | **Yawning:** *Observation during assessment*<br>0 no yawning<br>1 yawning once or twice during assessment<br>2 yawning three or more times during assessment<br>4 yawning several times/minute |
| **Pupil size:**<br>0 pupils pinned or normal size for room light<br>1 pupils possibly larger than normal for room light<br>2 pupils moderately dilated<br>5 pupils so dilated that only the rim of the iris is visible | **Anxiety or Irritability:**<br>0 none<br>1 patient reports increasing irritability or anxiousness<br>2 patient obviously irritable or anxious<br>4 patient so irritable or anxious that participation in the assessment is difficult |
| **Bone or Joint aches:** *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored*<br>0 not present<br>1 mild diffuse discomfort<br>2 patient reports severe diffuse aching of joints/muscles<br>4 patient is rubbing joints or muscles and is unable to sit still because of discomfort | **Gooseflesh skin:**<br>0 skin is smooth<br>3 piloerrection of skin can be felt or hairs standing up on arms<br>5 prominent piloerrection |
| **Runny nose or tearing:** *Not accounted for by cold – symptoms or allergies*<br>0 not present<br>1 nasal stuffiness or unusually moist eyes<br>2 nose running or tearing<br>4 nose constantly running or tears streaming down cheeks | Total Score _____<br>The total score is the sum of all 11 items<br><br>Initials of person completing assessment: _____ |

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

**Source:** Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). J Psychoactive Drugs, 35(2), 253–9.

**APPENDIX 3: CBHS Pharmacy Buprenorphine FAQ's for CBHS Prescribers**

**What services does CBHS Pharmacy provide for buprenorphine clients?**

CBHS Pharmacy provides specialty services for buprenorphine clients including the following:

Monitoring: Clients check in with a pharmacist every time they pick up buprenorphine. If the client appears intoxicated with a CNS depressant, clients will be referred to the buprenorphine prescriber for follow up and re-evaluation. Any reported/observed substance use, opioid withdrawal symptoms, side effects or sub-acute changes in client's condition will be reported to the buprenorphine prescriber. Providers can also order onsite urine drug screening and breathalyzers.
Observed dosing: Providers may request observed dosing for clients at the CBHS Pharmacy dispensing window.
Frequent dosing: Providers may request dosing schedules more frequent than every 28 days, including daily dosing (except holidays).
Alternative buprenorphine induction dosing support: Upon provider request, CBHS pharmacy provides prescriber consultation, medication bubble packing, in depth client counseling and close monitoring for clients prescribed alternative induction protocols (i.e. "micro-dosing").
Telebuprenorphine: For established clients with a gap in treatment or those in need of refills and unable to contact their provider, the pharmacy has designated ipads for clients to connect to a virtual clinic for a buprenorphine bridge prescription.
Buprenorphine Extended-Release Injection: The pharmacy processes and dispenses prescriptions for buprenorphine extended-release injections for providers that meet REMS requirements. The provider must pick up and administer the injection to the client on the date it is due.
Naloxone: Clients can be educated on the risks for opioid overdose and trained to respond to such overdose with naloxone. Pharmacists can furnish naloxone or it can be prescribed by a provider.
Smoking Cessation: Pharmacists can assess for tobacco use and furnish nicotine replacement therapy (patch, gum or lozenge). Providers may also prescribe nicotine replacement therapy and pharmacists will provide thorough smoking cessation counseling.
Clean injection kits: CBHS pharmacy provides clean injection kits with syringes to our clients at no charge.
Fentanyl Test Strips: CBHS pharmacy provides fentanyl test strips to clients at no charge. Programs can apply to stock a supply on site.
Medication and syringe disposal: Pre-paid postage medication take-away mail bags are available at the pharmacy. Used syringes can be disposed in receptacles provided in the building.

**What is CBHS Pharmacy's policy on early or late buprenorphine pick-ups?**
First early pick-up (ex: lost meds, vacation): CBHS pharmacy does not allow clients to routinely pick-up their medication before their assigned pick-up date without authorization by the prescriber. One early pick-up is allowed in a 365-day period. For example: Client pick-ups a 7-day supply on a Tuesday, making the following Tuesday their next assigned pick-up date. If the client returns any day prior to their assigned pick-up date, authorization from the prescriber will be required.

Second or subsequent early pick-ups in a 365-day period: The client is required to have consolidated daily observed dosing until their next pick-up date with prescriber authorization. For example: If client is taking 8 mg TID, they will take 24 mg at once daily observed until next assigned due date. Prior to next pick-up, prescriber should identify reasons for frequent early pick-ups and adjust take-home supply accordingly.

Late pick-ups: Clients that are ≥10 days late picking up from their assigned pick-up dates will require authorization from the prescriber to dispense buprenorphine. Clients <10 days late picking up will be counseled on adherence and given the prescription as written.

**Does CBHS Pharmacy have any policies that may affect the buprenorphine prescription I write?**
Dispense in 7-day increments: To keep clients assigned pick-up days the same day of the week, CBHS Pharmacy will dispense in increments of 7 days unless otherwise documented by the prescriber. Example: Prescription written for a 30-day supply will be dispensed for a 28-days supply.
Buprenorphine/naloxone film: In order to improve client safety, CBHS Pharmacy has recommendations for which dosage strengths to use based on total daily dose. (See: What buprenorphine products does CBHS stock?)

