

MaineHealth

Extended-Release Buprenorphine during Pregnancy and Postpartum

Alane O'Connor DNP

August 23, 2023

PATIENT
CENTERED

RESPECT

INTEGRITY

EXCELLENCE

OWNERSHIP

INNOVATION

Objectives and Disclosures

- Objectives

- Describe the basic logistics of acquiring extended-release buprenorphine (XRB) including REMS certification and the MaineCare coverage criteria.
- Identify pregnant and postpartum patients who may be appropriate for XRB and demonstrate an approach to discussing the potential risks and benefits of its use during the perinatal period.
- Explain XRB issues that are unique to the perinatal population including medication administration and appropriate monitoring for neonatal opioid withdrawal syndrome.

- Disclosures

- I have no disclosures of any kind. Sublocade = option 1; Brixadi = option 2.

Act with kindness and compassion.

Be an active listener.

Be a role model.

Set high standards.

Take responsibility.

Embrace change.

What is XRB?

- XRB is administered as a subcutaneous injection. It is a controlled substance (III) used to treat moderate to severe OUD.
- Like other forms of buprenorphine, XRB blocks the euphoric effect of other opioids, reduces a patient's opioid cravings and withdrawal symptoms.
- Patients are generally on sublingual buprenorphine prior to transitioning to XRB though “rapid challenges” are an option. Eligible patients are on at least 8 mg daily of the sublingual formulation (though other protocols exist to initiate those on lower doses, etc.)
- It is expensive and is generally used in our highest risk patients (e.g., those misusing their sublingual medication, those with severe complications from their OUD, those that are homeless/unable to safely control access to sublingual formulation) or those that require monotherapy.

Act with kindness and compassion.

Be an active listener.

Be a role model.

Set high standards.

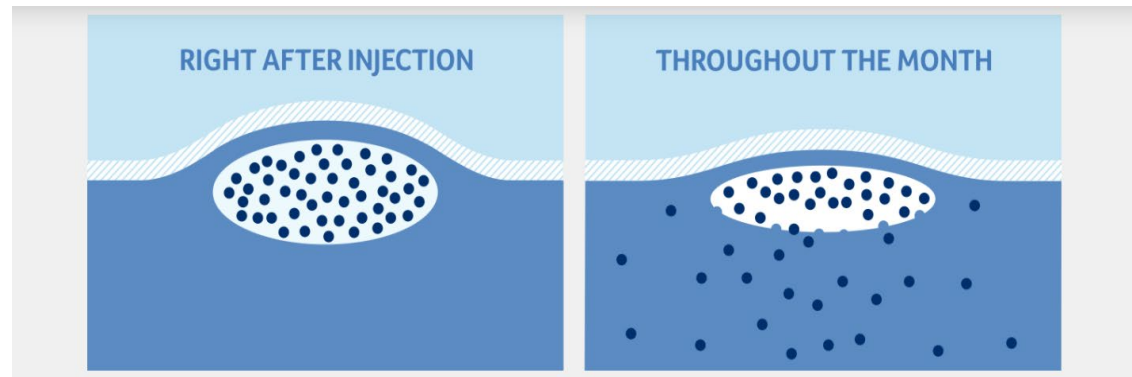
Take responsibility.

Embrace change.

MaineHealth

What is XRB?

- It is injected by a nurse/prescriber as a liquid and, once inside the body, turns to a solid gel. The depot gradually releases buprenorphine at a controlled rate. Pre-medicating the injection site with lidocaine and removing XRB from refrigerator in advance make the injection more comfortable.
- XRB is currently available in one formulation (option 1) that is injected into the abdomen every 28 days. It is available in a 300 mg and 100 mg dose. Patients are generally started on 300 mg. A second formulation (option 2) was recently approved by the US FDA and will be released in early September.



Act with
kindness and
compassion.

Be an active
listener.

Be a role
model.

Set high
standards.

