



# OPIOID USE DISORDER

## Treatment with Injectable and Implantable Buprenorphine

Accessible Version

August 2020

# GAO Highlights

Highlights of [GAO-20-617](#), a report to congressional committees

## Why GAO Did This Study

In 2018, SAMHSA estimated that about one-quarter of the estimated 2 million people with OUD had received some form of substance use treatment in the prior year. One form of treatment—medication-assisted treatment (MAT)—combines behavioral therapy with the use of certain medications. HHS has identified expanding access to treatment for OUD as an important strategy for reducing opioid morbidity and mortality, which includes increasing the number of injectable and implantable buprenorphine prescriptions.

Congress included a provision in the SUPPORT Act for GAO to review access to and the potential for the diversion of controlled substances administered by injection or implantation. This report focuses on injectable and implantable controlled substances that can be used to treat OUD and specifically, describes the process for treating OUD with injectable and implantable buprenorphine and what is known about their use.

GAO reviewed laws, regulations, and documentation from DEA, FDA, and SAMHSA governing the process of providing treatment with buprenorphine and interviewed officials from those agencies. GAO also interviewed representatives from stakeholder groups representing MAT providers; drug companies that manufacture injectable or implantable buprenorphine; and pharmacies that dispense these medications. HHS and DOJ reviewed a draft of this report, and GAO incorporated their technical comments, as appropriate.

View [GAO-20-617](#). For more information, contact James Cosgrove at (202) 512-7114 or [cosgrovej@gao.gov](mailto:cosgrovej@gao.gov).

August 2020

## OPIOID USE DISORDER

### Treatment with Injectable and Implantable Buprenorphine

## What GAO Found

Of the medications used to treat opioid use disorder (OUD), only buprenorphine is both a controlled substance and available as an injection or implant. Buprenorphine is used to treat patients with OUD because it reduces or eliminates opioid withdrawal symptoms and blunts the euphoria or dangerous side effects of other opioids, such as heroin. When used to treat OUD, buprenorphine, in any form, is subject to additional laws and regulations that are overseen by the Drug Enforcement Administration (DEA), within the Department of Justice (DOJ) and the Substance Abuse and Mental Health Services Administration (SAMHSA), within the Department of Health and Human Services (HHS). To ensure patient safety when injectable and implantable buprenorphine is used, the Food and Drug Administration (FDA), within HHS has also required drug companies to establish risk evaluation and mitigation strategies to help ensure the benefits of these medications outweigh their risks.

Providers and pharmacies must follow a number of specific steps based on federal requirements when providing treatment with injectable and implantable buprenorphine. Providers are responsible for prescribing, storing, and administering injectable and implantable buprenorphine, while pharmacies are responsible for dispensing these medications (see figure). Representatives GAO interviewed from provider groups and pharmacies said they did not find the steps involved in treating patients to be difficult overall. However, they stated that careful and timely coordination with each other and patients is needed at key steps of the process to ensure that the patient receives treatment.

Representatives from provider groups and pharmacies reported that the risk of diversion of injectable and implantable buprenorphine is low. For example, all of the provider groups GAO spoke with said that diversion of injectable or implantable buprenorphine is unlikely, and representatives from three of the six provider groups said that the design of these formulations reduces opportunities for diversion due to how they are administered.

#### Process for Treating Opioid Use Disorder with Injectable and Implantable Buprenorphine



Source: GAO analysis of Food and Drug Administration, Substance Abuse and Mental Health Services Administration, and Drug Enforcement Administration information. | [GAO-20-617](#)

The use of injectable and implantable buprenorphine to treat OUD is relatively low compared to oral forms of buprenorphine. HHS has reported that about 7,250 prescriptions were issued for injectable and implantable buprenorphine in fiscal year 2019, compared to over 700,000 patients who received buprenorphine prescriptions for oral formulations to treat OUD or pain in that year.

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# Contents

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Letter		1
	Background	4
	Treating OUD with Injectable and Implantable Buprenorphine Involves Specific Steps and Use Is Relatively Low	9
	Agency Comments	14
<hr/>		
Appendix I: GAO Contacts and Staff Acknowledgments		16
Appendix II: Accessible Data		17
	Data Table	17
<hr/>		
Related GAO Products		18
<hr/>		
Table		
	Table 1: Federal Requirements Providers and Pharmacies Must Meet to Treat Opioid Use Disorder with Injectable and Implantable Buprenorphine	8
<hr/>		
Figures		
	Figure 1: Administration of Injectable and Implantable Buprenorphine by Formulation	5
	Figure 2: Providers with SAMHSA Drug Addiction Treatment Act of 2000 Waivers by Patient Limit Level, as of December 31, 2019	7
	Figure 3: Process for Treating Opioid Use Disorder with Injectable and Implantable Buprenorphine	9
	Accessible Data for Figure 2: Providers with SAMHSA Drug Addiction Treatment Act of 2000 Waivers by Patient Limit Level, as of December 31, 2019	17

