HMA

Considerations for Use of Extended-Release Injectable Buprenorphine in Jails to Treat Individuals with Opioid Use Disorder

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INTRODUCTION

Offering clinically appropriate medication for opioid use disorder (MOUD) in jails significantly reduces mortality from overdose after release.[1]

The Food and Drug Administration (FDA) has three approved medications for opioid use disorder (MOUD) — methadone, extended-release (ER) injectable naltrexone, and buprenorphine. Healthcare providers should select the right medication for each individual patient based on clinical judgment and shared decision-making with the patient. Because of its effectiveness in managing withdrawal, buprenorphine is commonly provided in jails with mature MOUD programs.

Buprenorphine is available in transmucosal or sublingual (SL) and ER injectable formulations. The SL formulation is given once daily (sometimes twice) and dissolves under the tongue. The ER formulation is given as a shot under the skin (subcutaneously) and is administered either weekly or monthly.

Many jails identify several advantages to using the injectable form of buprenorphine, such as reduced potential for diversion and less staff time needed for daily medication administration; however, the injectable formulation has potential drawbacks. This brief is intended to assist jails in exploring the factors involved in implementing a program to administer injectable buprenorphine.

CLINICAL CONSIDERATIONS

Clinicians who provide care to patients with OUD should develop a patient-centered treatment plan and select the most appropriate medication and formulation of MOUD based on shared decision-making. Like medications used to treat diabetes, high blood pressure, and other chronic diseases, MOUD should be selected based on the patient's severity of OUD, past history with MOUD treatment, success or failure with treatment, preferences, risk factors, benefits, and alternatives. Compared with SL formulations, injectable formulations offer similar outcomes for treatment of OUD. These include increased stabilization of medical, mental health, and SUD issues, along with decreased cravings.[2] Some patients may prefer injectable buprenorphine.[3] At least one study has shown that individuals treated in jail with ER injectable buprenorphine were more likely to continue treatment in the community after release than people treated with SL buprenorphine.[4]

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[1] Green TC, Clarke J, Brinkley-Rubenstein L, Marshall BDL, Alexander-Scott N, Boss R, Rich JD. Postincarceration Fatal Overdoses After Implementing Medications for Addiction Treatment in a Statewide Correctional System
Postincarceration Fatal Overdoses After Implementing Medications for Addiction Treatment in a Statewide Correctional System. *JAMA Psychiatry*. 2018;75(4):405-407. doi: 10.1001/jamapsychiatry.2017.4614.

[2] Ling W, Nadipelli VR, Solem CT, et al. Patient-Centered Outcomes in Participants of a Buprenorphine Monthly Depot (BUP-XR) Double-Blind, Placebo-Controlled, Multicenter, Phase 3 Study. *Journal of Addiction Medicine*. 2019;13(6):442–449. doi: 10.1097/ADM.0000000000000517

[3] Cheng A, Badolato R, Segoshi A, et al. Perceptions and Experiences Toward Extended-Release Buprenorphine Among Persons Leaving Jail with Opioid Use Disorders Before and During COVID-19: An In-Depth Qualitative Study. Addiction Science & Clinical Practice. 2022;17(1):4. doi: 10.1186/s13722-022-00288-4

[4] Lee, JD, et. al. Comparisons of Treatment Retention of Adults with Opioid Addiction Managed with Extended-Release Buprenorphine vs Daily Sublingual Buprenorphine-Naloxone at Time of Release from Jail. *JAMA Open Network*. 2021;4(9):e2123032. doi:10.1001/jamanetworkopen.2021.23032

The FDA has approved two brands of ER injectable buprenorphine—Sublocade® and Brixadi®.[5] Sublocade® is available as a monthly injection and is approved to be given only after the individual has been on SL buprenorphine for at least seven days. [6] Brixadi® is available in both a weekly injectable formulation that can be given after only one SL dose of buprenorphine and a monthly injectable formulation for individuals who are already on buprenorphine.[7] Because the weekly injectable dose of Brixadi® can be given after only one SL dose of buprenorphine, it can be used for opioid withdrawal management, whereas Sublocade® cannot. However, even if jails move to using the ER injectable buprenorphine as the primary formulation of MOUD, they will be unable to completely eliminate use of the SL formulation because both injectable forms require at least one dose of SL buprenorphine and up to one week of SL buprenorphine.

