Injectable Buprenorphine (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)

For the most up to date information regarding Sublocade:

Full Prescribing Information: https://www.sublocade.com/Content/pdf/prescribing-information.pdf

FDA Medication Guide: https://www.sublocade.com/Content/pdf/medication-guide.pdf

For information about ordering Sublocade: https://www.insupport.com/specialty-product

Dosing

Available dosage strengths:

- 100 mg/0.5 mL
- 300 mg/1.5 mL

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.

- 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
- Doses should be given no less than 26 days apart.
- A patient who misses a dose of injectable buprenorphine should receive the next dose as soon as possible.
    - During clinical trials, delays in dosing up to 2 weeks did not have clinically significant treatment outcomes.

Safety

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, thrombolytic events and death.

Sublocade is available only through the SUBLOCADE REMS Program or specialty pharmacy due to the risk of serious harm that could result from intravenous self-administration.

Notable requirements of the SUBLOCADE REMS Program include:

- Certified Healthcare Settings and Pharmacies must establish processes and procedures to verify that Sublocade is provided directly to healthcare providers for administration by a healthcare provider, and that the drug is never dispensed to or handled by the patient.

- Certified Healthcare Settings and Pharmacies must not distribute, transfer, or sell Sublocade.

- Further information is available at www.SublocadeREMS.com or call 1-866-258-3905.

Storage and Handling

Injectable buprenorphine is a Schedule III medication. Handle with adequate security and accountability per federal and state regulations, as well as institutional protocols.

- Medication must be stored in a locked refrigerator unit.
- A logbook of injectable buprenorphine inventory and dispensing will be kept in the locked medication room.
- The receipt and administration of injectable buprenorphine will be documented in the logbook by two licensed providers.
- The inventory of the logbook will be audited on a regular (i.e. weekly) basis to verify completion of entries and appropriate stock of medication.
- All records related to controlled substances must be maintained and be available for inspection for a minimum of two years.
- It is highly recommended to contact your institutional legal and pharmacy teams to assist with establishing protocols for storing, dispensing, and documenting use of injectable buprenorphine.

Unrefrigerated, injectable buprenorphine can be stored at temperatures not exceeding 30 °C (86 °F) for no more than seven days prior to administration.

- Mark the medication each time it is removed and returned to the refrigerator.
- Discard Sublocade if left at room temperature for longer than 7 days.

Medication Disposal

A practitioner may dispose of out-of-date, damaged, or otherwise unusable or unwanted controlled substances by transferring them to a registrant who is authorized to receive such materials. These registrants are referred to as “Reverse Distributors.” The practitioner should contact the local DEA field office for a list of authorized Reverse Distributors. Copies of the records documenting the transfer and disposal of controlled substances must be maintained for a period of two years.

Injectable Buprenorphine: Patient Selection

Candidates for Treatment with Injectable Buprenorphine Include 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.
    - 8mg equivalents include: one 8-2mg SUBOXONE® (buprenorphine/naloxone) film, one 8-2mg sublingual buprenorphine-naloxone tablet, one 8mg buprenorphine-mono tablet, or one 5.7-1.4mg Zubsolv® (buprenorphine/naloxone) tablet.
- Patients who have a history of non-adherence to daily formulations of buprenorphine
- 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.

Contraindications:

× Patients who are opioid naïve

× Patients with advanced liver disease or acute hepatitis (LFTs >5x upper limits of normal).

× Patients with moderate to severe renal impairment.

× Patients with chronic or acute pain that requires full-opioid analgesics.

× Patients who have been shown to be hypersensitive to buprenorphine of any component of the ATRIGEL® delivery system.

Checklist: Prior to Monthly Buprenorphine Injection

✓ Treatment agreement and consents are reviewed and signed.

✓ Reinforce to patient the need for frequent appointment adherence, and establish whether this is realistic. If patient states it is not manageable, this needs to be addressed with the team prior to initiating treatment.

✓ Patients must be on an equivalent of 8mg – 24mg of transmucosal buprenorphine for at least one week prior to receiving the extended-release subcutaneous injection.

- This is to mitigate risk of precipitated withdrawal, allergic reactions, over-sedation, side effects, adverse reactions or any other intolerance of the medication.

- Verify that patients have tolerated and are dose adjusted on transmucosal buprenorphine before administering injectable buprenorphine.

- Toxicology screen completed and reviewed by OBAT team.

✓ Pregnancy test for women of childbearing age.

- If positive HCG, OBAT team will assist patient engagement with appropriate OB providers and will manage the patient in OBAT until a warm handoff occurs.

✓ Patient is approved for treatment with injectable buprenorphine by waivered provider.