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## Abbreviations

CSA	Controlled Substances Act
DATA 2000	Drug Addiction Treatment Act of 2000

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DEA	Drug Enforcement Administration
DOJ	Department of Justice
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
MAT	medication-assisted treatment
OTP	opioid treatment program
OUD	opioid use disorder
REMS	risk evaluation and mitigation strategies
SAMHSA	Substance Abuse and Mental Health Services Administration
SUPPORT Act	Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act

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August 4, 2020

The Honorable Lamar Alexander  
Chairman  
The Honorable Patty Murray  
Ranking Member  
Committee on Health, Education, Labor and Pensions  
United States Senate

The Honorable Frank Pallone, Jr.  
Chairman  
The Honorable Greg Walden  
Republican Leader  
Committee on Energy and Commerce  
House of Representatives

In 2018, the Substance Abuse and Mental Health Services Administration (SAMHSA) estimated that about 2 million people in the United States had an opioid use disorder (OUD).<sup>1</sup> SAMHSA also estimated that in 2018, one-quarter of individuals with OUD had received some form of substance use treatment in the past year.<sup>2</sup> Medication-assisted treatment (MAT) is a form of treatment for OUD that combines behavioral therapy with the use of certain medications, and buprenorphine is one of two controlled substances used in MAT for the treatment of OUD.<sup>3</sup> When

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<sup>1</sup>Department of Health and Human Services, SAMHSA. *Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health*, HHS Publication No. PEP19-5068, NSDUH Series H-54, (Rockville, MD.: August 2019). OUD is a pattern of opioid use leading to clinically significant impairment or distress as indicated by meeting certain criteria within a 12-month period, such as taking opioids in larger amounts than intended or unsuccessful efforts to reduce or control opioid use. See American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (Arlington, VA: 2013).

<sup>2</sup>Although the individuals included in this estimate had OUD, the treatment that they received may have been for substances other than opioids. See SAMHSA, *Results from the 2018 National Survey on Drug Use and Health: Detailed Tables*. Tables 5.1A and 5.18A (Rockville, MD.: August 2019).

<sup>3</sup>Methadone is the other controlled substance and the formulation most commonly used for MAT is an orally administered liquid. A third MAT drug—naltrexone—is not a controlled substance. Additionally, some oral forms of buprenorphine are also combined with naloxone, a drug that will reduce the chances of misuse or abuse.

used to treat OUD, buprenorphine is subject to additional requirements under the Controlled Substances Act (CSA) as well as regulations that are overseen by the Drug Enforcement Administration (DEA) within the Department of Justice (DOJ) and by SAMHSA within the Department of Health and Human Services (HHS).<sup>4</sup> Buprenorphine can be used in the short term to mitigate the immediate withdrawal symptoms associated with discontinuing opioids, and it may also be used over an extended period to maintain abstinence and prevent relapse. Buprenorphine may be administered in two oral formulations—(1) tablets for sublingual (under the tongue) administration, and (2) films for sublingual or buccal (inside the cheek) administration; as an implant; or as an injection. HHS has identified expanding access to treatment for OUD as an important strategy for reducing opioid morbidity and mortality, which includes increasing the number of prescriptions for injectable or implantable buprenorphine.<sup>5</sup>

In 2018, the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (SUPPORT Act) amended the CSA to allow pharmacies, under certain conditions, to deliver a prescribed injectable or implantable controlled substance to a provider, so the provider can administer the controlled substance to a patient for the treatment of OUD.<sup>6</sup>

The SUPPORT Act included a provision for GAO to report to Congress on access to, and the potential for the diversion of, controlled substances

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<sup>4</sup>Controlled substances are governed at the federal level by the CSA, which assigns them to one of five schedules based on the substance's medical use, potential for abuse, and risk of dependence. Buprenorphine is a Schedule III substance, meaning that it has recognized medical uses, less potential for abuse than Schedule I and II substances, and that abuse of it may lead to moderate or low physical dependence or high psychological dependence.

<sup>5</sup>Department of Health and Human Services, *Agency Priority Goal Action Plan: Reducing Opioid Morbidity and Mortality*, (Washington, DC: 2019), p. 3. We have previously reported on access to MAT. See GAO, *Opioid Addiction: Laws, Regulations, and Other Factors Can Affect Medication-Assisted Treatment Access*, [GAO-16-833](#) (Washington, D.C.: Sep. 27, 2016) and GAO, *Opioid Use Disorder: Barriers to Medicaid Beneficiaries' Access to Treatment Medications*, [GAO-20-233](#) (Washington, D.C.: Jan. 24, 2020).

<sup>6</sup>Pub. L. No. 115-271, § 3204, 132 Stat. 3894, 3945 (2018) (codified at 21 U.S.C. § 829a). Beyond this new provision, the CSA requires that prescriptions for controlled substances be delivered directly to the patient or a member of the patient's household. 21 U.S.C. § 802(10), (27).

administered by injection or implantation.<sup>7</sup> We focused our review on injectable and implantable controlled substances that can be used to treat OUD. Of the MAT drugs used to treat OUD, only buprenorphine is both a controlled substance and available as an injection or implant.<sup>8</sup> This report describes the process for treating OUD with injectable and implantable buprenorphine and what is known about their use.

