Protocol for Use of Long-Acting Injectable Buprenorphine (LAI-BUPE)

Epic Smartphrases
BUPESTABLENEW
BUPELAICOUNSELING
BUPELAIPATIENTHANDOUT
BUPELAIPATIENTHANDOUTSPANISH
BUPELAIRX
BUPELAIRAPIDSTART
BUPELAIRAPIDHX
BUPELAIADMIN
BUPELAIAP

Patient Selection

- Consider offering LAI-bupe to all patients newly initiating or already receiving buprenorphine treatment.
    - Patients already receiving bupe may be interested if they:
        - Are struggling to keep/safeguard/take sublingual buprenorphine (SL bupe)
        - Don't want to have to think about bupe treatment on a daily basis
        - Are re-starting bupe and anxious about precipitated withdrawal
        - Are ready to taper off bupe
- Relative contraindications:
    - Pregnancy: not well studied. Consider having a risk/benefit conversation with patient
    - Hepatic impairment: per manufacturer, patients with pre-existing moderate-severe hepatic impairment not candidates.
        - In patients with pre-existing moderate-severe hepatic impairment:
            - Primary risk is reduced clearance, leading to sedation
            - Potential hepatotoxicity of buprenorphine is not well-established and is based on a small number of case reports
            - If patient already tolerating sublingual, likely to tolerate LAI bupe. Consider having a risk/benefit conversation with patient
        - If no prior LFTs completed, consider ordering prior to administering first dose
        - ***Note: If patient is already tolerating sublingual, likely to tolerate LAI-bupe Have a risk/benefit conversation with patient for shared decision making.***

Patient Counseling

- Consider counseling all patients, including those stable on sublingual bupe, about LAI-bupe **(Smartphrase: .BUPESTABLENEW)**
- Counsel patients about benefits and risks **(Smartphrase: .BUPELAICOUNSELING)**
    - Counsel about long-acting medication, opioid blockade for a week or one month.
    - For patients not already on SL bupe, withdrawal symptoms are the primary risk.
        - Withdrawal symptoms generally occur during first 24-48 hours
        - Usually mild-moderate, rarely severe withdrawal
        - **Important! If initiating with COWS ≤ 4, patients should use their own opioid supply during the initiation (see flow diagram)**
        - Supportive meds will be prescribed: clonidine, loperamide, low-dose benzodiazepines
        - SL bupe should NOT be used until 24 hours after the injection
- Side effects
    - Primary side effects: Pain, redness, itching at injection site.
    - Potential for sedation in 48 hours after first injection (particularly with Sublocade and in geriatric patients and/or patients with low opioid tolerance)
    - Otherwise, same side effects as sublingual bupe
- Can give patient handout: (**Smartphrase: .BUPELAIPATIENTHANDOUT, .BUPELAIPATIENTHANDOUTSPANISH)**

Formulation selection (Sublocade vs. Brixadi)

- Decision is based on clinical judgment.
    - **Brixadi advantages**
        - Smaller needle

        - Smaller medication volume→smaller lump under skin
        - Less painful injection
        - Easy equivalency to SL bupe
        - Weekly and monthly formulations

    - **Sublocade advantages**
        - Higher plasma concentrations at maximum dosing (300 mg monthly)

Medication Prescribing (Smartphrase: .BUPELAIRX)

- Note: Buprenorphine prescriber's DEA license clinic address must match medication delivery address
- **Medicaid plans**: E-prescribe LAI-bupe to:
    a. Specialty Pharmacy
        i. Write in "Notes to Pharmacy":
            1. Medicaid member ID #
            2. Injection appt date. (*Appt information is so that pharmacy rep doesn't need to call patient*)
            3. Please deliver by: *date*
            4. Deliver to *Address* + *Point person*
        ii. Medications can be delivered for next business day with overnight shipping (plan for 2 days)
        iii. **Note: If ordering from *Specialty Pharmacy* for first order of the medication, email *point person's email* after sending the prescription for communication about any insurance processing**
            1. For subsequent ordering of the medication, emailing *Specialty Pharmacy* is not necessary
    b. No PA required for Medicaid plans

