

## Extended-Release Injectable Buprenorphine (Sublocade) Toolkit

1. [What Is Sublocade?](#)
2. [How To Set Up Your Program And Obtain Sublocade](#)
3. [Clinical Protocol For Storing And Administering Sublocade](#)
4. [Pregnancy Considerations](#)
5. [EPIC Tools](#)
6. [Appendix A – Lab And Point Of Care Standing Orders For Sublocade](#)
7. [Appendix B - Buprenorphine Extended Release \(Sublocade®\) Injection Order Form](#)
8. [Appendix C - SUBLOCADE REMS Program Information and Enrollment Form](#)

This toolkit is designed for use at any health system. If you have questions about the content or how to use these tools, please email the [MaineHealth Substance Use Training team](#).

## Section 1: What Is Sublocade?

Sublocade™ is the first, and currently only, once-monthly injectable buprenorphine product for the treatment of moderate-to-severe opioid use disorder in adult patients who have initiated treatment with a transmucosal buprenorphine-containing product. It is indicated for patients that have been on a stable dose of buprenorphine treatment for a minimum of seven days (FDA, 2017). Sublocade™ may only be prescribed by a physician or APP with an active buprenorphine X waiver.

Adult (18 years and older) candidates for Sublocade™ treatment include:

- a. Patients who have begun treatment on a transmucosal formulation of buprenorphine, delivering the equivalent of 8 to 24mg of buprenorphine daily for a minimum of 7 days AND
- b. Patients who have a history of non-adherence to daily formulations of buprenorphine OR
- c. Patients in sustained recovery utilizing a transmucosal formation of buprenorphine between 8 and 24mg daily, who would like to transition to a monthly injectable medication.

## Section 2: How To Set Up Your Program And Obtain Sublocade

What is the SUBLOCADE REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS is a strategy to manage known or potential risks associated with a drug, and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks. SUBLOCADE is intended for abdominal subcutaneous injection only by a healthcare provider. SUBLOCADE is available only through a restricted distribution program called the SUBLOCADE REMS Program because of the risk of serious harm or death that could result from intravenous self-administration.

What are the SUBLOCADE REMS Program requirements? Any pharmacy that dispenses SUBLOCADE as well as any healthcare setting (including a prescriber office) that purchases SUBLOCADE from a distributor must be certified prior to dispensing/purchasing SUBLOCADE. Prescriber offices that only order SUBLOCADE from a certified specialty pharmacy for a specific patient are exempt from certification.

Prescribers who are DATA 2000-waivered can obtain SUBLOCADE for their patients in two ways. Note that option A. below is preferred for MaineHealth

- A. By ordering SUBLOCADE directly through a distributor (“Buy and Bill”): To order SUBLOCADE through an authorized distributor, the healthcare setting in which you practice must first become certified.
  - a. To receive and store a supply of SUBLOCADE for a healthcare setting, all healthcare settings and pharmacies that dispense SUBLOCADE must:
    - i. Be certified in the SUBLOCADE REMS Program.
    - ii. Designate an “authorized representative” to complete the SUBLOCADE REMS Program Healthcare Setting and Pharmacy Enrollment Form and submit it to the SUBLOCADE REMS Program for certification.
    - iii. Train relevant staff involved in the dispensing of SUBLOCADE, to ensure that it is dispensed directly to a healthcare provider.
    - iv. Establish processes and procedures to verify that SUBLOCADE is dispensed directly to a healthcare provider. SUBLOCADE should never be dispensed directly to a patient.

If you are practicing in an office that is not on-site at a MaineHealth hospital with access to appropriate controlled substance storage and inventory, the best option is to obtain SUBLOCADE through an authorized distributor (eg. Besse, CuraScript, Henry Schein). Orders placed are not patient specific. An account is required to be set-up for each administering provider. Contact MaineHealth Supply Chain to assist with this set-up. Sublocade will be sent to the address where the provider’s X-DEA is set-up. Drug must be administered at same location where X-DEA is set-up.