To address our objective, we reviewed laws and regulations related to MAT medications.<sup>9</sup> We also reviewed documentation from SAMHSA, DEA, and the Food and Drug Administration (FDA) governing the process of providing treatment with buprenorphine, such as application templates for the Drug Addiction Treatment Act of 2000 (DATA 2000) waivers that providers must have to provide treatment with buprenorphine in office-based settings and documentation about the risk evaluation and mitigation strategies (REMS) in place for injectable and implantable buprenorphine.<sup>10</sup> We also analyzed SAMHSA data on the number of providers eligible to provide treatment with buprenorphine during calendar year 2019. Additionally, we reviewed information reported by HHS on the number of injectable and implantable buprenorphine prescriptions and the number of unique patients who received prescriptions for non-injectable or implantable forms of buprenorphine in fiscal year 2019. To assess the data's reliability, we reviewed related documentation, interviewed SAMHSA officials, and reviewed the data for obvious errors. We found these data to be sufficiently reliable for the purposes of our review.

In addition, we reviewed literature to examine information on the risk of diversion of injectable and implantable buprenorphine. We identified literature through searching the Scopus and ProQuest databases for articles published from January 2017 to March 2020. Finally, we interviewed agency officials from DEA, FDA, and SAMHSA;

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<sup>7</sup>Pub. L. No. 115-271, § 3204, 132 Stat. at 3946.

<sup>8</sup>There are extended-release and immediate-release injectable buprenorphine products, but only the extended-release injection is indicated for the treatment of OUD. The immediate release injection (Buprenex) is indicated for the management of severe pain, so it is outside the scope of this review. Throughout this report, "injectable buprenorphine" only refers to the extended-release buprenorphine injection.

<sup>9</sup>MAT medications are also sometimes referred to as medications to treat OUD.

<sup>10</sup>FDA is an agency within HHS. A REMS is required for a drug if FDA determines that one is necessary to ensure that the benefits of the drug outweigh its risks. A REMS requires additional actions beyond the drug's professional labeling.

representatives from six stakeholder groups representing providers; representatives from the only three drug companies that manufacture injectable or implantable buprenorphine; and representatives from two pharmacies that dispense these medications.<sup>11</sup> We selected provider groups that represent the different types of providers who treat OUD with buprenorphine, such as addiction medicine specialists, family physicians, and physician assistants, and the pharmacies we selected were pharmacies that are able to dispense both injectable and implantable buprenorphine. We conducted these interviews to obtain information on (1) general trends related to the use of injectable and implantable buprenorphine in MAT; (2) stakeholders' perceptions of federal requirements affecting MAT with these medications; and (3) the potential for or risk of diversion of injectable and implantable buprenorphine. The perspectives of the selected stakeholder organizations and pharmacies are not generalizable.

We conducted this performance audit from October 2019 to August 2020 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

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## Background

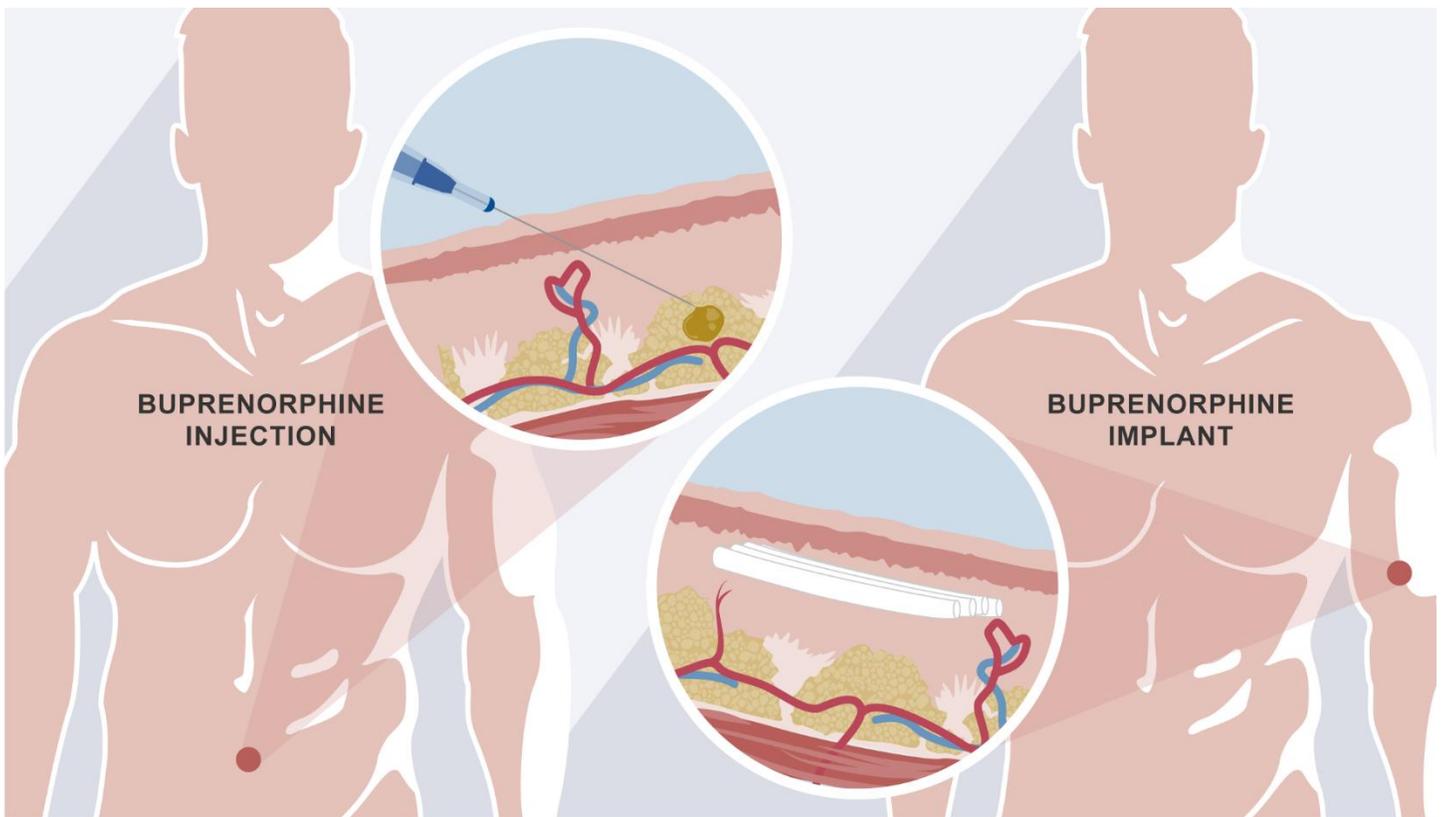
Buprenorphine is useful for treating OUD because it reduces or eliminates opioid withdrawal symptoms, including drug cravings, and blunts the euphoria or dangerous side effects of opioids, including heroin. Once administered, injectable and implantable buprenorphine deliver a sustained level of buprenorphine for the duration of treatment, which ranges from 1 month for the injection to 6 months for the implant (see fig. 1). Injectable buprenorphine is injected into the abdomen in the tissue layer between the skin and the muscle, where it remains and slowly releases the medication over a month. The implant, composed of four

