**Medication-Assisted Treatment**

MAT is the use of medications, in combination with counseling and behavioral therapies, to provide a whole-patient approach to the treatment of substance use disorders. Research shows that when treating substance-use disorders, a combination of medication and behavioral therapies is most successful. Medication assisted treatment (MAT) is clinically driven with a focus on individualized patient care.

**Medication-Assisted Treatment for Opioid Addiction**

This document contains a general discussion of medications approved by the U.S. Food and Drug Administration (FDA) for use in the treatment of opioid use disorder. These are extremely complex medical treatments and should be considered only after consultation with a physician who has received training in these therapies for individuals with opioid use disorders.

The FDA has approved three medications for use in the treatment of opioid dependence: methadone, naltrexone, and buprenorphine. With an array of medications now available for addressing the emerging prescription painkiller epidemic, it is crucial that providers in both primary and specialty care settings become trained in Medication-Assisted Treatment (MAT), an approach that uses FDA-approved pharmacological treatments, often in combination with psychosocial treatments, for patients with opioid use disorders. Equally important, insurers and policy makers must strive to learn about available medicines and promote policies that ensure that use of these medications is covered as part of a comprehensive approach to treating prescription and illicit drug dependence.

Because those who abuse opioids often abuse other substances as well, and because addiction is a chronic relapsing condition, a comprehensive approach to treatment should include assessment, diagnosis, treatment planning, psychosocial treatment, medication monitoring to promote adherence, and a host of social services to support patients as they build new drug-free lives and enter long-term recovery. Services may need to continue indefinitely, as relapse can be a lifelong risk.

***Medication Options***

**Opioid Addiction**

Medications for treating opioid addiction – including addiction to narcotic prescription painkillers such as oxycodone and hydrocodone as well as illegal opioids like heroin – work by interacting with some of the same receptors in the brain that are triggered by the abused drug. Three types of medications currently are used for treating opioid addiction: *agonists*, *partial agonists,* and *antagonists.*

As Nora Volkow, M.D., Director of the National Institute on Drug Abuse (NIDA), has explained, the rapid onset and short duration of an abused drug’s euphoric effects contribute to compulsive, escalating drug use.1 Oral **agonists**, therefore, are useful because their effects are less intense, come on more slowly, and last longer.2 Even when receptors are “turned on” by an agonist-type medication, the slower onset and longer duration of action help prevent withdrawal. **Partial agonists,** as the name implies, produce effects that are similar to but weaker than those of full agonists. **Antagonists** work by blocking the action of receptors. Should a patient undergoing treatment with an antagonist-type medication relapse and use the formerly abused substance, that drug’s power to trigger the receptors is often blocked or greatly diminished.

The following medications are approved by the FDA for use in opioid addiction treatment in conjunction with behavioral therapy:

***Methadone***

Methadone, a synthetic opioid, is an agonist that mitigates opioid withdrawal symptoms and, at higher doses, blocks the effects of heroin and other drugs containing opiates.3 Maintenance of opioid addiction treatment with methadone is approved “in conjunction with appropriate social and medical services.”4 Used successfully for more than 40 years in the treatment of opioid dependence, methadone at therapeutic doses (generally 80-120 mg) has been shown to eliminate withdrawal symptoms produced by stopping use of heroin and prescription opiate medications5 because it acts on the same targets in the brain as those drugs. Methadone compliance reduces injection opioid use, thereby helping to close off one route of HIV transmission for patients.6 Methadone can be dispensed only at an outpatient opioid treatment program (OTP) certified by SAMHSA and registered with the Drug Enforcement Administration (DEA) or to a hospitalized patient in an emergency.7 SAMHSA-certified OTP facilities provide daily doses until the patient is deemed stable enough to receive take-home doses.8

***Buprenorphine***

Buprenorphine, approved by the FDA in 2002 to treat opioid dependence, is a partial opioid agonist that, when dosed appropriately, suppresses withdrawal symptoms.9,10 Although buprenorphine can produce opioid agonist effects and side effects, such as euphoria and respiratory depression, its maximal effects are generally milder than those of full agonists like heroin and methadone.11 Physicians are permitted to distribute buprenorphine at intensive outpatient treatment programs that are authorized to provide methadone if providers are trained in its use.12 Additionally, a special program has been set up so that buprenorphine can be prescribed by physicians in office settings and dispensed by pharmacists.13

