



STATE OF MAINE
GOVERNOR'S OFFICE OF POLICY INNOVATION AND THE FUTURE
181 STATE HOUSE STATION
AUGUSTA, MAINE
04333-0181

GORDON SMITH, DIRECTOR
OPIOID RESPONSE

May 2022

To: Substance use treatment providers, pharmacy communities, and hospital and policy leaders

The Maine Opioid Response Clinical Advisory Committee consists of approximately 30 leaders in substance use disorder prevention, treatment and harm reduction in Maine including both prescribers and pharmacists. As part of our efforts, we have been working on developing clinical recommendations related to the management of patients with substance use disorders, particularly as they encounter barriers within the existing health care delivery system. One increasingly common challenge is utilizing extended-release buprenorphine (XRB) in patients with opioid use disorder (OUD). We have attached our proposed position on enhancing access to XRB including clinical, operational, policy and reimbursement considerations. These recommendations are intended to enhance your care and should not replace your own clinical judgement. If you have any questions, please do not hesitate to contact us.

Sincerely,
Maine Opioid Response Clinical Advisory Committee

Alane O'Connor DNP, Committee co-chair
alane.oconnor@mainehealth.org

Lisa Letourneau MD, MPH, Committee co-chair
lisa.letourneau@maine.gov

Gordon Smith, Director of Opioid Response, State of Maine
gordon.smith@maine.gov

Maine Opioid Response Clinical Advisory Committee: Proposed Position on Enhancing Access to Extended-Release Buprenorphine for Patients with Opioid Use Disorder

Extended-release buprenorphine (XRB) is a highly effective treatment for opioid use disorder (OUD) that is administered monthly by subcutaneous injection and provides treatment for at least 28 days. XRB offers unique advantages relative to other OUD treatment options, but it can be challenging for prescribers to identify patients who might best benefit from the medication, and it is often difficult to acquire the medication due to insurance restrictions, shipping, storage, and handling requirements. These factors have limited the ability of patients to take advantage of this treatment option. We want to acknowledge the hospitals, clinics and providers in Maine who are already providing XRB and encourage the continued efforts to safely expand access and reduce barriers to XRB, with an emphasis on ensuring equitable distribution in rural and underserved areas.

The literature and our clinical experience support the efficacy of XRB relative to sublingual buprenorphine-naloxone (SLB), especially for those who have not or are not stabilized with SLB and remain at the highest risk for overdose death. While SLB continues to be a highly effective treatment for OUD, it can be misused and diverted, and inconsistent adherence can be a barrier to stabilization.¹ XRB reduces these risks and has been shown to be safe, well tolerated and at least as efficacious as SLB in reducing illicit opioid use.²⁻⁴ Published rates of treatment retention for those utilizing XRB are high (82.8% at 24 weeks, 75% at 48 weeks).^{3,5} Relative to SLB, patients on XRB report high rates of treatment satisfaction and effectiveness, lower treatment burden, fewer aberrant medication behaviors, enhanced ability to avoid stigma at pharmacies and better physical functioning.⁶⁻⁸ Real-world implementation has demonstrated lower odds of illicit opioid and injection drug use as well as an increased quality of life and likelihood of being employed for those on XRB for 12 months relative to those on SLB or short-term XRB.^{5,9}

With the goal of safely expanding access to XRB in Maine, we offer the following clinical, operational and policy recommendations.

Clinical Considerations:

We recommend that providers consider utilizing XRB in patients with a variety of clinical indications including but not limited to:

- a known history of SLB misuse or diversion.
- significant medical complications of OUD and/or injection drug use (e.g., osteomyelitis, endocarditis).
- treatment-resistant OUD, including those with ongoing illicit substance use in the context of SLB treatment and/or further functional decline.
- difficulty keeping their medication safe (e.g., those experiencing homelessness, or living in unstable settings).
- patient initiated buprenorphine tapering if clinically appropriate.¹⁰

We strongly encourage utilization of XRB and/or referral to a higher level of care rather than abrupt cessation of prescribing SLB as this can have potentially lethal consequences.

We recommend that providers consider the following regarding XRB dosing and administration.

- While the FDA recommends a 7-day trial of SLB prior to administration of XRB¹¹, more recent literature¹² has supported a rapid induction approach which may be necessary in situations where overdose risk is high.
- While the recommended monthly dose of XRB is two initial doses of 300 mg followed by 100 mg maintenance doses, a monthly maintenance dose of 300 mg may be required for patients who continue to have symptoms.¹¹ Dose dependent hepatic effects have been observed and providers should consider monitoring the liver function in those continuing a monthly maintenance dose of 300 mg for an extended period.¹¹
- In the initial stages of XRB treatment, it is sometimes necessary to co-prescribe low-dose SLB for a limited period.
- XRB is not approved for use in pregnancy but may be considered in situations where benefits outweigh the risks. High doses of one of the solubility additives (N-Methyl-2-pyrrolidone) has been associated with adverse fetal outcomes in animal and some human studies.¹¹ However, other studies indicate that those who have become pregnant while on XRB did not have any adverse outcomes.¹³ There is an ongoing clinical trial to determine safety in this population.

Operational Considerations:

Because there are operational challenges to utilizing XRB, we recommend:

- ***Hospitals/clinics become REMS certified and utilize the XRB “buy and bill” option.*** Under the “buy and bill” approach, XRB is ordered in bulk (not for a specific patient) and insurance is billed when the medication is administered. Acquiring XRB through the “buy and bill” approach requires hospital pharmacies (as well as healthcare settings that purchase XRB from distributors) to become REMS (Risk Evaluation and Mitigation Strategy) certified. REMS certification enhances safety as the theoretical risk if a patient mishandled the medication is high. The REMS certification process is outlined at <https://www.sublocaderems.com/>.