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<sup>11</sup>The provider groups we interviewed were the American Academy of Addiction Psychiatry, American Academy of Family Physicians, American Academy of Physician Assistants, American Association for the Treatment of Opioid Dependence, American Society of Addiction Medicine, and Harm Reduction Coalition. The drug companies we interviewed were Braeburn, Indivior, and Titan Pharmaceuticals. The two pharmacies we contacted—Accredo and AllianceRx Walgreens Prime—responded to our questions in writing.

rods containing buprenorphine, is surgically inserted in the inner side of the upper arm and releases medication over 6 months.

**Figure 1: Administration of Injectable and Implantable Buprenorphine by Formulation**



Source: GAO. | GAO-20-617

DEA, SAMHSA, and FDA requirements for controlled substances, including injectable and implantable buprenorphine, aim to ensure patient safety and to limit the potential for diversion.

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## DEA Registration

Providers and pharmacies must adhere to the CSA and any relevant state laws governing the use of controlled substances and must have a valid DEA registration for each location where they prescribe, dispense, or administer controlled substances.<sup>12</sup>

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## SAMHSA Drug Addiction Treatment Act of 2000 (DATA 2000) Waiver

When used to treat OUD, buprenorphine can be dispensed or administered in an opioid treatment program (OTP) or by eligible providers in office-based settings who have a DATA 2000 waiver.<sup>13</sup> For office-based settings, eligible providers must obtain a DATA 2000 waiver from SAMHSA to dispense or prescribe buprenorphine to a limited number of patients to treat OUD.<sup>14</sup> In general, providers are limited to treating 30 patients in the first year under a DATA 2000 waiver and may apply to increase to 100 patients after a year. However, providers that meet certain criteria can treat 100 patients in their first year and may apply to increase to up to 275 patients after a year.<sup>15</sup> To qualify for a DATA 2000 waiver, providers must have a valid DEA registration, be

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<sup>12</sup>A provider can prescribe controlled substances at multiple locations using one DEA registration within the same state. However, the provider must maintain separate DEA registrations for each location where they store, administer, or dispense controlled substances.

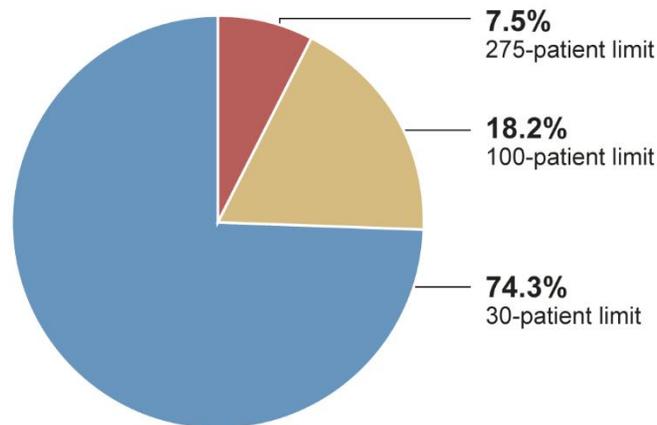
<sup>13</sup>OTPs, sometimes referred to as narcotic treatment programs or methadone clinics, offer opioid medications, counseling, and other services for individuals addicted to heroin or other opioids. OTPs are certified by SAMHSA and registered by the DEA. According to the Congressional Research Service, there were 1,674 federally certified OTPs in the U.S. as of June 1, 2019.