Furthermore, many clinicians report that they need to provide additional SL doses of buprenorphine in the first few days after the injection of ER buprenorphine to adequately control cravings. For Sublocade®, the ER formulation is the same dose for all patients regardless of weight and OUD history. Some patients report that they feel as though the dose is too weak to control cravings until they have received four or five monthly injections, which can further complicate clinical management. Brixadi® offers different injection dosages, but there is limited clinical experience with Brixadi® in the United States as it just was released here in September 2023.

Clinically, ER injectable buprenorphine may be a suboptimal choice for some people with OUD. For example, ER injectable buprenorphine can block the efficacy of opioid medications for pain management, so individuals anticipating surgery are poor candidates for injectable buprenorphine. Limited data are available on the use of injectable buprenorphine in pregnancy, whereas the SL buprenorphine is recommended for pregnant women.

Use of an injection or shot for individuals with a history of drug use, especially intravenous drug use, can be triggering for some people. Patients report that the shot is painful, further detracting from their satisfaction. In study data prepared for FDA approval, up to 16.5 percent of patients experience some type of injection site reaction (e.g., pain, itching, swelling) versus 9 percent of individuals who received a placebo injection.[8]

Accidental injection of buprenorphine into a blood vessel instead of the tissue under the skin can cause serious harm or death; therefore, the injectable formulations are available only through specialized pharmacy programs known as Risk Evaluation and Mitigation Strategy (REMS).[9] Healthcare settings and pharmacies that order and dispense injectable formulations must be certified in this program and comply with the REMS requirements.[10,11]

REMS PHARMACY CONSIDERATIONS

The FDA implemented the REMS program for ER injectable buprenorphine-containing products to mitigate the risk of accidental misplacement of the injection into a blood vessel, which has potentially lethal results.

[5] While information on different formulations is discussed in this brief, this is for informational purposes only. HMA does not endorse any specific brand of MOUD.
[6] Sublocade®. Prescribing Information. Available at: https://www.sublocade.com/Content/pdf/prescribing-information.pdf. Accessed October 10, 2023.
[7] Brixadi®. Prescribing Information. Available at: https://www.brixadihcp.com/pdfs/brixadi-prescribing-information.pdf. Accessed October 10, 2023.
[8] Sublocade®. Prescribing Information. Available at: https://www.sublocade.com/Content/pdf/prescribing-information.pdf. Accessed October 10, 2023.
[9] Ibid
[10] Brixadi®. Welcome to the BRIXADI REMS (Risk Evaluation and Mitigation Strategy). Available at: https://brixadirems.com/. Accessed October 10, 2023.
[11] Sublocade®. What is the SUBLOCADE® REMS (Risk Evaluation and Mitigation Strategy)? Available at: https://www.sublocaderems.com/#Main. Accessed October 10, 2023.

Another risk is that the injectable medication will be dispensed directly to the patient and misused as an IV injection and cause death.

There are two ways that jails can acquire ER injectable buprenorphine. Jails can purchase stock medication that is managed as a controlled substance and then used as needed for any patient, or jails can order injectable buprenorphine through a prescription specifically for a designated individual patient.

Jails that want to stock ER injectable buprenorphine (for either brand) must become REMS-certified. The process is relatively simple and requires designating an authorized representative, reviewing all materials, completing the enrollment process, developing processes and staff training, and complying with any manufacturing audits. Having stock medication versus patient-specific only enhances flexibility in the administration of ER injectable buprenorphine. Ordering patient-specific medication has drawbacks for jails because many detainees leave the jail without notice, and the medication is non-transferable to another patient.

Jails may order patient-specific injectable buprenorphine by sending a prescription for an individual patient to a REMS-certified specialty pharmacy for delivery to the address listed on the prescriber's DEA license. Prescribers who work at multiple clinical sites must have a separate DEA number for each location. The correctional facility is not required to be REMS-certified when using this pathway. Management of the REMS system requires slightly more administrative time than providing the SL formulation of buprenorphine, which does not require interaction with the REMS system or a REMS-certified pharmacy.