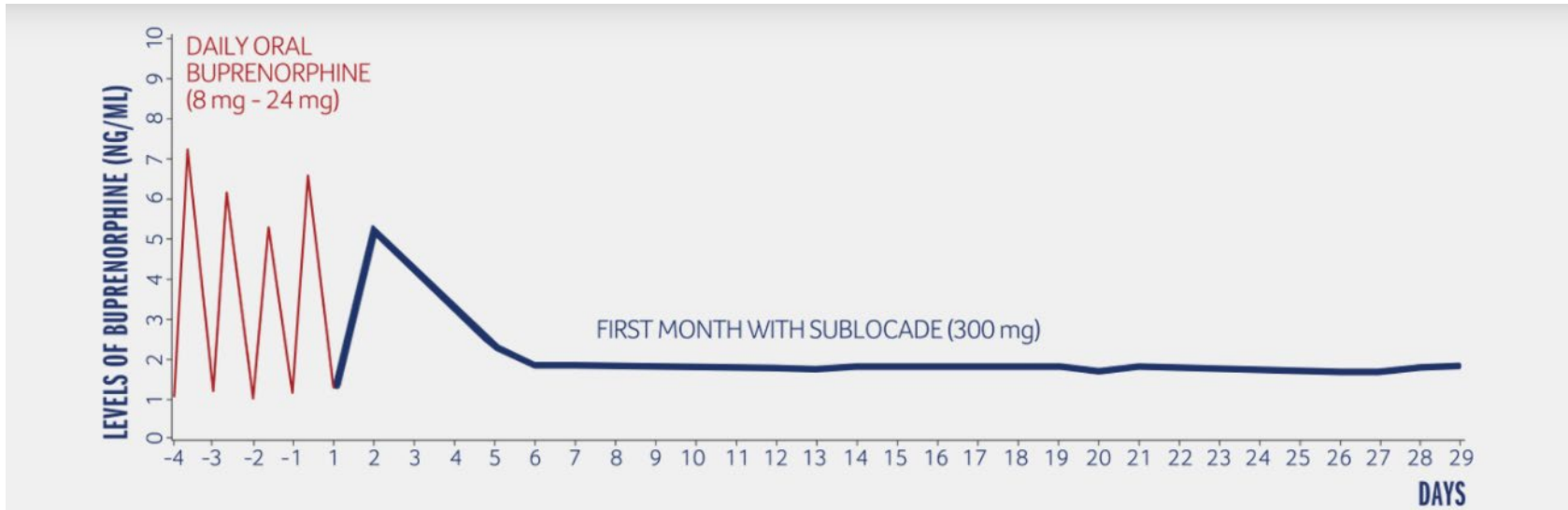
Take
responsibility.

Embrace
change.

MaineHealth

How does XRB work over time?

- Unlike the sublingual formulation, it results in a steady state serum level over time.



Act with kindness and compassion.

Be an active listener.

Be a role model.

Set high standards.

Take responsibility.

Embrace change.

MaineHealth

Risks/benefits of XRB

- The prescriber should discuss the risks/benefits of XRB with the patient prior to ordering the medication.
 - The most common side effects of XRB include constipation, headache, nausea, injection site itching, vomiting, increase in liver enzymes (may wish to order baseline LFTs in pregnancy to help differentiate potential preeclampsia later), tiredness, injection site pain. Lower extremity edema sometimes seen as well.
- Contraindications include patients who are opioid naïve, those with severe liver disease or renal impairment, and those who are hypersensitive to buprenorphine or any component of the ATRIGEL® delivery system.

Act with kindness and compassion.

Be an active listener.

Be a role model.

