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Approaches to Opioid Use Disorder Medication-Assisted Treatment Guideline

SCOPE: This Approaches to Opioid Use Disorder Medication-Assisted Treatment (OUD MAT) Guideline is intended to offer prescribing assistance for providers, clients and the interested general public to increase the effectiveness and safety of OUD MAT use 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 patient.

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 2015, heroin use disorder affected 0.2% and pain reliever use disorder affected 0.7% of people 12 years and older in the US. Locally in San Francisco, 5% of persons over the age 12 reported non-prescribed use of pain relievers between 2012 and 2014. In San Francisco public high-school students, 13% reported use of prescription drugs in 2015.

Opioids are associated with increased risk of death. In 2014, unintentional drug overdose was the leading cause of unintentional death in the United States at 14.7 per 100,000. The majority of the overdoses involved opioids at 9.0 per 100,000. This is a 200% 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.

Opioids are also associated with increased risk of multiple medical conditions. Opioids can lead to decreased gut motility and constipation. Taking opioids use can lead to sexual dysfunction including erectile dysfunction in men and changes in menstruation in women. Syringe and paraphernalia sharing or high risk behaviors such as unprotected sex can lead to multiple additional medical conditions. This includes viral infections, 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 on veins and, if severe enough, result in swelling in the legs.

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 the OUD as well as any co-occurring conditions that resulted from injecting opioids or jeopardize a person's treatment success.

Medication-Assisted Treatment (MAT) refers to the combination of medication therapy with counseling or behavioral interventions. MAT for OUD is recommended for those with moderate to severe OUD who are unsuccessful at ceasing opioid use without the assistance of medication or at risk for relapse.

While medication remains the cornerstone for treating the physiology of opioid dependence, withdrawal and cravings, non-medication supports and services are necessary components in the comprehensive treatment of OUD. A range of treatment modalities should be considered, including, but not limited to, cognitive behavioral therapy, intensive outpatient programs and residential treatment.

OPIOID WITHDRAWAL: 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 patients are provided with a humane and tolerable withdrawal experience that preserves their dignity and safety. Failure to do so may lead to patient 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.

EVALUATION: ASAM describes the comprehensive assessment and diagnosis of OUD that occurs during the initial phase of treatment as "a crucial aspect of patient 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. 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
- Sexual transmitted infections or diseases (STI/STD) risks/exposure (e.g., sharing needles, sex work, unprotected sex)
- 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)

OPIOID WITHDRAWAL MANAGEMENT: In general, opioid withdrawal management alone is not recommended due to significant relapse rates, especially in those with moderate and severe OUD. However, monitored inpatient or residential opioid withdrawal management may be necessary 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 addictions.

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, patients remain under daily management for MAT until such time as they earn take-home doses. 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 patients who require OUD MAT 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 OUD MAT including alcohol use disorder MAT, psychiatric medications, HIV treatment medications, hepatitis C treatment medications and others. DOT may benefit patients who have difficulty with medication adherence.

Office-Based Opioid Treatment (OBOT): Buprenorphine's originally intended use under Drug Addiction Treatment Act (DATA) 2000 was office-based opioid treatment (OBOT) rather than in the OTP setting. When considering buprenorphine for an office-based patient, an assessment of psychosocial functioning is crucial and should include the patient's capacity and ability to safely store medication, adhere with dosing instructions and an exploration of prior MAT treatment history, if any. Patients well-suited for OBOT buprenorphine typically are psychiatrically stable and show no evidence of concurrent substance use patterns that negatively impact their ability to engage in treatment. Patients with moderate to severe ETOH and/or sedative use disorders may benefit from the higher level of care found in OTP. Housing, employment and social and/or family support are important factors in recovery and be indicators of psychosocial stability. Alternatively, loss of dispensed buprenorphine may indicate diversion or the presence of functional impairments that preclude participation in office-based treatment.

OUD MAT PHARMACOTHERAPY SELECTION: Three medications, methadone, buprenorphine and naltrexone, are approved by the US Food and Drug Administration. Buprenorphine and methadone are indicated for the treatment of OUD and naltrexone is indicated for relapse prevention of OUD. (See Appendix 1). 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. Choice between these agents is based on availability in the chosen level of care. Methadone, and possibly buprenorphine, are available in OTPs, while buprenorphine is available for OBOT. Additional considerations include patient preference, past treatment experience with OUD MAT, level of motivation, their medical status and contraindications for each medication. For example, in a patient with underlying QTc prolongation, buprenorphine is a safer option. For a list of contraindications and cautions for each agent, see Appendix 1.