**What are CBHS Pharmacy's hours of operation and location?**
CBHS pharmacy is open 7 days per week. The window is open for pick-ups weekdays 9:00am-6:30pm and weekends 9:00am-4:00pm. Pharmacy staff are available by phone weekdays 8:30am-8:00pm and weekends 9:00am-5:00pm for any questions. CBHS pharmacy is located at 1380 Howard Street.

**What if my client is due to pick-up on a holiday and CBHS Pharmacy is closed?**
If a client's scheduled pick-up date falls on a holiday when CBHS Pharmacy is closed, the client will be allowed to pick-up their buprenorphine one business day before the holiday. CBHS Pharmacy posts signs reminding clients of holidays and this policy.

**What is CBHS Pharmacy's vacation supply policy?**
Approval from the prescriber is required. Other restrictions may apply and a prior authorization may be required by the client's insurance.

**What buprenorphine products does CBHS Pharmacy stock?**
CBHS Pharmacy stocks buprenorphine/naloxone sublingual tablets and films (Suboxone) and buprenorphine alone (Subutex) sublingual tablets. Product coverage varies by insurance or third-party payer. For films, CBHS Pharmacy recommends using the following table to determine product dosage strength selections. This is intended to improve client safety by minimizing dosage strengths dispensed to the client and the need to cut and dispose of unused product

| | Quantity of Films Per Day | | | |
|---|---|---|---|---|
| **Dose** | **2mg Film** | **4mg Film** | **8mg Film** | **12mg Film** |
| 32mg | | | 1 | 2 |
| 24mg | | | | 2 |
| 16mg | | | 2 | |
| 12mg | | | | 1 |
| 8mg | | | 1 | |
| 4mg | | 1 | | |
| 2mg | 1 | | | |

**Maintenance Doses to Avoid**

| | Quantity of Films Per Day | | | |
|---|---|---|---|---|
| **Dose** | **2mg Film** | **4mg Film** | **8mg Film** | **12mg Film** |
| 40mg[1] | | | 5 | |
| 32mg[1] | | | 4 | |
| 20mg[2] | | | 1 | 1 |
| 10mg[2] | 1 | | 1 | |
| 6mg[1] | 3 | | | |

[1] Maintenance doses requiring ≥3 strips should be avoided to reduce risk of diversion and minimize costs. Exception: TID dosing for pain

[2] Doses requiring 2 strengths should be avoided (exception for 32 mg) due to potential errors by prescriber, errors by pharmacy and unlikely to be covered by insurance

**I recently received my DATA 2000 waiver; does CBHS Pharmacy provide a pharmacy orientation for providers?**
Yes, we would be happy to meet with you, introduce you to our staff and orient you to our buprenorphine pharmacy services that we provide at CBHS Pharmacy. In addition, we can help you prepare for DEA audits.

**What are the record keeping requirements for prescribing buprenorphine?**
The DEA has additional record keeping requirements for controlled substances prescribed for office-based opioid therapy, such as buprenorphine, beyond the usual for Schedule III substances. The following are the record keeping requirements:
Buprenorphine Inventory Log: Prescribers must keep an inventory of buprenorphine dispensed (21 CFR Section 1304.03[b]). This log is *required* even if the prescriber does not stock buprenorphine products. Because no CBHS clinic stocks buprenorphine products, this is generally a log with a zero balance.
Buprenorphine Prescribed/Dispensed Log: Prescribers must keep a log of controlled substances prescribed for maintenance or detoxification. This can be accomplished by creating a log (client name, name of drug, strength, quantity and date of issuance) or keeping copies of each prescription. See 21 CFR Section 1304.03[c].

**Does OrderConnect meet the requirements of a Buprenorphine Prescribed/Dispensed Log?**
Yes, OrderConnect meets the requirements of a Buprenorphine Prescribed/Dispensed Log required by the DEA. However, prescribers still need to maintain a Buprenorphine Inventory Log. Use the following steps to access the information required for a Buprenorphine Prescribed/Dispensed Log in the case of a DEA audit:

1. On the OrderConnect "Prescriber Desktop" under "Reports" click "List of Patients with Active Orders by Prescriber."
2. In the drop down list, select yourself as the prescriber and "Prescribed Patients."
3. Use Ctrl+F to search the document. Enter "Suboxone" into the "Find" field. Click the "Next" button to scroll through clients. Write down clients names- this is your list of active buprenorphine clients.
4. If you are also prescribing a generic buprenorphine product, repeat Step 3 with the word "buprenorphine" in the "Find" field.
5. Close this report and return to the OrderConnect "Prescriber Desktop."
6. Under "Reports" click "Individual Medication Profile."
7. Using your list of active buprenorphine clients you made in Step 3, type in the first client's name.
8. From this report you can determine the information required for the Buprenorphine Prescribed/Dispensed Log: drug name, strength, days supply (click the drug name), and date of issuance.
9. You may need to click "Display Entire History" at the bottom right corner of the screen to see older history.
10. Repeat Steps 6-9 with each of your active buprenorphine clients.