LEGAL CONSIDERATIONS

The ideal MOUD program provides all three types of FDA-approved MOUD in all formulations and selects the most appropriate course of treatment based on shared decision-making between the clinician and the patient. Some states, such as New York, recognize the value of a patient-centered program and require correctional facilities to offer all forms of MOUD.[12] Many jails are influenced by legal considerations when developing a MOUD program. The US Department of Justice has issued clear guidance that failure to continue community-prescribed MOUD in correctional facilities is a violation of the Americans with Disabilities Act.[13] Furthermore, several lawsuits have been settled in favor of the plaintiff for wrongful death related to failure to adequately manage opioid withdrawal.[14]

To date, no detainees have successfully won a lawsuit because a correctional facility failed to offer a specific form of MOUD. However, the Justice Department has investigated and sometimes sued entities—including a jail,[15] a parole board,[16] and many others across sectors[17]—that have a one-size-fits-all approach to SUD-

[12] New York State S. 1795/A. 533 was signed into law in October 2021. This law mandates the establishment of a program offering all forms of MOUD in state correctional facilities. Such programs also must include conditions for a reentry strategy.
[13] US Department of Justice Civil Rights Division. The Americans with Disabilities Act and the Opioid Crisis: Combating Discrimination Against People in Treatment or Recovery. Available at: https://archive.ada.gov/opioid_guidance.pdf. Accessed October 10, 2023.
[14] US Department of Justice, Bureau of Justice Administration. Managing Substance Withdrawal in Jails: A Legal Brief. February 2022. Available at: https://bja.ojp.gov/library/publications/managing-substance-withdrawal-jails-legal-brief. Accessed October 10, 2023.
[15] US Department of Justice, Civil Rights Division, and US Attorney's Office, District of New Jersey Department of Justice. Investigation of the Cumberland County Jail. January 14, 2021). Available at: https://www.justice.gov/opa/press-release/file/1354646/download.
[16] Settlement Agreement Between the U.S. and the Mass. Parole Board (Dec. 14, 2021).
[17] Voluntary Resolution Agreement Between Department of Justice, Department of Health & Human Services, and Genesis Healthcare's Designated Nursing Home Facilities. August 4, 2021. Available at: https://www.hhs.gov/civil-rights/for-providers/compliance-enforcement/agreements/genesis-healthcares-designated-nursing-home-facilities-agreement/index.html. Accessed October 10, 2023.

related medical needs. Providing MOUD is the standard of care for correctional centers, and jails should consider their legal risk in restricting detainee access to specific formulations of MOUD. [18]

STAFFING CONSIDERATIONS

Correctional settings often prefer to administer medication on a monthly rather than daily basis. Both clinical and custody staff are responsible for administering SL buprenorphine to reduce the risk of diversion and for monitoring individuals until the sublingual preparation has dissolved, which takes several minutes. A weekly or monthly injection potentially reduces the amount of clinical and custody staff time required to administer medication.[19]

Because of the risk of serious harm or death resulting from a misplaced injection, clinical staff who are injecting the ER buprenorphine must be specially trained.

Correctional settings also should assess nursing staff for competency to administer buprenorphine safely and effectively.[20] Though use of the ER injectable formulation may reduce daily staff medication administration time, it requires a minor additional initial and ongoing investment in training time. Use of any injectable medications increases the risk of needlestick injuries to staff and may increase risk for blood-borne disease like HIV or hepatitis.

ORDERING, STORING, AND ADMINISTERING CONSIDERATIONS

Ordering and Storage

ER injectable buprenorphine must be treated like any other controlled substance in terms of storing in a double-locked system, tracking with medication logs, reconciliation of discrepancies in inventory, and maintenance of records. It is beyond the scope of this discussion to describe all those procedures, but correctional settings considering ER injectable buprenorphine should have those systems in place already for SL formulations of buprenorphine and other controlled medications.

Sublocade® should be stored in a refrigerator at 2−8°C (35.6−46.4°F). Once outside the refrigerator, this product can be stored in its original packaging at room temperature, 15–30°C (59–86°F), for up to seven days prior to administration. The product packaging instructs staff to discard Sublocade® if left at room temperature for longer than 12 weeks.[21] Brixadi® does not require refrigeration.[22]

Medication Administration

Some jails administer SL buprenorphine at a dedicated med line in the clinic area. Other facilities routinely administer SL buprenorphine from a cart on the units during routine med pass. Administration of the injectable formulation generally is performed in the clinic area where detainees are escorted to receive their weekly or monthly injection. Injections must be provided according to a fairly rigid schedule. For example, monthly

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[18] National Sheriff's Association and National Commission on Correctional Health Care. Jail-Based Medication Assisted Treatment: Promising Practices, Guidelines, and Resources for the Field. October 2018. Available at: https://www.sheriffs.org/publications/Jail-Based-MAT-PPG.pdf; Accessed October 11, 2023.