✓ NCM consults with waivered provider, obtains the prescription from the waivered provider and reviews the injection plan.

✓ NCM coordinates with pharmacy delivery of injectable buprenorphine (Sublocade) to locked medication refrigerator in clinic.

✓ NCM reviews details of injection appointment with patient including date, time, location, expectations.

INJECTABLE BUPRENORPHINE ADMINISTRATION

- Obtain injectable buprenorphine from pharmacy per written prescriber order. The recommended dose of injectable buprenorphine is 300mg monthly for the first two months, followed by a maintenance dose of 100mg monthly.

- Injectable buprenorphine should be stored in the locked 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.

    - When removing the medication from the locked refrigerator, the healthcare provider must appropriately document its removal in the designated medication log.
    - Each dose is provided in a prefilled syringe with a 19 gauge 5/8- inch needle
    - Do not open the foil pouch or prepare the medication until the patient has arrived for his or her office visit.

- Patients should be advised not to take a morning dose of transmucosal buprenorphine on the day of injection.

- After meeting with the patient and ensuring appropriateness for injectable buprenorphine, the healthcare provider (i.e. NCM) then prepares and administers medication, following the specific detailed directions contained in the injectable buprenorphine medication package insert.

    - Appropriate patients:
        - Have a recent UTS available that is positive for buprenorphine
        - Are not currently sedated or under the influence of other substances.

- Injectable buprenorphine should be administered as a subcutaneous injection between the transpyloric and transtubercular planes of the abdomen monthly with a minimum of 26 days between doses. 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.

- Subcutaneous injection to occur between the transpyloric and transtubercular places of the abdomen.

    - 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, thrombolytic events and death.

    - Only healthcare providers should prepare and administer Sublocade

- 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.

- Advise patient to contact the OBAT clinic, or go to the Emergency Department in the event of suspected injection site or other adverse reaction.

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 should be handled with adequate care as this is a biohazardous material as well as a Schedule III substance.

Injectable Buprenophine (Sublocade) Maintenance

- Once stable, clinic visits every two to four weeks.
- ***Goal:*** Clinic visits every 28 days, occurring on the date of the patient's buprenorphine injection.
    - Each decrease in visit frequency requires treatment team review.

Clinic Visits to Include (See Appendix 6: Nursing Follow-up Form):

- Collection of sample for toxicology screening.
- Check injection site for signs or irritation or attempts of tampering to remove the depot.
- Assessment of status: recovery, relapse, and medical, social and psychiatric issues should be addressed as indicated.
- Monitor and assess for potential medication side-effects or adverse reactions: injection site reaction, hepatic complications, gastrointestinal distress, etc.
- Review of treatment plan: visit frequency, counseling, assess need for additional support.
- If there is a history of risky alcohol use, address concerns with patient, consider use of breathalyzer at each visit.
    - Acamprosate (Campral) and disulfiram (Antabuse) may also be offered to patients with problematic alcohol use with provider input and agreement.
- Lab testing: if liver function tests were elevated at induction, consider rechecking within one to two months or sooner depending on degree of elevation. Continue to regularly monitor LFTs thereafter.
- Coordinate care with other OBAT team members as needed, including OBAT provider and PCP if different and warranted.
- Review contact information at each visit.
- OBAT provider visits at least every three to four months
- In addition to office visits, OBAT NCM performs telephone contact for support as needed.

BUPRENORPHINE DISCONTINUATION

- A substance use disorder is a chronic and complex health condition, therefore enforcing a predefined treatment duration is not recommended nor is it advised.

- Some patients may choose to taper off of or discontinue buprenorphine treatment. These patients will continue to be supported by the OBAT team and receive assistance with dose adjustments and management of withdrawal symptoms. The taper duration is individualized to the patient and should be continually adjusted to meet the patient's needs.

- If injectable buprenorphine (Sublocade) is discontinued, its extended release qualities should be considered and the patient should be monitored for several months for signs and symptoms of withdrawal and treated appropriately.

    - Of note, after a steady-state has been achieved (which per clinical trial data occurs following 4-6 months of treatment), patients who discontinue Sublocade may have detectable plasma levels of buprenorphine for twelve months or longer. The correlation between plasma levels and urine levels is not known.

Resources:

FDA (2017). FDA approves first once-monthly buprenorphine injection, a medication-assisted treatment option for moderate-to-severe opioid use disorder. Retrieved 1/23/2019 from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm587312.htm

Indivior (2018) Sublocade Prescribing Information. Retrieved 1/22/2019 from: https://www.sublocade.com/Content/pdf/prescribing-information.pdf