- **Non-Medicaid insurances**:
    a. CVS Specialty Pharmacy
    b. Accredo Health Group
    c. Other Specialty pharmacies
    d. Write in "Notes to Pharmacy":
        i. Medicaid member ID #
        ii. Injection appt date
        iii. Please delivery by: *date*
        iv. Deliver to *Address* + *Point person*
    e. Usually pharmacy will need to call patient to confirm that patient wants medication before billing and delivery

- **Refills:** Specialty pharmacies will **NOT** automatically ship refills.
    - **Best practice is to order the next dose during the patient's injection appointment:**
        - After medication is administered in clinic, the physician for encounter can click refill under the "Plan" tab and then to "Med Management" section.
        - Once refill is clicked, please change the appointment and delivery dates in the instructions to the pharmacy, the rest of the instructions do not need to be changed.
        - Confirm that the specialty pharmacy is selected prior to ordering the refill
    - Subsequent communications are not needed with the specialty pharmacy unless medications have not been delivered or there are other concerns about the insurance (i.e. change in insurance)

Site-specific communication guidance:

- Email *Contact person* with: 1) Patient name & MRN; 2) Date LAI bupe ordered; 3) Specialty pharmacy Rx sent to; 4) Injection appt. date.

Medication Delivery and Storage

- RN/LPN/PharmD should document arrival date of medication and place in double-lock lockbox for controlled medications.
- Medications received should be documented on paper log with dose and date received, medications within lockbox should be counted twice daily by nursing staff using this physical log.
- Nurse leader will email or EPIC telephone note ordering provider when medication arrives and clinic excel spreadsheet should be updated according to clinic specific workflow.
- Note: Brixadi should be stored at room temperature. It should NOT be refrigerated. Sublocade can be stored at room temperature for 12 weeks, after which should be discarded if not used. Otherwise, can be refrigerated until expiration date.

Dosing and initiation

- **See Rapid LAIB start algorithm below (Brixadi and Sublocade)**
  - **Please use Smartphrase .BUPELAIRAPIDHX to document pertinent history for patients not already on sublingual buprenorphine.**
- **Sublocade dosing**
  - A single dose of sublingual buprenorphine is recommended before administering the injection, per package insert. Thus, Sublocade is generally not used to initiate when COWS≤4 due to increased risk of precipitated withdrawal with sublingual formulation.
  - First injection is 300 mg
  - Subsequent injections are either 100 mg or 300 mg administered **one week later**. Recommend continuing 300 mg monthly for patients with very high opioid tolerance.
  - Requires 4-6 injections to reach steady state

Medication Administration:

- Buprenorphine provider
  - Place clinic administration order.
    - For Sublocade: Place Sublocade in clinic administration order (specify if 100mg or 300mg dosing).
    - For Brixadi: Place Brixadi in clinic administration order (confirm and specify dosing)
- RN/ LPN/Other provider administering
  - **Prior to injection, consider pre-treatment with options below**
    - Ice
    - Ethyl chloride spray
    - Topical or intradermal lidocaine (especially for Sublocade given larger needle and medication volume)
  - RN/LPN administers LAI-buprenorphine to patient and documents the administration in Epic. Administrations are all SUBCUTANEOUS.
  - Follow administration instructions from the package insert, which can also be found at the end of the protocol.
  - Additional video demonstration can be accessed here: https://www.youtube.com/watch?v=cBNLabyxNbM

Post-Injection:

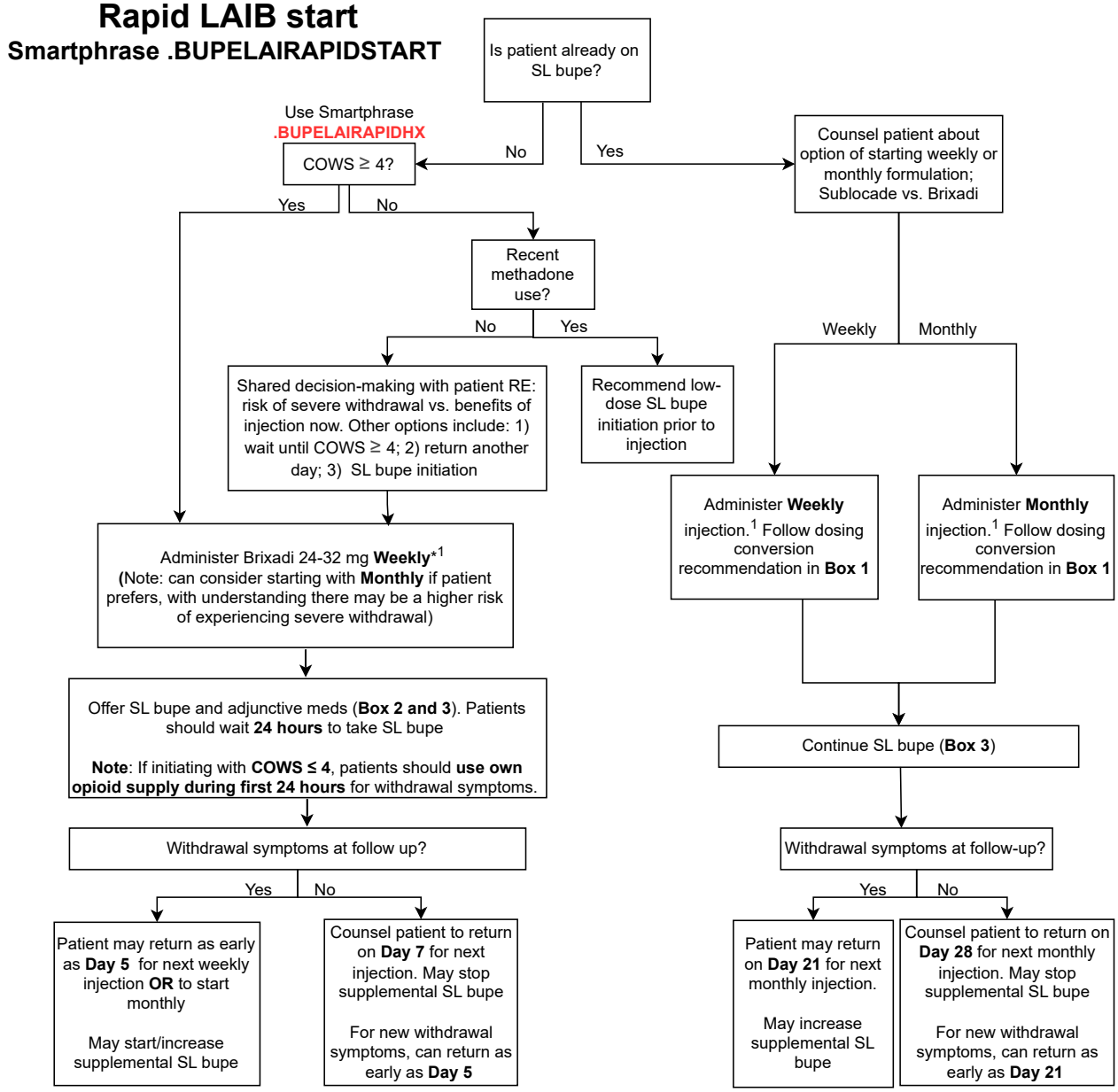
- No special monitoring is required post administration. Can provide cold pack post injection to aid in post injection site pain. Can monitor for ongoing withdrawal with COWS and provide supportive medications as needed.

Follow-Up:

- When scheduling follow-up please note the following
    - **Weekly dosing**: patient may return as early as 5 days after the last injection
    - **Monthly dosing**: patient may return as early as 21 days after the last injection
- **It is our policy to prescribe supplemental SL buprenorphine as LAI bupe needs multiple injections to reach steady state and to be optimally effective.**
    - Insurance typically approves supplemental prescriptions.

Rapid LAIB start

Smartphrase .BUPELAIRAPIDSTART



Box 1: Sublingual to LAI dose conversion

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

Box 2: Adjunctive medications:

Purpose: Treat withdrawal during 24-48 hours after Brixadi administration.

