QUESTIONS?

Given the complex nature of starting an injectable buprenorphine formulation especially in the age of fentanyl, alternative strategies have been utilized in several case studies to demonstrate potential use of this formulation, especially in those who are not stable on sublingual buprenorphine for at least 7 days. For individualized "in-the-moment" consultation regarding specific patient cases, please contact the COE clinical hotline at 1-844-HELP-OUD. For non-urgent questions, please reach out to your respective COE:
Northern COE: coe@njms.rutgers.edu
Southern COE: southernnjcoe@rowan.edu

REFERENCES:

1) Sublocade [prescribing information]. Indivior Inc.; 2012.

2) Mariani, et al. Am J Addict. 2020 Jul;29(4):345-48.

3) Haight BR, et al. Lancet. 2019 Feb 23;393(10173):778-90.

4) Peckham AM, et al. J Subst Abuse Treat. 2021.

5) Jones AK, et al. Clin Pharmacokinet. 2021 Apr;60(4):527-40.

6) https://www.insupport.com/specialty-product/specialty-pharmacy/how-works

7) https://www.insupport.com/specialty-product/buy-bill/how-works

MEDICATION-ASSISTED TREATMENT CENTERS OF EXCELLENCE

sites.rutgers.edu/mat-coe

coe@njms.rutgers.edu

@Rutgers_ADM

844-HELP-OUD (844-435-7638)

March 2022

Printing instructions: Be sure your printer options are set to double-sided and "flip on short edge"

USING INJECTABLE BUPRENORPHINE (SUBLOCADE®):

A GUIDE FOR PROVIDERS

MEDICATION-ASSISTED TREATMENT CENTERS OF EXCELLENCE

WHAT IS INJECTABLE BUPRENORPHINE?

Extended-release buprenorphine injection (Sublocade®, XR-bup) is a once-monthly subcutaneous injection for patients with moderate-to-severe OUD. XR-bup is equivalent to approximately 16-24 mg/day of sublingual buprenorphine. According to the package insert, patients should be treated with a transmucosal formulation of buprenorphine for at least 7 days and on stable doses of buprenorphine 8-24mg/day before starting XR-bup. XR-bup may be a good option for patients in whom adherence or diversion is a concern. Use of SR-bupe can also help with patient concerns such as having their prescription bottles stolen or needing to store their medication safely away from children.

NOTE: There is new literature suggesting that patients can be started on extended-release buprenorphine without being stable on a transmucosal formulation of buprenorphine for at least 7 days. For more information, please contact the MAT Hotline Provider line at 844-HELP OUD or contact your Center of Excellence (coe@njms.rutgers.edu or southernnjcoe@rowan.edu.)

In addition to providing effective physical security, practitioners also have an obligation to set up additional procedures or alarm systems where necessary to reduce access to controlled substances by unauthorized persons. There are specific federal record keeping requirements for providers who prescribe buprenorphine beyond standard Schedule III requirements. Providers must keep records and inventories of all controlled substances dispensed, including buprenorphine. Providers are also required to keep documentation of their protocols, practice guidelines or practice agreements readily available. (See also: https://www.deadiversion.usdoj.gov/21cfr/cfr/1304/1304_21.htm)
Primary care providers cannot store and dispense controlled substances that have been obtained from prescriptions filled at outside pharmacies.

* For specific state requirements, visit the sites.rutgers.edu/mat-coe/ and find DEA Requirements for Medication Storage Module under “Toolkits”

PRIMARY WAY TO OBTAIN SUBLOCADE:

1. Initiate a benefit investigation by filling out the patient enrollment form and submit to INSUPPORT® via fax, along with the prescription; https://www.insupport.com/pdf/patient-enrollment-form-en.pdf.

   * You may also fill out the form electronically at www.INSUPPORTportal.com

2. The specialty pharmacy selected will determine coverage for Sublocade®, which is covered by all NJ Medicaid plans, and will provide a prior authorization form and additional information if necessary.

3. If a co-pay is needed, the specialty pharmacy will contact the patient to collect costs or advise the patient of the cost that the patient will be billed after the appointment.