- b. Hospital Site Option - If your practice is on-site at a MaineHealth hospital with access to appropriate controlled substance storage and inventory, talk with your local pharmacy leader about ordering options. Currently Maine Medical Center and Franklin Memorial pharmacy departments are registered with the REMS program to dispense Sublocade to clinics on-site as well as inpatients. Maine Medical Center uses Curascript.
- B. Through a certified pharmacy for a specific patient (sometimes referred to as “white bagging”\*):
  - a. In advance of the patient’s appointment, send a prescription for your named patient to a certified pharmacy. The certified pharmacy will send SUBLOCADE to either you (the prescribing practitioner) or the practitioner administering the controlled substance, as applicable, to administer it directly to that patient. SUBLOCADE should never be dispensed directly to the patient. It should be administered by a healthcare professional in a healthcare setting.
  - b. Your healthcare setting does not need to be certified in the SUBLOCADE REMS Program for you to administer SUBLOCADE to an individual named patient obtained through a certified pharmacy.
  - c. A list of certified pharmacies is appended to each mailing of the SUBLOCADE REMS Program Dear Healthcare Provider Letter. Additionally, the current list may be obtained on the SUBLOCADE REMS website or from the SUBLOCADE REMS Program at 1-866-258-3905.
  - d. This option can only be done on a case-by-case basis and needs to be approved by the Hospital Pharmacy Director.

#### For Rural Health Clinics:

Due to the fixed payment structure for government payors to Rural Health Clinics, obtaining Sublocade through a Buy and Bill option for these patients is a challenge. Reimbursement will not cover the cost of the medication. One option is to proceed through the “White Bagging” option described above. This would allow the provider to administer the medication directly in the office. Another possibility would be to work with your hospital pharmacy and infusion center to establish a workflow that would allow for a buy and bill option and have the patient receive their dose at the infusion center. MaineHealth is working with representatives from MaineCare on solutions to address this issue.

## Section 3: Clinical Protocol For Storing And Administering Sublocade

The following protocol was approved in 2020 at Maine Medical Center. It can be modified for use at any local health system.



### Buprenorphine Extended Release (Sublocade™) Protocol

**Purpose:** This protocol provides guidance for the administration of subcutaneous extended release buprenorphine (Sublocade™) for the treatment of opioid use disorder.

**Policy:** Sublocade™ is the first, and currently only, once-monthly injectable buprenorphine product for the treatment of moderate-to-severe opioid use disorder in adult patients who have initiated treatment with a transmucosal buprenorphine-containing product. It is indicated for patients that have been on a stable dose of buprenorphine treatment for a minimum of seven days (FDA, 2017). Sublocade™ may only be prescribed by a physician or APP with an active buprenorphine X waiver. This protocol reviews the informed consent of patients to whom Sublocade™ is being prescribed. It covers patient selection and preparation, as well as the ordering, storage and administration of the medication. Sublocade™ is approved for adults 18 and older.

## Procedures

### Informed Consent

1. The prescriber will discuss the risks, benefits and alternatives to Sublocade™ as a treatment for opioid use disorder.
2. Explain the risks of:
  - a. Overdose, especially if combined with other respiratory depressants like alcohol and benzodiazepines
  - b. Physical dependence and withdrawal
  - c. Allergic reaction
  - d. Decrease in blood pressure
  - e. Liver inflammation
  - f. Fertility problems (with any long term opioid therapy)
  - g. Common side effects, including constipation, nausea, headache, injection site itching or pain, vomiting, increase in liver enzymes, tiredness

3. Sublocade™ forms a solid mass upon contact with body fluids and therefore must be administered into subcutaneous tissue. Intravenous use of Sublocade poses a significant risk including occlusion, local tissue damage, thromboembolic events and death.
4. Because of the serious risk of harm or death from self-administering Sublocade™ into a vein (intravenously), it is only available through a restricted program called the SUBLOCADE™ REMS Program.
5. In an emergency, the patient must tell emergency medical staff that they are physically dependent on an opioid and are being treated with Sublocade™. Provider will inform patient of required lab work prior to injection (listed under Patient Selection and Preparation section).