Medications:

Clonidine 0.1 mg tablets, 6 tablets
Lorazepam 1 mg tablet, 6 tablets
Zofran 8 mg, 4 tablets
Other: Acetaminophen/NSAIDs, Loperamide

* Consider **16 mg injection** if patient not regularly using fentanyl, low-opioid tolerance, and/or age>=65; Consider **24 mg injection** if patient using 2 bags or less fentanyl daily

Box 3: Supplemental SL bupe

Dosing

- For patients NOT on SL bupe:
  - Provide 8-16 mg SL bupe daily x 1 week, explain they may not need it
  - Encourage them to **WAIT** to take it until 24 hours after *weekly* injection or 8-12 hours after *monthly* injection administered to avoid precipitated withdrawal.
  - At follow up, can increase or decrease according to symptoms
- For patient on SL bupe: ensure patient has their previous SL dose x1 week but encourage them to take half or less (i.e. if patient on 16 mg daily, encourage starting with 8 mg daily)

Duration

- Reassess one week after injection whether they require additional SL bupe
- Some patients may require supplemental SL bupe until steady state is reached (i.e. after 4-6 injections)

[1]Do NOT give weekly Brxiadi injections in arm until steady state has been reached (after 4-6 injections). Monthly injections okay.

Missed doses

- For missed dose of **weekly**:
    a. Patients not yet at steady state (received fewer than 4-6 injections):
        i. **10-12 days** since last injection: Give injection
        ii. **13-20 days** since last injection: Shared decision making: Give injection vs. Reinitiate per quick-start algorithm
        iii. **21 or more days:** Reinitiate per quick-start algorithm
    b. Patients at steady state (received 4-6 injections):
        i. **10-20 days** since last injection**:** Give injection
        ii. **21-30 days**: Shared decision making: Give injection vs. Reinitiate per quick-start algorithm
        iii. **31 or more days:** Reinitiate per quick-start algorithm
- For missed dose of **monthly**:
    a. Patients not yet at steady state (received fewer than 4-6 injections):
        i. **4-6 weeks** since last injection**:** Give injection
        ii. **6-8 weeks** since last injection**:** Shared decision making: Give injection vs. Reinitiate per quick-start algorithm
        iii. **>8 weeks:** Reinitiate per quick-start algorithm
    b. Patients at steady state (received 4-6 injections):
        i. **4-12 weeks** Since last injection: administer injection
        ii. **12-16 weeks:** Shared decision making: Give injection vs. Reinitiate per quick-start algorithm
        iii. **>16 weeks:** Reinitiate per quick-start algorithm

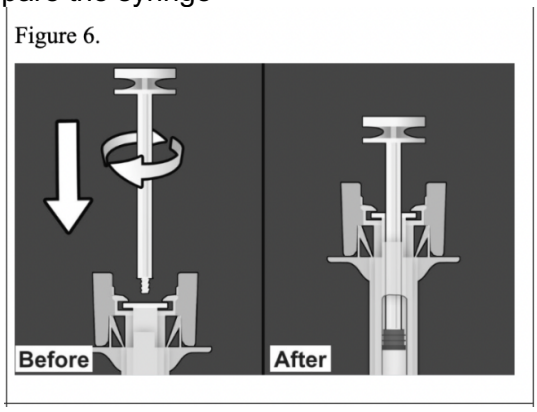
Tapering

- LAI formulation is self-tapering: It is possible to give even a single dose of monthly and it will self-taper without the patient experiencing withdrawal symptoms.
- Develop an individualized plan with patient for tapering, based on their preferences and timeline (limited data to support one option over another). Options include:
    a. Administer just 1-2 monthly injections then stop.
    b. Administering 4 injections to reach steady state then stop.
    c. Gradually decrease dose of monthly (i.e. 128 mg→96 mg→64 mg→stop)
    d. Gradually increase time between injections: 6 weeks→8 weeks→12 weeks→stop
- Schedule periodic check-ins to ensure patient not experiencing cravings or withdrawal symptoms.