**What is the preferred method to prescribe buprenorphine through OrderConnect?**
eRx is the preferred method, but eFax is also accepted.

**Who can I contact if I have further questions regarding buprenorphine at CBHS Pharmacy?**
CBHS substance use disorder pharmacists can help! Call 415-255-3659 or 415-255-3705 to request a phone consult. Or, reach out by email at druginfo.bhs@sfdph.org.

## APPENDIX 4: Alternative Buprenorphine Induction Dosing

Standard protocols for buprenorphine induction are well established and work for many individuals with OUD. However, there are various clinical circumstances when alternative buprenorphine induction strategies may be desired such as:

- Difficulty starting buprenorphine in the past
- Currently on methadone
- Transitioning from prescribed full opioid agonists for pain to buprenorphine
- Using fentanyl daily

Alternative methods for dosing buprenorphine are referred to as "microdosing", "cross-tapering", "rapid microdosing" and others. There is limited but growing evidence for these dosing methods, in particular in the outpatient setting and they are not universally accepted. Additionally, these dosing protocols have not been rigorously studied and are not FDA approved. These alternative induction strategies aim to use very small doses of buprenorphine that are gradually increased while the client continues to use opioids. This allows buprenorphine levels to build up slowly and prevents clients from experiencing withdrawal. CBHS pharmacy utilizes and supports the use of these alternative induction dosing methods and has developed 2 protocols which are shown below and are accompanied by client education and counseling points.

**Client Selection**

- Preference (for any reason) for a micro-dosing strategy and/or frequent fentanyl use or history of precipitated withdrawal
- Able to manage multiple times per day dosing
- Client understands there is not a need to stop full agonist opioids during the protocol and the buprenorphine dose is not protective from overdose so should continue to practice overdose prevention strategies

**Prescribing/Dispensing Tips:**

- All take home doses for >1 day will be blister-packed for ease of use
- See table below for an example regimen-> schedule should be adjusted depending on how client tolerates the start or if they miss doses
- Buprenorphine mono product is recommended when the tablets are being cut into quarters
- First dose may be observed upon provider request

**CBHS Pharmacy Buprenorphine "Microdosing" Protocol**

| | |
|---|---|
| **Buprenorphine Mono-Product 2 mg tablets (NDC 50383-0924-93)<br>Blister-pack Days 1-3 and dispense #2 tablets** | |
| Day 1 | Dissolve ¼ of a 2mg tablet (0.5mg) under your tongue in the morning |
| Day 2 | Dissolve ¼ of a 2mg tablet (0.5mg) under your tongue twice daily |
| Day 3 | Dissolve ¼ of a 2mg tablet (0.5mg) under your tongue in the AM Then Dissolve ½ tablet (1mg) in the afternoon and evening |
| **Buprenorphine-Naloxone or Buprenorphine Mono-Product 2 mg Tablets<br>Blister-pack Days 4-6 and dispense #9 tablets** | |
| Day 4 | Dissolve 1 (2mg) tablet under your tongue twice daily |
| Day 5 | Dissolve 1 and ½ (3mg) tablets under your tongue twice daily |
| Day 6 | Dissolve 2 (4mg) tablets under your tongue twice daily |
| **Buprenorphine-Naloxone or Buprenorphine Mono-Product<br>Provider can change to films based on client preference** | |
| Day 7 | Custom (12-32 mg depending on clinical situation) |

**CBHS Pharmacy Buprenorphine "Rapid Microdosing" Protocol**

| **Buprenorphine mono-product 2mg tablets (NC 50383-0924-93)<br>Blister-pack and dispense #7 tablets** | |
|---|---|
| Day 1 | Dissolve ¼ of a 2mg tablet (0.5mg) under your tongue observed now, then every 6 hours for a total of 4 doses |
| Day 2 | Dissolve 1/2 of a 2mg tablet (1mg) under your every 6 hours for a total of 4 doses |
| Day 3 | Dissolve 1 (2mg) tablet under your every 6 hours for a total of 4 doses |

**Client Education Key Points:**

- This is a gentle and gradual way for you to start buprenorphine that will not require you to stop using opioids until later.
- We blister-pack your medication to help you stay on your dosing schedule. It is very important that you follow the schedule to avoid symptoms of withdrawal.
- If you skip doses of buprenorphine please check in with your provider ASAP so they can help guide you.
- You may continue to use opioids. You can try to cut down on your opioid use gradually over the week. However, you do not have to. This can happen later when you're on a higher dose.
- Do not try to quantify how much opioid that you need to decrease per day – let your body naturally cut down. As the buprenorphine builds up in your body, you will notice that the same amount of opioid does not cause the same effect and you can begin to try less.
- You may not notice a decrease in opioid use during the first few days as the buprenorphine slowly builds up. You may begin to a notice a difference as you move into days 4-6.
- You may not feel 100% better right away. Your body is transitioning, and most people feel better and better with time.