For relapse prevention in a patient who has successfully completed opioid detoxification, naltrexone has been shown to be an effective choice for the highly motivated, high functioning individual willing to engage in the requirements of therapy. Barriers to effective treatment with naltrexone include continued opioid use vis a vis an inability to abstain long enough to achieve the required full two week post-detoxification period necessary to initiate the medication. Failure of the medication to reduce opioid cravings may be related to treatment efficacy outcome or poor medication adherence.

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 patient will negatively impact the course and prognosis of recovery. Accordingly, a fundamental principle of effective OUD emphasizes the need for comprehensive treatment of both conditions in this patient, who is 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 patients presenting with possible OUD. A barrier to comprehensive and integrated treatment is the 42 Code of Federal Regulations (CFR) Part 2 confidentiality regulations that 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 patient 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. Patients should be assessed for psychiatric disorders, including a detailed mental status examination prior to beginning OUD pharmacotherapy, and treated accordingly. Likewise, reassessment should occur after stabilization of OUD MAT to identify previously undiagnosed psychiatric disorders. It is also prudent clinical practice to consider the existence of undiagnosed psychiatric conditions in the patient who repeatedly is unable to adhere with the established OUD management plan.

While there is no absolute contraindication to concurrent pharmacotherapy in patients with co-occurring psychiatric and OUD, prescribers should remain aware of potential interactions between these medications. ASAM recommends the concurrent initiation of antidepressant and OUD MAT in patients that present with symptoms of depression, and the concurrent initiation of antipsychotics and OUD MAT in patients with a psychotic disorder, including the use of depot formulations as a strategy for increasing adherence. Patients with more severe psychiatric impairments may benefit from greater coordination between involved providers, or a referral for intensive case management. Patients 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. Taking other substances during OUD treatment is associated with poorer treatment outcomes. Treatment recommendations for patients who drink alcohol and/or take other drugs depends on the substance used and the presence and severity of a use disorder.

OUD MAT can be initiated and should not be withheld when the substance used does not interact with opioids and should not be discontinued when benefit has been shown. This includes marijuana, tobacco, cocaine, methamphetamine or other non-CNS depressant substances.

Alcohol, benzodiazepines or other CNS depressants use should be considered when selecting OUD MAT. Combining CNS depressants with buprenorphine or methadone can have additive CNS depressant effects and increase a patient's risk for accidental overdose. Patients with co-occurring alcohol use disorder or other CNS depressant use disorders may require detoxification prior to initiating OUD MAT. If naltrexone is chosen for relapse prevention, it may also help with treating co-occurring alcohol use disorder.

CO-OCCURRING CHRONIC PAIN: Among people with chronic pain, approximately 10-20% of people have a co-occurring opioid use disorder. General approaches to the management of co-occurring chronic pain include using nonpharmacological treatments and non-opioid treatments as first-line treatments. In patients 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 should be used.

CO-OCCURRING HIV: Injection drug use (IDU) of heroin and stimulants 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 life instability commonly associated with repeated use and/or withdrawal. Engagement and offering OUD MAT to opioid users is crucial to decreasing 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 opioid use disorder.

*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 patients on concurrent INSTIs. While non-first-line agents, OUD MAT prescribers may encounter patients 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.

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: The ASAM consensus opinion is adolescents can be considered for treatment with OUD MAT. However, there are few studies in this patient population. There are no studies comparing the effects of the agents in adolescents. There are no methadone or naltrexone placebo controlled trials in patients under the age of 18. Buprenorphine is indicated for patients 16 years and older. Psychosocial treatment is recommended for all adolescents with OUD. This includes family intervention approaches, vocational support and behavioral interventions to reduce opioid use.

Pregnancy/Lactation: The decision to treat OUD with an opioid agonist should include a discussion of the risks and benefits of treatment. 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 abstinence syndrome (NAS), where the infant experiences withdrawal if not treated, can occur with opioid agonist treatment during pregnancy. However, the risks of NAS are much less substantial than untreated OUD. Therefore, the ASAM consensus opinion is opioid agonist treatment should be offered if opioid use is likely during pregnancy. In addition, treatment should begin early in pregnancy to avoid the harms of illicit drug use. Women currently taking opioid agonist treatment who become pregnant should be encouraged to continue treatment during pregnancy.