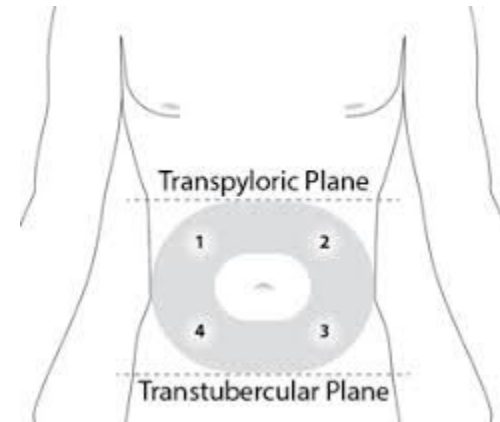
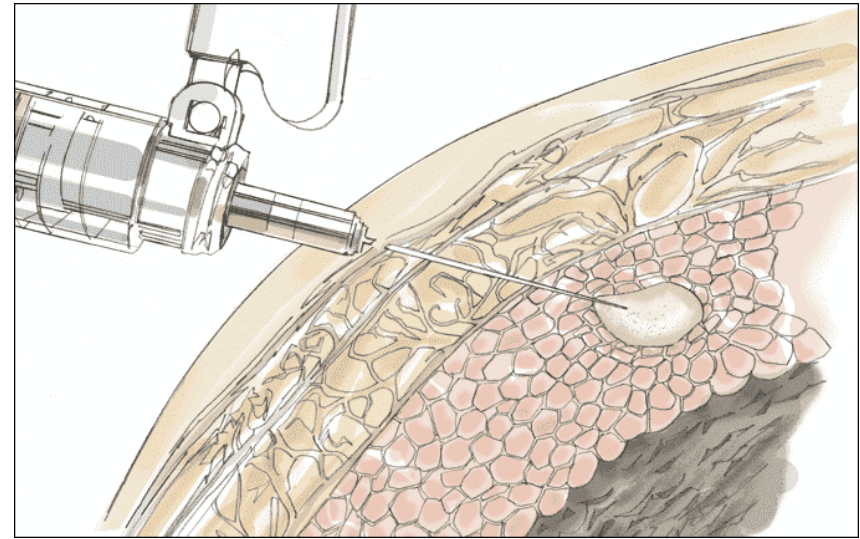
Set high standards.

Take responsibility.

Embrace change.

MaineHealth

XRB



Act with kindness and compassion.

Be an active listener.

Be a role model.

Set high standards.

Take responsibility.

Embrace change.

MaineHealth

Tools and resources

- A few logistical challenges:
 - Requires Risk Evaluation and Mitigation Strategy (REMS) certification.
<https://www.sublocaderems.com/#Main>
 - DEA license address must match delivery address. Likely simpler to use “buy and bill” than “white bagging.”
 - Like all other forms of buprenorphine for MOUD, no longer requires an X waiver per the MAT Act.
- MaineHealth XRB Toolkit:
 - [Long-Acting-Injectable-Buprenorphine-Toolkit.pdf \(mainehealth.org\)](#)
- Training Video:
 - [220502 PM Sublocade Injection - YouTube](#)



What about Mainecare coverage for XRB?

- Prior authorization required under pharmacy benefit or prescriber attestation under medical benefit that:
 - Member has documented history of OUD
 - XRB is being used for treatment of OUD
 - Member's total daily dose of sublingual buprenorphine is ≤ 24 mg daily
- AND any one of the following is true:
 - Previous use of sublingual buprenorphine included misuse, overuse or diversion
 - Difficulty keeping OUD treatment medications safe (e.g., unhoused)
 - Member is in ongoing treatment with XRB and would like to continue
 - Treatment resistant OUD (e.g., ongoing illicit substance use while on sublingual)
 - Significant intolerance of sublingual
 - Significant medical complications of OUD or injection drug use
 - High risk for overdose (e.g., leaving incarceration, potential gaps in care)

Act with
kindness and
compassion.

Be an active
listener.

Be a role
model.

Set high
standards.

Take
responsibility.

Embrace
change.

MaineHealth

What about pregnancy?

- Across the US, we are seeing an increased utilization of XRB in pregnant patients, particularly among high-risk individuals in rural settings with limited access to care.
- Providers are reporting considerable success in these patients, especially those who are having difficulty taking sublingual buprenorphine daily either because of tolerance issues, going “on and off” the medication as we often see early in recovery or because of access issues (e.g., pharmacy/transportation problems, unstable social situations).
- The use of XRB in pregnancy may be complicated as it can sometimes be hard to find the right dose. XRB is more of a “one size fits all” medication. Supplementing with sublingual may be required. Expect potential dose changes, most likely in the second trimester, because of pregnancy related metabolism changes.