4. Once the Sublocade® is approved, the specialty pharmacy will work with your office to coordinate shipment directly to your office, which requires the patient’s consent to ship. Ensure you notify your patient that the specialty pharmacy will contact the patient directly to receive this consent.

   Following the administration of Sublocade, submit a claim to the payer to get reimbursed for the administration.

   If applicable, the specialty pharmacy will refill Sublocade when appropriate and contact your office and the patient to coordinate the next shipment.

* *Providers may also choose to obtain Sublocade via the “buy-and-bill” method. For more information, visit the following checklist - https://www.insupport.com/pdf/buy-and-bill-checklist.pdf*

STORAGE REQUIREMENTS:

XR-bup is a Schedule III controlled substance subject to regulation by the DEA, including storage and security requirements. Federal regulations require that practitioners store Schedule III drugs, "in a securely locked, substantially constructed cabinet" with limited access by office staff. Federal regulations do not specifically define how locked cabinets should be constructed, but the DEA notes in its security requirements that "the intent of the law is that controlled substances must be adequately safeguarded. Therefore, depending on other security measures, a wooden cabinet may or may not be considered adequate. In an area with a high crime rate, a strong metal cabinet or safe may be required."

Additional factors that the DEA considers when evaluating a practitioner's controlled substances security include:

- The number of employees, customers and/or patients who have access to the controlled substances.
- The location of the registrant (high or low crime area).
- Use of an effective alarm system (usually suggested on the cabinet).
- Quantity of controlled substances to be kept on hand.
- Prior history of theft or diversion.

CLINICAL PEARLS: [1,2,3]

- Steady state of XR-bup achieved at 4-6 months
- Both 100mg & 300mg doses should suppress opioid withdrawal and cravings
- Average steady state concentration of both the 100mg & 300mg doses are higher than 24mg sublingual buprenorphine (see table).
- Levels of 2-3 ng/mL are required to occupy at least 70% of mu-opioid receptors and reduce illicit opioid use
- At steady state (4-6 months after starting Sublocade®), levels of buprenorphine >2 ng/mL may be maintained for at least 2 months after last monthly injection
- Patients may need to be maintained at 300mg monthly of XR-bup especially in the age of fentanyl and amongst those who inject drugs

Table 6. Comparison of Buprenorphine Mean Pharmacokinetic Parameters Between SUBUTEX and SUBLOCADE

Pharmacokinetic parameters	SUBUTEX daily stabilization		SUBLOCADE		
Mean	12 mg (steady-state)	24 mg (steady-state)	300 mg# (1st injection)	100 mg* (steady-state)	300 mg* (steady-state)
C_{max} (ng/mL)	1.71	2.91	2.19	3.21	6.54
$C_{min,ss}$ (ng/mL)	5.35	8.27	5.37	4.88	10.12
$C_{min,ss}$ (ng/mL)	0.81	1.54	1.42†	2.48	5.01

#Exposure after 1 injection of 300 mg SUBLOCADE following 24 mg SUBUTEX stabilization
†Mean plasma concentration of 1.86 ng/mL was observed on last day of the dosing interval (Day 29)
*Steady-state exposure after 4 injections of 100 mg or 300 mg SUBLOCADE, following 2 injections of 300 mg SUBLOCADE

Image from: Sublocade [prescribing information]. Indivior Inc.; 2012.

KEY STUDY FINDINGS: [3,4]

XR-bup in both the 100mg and 300mg maintenance groups had greater % opioid abstinence at 6 months compared to placebo; ~40% vs. 5% in the pivotal study