## Patient Selection and Preparation

1. Adult (18 years and older) candidates for Sublocade™ treatment include:
  - a. Patients who have begun treatment on a transmucosal formulation of buprenorphine, delivering the equivalent of 8 to 24mg of buprenorphine daily for a minimum of 7 days AND
  - b. Patients who have a history of non-adherence to daily formulations of buprenorphine OR
  - c. Patients in sustained recovery utilizing a transmucosal formation of buprenorphine between 8 and 24mg daily, who would like to transition to a monthly injectable medication.
2. Contraindications include:
  - a. Patients who are opioid naïve
  - b. Patients with moderate to severe liver disease including acute hepatitis (LFTs >5x upper limits of normal) or decompensated cirrhosis.
  - c. Patients with moderate to severe renal impairment.
  - d. Patients with chronic or acute pain that require full-opioid analgesics.
  - e. Patients who have been shown to be hypersensitive to buprenorphine or any component of the ATRIGEL® delivery system.
3. Clinical staff will order the following lab work and point of care testing (see Appendix A):

### One Week prior to appointment

- liver and renal function tests (if not done within the prior 3 months)
- HIV Ag/Ab, Hep B surface Ag/core Ab/surface Ab, hepatitis C antibody testing with reflex to PCR. For patients with prior negative tests, but might have been exposed to HIV or viral hepatitis within the past 6 months, follow-up testing is recommended - check with provider.

### Day of appointment

- POC Urine drug screen-results must be positive for buprenorphine and negative for opioids

- Urine Pregnancy (HCG)

Provider will review results prior to the patient receiving Sublocade™.

## Medication Administration

### Obtaining Medication per REMS Program:

#### a. When ordering from MMC Pharmacy:

- Fill out MMC Sublocade Requisition Form signed prescription by provider with DATA 2000 waiver.
- Fax Sublocade form to number on form (Appendix B)
- Email Sublocade form to Controlled substance team
- Medication will be stored in the vault in the refrigerator at the pharmacy.
- On the day of administration designated staff will pick up from the pharmacy.
- Sublocade is placed in the lock box in the refrigerator in the medication room.
- Medication is removed prior to administration as detailed in this policy; be sure to keep medication locked in medication room while out of the refrigerator.

#### b. Buy and Bill through provider's X-DEA (preferred):

- Drug shipped from one of the specific specialty distributors (eg. Besse, CuraScript, Henry Schein). Orders placed are not patient specific. An account is required to be set-up for each administering provider. Contact MaineHealth Supply Chain to assist with this set-up.
- Drug will be sent to address where X-DEA is set-up. Drug must be administered at same location where X-DEA is set-up.
- Clinic address where X-DEA is set-up must register with the REMS program (<https://www.sublocaderems.com/>). A primary contact must be designated.
- Clinic is responsible for meeting all required security and storage requirements for the medication.
- Clinic will maintain ownership of the prior authorization and financial reimbursement.

#### c. Specialty Pharmacy Supplied (White Bagging):

- Provider writes an RX to one of the specific specialty pharmacies in the Sublocade network.
- Drug will be shipped from the Specialty Pharmacy to the address connected to the X-DEA.
- Clinic will still bill an administration fee.
- This option (white bagging) will require Pharmacy Director approval per policy.

## Dosing:

- a. Available dosage strengths:
  - 100 mg/0.5 mL
  - 300 mg/1.5 mL
- b. The recommended dose of injectable buprenorphine following induction and stabilization with transmucosal buprenorphine is 300mg monthly for the first two months, followed by a maintenance dose of 100mg monthly.
- c. While the majority of patients will be appropriate to receive 100mg maintenance doses, certain individuals may benefit from continued 300mg maintenance doses such as persons with: high daily opioid requirement, persistent toxicology screens positive for opioids, persistent opioid cravings, or other unsatisfactory clinical response
- d. Doses will be given no less than 26 days apart.
- e. A patient who misses a dose of injectable buprenorphine will receive the next dose as soon as possible.
- f. During clinical trials, delays in dosing up to 2 weeks did not have clinically significant treatment outcomes.