Both methadone and buprenorphine can be used during pregnancy. Methadone has generally been the standard treatment in pregnancy. However, buprenorphine is associated with a shorter duration of NAS and is an appropriate alternative to methadone. When using buprenorphine in pregnancy, the mono-product should be used to decrease exposure to the small amount of naloxone absorbed. When using methadone, a higher dose and/or split dosing may be needed in the second and third trimester.

Women can breastfeed when taking methadone or the buprenorphine mono-product and should be encouraged. Breastfeeding with both agents is associated with decreased NAS.

See Local Resources for local resources for pregnant women.

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, patients 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 patients 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 patients 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. Oral naltrexone has not been studied in moderate to severe 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*:* Death from unintentional opioid overdose is a growing epidemic. Unintentional poisonings have surpassed motor vehicles accidents as the number one cause of unintentional death in the United States. 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.

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.

LOCAL RESOURCES:

Program Name	Overview
Treatment Access Program (TAP) 1380 Howard St, 1st Floor San Francisco, CA 94103 Phone: (415) 503 – 4730 Hours of Operation: Mon – Fri: 8:00AM – 5:00PM *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.
OBIC- Office-based Buprenorphine Induction Clinic 1380 Howard St, 2nd Floor San Francisco, CA 94103 Phone: (415) 552 – 6242 Hours of Operation: Mon – Fri: 8:30AM – 5:00PM *Closed on major holidays*	Medication-assisted treatment for opioid use disorder, using buprenorphine (Suboxone). Not a detox program, OBIC initiates and stabilizes patients on buprenorphine then coordinates transfer out for ongoing buprenorphine maintenance with a community provider. Clients eligible for treatment at OBIC must reside in San Francisco and be enrolled in or eligible for San Francisco Medi-Cal. Provider and self-referrals are welcome No private insurance or cash are accepted.
Ward 93 at Zuckerberg San Francisco General (ZSFG) 1001 Potrero Ave. Building 90 Ward 93 San Francisco, CA 94110 Phone: (415) 206-8412 <u>Dosing Hours:</u> M-F: 6:45am-11:00am, 12:30-2:00pm Sa-Su/Holidays: 7:30am-11:30am, 12:30pm-2:00pm	Opioid Treatment Program (OTP) on the ZSFG campus. New patient instructions: first-come, first-served. For initiating treatment, arrive early. After initiation, may transfer to a van at Newcomb & Newhall or Sunnydale at Leland House.
BAART Turk Street Clinic 433 Turk St San Francisco, CA 94102 Phone: (415) 928-7800 <u>Business Hours:</u> M-F: 7:00am-3:00pm Sa-Su: 8:00am-12:00pm <u>Dispensing Hours:</u> M-F: 7:00am-2:30pm Sa-Su: 8:00am-12:00pm Holidays: 9:00am-12:00pm	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. Patients may pay cash for services. New patient instructions: First-come, first-served. Early arrival recommended.
BAART Market Street Clinic 1111 Market St #1 San Francisco, CA 94103 Phone: (415) 863-3883 <u>Business Hours:</u> M-F: 6:00am-2:00pm Sa-Su: 8:00am-12:00pm <u>Dispensing Hours:</u> M-F: 6:00am-1:30pm	OTP with additional services including primary care and mental health. Patients may pay cash for services. New patient instructions: First-come, first-served. Early arrival recommended.