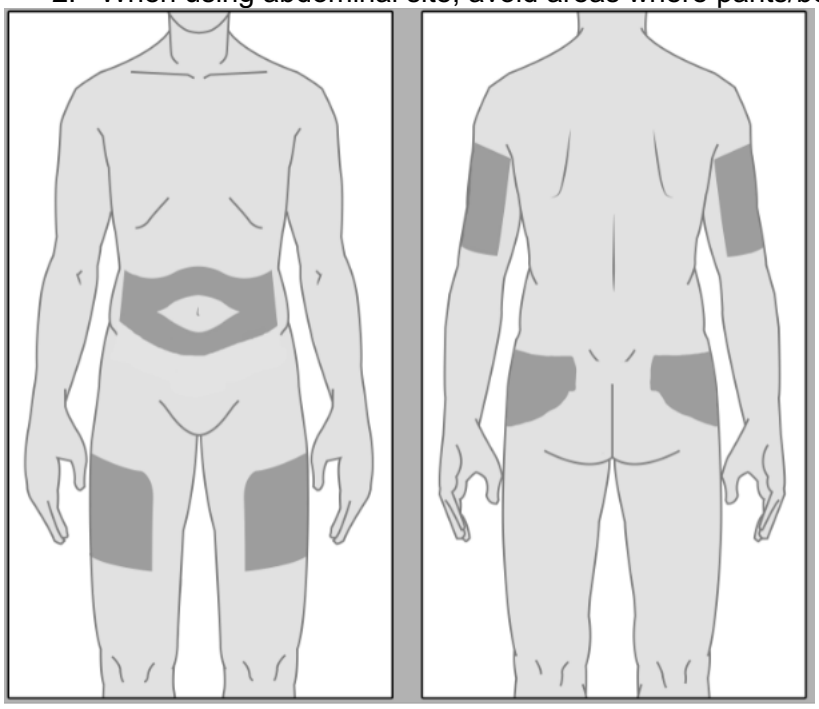
Medication Disposal: Please dispose of expired medications according to Institutional policies.

<u>Brixadi administration instructions</u> (Smartphrase: .BUPELAIADMIN)

- Buprenorphine provider places Brixadi order in Epic
- RN/ LPN administers Brixadi to patient and documents the administration in Epic.
- Follow administration instructions from the package insert, which can also be found here (starting on page 8)
    a. Highlights from instructions:
        i. Prepare the syringe



        ii. Site selection
            1. Do NOT use upper arm for **weekly** injection until at least 4 injections have been given (steady state reached) due to worse absorption. **Okay to use all sites for monthly.**
            2. When using abdominal site, avoid areas where pants/belt will rub

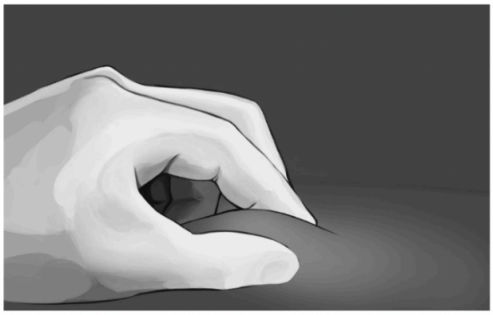


iii. Giving the injection

Step 6:

Pinch the skin at the injection site between your thumb and index finger as shown in Figure 8.

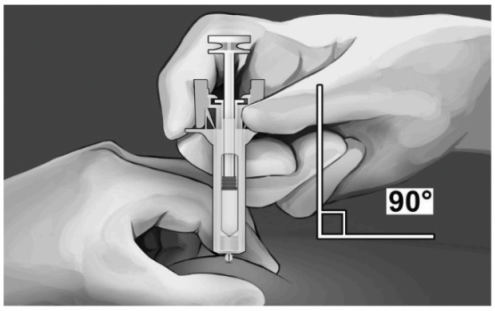
Figure 8.



Step 7:

Hold the syringe, as shown, and insert the needle at an angle of approximately 90° (see Figure 9). The needle is designed to inject into the subcutaneous space. It is important to fully insert the needle.