<sup>14</sup>Until 2016, only physicians were eligible to obtain a DATA 2000 waiver. The Comprehensive Addiction and Recovery Act of 2016 and the SUPPORT Act amended the CSA to allow nurse practitioners and physician assistants to obtain DATA 2000 waivers and to allow certified registered nurse anesthetists, certified nurse midwives, and clinical nurse specialists to obtain DATA 2000 waivers until October 1, 2023. Pub. L. No. 114-198, § 303(a)(1), 130 Stat. 695, 720 (2016); Pub. L. No. 115-271, § 3201(b), 132 Stat. 3894, 3943 (2018). In this report, we refer to these health care practitioners with a DATA 2000 waiver as providers.

<sup>15</sup>Providers are eligible to treat 100 patients in their first year with a DATA 2000 waiver if they (1) hold a board certification in addiction medicine or addiction psychiatry; or (2) provide MAT in a "qualified practice setting," which must provide coverage for patient medical emergencies outside of office hours, and patient access to case-management services, among other requirements.

appropriately licensed under state law, and meet applicable certification, training, or experience requirements. As of December 2019, 78,123 providers had DATA 2000 waivers, with the majority of these providers (about 74 percent) being eligible to treat at the 30 patient limit (see fig. 2).

**Figure 2: Providers with SAMHSA Drug Addiction Treatment Act of 2000 Waivers by Patient Limit Level, as of December 31, 2019**



Source: GAO analysis of Substance Abuse and Mental Health Services Administration (SAMHSA) data. | GAO-20-617

## FDA Risk Evaluation and Mitigation Strategies (REMS)

Providers and pharmacies also must comply with the requirements outlined in the REMS for FDA-approved injectable and implantable buprenorphine formulations. REMS impose one or more risk-mitigation strategies beyond the drug's professional labeling to ensure the benefits of the drug outweigh its risks, such as by helping mitigate or prevent serious risks of adverse side effects.<sup>16</sup> FDA required a REMS for the 6-month buprenorphine implant and the monthly buprenorphine injection when it approved these formulations in May 2016 and November 2017,

<sup>16</sup>According to FDA, most REMS are designed to reinforce patients' and providers' behaviors and actions that support the safe use of the particular drug they cover. For example, FDA may require drug companies to give patients and providers additional information to reinforce certain safe use conditions or specific risks described in the approved labeling of a certain drug. See GAO, *Generic Drug Development: Stakeholders' Views of Risk Evaluation and Mitigation Strategies Differ*, GAO-20-94 (Washington, D.C.: Oct. 15, 2019).

respectively.<sup>17</sup> REMS were required for these medications due to the serious risks associated with their use. For the injection, a REMS is required to mitigate the risks of serious harm or death that could result from intravenous self-administration. The injectable formulation forms a solid mass upon contact with bodily fluids, so if it is administered intravenously, it may cause occlusion (i.e., blockage), local tissue damage, or an embolism that could result in serious harm or death. For the buprenorphine implant, the insertion or removal of the implant is associated with the risk of implant migration, protrusion, expulsion, and nerve damage that in rare cases could result in serious complications, such as an embolism. As a result, under the REMS, providers who want to provide MAT with implantable buprenorphine must complete training to be certified in the REMS program for that medication and every year thereafter in which they provide treatment with the implant.<sup>18</sup> Further, pharmacies must enroll in the REMS program for a particular medication to be eligible to be certified to dispense injectable and implantable buprenorphine to providers (see table 1).

**Table 1: Federal Requirements Providers and Pharmacies Must Meet to Treat Opioid Use Disorder with Injectable and Implantable Buprenorphine**

na Requirement	Injectable buprenorphine		Implantable buprenorphine	
	Providers	Pharmacies	Providers	Pharmacies
Drug Enforcement Agency (DEA) registration	● requirement applies	● requirement applies	● requirement applies	● requirement applies
Drug Addiction Treatment Act of 2000 (DATA 2000) waiver <sup>a</sup>	● requirement applies	— na	● requirement applies	— na
Risk Evaluation and Mitigation Strategy (REMS) certification <sup>b</sup>	— na	● requirement applies	● requirement applies	● requirement applies

Legend:  
 ● = requirement applies  
 — = not applicable

<sup>17</sup>A third buprenorphine medication—a weekly or monthly injection—received tentative approval from the FDA in December 2018. This medication is not yet on the market, pending the expiration of a marketing exclusivity period for the injectable buprenorphine medication approved in 2017.

<sup>18</sup>The REMS for the buprenorphine implant has three certification categories (1) prescriber-only, (2) inserter-only, or (3) dual (prescriber and inserter). The annual training requirement is only applicable to the providers who perform the actual insertion and/or removal of the implant (i.e., providers in the latter two categories).

Source: GAO analysis of Substance Abuse and Mental Health Services Administration, DEA, and Food and Drug Administration documentation. | GAO-20-617

<sup>a</sup>A DATA 2000 waiver is required for providers to prescribe or dispense buprenorphine to patients with opioid use disorder in office-based settings. Providers treating patients in opioid treatment programs do not need a DATA 2000 waiver.