Sa-Su: 8:00am-12:00pm Holidays: 8:00am-12:00pm	
Westside Methadone Detoxification & Maintenance Programs 1301 Pierce St (at Ellis St) San Francisco, CA 94115 Phone: (415) 563-8200 Business Hours: M-F: 7:00am-3:30pm Dosing Hours: M-F: 7:00am-10:45am & 12:00pm-1:45pm Sa-Su/Holidays: 8:00am-11:00am *Walk-ins accepted, calling beforehand is recommended to ensure MD availability.* *Photo ID required.*	OTP New patient instructions: Walk-ins accepted, calling beforehand is recommended to ensure MD availability. Photo ID required.
Fort Help 915 Bryant St San Francisco, CA 94103 Phone: (415) 777-9953 Hours of Operation:	OTP
Fort Help 1101 Capp Street San Francisco, CA 94110 Phone: (415) 821-1427	OTP with additional services including primary care.
Bayview Hunters Point Foundation 1625 Carroll Ave. San Francisco, CA 94124 Phone: (415) 822-8200 Program Hours: M-F: 6:00am-2:00pm Sa-Su: 7:00am-10:00am Holidays: 6:15am-10:00am Dosing Hours: M-F: 6:15am-11:00am	OTP New patient instructions: Call intake coordinator, to make an appointment.
Veterans Affairs Medical Center Substance Abuse Programs 4150 Clement St, Unit 116-E San Francisco, CA 94121 Phone: (415) 221-4810 ext. 22823 Business Hours: M-F: 7:00am-12:00pm Dosing Hours: M-Sa: 7:00am-12:00pm	OTP for veterans only New patient instructions: Call beforehand to make an appointment.
healthRight 360 Central Intake Office 1563 Mission St San Francisco, CA 94103 Phone: (415) 760-9263 **Hours:** Monday – Friday 8:30am – 1:30pm. Earlier arrival is always best.	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) provides access and placement into detox when TAP is closed. This office works very closely

Weekends: Saturday and Sunday, clients may present at the Daily Reporting Center at from 9am-1pm to request detox.	with TAP and provides an alternative location for accessing healthRIGHT360 SUD services.
12-Step Programs (NA, AA, Al-Anon, etc) 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. Narcotics Anonymous (NA): http://sfna.org/ Alcoholics Anonymous (AA): http://www.aasf.org
LifeRing Various dates, times and locations	A network of support groups for people who want to live free of alcohol and other addictive drugs. http://liferingsf.org/
CBHS Pharmacy 1380 Howard St San Francisco, CA 94103 Phone: (415) 255-3659 **Hours:** Monday – Friday 9:00am – 4:30pm	Specializes in substance use and mental health disorders. Provides safe injection kits and naloxone furnishing without a prescription. Provides additional services for buprenorphine patients including daily dosing, urine drug screening, breathalyzers, and directly observed treatment (DOT) for buprenorphine, mental health, and alcohol use disorder maintenance medications.
Needle Access 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. Schedule: http://sfaf.org/client-services/syringe-access/site-schedule.html
Integrated Soft Tissue Injection Service (ISIS) Clinic San Francisco General Hospital, Main Building, 4th Floor, Suite 4C 1001 Potrero Avenue San Francisco, CA 94110 Phone: (415) 206-3719 **Hours:** Mon, Wed-Fri: 8:00am-4:30pm (closed noon-1pm) Sat: 8:00am-11:am	Treats patients with fulminating or emergent soft tissue infections. Serves patients with previously untreated abscesses and cellulitis and offers treatment such as incision and drainage of abscesses and antibiotics prescriptions. ISIS patients are drop-in and seen on a first-come, first-served basis. Patients with chronic wounds and previously treated abscesses are not appropriate for referral to the ISIS clinic.
Kaiser Chemical Dependency Recovery Program (CDRP) 1201 Fillmore St San Francisco, CA 94115 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.
Women's Health Center 5M (includes high-risk OB)	Obstetrics and gynecology practice that includes prenatal care, including managing high-risk

San Francisco General Hospital, Main Hospital, Ward 5M 1001 Potrero Avenue San Francisco, CA 94110 Phone for Appointments: (415) 206 – 3409	pregnancies. Patients have access to mental health and psychiatric support. Partners closely with Homeless Prenatal Program.
Homeless Prenatal Program 2500 18th St. San Francisco, CA 94110 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.

REFERENCES AND FURTHER READING:

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Vowles K, McEntee M, Julens P, et al. Rates of opioid misuse, abuse and addiction in chronic pain: a systematic review and data synthesis. Pain 2015;156:569-76.