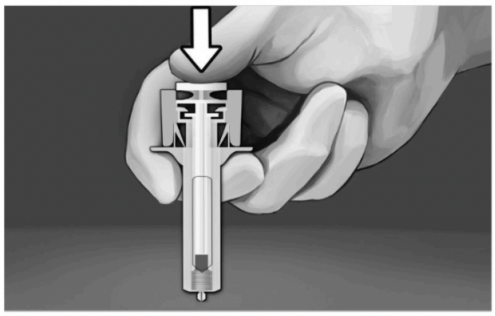
Figure 9.



Step 8:

- After the needle is completely inserted into the subcutaneous tissue, release the skin that you are grasping. Slowly press down the plunger head until it latches in the safety device 'wings' (see Figure 10). This will ensure that all of the medication has been injected.
- **Keep the plunger pressed fully down while you hold the safety syringe in place for an additional 2 seconds.**

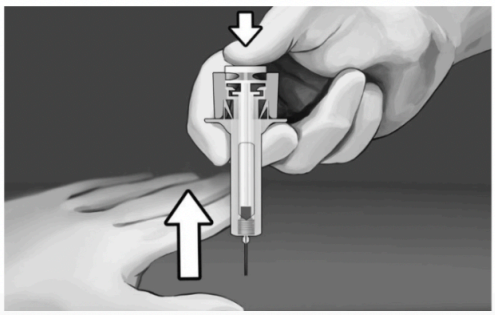
Figure 10.



Step 9:

- Gently pull the needle out of the skin.
- Keep the plunger fully depressed while you carefully lift the needle straight out from the injection site (see Figure 11).

Figure 11.



iv. If there is blood from injection site, press a cotton ball or gauze on the site. Do NOT rub injection site.

v. Can administer ice after injection

Sublocade administration instructions

Full Prescribing Information: https://www.sublocade.com/Content/pdf/prescribing-information.pdf
FDA Medication Guide: https://www.sublocade.com/Content/pdf/medication-guide.pdf

Sublocade Administration Instruction Video: https://www.sublocadehcp.com/resources

---

Sublocade Administration: (See pictures below)

(*Pictures taken from Sublocade prescribing information)*

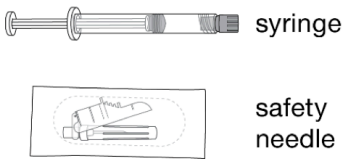
- Sublocade should only be prepared and administered by a trained health care provider
- Remove Sublocade from the refrigerator prior to administration. The product requires at least 15 minutes to reach room temperature. Do not open the foil pouch until the patient is ready for their injection.
    - Product can also be stored for up to 12 weeks at room temperature.
- Application of an ice pack to the injection side for 15 minutes prior to administration can decrease injection pain.
- Patients can also be offered topical anesthetic with lidocaine or EMLA if needed.
- Each dose is provided in a prefilled syringe with a safety needle
- Note: LAIB ranges in color from clear, to yellow, to amber. Variations within this range do not affect safety or potency of the medication.
- DO NOT administer intravenously or intramuscularly
- It is recommended that the patient receive **LAIB subcutaneously in the abdomen, thigh, buttock, or back of the upper arm.**
- 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.
- Record the location of the injection to ensure that a different site is used at the time of the next injection.
- For abdominal subcutaneous injection only. Log LAIB administration in the health record of the patient, noting the site of injection to avoid duplicate injections

STEP 1: GETTING READY

Remove the foil pouch and safety needle from the carton. Open the pouch and remove the syringe.

Discard the oxygen absorber pack. It is not needed.

Figure 1

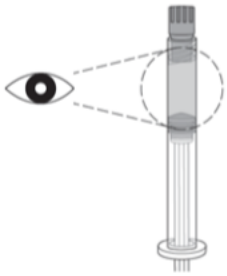


STEP 2: CHECK THE LIQUID CLARITY

Check that the medication does not contain contaminants or particles. SUBLOCADE ranges from colorless to yellow to amber. Variations of color within this range do not affect the potency of the product.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Figure 2



STEP 3: ATTACH THE SAFETY NEEDLE

Remove the cap from the syringe and the safety needle supplied in the carton from its sterile package.