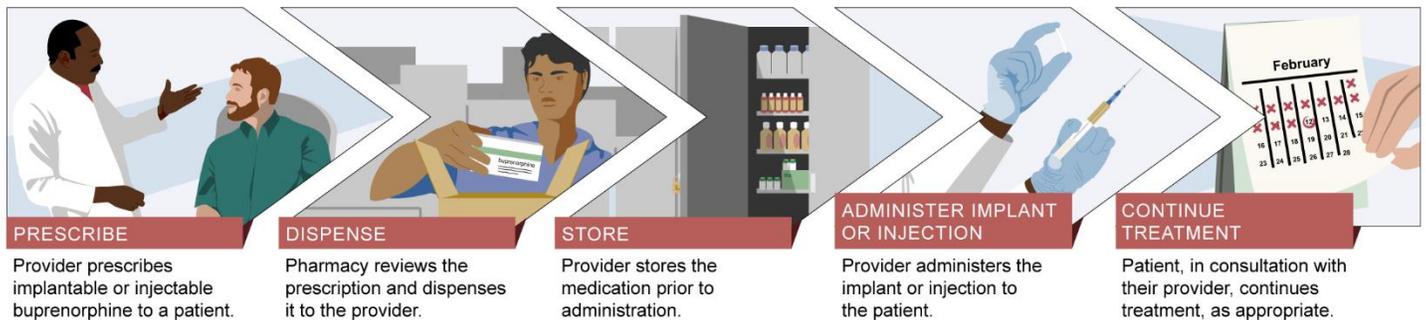
<sup>b</sup>Health care settings or individual providers participating in “buy-and-bill” must also receive REMS certification for a particular buprenorphine formulation. In “buy-and-bill,” providers purchase the medication from the manufacturer or distributor and store it until the provider administers it to the appropriate patient. After the medication is administered, the provider bills the relevant payer for the cost.

## Treating OUD with Injectable and Implantable Buprenorphine Involves Specific Steps and Use Is Relatively Low

### Providers and Pharmacies Must Follow Specific Steps That Align with Federal Requirements to Treat OUD with Injectable and Implantable Buprenorphine

To ensure patient safety and prevent diversion when treating with injectable and implantable buprenorphine, providers and pharmacies must follow a number of specific steps based on federal requirements. Providers are responsible for prescribing, storing, and administering these medications, while pharmacies are responsible for dispensing these medications to providers (see fig. 3).

Figure 3: Process for Treating Opioid Use Disorder with Injectable and Implantable Buprenorphine



Source: GAO analysis of Food and Drug Administration, Substance Abuse and Mental Health Services Administration, and Drug Enforcement Administration information. | GAO-20-617

Representatives from provider groups and pharmacies said they did not find the steps involved in treating patients with injectable and implantable buprenorphine to patients to be difficult overall, though they reported a

need for careful and timely coordination with each other and with patients at key steps of the process.

- **Prescribing.** Providers must prescribe injectable or implantable buprenorphine in accordance with the REMS for each of these medications.<sup>19</sup> Providers we spoke with stated that they typically prescribe injectable or implantable buprenorphine to patients who are stabilized on oral forms of buprenorphine or who are at risk of diverting the oral form. According to the product labeling for each medication, patients may receive the injection after a minimum stabilization period of 7 days on oral buprenorphine and the implant after a 3-month stabilization period. Providers also may need to seek prior authorization from a third-party payer, which some provider groups said can make the process of prescribing these medications to patients more difficult.<sup>20</sup>
- **Dispensing.** After receiving the prescription from the provider, specialty pharmacies must review the prescription and perform checks to confirm that the provider is eligible to prescribe or administer the prescription.<sup>21</sup> For example, pharmacies may review the state's prescription drug monitoring program to identify other medications the patient has received and they are to confirm that the provider has a DATA 2000 waiver.<sup>22</sup> After their review is complete, the specialty pharmacy fills the prescription and sends the medication to the location listed on the provider's DEA registration.
- Since both injectable and implantable buprenorphine have serious risks associated with their administration, the REMS

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<sup>19</sup>Providers who prescribe or those that insert and remove the buprenorphine implant must be enrolled in the REMS and complete requisite training, and they must maintain records of the insertion and removal of the implant. Health care settings and pharmacies that dispense injectable buprenorphine must establish processes and procedures to verify that it is dispensed directly to a provider and not to the patient.

<sup>20</sup>Prior authorization requires that certain conditions be met before services can be provided to patients, in part, to control utilization, ensure appropriate use, and prevent improper payments.

<sup>21</sup>Specialty pharmacies are non-retail pharmacies that primarily dispense drugs to treat serious health conditions requiring complex therapies or drugs that require special handling to providers, hospitals, or other institutions.

<sup>22</sup>Prescription drug monitoring programs are state-run databases that track the prescribing, dispensing, and purchasing controlled substances by individuals.

do not allow pharmacies to dispense injectable and implantable buprenorphine directly to patients. Specialty pharmacies and provider groups we spoke with said that medication deliveries require careful coordination. Specialty pharmacies told us that they must confirm that the provider's address for the delivery matches the address associated with their DEA registration, and provider groups and drug companies told us that timely deliveries allow patients to have appointments for administration of medication coincide with when the medication is delivered.