Act with
kindness and
compassion.

Be an active
listener.

Be a role
model.

Set high
standards.

Take
responsibility.

Embrace
change.

What about pregnancy?

- If you are thinking about XRB during pregnancy, always good to step back and ask whether methadone is a good option.
- Until more is known, it is vitally important to consent patients to the potential risks of exposure to N-methyl-2-pyrrolidone (NMP).
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209819s000lbl.pdf
- In terms of administration, most providers report that they can still find subcutaneous tissue on the abdomen in pregnant patients but have gone lateral into the flank/lower waist (i.e., “love handles”) in pregnant patients with lower BMI.



Act with kindness and compassion.

Be an active listener.

Be a role model.

Set high standards.

Take responsibility.

Embrace change.

Implications at delivery

- Buprenorphine will remain in maternal serum for an extended period when utilizing XRB. A case report of two pregnant patients who opted to taper off were still positive 30 and 37 weeks after last injection.
- Infants still need to be monitored for neonatal opioid withdrawal syndrome for at least 5-days! Infant exposure to XRB in utero is no different than exposure to sublingual. Do not assume that pediatric providers are familiar with XRB.
- Likely still requires referral to CPS.
- Continue to monitor UDS. Likely impossible to determine whether patient is also using sublingual buprenorphine (monitor levels?).

Act with kindness and compassion.

Be an active listener.

Be a role model.

Set high standards.

Take responsibility.

Embrace change.

Option 2

Daily dose of sublingual buprenorphine	BRIXADI (weekly)	BRIXADI (monthly)
≤ 6 mg	8 mg	--
8-10 mg	16 mg	64 mg
12-16 mg	24 mg	96 mg
18-24 mg	32 mg	128 mg

- Weekly and monthly options (weekly option does NOT have NMP)
- More dosing options
- Does not require refrigeration and is a much smaller volume injection both of which likely reduce injection related discomfort. Premedicating with lidocaine likely not necessary.
- Can be given in sites other than the abdomen (thigh, buttocks, upper arm).
- Does not form a “bump” at the injection site and is more readily absorbed into the surrounding tissues.
- Rapid initiation.

Act with kindness and compassion.

Be an active listener.

Be a role model.

Set high standards.

Take responsibility.

Embrace change.

Ongoing questions

- Use during postpartum likely less controversial though it is not known whether NMP or its metabolites enter human breast milk.
- “Intoxication” after initial dose?
- Need to supplement with sublingual?
- Ongoing NIDA trial using the weekly injection in pregnant patients seems to be going well. Studying maternal and infant serum concentrations after exposure to XRB and concentrations in breastmilk which will hopefully inform future care.



Act with
kindness and
compassion.

Be an active
listener.

Be a role
model.

Set high
standards.

Take
responsibility.

Embrace
change.

References

- Cleary EM, Byron RK, Hinely KA, Talley AW, Costantine MM, Rood KM. Subcutaneous Buprenorphine Extended-Release Use Among Pregnant and Postpartum Women. *Obstet Gynecol.* 2020 Nov;136(5):902-903. doi: 10.1097/AOG.0000000000004126. PMID: 33030872; PMCID: PMC7771390.
- Coe MA, Lofwall MR, Walsh SL. Buprenorphine Pharmacology Review: Update on Transmucosal and Long-acting Formulations. *J Addict Med.* 2019 Mar/Apr;13(2):93-103. doi: 10.1097/ADM.0000000000000457. PMID: 30531584; PMCID: PMC7442141.
- Towers CV, Deisher H. Subcutaneous Extended-Release Buprenorphine Use in Pregnancy. *Case Rep Obstet Gynecol.* 2020 Jul 17;2020:3127676. doi: 10.1155/2020/3127676. PMID: 32724686; PMCID: PMC7382717.

Act with
kindness and
compassion.

Be an active
listener.

Be a role
model.

Set high
standards.

Take
responsibility.

Embrace
change.