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Medication-Assisted Treatment for Opioid Use Disorder

Opioids, such as heroin, fentanyl, and some prescription pain medications (including morphine and oxycodone), are substances that act on receptors in the brain important in regulating pain and emotion. Opioids have high potential for misuse, dependence, and overdose. The label *opioid use disorder* (OUD) is the diagnostic term for "a problematic pattern of opioid use leading to clinically significant impairment or distress," as defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR).

Medication-Assisted Treatment (MAT)

Medication-assisted treatment is the combined use of medication and other services (such as counseling) to treat substance use disorders. Three medications are currently used in MAT for opioid use disorder: methadone, buprenorphine, and naltrexone.

Methadone and buprenorphine are both opioids; their use to treat opioid use disorder is often called *opioid substitution therapy*, *opioid replacement therapy*, or *opioid agonist treatment*. These medications can reduce the cravings and withdrawal symptoms that often accompany discontinuation of misused opioids, typically without producing the same euphoria or "high" as the substances they replace. Research on MAT has found it to be the most effective treatment for OUD.

Methadone

Methadone is a full opioid agonist, meaning it binds to and activates opioid receptors in the brain. Methadone carries risk of misuse but poses fewer risks of dependence and overdose than some other full opioid agonists (e.g., heroin). Methadone suppresses withdrawal symptoms in detoxification therapy and controls the craving for opioids in maintenance therapy.

Buprenorphine

Buprenorphine is a partial opioid agonist, meaning it binds to opioid receptors in the brain and activates them, but not as much as full opioid agonists. Buprenorphine also carries risk of misuse but poses fewer risks of dependence and overdose than full opioid agonists. Like methadone, buprenorphine is used for detoxification and maintenance therapy.

Naltrexone

Naltrexone is an opioid antagonist, meaning it binds to opioid receptors but does not activate them; it prevents opioid agonists from binding to and activating opioid receptors. Naltrexone carries no known risk of misuse. Naltrexone is used for relapse prevention because an individual on naltrexone who uses opioids will not experience the effects of those opioids. Naltrexone is different from *naloxone* (e.g., Narcan), which is used to reverse opioid overdose, but not used to treat opioid use disorders.

Regulatory Framework

Two overlapping systems of federal law apply to MAT for opioid use disorder: one regulating pharmaceuticals and the other regulating controlled substances.

Federal Food, Drug, and Cosmetic Act (FFDCA)

Under the Federal Food, Drug, and Cosmetic Act (FFDCA, 21 U.S.C. §§301 et seq.), the Food and Drug Administration (FDA) in the Department of Health and Human Services (HHS) has primary responsibility for ensuring the safety and effectiveness of pharmaceuticals, regardless of whether they are controlled substances. (For more information, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*.) Methadone, buprenorphine, and naltrexone are subject to the FFDCA.

Controlled Substances Act (CSA)

Under the Controlled Substances Act (CSA, 21 U.S.C. §§801 et seq.), the Drug Enforcement Administration (DEA) in the Department of Justice (DOJ) has primary responsibility for regulating the use of controlled substances for legitimate medical, scientific, research, and industrial purposes, and for preventing these substances from being diverted for illegal purposes. The CSA assigns various drugs and other substances to one of five schedules based on accepted medical use, potential for misuse, and severity of potential psychological or physical dependence. Schedule I contains substances that have no currently accepted medical use and are not available by prescription (such as heroin). Schedules II, III, IV, and V include substances that have recognized medical uses and are progressively less dangerous and pose fewer risks. As shown in **Table 1**, methadone, buprenorphine, and naltrexone are classified differently under the CSA. For more information, see CRS Report R45948, *The Controlled Substances Act (CSA): A Legal Overview for the 118th Congress*.

Table 1. FDA-Approved Medications for Opioid MAT

Medication	Class	CSA Schedule
Methadone	Full Opioid Agonist	II
Buprenorphine	Partial Opioid Agonist	III
Naltrexone	Opioid Antagonist	none

Source: Congressional Research Service, based on information publicly available from FDA and DEA.

Under the CSA, responsibility for regulating schedule II medications used in MAT (i.e., methadone) falls to both

DEA in DOJ and the Substance Abuse and Mental Health Services Administration (SAMHSA) in HHS. The CSA requires most persons who handle controlled substances to register with DEA. It further requires individuals treating OUD with methadone to obtain a separate DEA registration but leaves specific criteria for obtaining this registration up to the executive agencies.