## Storage and Handling:

- a. Store refrigerated at 2 - 8°C (35.6 - 46.4°F). Once outside the refrigerator this product may be stored in its original packaging at room temperature 15 – 30°C (59 – 86°F), for up to 7 days prior to administration. Discard Sublocade™ according to the MMP Policy for Controlled Substance Handling if left at room temperature for longer than 7 days.
- b. Sublocade™ is a Schedule III drug product. Handle with adequate security and accountability. Please refer to MMP Policy for Controlled Substance Handling regarding the storage of controlled medications on site. Sublocade™ will be stored using a double locking system.
- c. After administration, syringes will be properly disposed, per facility procedure (MMP Policy for Pharmaceutical Waste Management and Disposal) for a Schedule III drug, and per applicable federal, state, and local regulations.

## Administration:

- a. Injectable buprenorphine will be stored in the refrigerator at 2 - 8°C (35.6 - 46.4°F). Prior to preparation, allow the drug to reach room temperature. This takes at least 15 minutes. Experience to date suggests removing the medication from refrigeration an hour prior to administration decreases patient complaints of discomfort with the injection. Once at room temperature, Sublocade™ will be discarded if left out for more 7 days.
- b. Each dose is provided in a prefilled syringe with a 19-gauge 5/8- inch needle

- c. Do not open the foil pouch or prepare the medication until the patient has arrived for his or her office visit.
- d. Patients will be advised not to take a morning dose of transmucosal buprenorphine on the day of injection.
- e. Sublocade™ will be administered by a licensed medical professional (RN, LPN, MD, DO, APP, RPh) following the specific detailed directions contained in the injectable buprenorphine medication package insert. Additionally, patients may be offered a subcutaneous dose of lidocaine without epinephrine (1-2 cc) into the area of injection prior to administration of Sublocade to minimize the burning sensation caused by the medication.
- f. Injectable buprenorphine will be administered as a subcutaneous injection between the transpyloric and transtuberular planes of the abdomen monthly with a minimum of 26 days between doses, rotating sites. Do not substitute any components of the carton.

**SPECIAL NOTES:**

- Sublocade™ ranges in color from clear, to yellow, to amber. Variations within this range do not affect safety or potency of the medication.
- Administer each injection only using the syringe and safety needle included with the product.
- It is recommended that the patient is in the supine position during administration.
- Do not inject intravenously or intramuscularly as Sublocade™ forms a solid mass upon contact with body fluids and therefore intravenous administration poses a significant risk including occlusion, local tissue damage, thromboembolic events and death.
- Many patients report a burning sensation during injection that resolves in about one minute.
- Advise the patient that they may have a lump for several weeks that will decrease in size over time.
- Do not rub the injection area after administering the injection. If there is bleeding, lightly apply a gauze pad or bandage, using minimal pressure.
- Instruct the patient not to rub or massage the injection site and to be aware of placement of belts or clothing waistbands.
- To avoid irritation, rotate injection sites. Record the location of the injection to ensure that different site is used at the time of the next injection.
- Dispose of all syringe components into a secure sharps disposal container.

**Removal of Depot:** In the event the depot must be removed, it can be surgically excised under local anesthetic within 14 days of injection. Only the most recent depot can be removed. The removed depot will be handled with adequate care and disposed of in red biohazard bins.

## Monitoring

- a. Patients starting on Sublocade™ will be seen at a minimum 2 weeks after the initial injection to evaluate their clinical response to the medication. A decrease in frequency of visits will be made at the discretion of the treatment team and is dependent on patient stability and response to treatment. While on Sublocade™ patients will be seen at least every 4 weeks, ideally occurring on the date of the next injection.
- b. LFTs will be checked at least monthly while patients are on the higher 300 mg dose due to increased risk of hepatic impairment. Once on the 100 mg dose, LFTs will be checked every 3-6 months.

## Documentation

Documentation in the electronic health record:

- Provider will order medication that is administered in the clinic.
- The clinical staff will document in the MAR including site of injection.

## Staff Training and Competency

Primary care clinical staff will be trained on applicable roles such as how to request from MMC, store, log, prepare and administer Sublocade™ by a qualified clinical staff member. Documentation of this training will be maintained.