Opioid Treatment Resources: https://store.samhsa.gov/facet/Substances/term/Opioids-or-Opiates?pageNumber=1

Substance use disorder-specific privacy and confidentiality requirements: https://www.ecfr.gov/cgi-bin/text-idx?SID=0f9b2a146b539944f00b5ec90117d296&mc=true&node=pt42.1.2&rgn=div5

APPENDIX 1: OPIOID USE DISORDER MEDICATION ASSISTED TREATMENT PHARMACOTHERAPY

Medication	Mechanism of Action	Dose & Administration	Contra-indications	Adverse Effects	Comments
Methadone	Full 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.	*Only available from a Narcotic Treatment Program when treating OUD.* **Oral:** 10-30mg PO daily titrated every 5 days to a maintenance dose of 60 – 120mg daily. A maintenance dose is established when a patient no longer experiences opioid cravings or opioid withdrawal. *Hepatic impairment:* no adjustments providers in package insert *Renal impairment:* CrCl ≥10mL/min: no dose adjustment. CrCL <10mL/min: use 50-75% of normal dose	Contraindications: Paralytic ileus, documented Torsade de pointes (Tdp) on methadone, use of opioids antagonists 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	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). 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. 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. OTP's have additional confidentiality requirements under Code of Federal Regulations 42, therefore methadone will not be present on CURES. ***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 Medications to avoid with methadone include efavirenz, ketoconazole, rifampin ***Monitoring:*** Check LFTs prior to initiation and monitor periodically while on treatment EKG monitoring practices are variable in terms of timing and dose. Expert consensus from the

					American Society of Addition Medicine (ASAM) recommends EKG in patients on methadone doses >120mg per day, patients with a history of QTc prolongation and in patients taking medications that prolong the QTc interval
Buprenorphine **Buprenorphine implant**	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.	*Patients should be in mild to moderate opioid withdrawal (COWS >10) when initiating buprenorphine to prevent precipitated withdrawal* **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. A maintenance dose is established when a patient no longer experiences opioid cravings or opioid withdrawal. **Implant:** Insert four implants subdermally in the upper arm for 6 months *Renal impairment:* no adjustment *Hepatic impairment:* Buprenorphine: decrease	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/. 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. In addition to treating opioid withdrawal and cravings, maintenance treatment with buprenorphine is associated with increased treatment retention compared to detoxification. 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. 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

		dose by 50% in severe impairment. Naloxone: avoid naloxone containing products in severe (and possibly moderate) impairment			Hepatic Impairment for exceptions). If the co-formulated product is injected by an opioid physically dependent person precipitated withdrawal can occur. ***Implant:*** Only indicated for people stable on 8mg of buprenorphine per day. ***Drug Interactions:*** Metabolized by CYP3A4 ***Monitoring:*** Check LFTs prior to initiation and monitor periodically while on treatment
Naltrexone **Naltrexone long acting injection**	μ opioid antagonist which may block the effects of opioids	**Oral:** 25mg/day for 3 days then 50mg/day. Can increase to 100mg after 4 weeks if drinking continues. **Injection:** 380mg IM monthly Recommend patient take with a meal to mitigate nausea Patients 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 challenge to assess for opioid withdrawal.	Decompensated cirrhosis as manifested by AST/ALT > 5x ULN, INR >1.5, ascites, esophageal varices, hepatorenal syndrome, spontaneous bacterial peritonitis, encephalopathy *Pregnancy: C*	Nausea, headache, anxiety, sedation. Warnings of hepatotoxic effects are derived from studies using dosages up to 300mg/day for obesity and dementia. No reports of hepatotoxicity at recommended daily dose of 50mg.	Naltrexone that has no required certifications to prescribe or requirements for treatment setting. Does not treating opioid cravings. A person must be opioid free 7-10 days prior to initiating naltrexone to avoid precipitated withdrawal. Long acting injection may improve adherence however is cost prohibitive and has limited availability as an outpatient drug benefit through Medi-Cal. ***Monitoring:*** Check LFTs and INR prior to initiation and monitor LFTs periodically while on treatment (annually unless signs or symptoms of hepatitis develop).

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:_____

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying 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	**GI Upset:** *Over last 1/2hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *Over past 1/2hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**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
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 movements of legs/arms 5 unable to sit still for more than a few seconds	**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
Pupil size: 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**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
Bone or Joint aches: *If patient was having pain previously, only the additional component attributed to opiates 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	**Gooseflesh skin:** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing: *Not accounted for by cold – symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items 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.