- **Storing.** After receiving the prescription, the provider must securely store the medication until administering it to the patient.<sup>23</sup> The provider can only store the medication for up to 14 days after delivery.<sup>24</sup> As a result, providers must schedule appointments with patients accordingly. As controlled substances, injectable and implantable buprenorphine must be stored in a securely locked, substantially constructed cabinet to reduce the potential for diversion. One provider told us that providers generally have checks in place, such as provider check-ins and check-outs into storage areas to further control access to these medications while in storage.
- **Administering.** Providers receive injectable buprenorphine pre-packaged in a syringe. After the patient receives his/her first injection, patients should continue to visit the provider for the administration of a monthly maintenance injection. After administering the injection, providers must dispose of any supplies used in accordance with established procedures for controlled substances and applicable federal, state, and local regulations. For implantable buprenorphine, the REMS requires providers who insert and remove the product to have appropriate surgical equipment onsite for insertion and removal of the device. For the implant, patients may receive the implant, which lasts up to 6 months, once in each arm.

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<sup>23</sup>Pharmacies are also responsible for securely storing the medication prior to dispensing it to the provider.

<sup>24</sup>Pub. L. No. 115-271, § 3204, 132 Stat. 3894, 3945 (2018). Providers must administer the medication within 14 days of receiving the medication. If the provider is unable to do so, they may transfer the medication to a DEA-registered company who handles the disposal of controlled substances. Injectable buprenorphine should be refrigerated but can be stored at room temperature for up to 7 days, while implantable buprenorphine is stored at room temperature.

They may continue treatment with oral buprenorphine after that 1-year period, if necessary.<sup>25</sup> Providers must dispose of the implant after removal as it will contain residual amounts of buprenorphine.

Stakeholders told us many of the federal requirements are in place to prevent diversion and reported that the risk of diversion of injectable and implantable buprenorphine is low. Representatives from all of the provider groups and pharmacies we spoke with said that diversion of injectable or implantable buprenorphine was unlikely. In addition, representatives from three of the six provider groups and two studies indicate that the design of these formulations reduces opportunities for diversion due to how they are administered.<sup>26</sup> Further, representatives from one of the specialty pharmacies noted that DEA registration and the REMS requirements make the risk of diversion unlikely. Consistent with this view, a 2017 study found that because patients lack control over the administration of injectable and implantable buprenorphine, patients receive consistent treatment exposure and therefore experienced improved health outcomes and reduced opportunities for diversion.<sup>27</sup>

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## Use of Injectable and Implantable Buprenorphine Is Relatively Low

As of 2019, the use of injectable and implantable buprenorphine to treat OUD is relatively low compared to use of oral buprenorphine. According to HHS reporting, providers issued 7,249 prescriptions for injectable and implantable buprenorphine in fiscal year 2019.<sup>28</sup> This means that injectable and implantable buprenorphine represent a small portion of

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<sup>25</sup>The buprenorphine implant's label indicates that no studies have been conducted in which a patient has received an implant more than once in each arm.

<sup>26</sup>Haight, Learned, et. al., "Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial," *The Lancet*, vol. 393, (2019): p. 780.

Shephard & Drovandi, "Sustained-release subdermal buprenorphine implants: the future of opioid use disorder management?" *Journal of Pharmacy Practice and Research*, vol. 49, (2019): p. 42.

<sup>27</sup>Rosenthal, R. N., Goradia, V. V., "Advances in the delivery of buprenorphine for opioid dependence," *Drug Design, Development and Therapy*, vol. 11, (2017): p. 2502.

<sup>28</sup>Department of Health and Human Services, *Agency Priority Goal Action Plan: Reducing Opioid Morbidity and Mortality*, (Washington, DC: 2019).

MAT treatment with buprenorphine given that according to HHS over 700,000 patients received buprenorphine prescriptions for oral formulations to treat OUD or pain in fiscal year 2019.<sup>29</sup> Representatives from five of the six provider groups in our review told us that this is due to factors such as the high cost of injectable and implantable formulations, providers' lack of familiarity with them, and the fact that patients must be on a stable dosage of oral buprenorphine prior to initiating treatment with injectable or implantable formulations. One study found that injectable and implantable buprenorphine medications can cost at least four times the price of oral buprenorphine formats.<sup>30</sup> Additionally, three of the six provider groups told us that because injectable and implantable buprenorphine are newer formulations, providers are still gaining an understanding of them. In addition, representatives from three of the six provider groups said that of the injectable and implantable formulations, providers primarily prescribe injectable buprenorphine because of the additional training required or some patients' concerns of implantable drugs. For example, the REMS for implantable buprenorphine requires providers who insert and remove the product to annually complete surgical training for the insertion and removal procedure.