[19] Ling R, White B, Roberts J, et al. Depot Buprenorphine as an Opioid Agonist Therapy in New South Wales Correctional Centres: A Costing Model. *BMC Health Services Research*. 2022;22:1326. doi: 10.1186/s12913-022-08687-8

[20] Boston Medical Center (BMC) Grayken Center for Addiction Training & Technical Assistance. Injectable Buprenorphine Implementation Guide. February 2023. Available at https://www.addictiontraining.org/documents/resources/327_Injectable_Buprenorphine_Implementation_Guide_2.2023.pdf. Accessed October 11, 2023.

[21] Indivior. Sublocade. Available at: https://www.sublocadehcp.com/. Accessed October 9, 2023.

[22] Braeburn. Brixadi Prescribing Information. Available at: https://braeburnrx.com/wp-content/uploads/2023/05/brixadi-prescribing-information.pdf. Accessed October 11, 2023.

injections of Sublocade® require at least 26 days between doses, so potential interruptions to clinical staffing need to be considered. Weekly Brixadi® injections should be administered at seven-day intervals (or more frequently during the withdrawal phase). As a result, clinical staff who are able to administer the injection need to be available at those times, which can be troublesome for facilities with limited clinical staffing.

Custody staff frequently cite reduced risk of diversion as a key factor in selecting the ER injectable formulation. Documented diversion of SL buprenorphine is less frequent than custody staff predict prior to starting an MOUD program.[23] Jails report that patient education, monitoring, and appropriate assessment of potential diversion reduces the incidence of diversion. Problems created by diversion are frequently balanced by decreased contraband and reduced aggression after MOUD programs are implemented. If diversion, threats, or victimization are a concern, then ER injectable formulations are a better alternative. Distressingly, there are rare reports of individuals who have attempted to "divert" ER injectable buprenorphine by digging out the tissue around the injection site. ER injectable formulations do not have a peak effect and are therefore less likely to be diverted by staff. However, as a controlled substance, both SL and injectable formulations require the same level of controls as any other controlled substance.

COST CONSIDERATIONS

A major drawback to ER injectable buprenorphine is the cost. Sublocade® typically costs approximately $2,000 per injection. Brixadi® typically costs $450 for weekly injection and $1,700 for monthly injections. The cost of medication may be partially offset by the savings in staff time. Each institution should consider a careful cost analysis when deciding whether to offer the ER injectable formula as the primary form of buprenorphine. Jails are encouraged to compare SL and ER injectable costs using Health Management Associates' cost comparison tool.[24]

Many jails that provide ER injectable formulations have alternative sources of funding, such as opioid settlement grants. Some facilities participate in group purchasing arrangements, such as the Minnesota Multistate Contracting Alliance for Pharmacy (MMCAP) Infuse program,[25] which may lower the cost of the medication from the wholesale price. Other states are seeking 1115 waivers from the Centers for Medicare & Medicaid Services (CMS), which will provide Medicaid coverage for a period of time prior to release, allowing correctional facilities to shift the cost for all forms of MOUD to Medicaid.[26] CMS approved California's waiver request, which makes certain healthcare services, including MOUD, billable to MediCal beginning 90 days before release.[27]

CONSIDERATIONS UPON REENTRY OR TRANSITION

Because correctional centers cannot implement a MOUD program with ER injectable buprenorphine as a routine choice, providing one injection at release is a reasonable option. Use of ER injectable formulation at release can increase retention in treatment post-release.[28] Individuals released with an ER injection benefit from the extended duration of the medication dosage until they can establish care for continued MOUD,