An alternative to “buy and bill” is the “white bagging” option (where XRB is ordered from a specialty pharmacy for a specific patient). This approach presents some challenges (i.e., medication not arriving in time due to insurance delays and/or specialty pharmacy requirements to obtain patient consent prior to shipping the medication, and the medication needing to be wasted if unused rather than returned to the pharmacy as with “buy and bill”). **“White bagging” is a better alternative to not providing XRB at all,** but consensus is that “buy and bill” has fewer potential complications.

- ***Hospital-based and free-standing infusion clinics implement clinical pathways so that XRB can be offered/administered.*** This should include a pathway that enables prescribers not on the hospital’s medical staff to refer patients for XRB administration. This can be achieved by having an X-waivered member of the hospital’s medical staff co-sign the orders if necessary. Utilizing infusion clinics will expand XRB access for patients in community treatment programs not affiliated with a hospital, those utilizing telehealth services, and patients at some federally qualified health centers/rural health centers where capitated payment models do not reimburse for the cost of the medication.
- ***Hospitals and infusion centers offering XRB utilize the MaineHealth “how to” toolkit*** for becoming REMS certified/acquiring XRB. The toolkit includes instructions for how to acquire XRB, a clinical protocol, a procedure smartphrase, implications for use, and patient instructions. The toolkit may need to be modified for a particular setting (i.e., those without on-site point of care drug testing) and can be found at <https://www.mainehealth.org/-/media/Maine-Behavioral-Healthcare/MBH-Files/Work-Files/Content/Long-Acting-Injectable-Buprenorphine-Toolkit.pdf>. A 10-minute instructional video on how to administer XRB is available at <https://www.youtube.com/watch?v=dfO-jVvynuk>.

Policy & Reimbursement Considerations:

We encourage state leaders to consider the following policy and reimbursement changes:

- ***Begin the legislation and rule changes needed to require that XRB administered in all settings is included in the Maine Prescription Monitoring Program (PMP).***
- ***All payers should remove any prior authorization requirements for XRB within both medical and pharmacy benefits.*** This approach would be consistent with Medicaid programs in several other states (e.g., DC, FL, KY, PA) where providers are not required to complete prior authorizations when the medication is prescribed per FDA labeled dosing.
- While we recognize that medication costs and reimbursements will vary depending upon the setting in which XRB is administered, ***we advocate that all payors be required to reimburse providers at a rate that covers the provider’s costs of acquiring XRB.***
- ***Consider using state, federal or other available funds to provide grants that incentivize programs to implement and/or expand access to XRB*** to reflect the challenges encountered acquiring the medication and implementing treatment protocols.

References

1. Chilcoat H.D., Amick H.R., Sherwood M.R., Dunn K.E. Buprenorphine in the United States: Motives for abuse, misuse and diversion. *J Subst Abuse Treat.* 2019; 104: 148-157.
2. Lofwall M.R., Walsh S.L., Nunes E.V.... Kim S. Weekly and monthly subcutaneous buprenorphine depot formulations vs daily sublingual buprenorphine with naloxone for treatment of opioid use disorder. *JAMA Intern Med.* 2018; 17(6): 764-773.
3. Frost M., Bailey G.L., Lintzeris N.... Tiberg F. Long-term safety of a weekly and monthly subcutaneous buprenorphine depot (CAM2038) in the treatment of adult out-patients with opioid use disorder. *Addiction.* 2019; 114: 1416-1426.
4. Adorn A.C., Haight BR., Shinde S.... Rutrick D. Treating opioid use disorder with a monthly subcutaneous buprenorphine depot injection: 12-month safety, tolerability and efficacy analysis. *J Clin Psychopharmacol.* 2020; 40: 231-239.
5. Farrell M., Shahbazi J., Byrne M.... Degenhardt L. Outcomes of a single-arm implementation trial of extended-release subcutaneous buprenorphine depot injections in people with opioid dependence. *Int J Drug Policy.* 2022; 100: 103492.
6. Lintzeris N., Dunlop A.J., Haber P.S.... Tiberg F. Patient-reported outcomes of treatment of opioid dependence with weekly and monthly subcutaneous depot vs sublingual buprenorphine. *JAMA Network Open.* 2021; 4(5): e219041.
7. Cheng A., Badolato R., Segoshi A.... Tofighi B. 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. *Addict Sci Clin Prac.* 2022; 17(4).
8. Barnett A., Savic M., Lintzeris N... Hayes V. Tracing the affordances of long-acting injectable depot buprenorphine: A qualitative study of patients' experiences in Australia. *Drug Alcohol Depend.* 2021; 227: 108959.
9. Ling W., Nadipelli V.R., Aldridge A.P.... Heidbreder C. Recovery from opioid use disorder (OUD) after monthly long-acting buprenorphine treatment: 12-month longitudinal outcomes from RECOVER, an observational study. *J Addict Med.* 2020; 14(5): e233-e240.
10. Ritvo A.D., Calcaterra S.L., Ritvo J.I. Using extended release buprenorphine injection to discontinue sublingual buprenorphine: A case series. *J Addict Med.* 2021; 15(3): 252-254.
11. Prescribing Information for Sublocade. Available at <https://www.sublocade.com/Content/pdf/prescribing-information.pdf>.
12. Mariani J.J., Mahony A., Iqbal M.N.... Levin, F.R. Case series: Rapid induction onto long acting buprenorphine injection for high potency synthetic opioid users. *Am J Addict.* 2020; 29(4): 345-348.
13. Towers C.V., Deisher H. Subcutaneous extended-release buprenorphine use in pregnancy. *Case Rep Obstet Gynecol.* 2020; Article ID 3127676.