In order to prescribe this medication, physicians must complete a training course and receive a waiver granted by the DEA.14 Buprenorphine was tested in clinical trials for addiction treatment in the United States both by itself and in combination with naloxone,15 a drug used to counter the effects of an overdose of opiates such as heroin or morphine. The buprenorphine/naloxone combination is sometimes referred to as Bup/Nx (marketed under the brand name Suboxone®). Formulations approved for drug abuse treatment are intended to be taken sublingually (placed under the tongue and allowed to dissolve).16 When taken this way, the naloxone has little effect. However, if a patient injects Bup/Nx, the naloxone (an antagonist) enters the bloodstream and will block the buprenorphine, causing the patient to enter opioid withdrawal.17 This combination formulation may deter abuse through injecting because abusers are motivated to avoid unpleasant withdrawal symptoms.18

Buprenorphine without naloxone – sometimes called “buprenorphine mono-formulation” or simply “bup” – has been used routinely for inducting patients onto buprenorphine. Induction occurs in the provider’s presence, where risk of intravenous use is low and injection deterrence is generally unnecessary. Once patients are stabilized on the mono-formulation, those who can tolerate naloxone are switched to the combination product for ongoing maintenance.

***Naltrexone***

Naltrexone is a non-addictive antagonist19 used in the treatment of opioid dependence. The medication blocks opioid receptors so they cannot be activated.20 This “blockade” action, combined with naltrexone’s ability to bind to opioid receptors even in the presence of other opioids, helps keep abused drugs from exerting their effects when patients have taken or have been administered naltrexone.21 As an antagonist, naltrexone does not mimic the effects of opioids. Rather, it simply blocks opioid receptor sites so that other substances present in a patient’s system cannot bind to them. If a patient who has been administered naltrexone attempts to continue taking opioids, he or she is unable to feel any of the opioid’s effects due to naltrexone’s blocking action. Theoretically, it is possible to override the blockade by taking very large doses of opioid, but this is rarely reported because the quantities required are so large.

Naltrexone is administered in an injectable long-acting formulation (marketed under the brand name Vivitrol®), sometimes called “depot naltrexone,” which is designed for once-monthly dosing.22 The FDA approved this medication for use in people with opioid use disorders to prevent relapse.23 FDA recommends that Naltrexone should be used only in patients who have been detoxified from opioids and have been opioid free for 7 – 10 days.24

Although naltrexone is non-narcotic and non-addictive, as with other medications that interact with the opioid receptors, there is a risk of narcotic overdose if a patient who is being treated with naltrexone misses a dose and takes an opioid, or if the patient takes large quantities of opioids in an attempt to “break the blockade.”25,26 Compliance measures that closely monitor patients during the treatment period may be beneficial.

***Detoxification vs. Stabilization and Maintenance***

For opioid abusers who do not wish to enter treatment or do not qualify for ongoing maintenance therapy, some treatment programs provide medically assisted detoxification services, which involve weaning patients off addictive substances and managing withdrawal. However, research shows such programs are closely associated with relapse.27 And because tolerance to opioids fades rapidly even during a short period of abstinence, one episode of opioid misuse following detoxification can result in a life-threatening or deadly overdose.

Before medications became available for addiction treatment, detoxification routinely took place at the beginning of treatment. This is still the case in programs that set complete drug abstinence as a goal and in the treatment of addictions for which medications are not yet approved. However, in the case of methadone, researchers supported by the National Institute on Drug Abuse (NIDA) formulated a “phased approach” that does not necessarily emphasize complete detoxification.28,29 This approach, recently expanded, has been recommended by a consensus panel from the Substance Abuse and Mental Health Services Administration (SAMHSA).

According to the phased approach, the first step in treatment is not detoxification. Rather, it involves intensive stabilization, including withdrawal management, assessment, medication induction, and involvement in psychosocial counseling. The middle phase of care emphasizes medication maintenance and deeper work in and out of counseling on patient goals. In the third phase, “ongoing rehabilitation,” the patient and provider might choose to detoxify from all medication or pursue indefinite maintenance, depending on the patient’s needs.30,31 Treatment in a phased model, regardless of how long medication is used, involves participation in psychosocial treatment, and engagement with the self-help community is recommended. As such, participants in MAT can transition to a lifestyle consistent with being “in recovery” while using FDA-approved medication to treat their substance use disorder. One study found it was common for patients in long-term methadone maintenance who taper off their medicine (gradually reduce their doses) to fail during the process or relapse within 6 months of becoming abstinent.32 The SAMHSA consensus group recommended that detoxification be optional and that patients never be coerced into tapering.33 Research in which patients have been discontinued from buprenorphine also shows high rates of relapse.34 For this reason, ongoing MAT may be the safest and best approach for opioid rehabilitation.