CBHS Pharmacy Buprenorphine FAQ's for CBHS Prescribers

What services does CBHS Pharmacy provide for buprenorphine patients?
We provide special services for buprenorphine patients at CBHS Pharmacy including the following:

Refill requests**:** We fax refill requests to the prescriber approximately 7-days prior to the patient's next pick-up date. This allows for uninterrupted therapy.
Monitoring: Patients check in with a pharmacist every time they pick up buprenorphine. If the patient appears intoxicated with a CNS depressant, patients 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 patient's condition will be reported to the buprenorphine prescriber. Prescribers can also order onsite urine drug screening and breathalyzers.
Observed dosing: Providers have the option to request observed dosing for patients at CBHS Pharmacy dispensing window.
Frequent dosing: Providers have the option to request dosing schedules more frequent than every 28 days. Including daily with the exception of Holidays or weekends.
Naloxone: Patients 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 prescriber.
Smoking Cessation: Patients can receive smoking cessation counseling and medications from the pharmacist.
Clean injection kits: We provide clean injection kits with syringes to our patients at no charge.
Medication and syringe disposal: Patients can dispose of unwanted medications (accept aerosols) and syringes in provided receptacles in the building.

What is CBHS Pharmacy's policy on early or late buprenorphine pick-ups?
Early pick-ups: We do not allow patients to pick-up before their assigned pick-up date without permission by the prescriber. Example: Patient pick-ups a 7 day supply on a Tuesday, making the following Tuesday their next assigned pick-up date. If the patient comes back the next Monday, permission from the prescriber will be required.
Late pick-ups: Patients that are ≥10 days late picking up from their assigned pick-up dates will require permission from the prescriber to dispense buprenorphine. Patients <10 days late picking up will be counseled on adherence and given the prescription as written.

Does CBHS Pharmacy have any policies that may effect the buprenorphine prescription I write?
Dispense in 7 day increments: Because we are not open on weekends and to keep patients assigned pick-up days the same day of the week, CBHS Pharmacy will dispense in increments of 7 day supplies unless otherwise documented by the prescriber. Example: Prescription written for a 30 days supply will be dispense for a 28 days supply.
Buprenorphine/naloxone film: In order to improve patient 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?
We are open Monday through Friday and located at 1380 Howard St. The window is open for pick-ups 9:00am – 4:30pm. Pharmacy staff are available by phone 8:30am – 5:00pm for any questions.

What if my patient is due to pick-up on a holiday and CBHS Pharmacy is closed?
If a patient's scheduled pick-up date falls on a holiday when CBHS Pharmacy is closed, the patient will be allowed to pick-up their buprenorphine one business day before the holiday. CBHS Pharmacy posts signs reminding patients 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 depending on the patient's insurance.

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

	Quantity of Films Per Day			
Dose	**2mg Film**	**4mg Film**	**8mg Film**	**12mg Film**
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 due to potential errors by prescriber, errors by pharmacy and unlikely to be covered by insurance

Does CBHS Pharmacy provide buprenorphine only tablets?
We do stock buprenorphine only sublingual tablets and may be prescribed to any patient. We recommend buprenorphine only tablets be considered in the following patient groups:
Low risk for diversion: Patients with a low suspicion of diversion and history of stability. The buprenorphine pharmacist, Michelle Geier, PharmD can assess your patient's refill history to aide in this decision by calling (415) 503 – 4755.
Pregnancy: We recommend the buprenorphine only product for all pregnant women

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 (patient name, name of drug, strength, quantity and date of issuance) or keeping copies of each prescription. See 21 CFR Section 1304.03[c].

Does Infoscriber meet the requirements of a Buprenorphine Prescribed/Dispensed Log?
Yes, Infoscriber meets the requirements of a Buprenorphine Prescribed/Dispensed Log required by the DEA. However, you will still need to to have 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 Infoscriber "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 patients. Write down the patients names, this is your list of active buprenorphine patients.
4. If you are also prescribing a buprenorphine generic product, repeat Step 3 with the word "buprenorphine" in the "Find" field.
5. Close this report and return to the Infoscriber "Prescriber Desktop"
6. Under "Reports" click "Individual Medication Profile"
7. Using your list of active buprenorphine patients you made in Step 3, type in the first patient's name
8. From this report you can determine 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 your active buprenorphine patients.

What is the preferred method to prescribe buprenorphine through Infoscriber?
eRx is our preferred method, but we also accept eFax.

Who can I contact if I have further questions regarding buprenorphine at CBHS Pharmacy?

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