**Definition:** Qualified Clinical Staff member – Medical Assistant, Licensed Practical Nurse, Registered Nurse

### MMC Policy Reference:

Institutional Standing Physician Orders

MMC Policy for Controlled Substance and Handling

MMP Policy for Pharmaceutical Waste Management and Disposal

### Original Date:

### Review Date:

Administrative Approval:

---

*Medical Director of Primary Care* *Date*

Administrative Approval:

---

*Chief Medical Officer* *Date*

## Section 4: Pregnancy Considerations

*Clinical Guidance from Alane O'Connor, DNP  
Director, MMC Perinatal Addiction Medicine*

In terms of its use in pregnancy, [Sublocade] is not approved for use but a prescriber may consider it in very high-risk situations (e.g., injecting transmucosal buprenorphine, when the patient has significant complications associated with drug use (endocarditis, etc.), or cases where patient is intermittently going without medication (missing many appointments) and/or is using significant amounts of illicit drugs). One of the solubility additives (N-Methyl-2-pyrrolidone) has been associated with adverse fetal outcomes in animal studies and potentially high dose frequent occupational exposure in pregnant women. So I would think carefully about that but, again, in situations where maternal overdose death risk was very high, I would certainly consider it. A once a week injectable formulation (currently called CAM2038, will be marketed as Brixadi) will likely be available later this year and it will not contain this additive.

Two helpful resources can be found here:

<https://pubmed.ncbi.nlm.nih.gov/32353544/>

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2017/209819s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209819s000lbl.pdf)

## Section 5. EPIC Tools

### Procedure Note:

The following smartphrase has been developed to help with documenting the administration of Sublocade

.SUBLOCADEINJ

After review of the risks, benefits and alternatives to Sublocade as a treatment for opioid use disorder, @FNAME@ agreed to proceed with Sublocade injection today. Recent labs including today's urine drug screen were reviewed prior to injection. The patient was placed in the supine position and the location of the injection was determined between the transpyloric and transtuberular planes of the abdomen. The area was cleansed with an alcohol pad and 1.5 cc of lidocaine without epinephrine was injected into the subcutaneous injection area. After waiting 2 minutes, Sublocade was injected at a 45 degree angle to the skin. The complete contents of the syringe were administered.

A band-aid was applied to the skin. The patient tolerated the injection well and was advised not to rub the site following the injection. @FNAME@ was advised that there may be a lump under the skin for several weeks which will decrease over time.

Dosage administered: 300 mg/1.5 ml OR 100 mg/0.5 ml

Location of injection:

### Patient Education:

The following smartphrase will add vetted and approved patient education to the After Visit Summary or MyChart message

.SUBLOCADEPATIENTEDUCATION

#### **Patient Medication Guide for Sublocade (SUB-lo-kade)**

Sublocade is a medicine used to treat adults with an addiction to opioids. It is part of a complete treatment plan that may include counseling and other supports.

#### **How is Sublocade given?**

Sublocade is injected just under the skin in your stomach (abdomen) area. You will receive this once a month. After each injection, you may see or feel a small bump under your skin. This is normal and the bump should get smaller over time.

If you notice this bump:

- Do not try to remove it
- Do not rub or massage it
- Try not to let belts or clothing waistbands rub against it

**Who should not have Sublocade?**

Buprenorphine, the medicine in Sublocade, can cause serious and life-threatening problems, especially if you take or use certain other medicines or drugs.

For your safety, you **MUST** tell your healthcare provider if you:

- Are allergic to the medicine buprenorphine
- Drink alcohol
- Take certain other medicines including:
  - anxiety medicines or benzodiazepines like Valium or Xanax
  - sleeping pills
  - tranquilizers
  - muscle relaxants or sedatives
  - antidepressants
  - antihistamines

Some medicines could cause death or serious harm when taken with Sublocade.

**Important information to know before starting Sublocade**

Tell your healthcare provider about all medicines and drugs that you currently take. This includes:

- Prescriptions
- Over-the-counter medicines
- Vitamins
- Herbal supplements

Tell your healthcare provider about all of your medical conditions, including:

- Trouble breathing or lung problems
- An enlarged prostate gland (men)
- A head injury or brain problem
- Problems urinating
- Liver problems
- Are breastfeeding or plan to breast feed
- Mental problems such as hallucinations (seeing or hearing things that are not there)
- A curve in your spine that affects your breathing (scoliosis)
- Adrenal gland problems
- Addison's disease
- Low thyroid hormone levels (hypothyroidism)
- A history of alcoholism
- Gallbladder problems
- Are pregnant or plan to become pregnant

**Things to avoid while taking Sublocade**

Do not drive, operate heavy machinery, or do any other dangerous activities until you know how you feel taking this medicine. Sublocade can make you sleepy and slow your reaction time.