***Other Resources***

These free resources provide more information about Medication-Assisted Treatment:

* *http://www.ncbi.nlm.nih.gov/pubmed/25984838***Opioid use in pregnant women and the increase in neonatal abstinence** **syndrome: what is the cost**? Roussos-Ross K(1), Reisfield G, Elliot I, Dalton S, Gold M**Opioid use in pregnant women and the increase in neonatal abstinence** **syndrome: what is the cost**?

http://www.ncbi.nlm.nih.gov/pubmed/25984838

Roussos-Ross K(1), Reisfield G, Elliot I, Dalton S, Gold M.

* **Medication for the Treatment of Alcohol Use Disorder: A Brief Guide .**

*http://store.samhsa.gov/product/Medication-for-the-Treatment-of-Alcohol-Use-Disorder-A-Brief-Guide/SMA15-4907*Provides **guidance** for the use of **medication**-assisted **treatment** for alcoholism and alcohol abuse in clinical practice. Summarizes approved **medications** and ...

* [**National Practice Guideline for the Use of Medications in the in the Treatment of Addiction Involving Opioid Use** **...**](http://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/national-practice-guideline.pdf?sfvrsn=22)

*http://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/national-practice-guideline.pdf%3Fsfvrsn%3D22*May 27, 2015 **...** 2. **ASAM National Practice Guideline for the Use of Medications** in the **Treatment** **of Addiction Involving Opioid Use**. Guideline Committee ...

• **Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction** http://buprenorphine.samhsa.gov/Bup\_Guidelines.pdf

• **Medication-Assisted Treatment for Opioid Addiction: Facts for Family & Friends** http://store.samhsa.gov/shin/content/SMA09-4443/SMA09-4443.pdf

**• NIDA Info Facts: Treatment Approaches to Drug Addiction** http://www.drugabuse.gov/publications/infofacts/treatment-approaches-drug-addiction

• **Medication Assisted Therapy Toolkit** http://www.niatx.net/PDF/NIATx-MAT-Toolkit.pdf

* The revised **Federal Guidelines for Opioid Treatment Programs**, published by the Substance Abuse and Mental Health Services Administration ...

[*http://www.samhsa.gov/newsroom/press-announcements/201503271100*](http://www.samhsa.gov/newsroom/press-announcements/201503271100)

1 Nora Volkow, M.D., Director, National Institute on Drug Abuse (NIDA).

2 Gerra G., Maremmani I., Capovani B., Somaini L., Berterae S., Tomas-Rossello J., Saenz E., Busse A., & Kleber H. (2009). Long-Acting

Opioid-Agonists in the Treatment of Heroin Addiction: Why Should We Call Them “Substitution?” *Substance Use Misuse*. *44(5)*, 663-671.

3 U.S. Food and Drug Administration. Methadone Oral Concentrate (methadone hydrochloride oral concentrate USP) and Methados Sugar-Free Oral Concentrate (methadone hydrochloride oral concentrate USP) dye-free, sugar-free, unflavored. Retrieved 02/28/2012 from http://www.accessdata.fda.gov/drugsatfda\_docs/label/2008/017116s021lbl.pdf

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| 4 Ibid. **FDA-Approved Medications for Substance Use Disorders**  |
| **Name**  | **Naltrexone** **(Vivitrol®)**  | **Buprenorphine**  | **Methadone**  |
| **Molecular Structure**  | Antagonist  | Agonist  | Agonist  |
| **Treatment Use**  | Opioid dependence  | Opioid dependence  | Opioid dependence  |
| **Controlled Substance?**  | Schedule 0  | Schedule III  | Schedule II  |
| **Abuse Potential**  | No  | Yes  | Yes  |
| **Trade Name**  | Vivitrol  | Suboxone®\* \*includes naloxone  | Methadone  |
| **How administered**  | Intramuscular injection  | Oral tablet or sublingual film taken once daily  | Oral Solution  |
| **How the medication works**  | By blocking opioid receptors, it blocks cue-triggered craving  | A long-acting partial opioid, it relieves withdrawal, decreases craving, and prevents euphoria if other opioids are used  | A long-acting “full” opioid that relieves withdrawal, blocks craving, and prevents euphoria if other opioids are used  |
| **Special licensing or credential required?**  | No  | Varies by state  | Yes  |
| **Year approved by FDA for Addiction Treatment**  | 2006  | 2002  | 1947 - Approved dispersible tablet for treatment of addiction  |
| **Physician training required?**  | No  | Yes – 8 hours of training required  | No  |
| **Typical Duration**  | Up to 30 days  | 1 day  | 1 day  |
| **Detoxification or Stabilization**  | Detoxification & 7 – 10 days of complete abstinence from opioids  | Detoxification  | Can be used for detoxification and/or stabilization  |