Opioid Treatment Programs (OTPs)

The use of methadone to treat OUD is subject to federal regulations beyond those that apply to the same medication used for other purposes (e.g., treating pain) or other controlled substances. Both DEA and SAMHSA promulgate rules for methadone treatment provided at federally certified *opioid treatment programs* (known as *narcotic treatment programs* in DEA lexicon). Requirements for OTPs are specified in the *Code of Federal Regulations* (21 CFR Chapter II and 42 CFR Part 8).

According to these regulations, OTPs must obtain

- accreditation from a SAMHSA-approved accreditor,
- certification from SAMHSA, and
- registration from DEA.

Programs meeting all requirements may "administer or dispense directly (but not prescribe)" any drug approved by FDA for treatment of opioid use disorder. They may also administer a drug being studied for treatment of OUD, as authorized by FDA under an investigational new drug application.

With few exceptions, the use of methadone to treat OUD is limited to OTPs, which may also offer other forms of MAT, including buprenorphine for detoxification or maintenance and naltrexone for relapse prevention. OTPs generally administer methadone on a daily basis, with staff observing as a patient takes an oral dose of liquid methadone. Stable patients may be allowed to receive a few take-home doses (e.g., for a weekend or longer).

OTP Accreditation

Accreditation is based on a peer review process in which SAMHSA-approved accrediting organizations evaluate OTPs by making site visits and reviewing policies, procedures, and practices. Examples of accrediting organizations include The Joint Commission and the Commission on Accreditation of Rehabilitation Facilities.

OTP Certification

Certification is based on SAMHSA's determination that an accredited program is qualified to carry out treatment conforming to standards in federal regulation. SAMHSA uses the results of the accreditation process as well as other information to determine whether a program is qualified. SAMHSA promulgates guidelines to help accrediting organizations and OTPs conform to treatment standards.

OTP Registration

Registration with DEA as an OTP is separate from—and in addition to—the DEA registration required of any "person" (including a hospital, pharmacy, or doctor, among others) who handles controlled substances. OTPs must also comply with relevant DEA regulations addressing records maintenance, security controls, and other matters. They must also comply with any applicable state laws.

COVID-19 OTP Flexibilities

During the COVID-19 public health emergency (PHE), SAMHSA and DEA allowed greater flexibilities for take-home methadone. Beginning in March 2020 and throughout the duration of the PHE, SAMHSA has allowed states to request a "blanket exception for all stable patients in an OTP to receive 28 days of take-home doses" or 14 days for patients who are less stable. SAMHSA is currently considering mechanisms to make this flexibility permanent after the PHE expires.

Office-Based Opioid Treatment

The use of buprenorphine and naltrexone outside of an OTP is often referred to as *office-based opioid treatment* (OBOT) or office-based MAT (though it may occur in various settings). Office-based opioid treatment is not subject to the same regulations governing OTPs. The use of buprenorphine in OBOT is subject to CSA provisions regulating controlled substances in medical treatment or telemedicine generally.

Prior to the December 2022 enactment of the Restoring Hope for Mental Health and Well-Being Act (Division FF, Title I of P.L. 117-328, the Consolidated Appropriations Act, 2023), practitioners meeting certain criteria were required to obtain a separate waiver via DEA and SAMHSA (known as a *DATA waiver* or *X waiver*) in order to treat OUD with buprenorphine outside of an OTP. Practitioners with DATA waivers were subject to limits on the number of patients they could treat at any time. P.L. 117-328 repealed the DATA waiver requirement and patient limit. Thus, under current law, any practitioner registered with DEA to dispense (i.e., prescribe or administer) controlled substances is authorized to use buprenorphine to treat OUD outside of an OTP, subject to state laws.

Naltrexone is not a controlled substance, and therefore its use is not governed by the CSA. Any practitioner with prescribing authority (as determined by the state) can use naltrexone in the treatment of OUD.

COVID-19 OBOT Telemedicine Flexibilities

Prior to the COVID-19 PHE, practitioners initiating patients with buprenorphine for OUD were required to conduct an in-person medical evaluation (21 U.S.C. §829). During the COVID-19 PHE, SAMHSA and DEA allowed practitioners to prescribe buprenorphine via telemedicine without first conducting such evaluation. In March 2023, DEA issued a proposed rule that would permanently allow practitioners to initiate patients with buprenorphine for OUD via telemedicine without first conducting an in-person evaluation, provided such evaluation took place within 30 days (88 FR 12890).

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