Gently twist the needle clockwise until it is tight and firmly attached.

Do not remove the plastic cover from the needle.

Figure 3

STEP 4: PREPARE THE INJECTION SITE

Choose one of the following body regions for subcutaneous injection (see Figure 4):

- Abdomen between the transpyloric and transtubercular planes
- Back of the upper arm
- Buttock
- Thigh

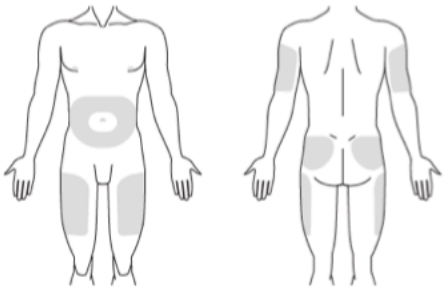
Ensure that the selected injection site has adequate subcutaneous tissue that is free of skin conditions (e.g., nodules, lesions, excessive pigment).

Do not inject into an area where the skin is irritated, reddened, bruised, infected or scarred in any way.

To avoid irritation, rotate injection sites.

Clean the injection site well with an alcohol swab.

Figure 4



STEP 5: REMOVE EXCESS AIR FROM SYRINGE

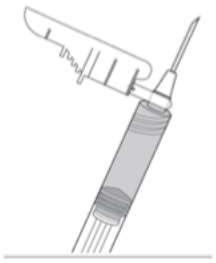
Hold the syringe upright for several seconds to allow air bubbles to rise. Due to the viscous nature of the medication, bubbles will not rise as quickly as those in an aqueous solution.

Remove needle cover and slowly depress the plunger to push out the excess air from the syringe.

- Small bubbles may remain in the medication. Large air gaps, however, can be minimized by pulling back on the plunger rod to pop air bubbles prior to expelling the air very slowly. Air should be expelled very carefully to avoid loss of medication.

If medication is seen at the needle tip, pull back slightly on the plunger to prevent medication spillage.

Figure 5



STEP 6: PINCH THE INJECTION SITE

Pinch the skin around the injection area. Be sure to pinch enough skin to accommodate the size of the needle. Lift the adipose tissue from the underlying muscle to prevent accidental intramuscular injection.

Figure 6

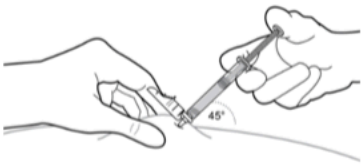
STEP 7: INJECT THE MEDICATION

SUBLOCADE is for subcutaneous injection only. Do not inject intravenously, intramuscularly, or intradermally *[see Warnings and Precautions (5.1, 5.6)]*.

Insert needle fully into the subcutaneous tissue. Actual angle of injection will depend on the amount of subcutaneous tissue.

Use a slow, steady push to inject the medication. Continue pushing until all of the medication is given.

Figure 7



STEP 8: WITHDRAW THE NEEDLE

Withdraw the needle at the same angle used for insertion and release the pinched skin.

Do not rub the injection area after the injection. There may be a small amount of blood or fluid at the injection site; wipe with a cotton ball or gauze before applying a gauze pad or bandage using minimal pressure.

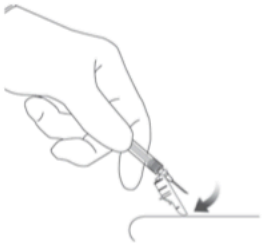
Figure 8

STEP 9: LOCK THE NEEDLE GUARD AND DISCARD THE SYRINGE

Lock the needle guard into place by pushing it against a hard surface such as a table (Figure 9).

Dispose of all syringe components in a secure sharps disposal container.

Figure 9



STEP 10: INSTRUCT THE PATIENT

Advise the patient that they may have a lump for several weeks that will decrease in size over time. Instruct the patient not to rub or massage the injection site and to be aware of the placement of any restrictive clothing, such as belts, waistbands, or sleeves.