Do not drink alcohol during treatment with this medicine.

Do not stop taking Sublocade without talking to your healthcare provider. If you stop taking it, you could have opioid withdrawal symptoms.

### **Possible side effects of Sublocade**

The most common side effects of this medicine include:

- Constipation
- Vomiting
- Headache
- Increased liver enzymes
- Nausea
- Tiredness
- Injection site itching
- Injection site pain

Long-term use of Sublocade may cause fertility problems in males and females.

Your body can develop a physical need (dependence) on this medicine. If you stop taking it, you could have opioid withdrawal symptoms.

These are not all the possible side effects of Sublocade. For more information, go to [www.sublocade.com](http://www.sublocade.com) or call 1-877-782-6966.

### **Other considerations when taking Sublocade**

In an emergency, you or your family should tell the emergency medical staff that you are being treated with Sublocade.

If a healthcare provider is considering prescribing medication for you, remind them that you are being treated with Sublocade.

You may have detectable levels of this medicine in your body for a long time after stopping treatment.

**If you are experiencing any issues related to your treatment or Sublocade, call your doctor.**

## Appendix A

### Lab and Point of Care Standing Orders for Sublocade™

#### Patient Qualifications:

- Patient scheduled to receive Buprenorphine Extended Release (Sublocade™):

Clinical staff will order at least 1 week prior to first injection:

- Lab order CMP (Lab17)
- HIV Ag/Ab, Hep B surface Ag/core Ab/surface Ab, hepatitis C antibody testing with reflex to PCR (For patients with prior negative tests, but might have been exposed to HIV or viral hepatitis within the past 6 months, follow-up testing is recommended - check with provider) (LAB11153, LAB471, LAB1242, LAB472, LAB 20314)

Day of injection:

- POC 717 (CLIA-WAIVED Urine Tox Cup)
- POC7 Urine Pregnancy(HCG) (only in females ages 18-55)

#### Electronic health record workflow:

- Associate order with one of the following diagnoses based on problem list
  - F11.20 - Opioid use disorder – severe – dependence
- Sign order  
Document in encounter: “Liver, renal function, viral serologies lab order per standing order protocol” and “Point of Care urine pregnancy and Urine Tox order per standing order protocol”
- Close encounter

Definition: Clinical Staff- Medical Assistant, Registered Nurse, Licensed Practical Nurse

Administrative Approval: \_\_\_\_\_  
*Medical Director of Primary Care* *Date*

Administrative Approval: \_\_\_\_\_  
*Chief Medical Officer* *Date*

# MaineHealth

## Buprenorphine Extended Release (Sublocade®) Injection Order Form

Fax orders to pharmacy at 207-662-6273 at least 3 days prior to the procedure.

### Patient Information:

Name: \_\_\_\_\_

DOB: \_\_\_\_\_ Date Needed: \_\_\_\_\_

Allergies: \_\_\_\_\_

Prescriber Name: \_\_\_\_\_ (print)

DEA: \_\_\_\_\_ Telephone Number: \_\_\_\_\_

### Buprenorphine Extended Release (Sublocade®) Injection

☐ 100 mg/0.5 ml                      Quantity \_\_\_\_\_

☐ 300 mg/1.5 ml                      Quantity \_\_\_\_\_

Directions: Use as directed. For Subcutaneous Use only

\_\_\_\_\_

Prescriber Signature

\_\_\_\_\_

Date

Staff from Adult Medicine Clinic will pick up from the Pharmacy on required date.

## Appendix C

### SUBLOCADE REMS Program Information And Enrollment Form

- [SUBLOCADE REMS Program Dear Healthcare Provider Letter](#)
- [SUBLOCADE REMS Program Fact Sheet: How to Obtain SUBLOCADE](#)
- [SUBLOCADE REMS Program Healthcare Setting and Pharmacy Enrollment Form](#)