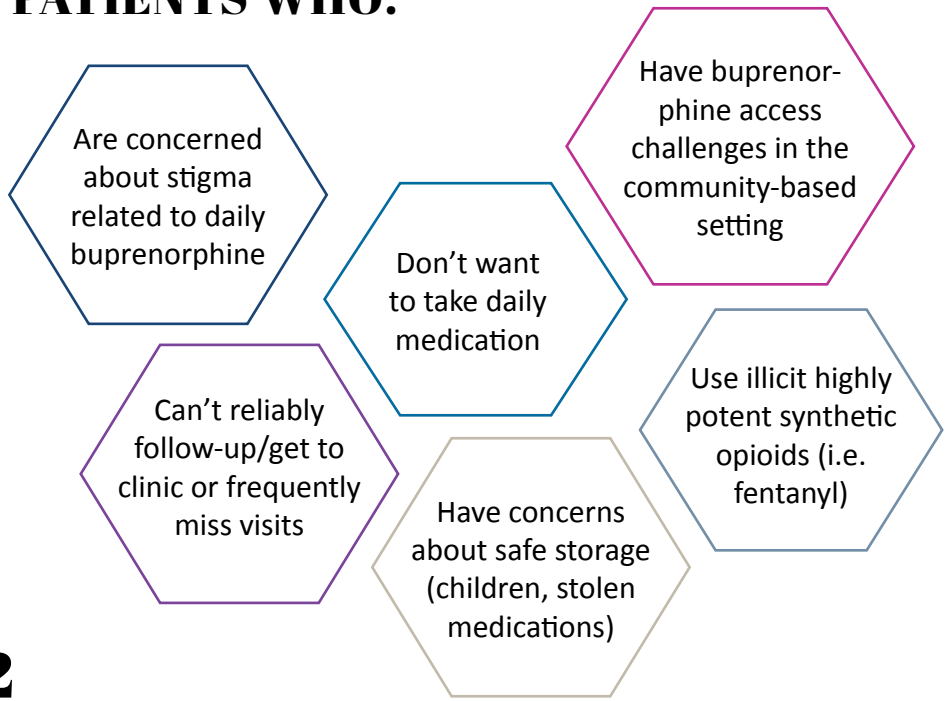
Greater than 40% opioid abstinence vs. placebo and upwards to 65% opioid abstinence amongst a real-world chronically homeless population

Quality of life improvement over sublingual buprenorphine

Several case series showed the tolerability and safety of initiating XR-bup in those on sublingual buprenorphine for <7 days

Similar side effect profile to sublingual buprenorphine except for injection-site reactions (5-10% of patients)

XR-BUP MAY BE ADVANTAGEOUS FOR PATIENTS WHO:



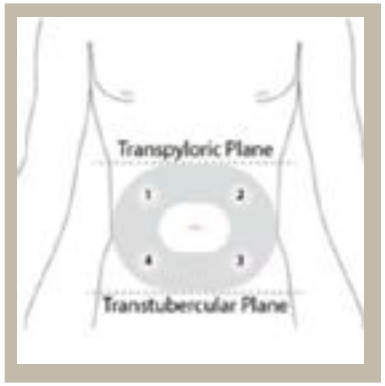
DOSING: [1]

Patients should be able to tolerate 8-24 mg of transmucosal buprenorphine before starting XR-bup. This is to ensure sufficient opioid tolerance to avoid adverse events such as excessive sedation or nausea with XR-bup. The recommended dose of XR-bup is 300 mg monthly for the first 2 months, followed by a maintenance dose of 100 mg monthly. Some patients may require supplementary sublingual buprenorphine during initiation of XR-bup. The maintenance dose may be increased to 300 mg monthly for patients who continue to experience withdrawal and/or craving symptoms or continue to use opioids on the 100 mg maintenance dose. A patient who misses a dose should receive the next dose as soon as possible. The minimum number of days between doses is 26 days. Occasional delays in dosing up to 2 weeks are not expected to have a clinically significant impact on treatment effect. If XR-bup is discontinued, plasma levels decrease slowly over time and may be detectable for 12 months or longer once at steady state. Therefore, patients should be monitored for several months for signs of opioid withdrawal after stopping treatment.

STORAGE & ADMINISTRATION: [1]

XR-bup is injected subcutaneously into the abdomen by a healthcare provider. The injection site should have adequate subcutaneous tissue free of nodules or lesions and the area should not be irritated, reddened, bruised, infected, or scarred in any way. Patients should be educated that they will have a lump present for several weeks that will decrease in size over time.

- Inject as a slow, steady push
- Provide at least a minimum of 15 minutes at room temperature before injection to minimize pain
- An injection containing lidocaine HCL 10-15 minutes prior to administering XR-bup may help to minimize pain. Ice packs may also be used.
- Store at 2C - 8C in a refrigerator. If stored at room temperature, it must be used within 30 days



Images from: https://www.rxlist.com/sublocade-drug.htm#indications