In January 2020, the HHS Office of Inspector General reported that the majority of providers with a DATA 2000 waiver do not prescribe buprenorphine at or near their patient-limit capacity.<sup>31</sup> SAMHSA data indicates that waived providers had the capacity to provide MAT with buprenorphine to about 4.8 million patients, as of December 2019. However, only slightly more than 2,000 waived providers have indicated

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<sup>29</sup>Some of the 700,000 patients receiving prescriptions for oral buprenorphine formulations may have received them for the treatment of pain rather than for treating OUD. However, according to HHS, the proportion receiving them for pain is not expected to shift over time, so tracking the overall number of patients treated with these medications should provide a stable estimate of the change in the number of patients treated for OUD.

<sup>30</sup>Chua & Conti, "Revocation Of Orphan Drug Designation For Extended-Release Buprenorphine Injection: Implications And Next Steps," (Health Affairs, March 5, 2020), Accessed March 9, 2020, <https://www.healthaffairs.org/doi/10.1377/hblog20200302.846103/full/>. The authors analyzed a national sample of claims from 27 million non-elderly Americans with employer-sponsored coverage from medium-to-large firms. The price that patients ultimately pay for injectable and implantable buprenorphine may vary based on their health care coverage.

<sup>31</sup>Department of Health and Human Services, Office of Inspector General, *Geographic Disparities Affect Access to Buprenorphine Services for Opioid Use Disorder*, OEI-12-17-00240 (Washington, DC: January 2020).

that they would like to be listed on SAMHSA's online treatment locator as offering injectable and implantable buprenorphine as of December 2019.<sup>32</sup> Representatives from three provider groups told us that various issues, such as the cost of the medications and stigma toward addiction treatment, may affect the extent to which providers obtain or utilize their waiver. Representatives from one provider group told us that they were more likely to prescribe less costly oral buprenorphine formats, especially when they cannot guarantee they will be reimbursed for the cost of the medication. Also, representatives from two provider groups told us that due to the negative stigma associated with MAT, some providers may not want to publicize that they have a DATA 2000 waiver because they only want to provide MAT to existing patients and do not want to be perceived as solely a MAT provider.

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## Agency Comments

We provided a draft of this report to HHS and DOJ for review and comment. HHS and DOJ provided technical comments, which we incorporated as appropriate.

We are sending copies of this report to the appropriate congressional committees, the Secretary of Health and Human Services, the Attorney General, and other interested parties. In addition, the report is available at no charge on the GAO website at <http://www.gao.gov>.

If you or your staff members have any questions about this report, please contact me at (202) 512-7114 or [cosgrovej@gao.gov](mailto:cosgrovej@gao.gov). Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix I.



James Cosgrove

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<sup>32</sup>These data are self-reported and may not fully reflect the number of providers who currently prescribe injectable or implantable buprenorphine. Some providers who have indicated that they provide treatment with these medications may not be current, and there may be other providers who do prescribe these medications that do not want this information posted on SAMHSA's treatment locator at <https://www.findtreatment.gov/>.

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Letter

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Director, Health Care

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# Appendix I: GAO Contacts and Staff Acknowledgments

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## GAO Contact

James Cosgrove, (202) 512-7114, [cosgrovej@gao.gov](mailto:cosgrovej@gao.gov)

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## Staff Acknowledgments

In addition to the contact named above, Leslie V. Gordon (Assistant Director), Alison Goetsch (Analyst-in-Charge), Sam Amrhein, Sarah Gilliland, Diona Martyn, Ethiene Salgado-Rodriguez, Emily Wilson Schwark, and Meghan Shrewsbury made key contributions to this report.

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# Appendix II: Accessible Data

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## Data Table

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**Accessible Data for Figure 2: Providers with SAMHSA Drug Addiction Treatment Act of 2000 Waivers by Patient Limit Level, as of December 31, 2019**

<b>Patient limit level</b>	<b>Percentage</b>
275-patient limit	7.5
100-patient limit	18.2
30-patient limit	74.3

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## Related GAO Products

*Opioid Use Disorder: Barriers to Medicaid Beneficiaries' Access to Treatment Medications.* [GAO-20-233](#). Washington, D.C.: January 24, 2020.

*Generic Drug Development: Stakeholders' Views of Risk Evaluation and Mitigation Strategies Differ.* [GAO-20-94](#). Washington, D.C.: October 15, 2019.

*Drug Policy: Assessing Treatment Expansion Efforts and Drug Control Strategies and Programs.* [GAO-19-535T](#). Washington, D.C.: May 9, 2019.

*Illicit Opioids: While Greater Attention Given to Combating Synthetic Opioids, Agencies Need to Better Assess their Efforts.* [GAO-18-205](#). Washington, D.C.: March 29, 2018.

*Opioid Use Disorders: HHS Needs Measures to Assess the Effectiveness of Efforts to Expand Access to Medication-Assisted Treatment.* [GAO-18-44](#). Washington, D.C.: October 31, 2017.

*Opioid Addiction: Laws, Regulations, and Other Factors Can Affect Medication-Assisted Treatment Access.* [GAO-16-833](#). Washington, D.C.: September 27, 2016.

*Controlled Substances: DEA Should Take Additional Actions to Reduce Risks in Monitoring the Continued Eligibility of Its Registrants.* [GAO-16-310](#). Washington, D.C.: May 26, 2016.

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