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[23] Evans EA, Pivovarova E, Stopka TJ, et al. Uncommon and Preventable: Perceptions of Diversion of Medication for Opioid Use Disorder in Jail. *Journal of Substance Abuse Treatment*. 2022;138:108746. doi: 10.1016/j.jsat.2022.108746.
[24] Counties participating in one of HMA's Jail MAT Learning Collaboratives can request tool through their assigned HMA coach.
[25] Minnesota Multistate Contracting Alliance for Pharmacy. MMCAP Infuse. Available at: https://infuse-mn.gov/. Accessed October 11, 2023.
[26] Kaiser Family Foundation. Medicaid Waiver Tracker: Approved and Pending Section 1115 Waivers by State. September 26, 2023. Available at: https://www.kff.org/medicaid/issue-brief/medicaid-waiver-tracker-approved-and-pending-section-1115-waivers-by-state/. Accessed October 10, 2023.
[27] Centers for Medicare & Medicaid Services (CMS). HHS Approves California's Medicaid and Children's Health Insurance Plan (CHIP) Demonstration Authority to Support Care for Justice-Involved People. January 26, 2023. Available at: https://www.cms.gov/newsroom/press-releases/hhs-approves-californias-medicaid-and-childrens-health-insurance-plan-chip-demonstration-authority
[28] Lee JD, Malone M, McDonald R, et al. Comparison of Treatment Retention of Adults with Opioid Addiction Managed With Extended-Release Buprenorphine vs Daily Sublingual Buprenorphine-Naloxone at Time of Release From Jail. *JAMA Network Open*. 2021;4(9):e2123032. doi: 10.1001/jamanetworkopen.2021.23032

thereby reducing the risk of relapse. Some jails have used ER injectable formulations when detainees are scheduled for transfer to another facility that does not offer MOUD, as the ER injection wears off gradually and, hence, provides a smoother withdrawal process.

For jails that provide regularly scheduled monthly injections, timing of release may be problematic if a detainee is due for a shot and then is precipitously released. Of course, this challenge is the same for individuals taking the SL formulation. Whatever formulation is chosen, continuity of MOUD at release is paramount. Individuals who have received ER injectable buprenorphine during incarceration or at release can switch back to the SL preparation if the individual and treating clinician prefer that option. Many insurers, especially commercial carriers, require prior approval for the ER injectable formulation, so coordination of insurance benefits may be more difficult than when administering the SL preparation. Additionally, many community providers can prescribe the SL formulation of buprenorphine but do not participate in the REMS program or offer ER injectable formulations in the office, necessitating a transition back to SL formulation at reentry. Jails that are considering broad use of the ER injectable formulation should speak with their community providers about continuity of care at reentry.

TWO CARCERAL SYSTEMS USING ER INJECTABLE BUPRENORPHINE

Orange County, CA

Orange County has a broad program to provide MOUD in their jails. Orange County offers both SL and ER injectable formulations, and patients and prescribers engage in shared decision-making to determine the best option. The Orange County MOUD team includes a pharmacist and technicians who handle medication ordering and processing, a licensed vocational nurse who administers the injections, a full-time case manager who works on discharge planning, and addiction and primary care physicians for clinical management. Orange County has an arrangement with a community provider who routinely offers ER injectable buprenorphine to facilitate reentry coordination.

Jail staff note that cost is a significant barrier. Even though administration time may be reduced with the ER injectable, they still find that the ER injectable formulation is more expensive. Patient acceptance of the injection can also be a barrier to use. Nonetheless, facility staff cite decreased diversion, efficiency in medication administration, and longer window to link to care upon release as primary advantages to use.

Pennsylvania Department of Corrections

Steven Seitchik, the Medication Assisted Treatment Statewide Coordinator for the Pennsylvania Department of Corrections (PA DOC), presented data on Pennsylvania's experience during the American Correctional Association's 153rd Congress of Correction, August 2023, in Philadelphia.[29] PA DOC offers ER injectable buprenorphine to detainees who prefer the injection over the SL tablet, detainees sent to county jails, and detainees caught diverting their SL forms. They report a 3−5 percent diversion rate for SL forms of buprenorphine.

In January 2022, 149 detainees received ER injectable buprenorphine, and 690 individuals received SL. By June 2023, 392 PA DOC detainees were on ER injectable buprenorphine and 599 on SL.

The DOC works with the Pennsylvania Department of Human Services to ensure that detainees have Medicaid benefits upon release through an automated process and coordinates referrals to Addiction Centers of Excellence. According to Mr. Seitchik, "Lack of champions for the program [is a barrier]. Leaders need to voice support for the program, or it will fail. The stigma and the diversion risk make it an uphill battle in a prison environment, but hundreds of studies show that addiction is a disease, and it needs to be treated as such."

[29] International Corrections and Prisons Association. ACA's 153rd Congress of Correction. Philadelphia, PA. August 10−13. Available at: https://icpa.org/events/upcoming-events/aca-s-153rd-congress-of-correction.html. Accessed October 11, 2023.