Delivering XR Buprenorphine in a Maine Practice: Long-Acting Injectable Buprenorphine

Concept to Reality

Your Faculty

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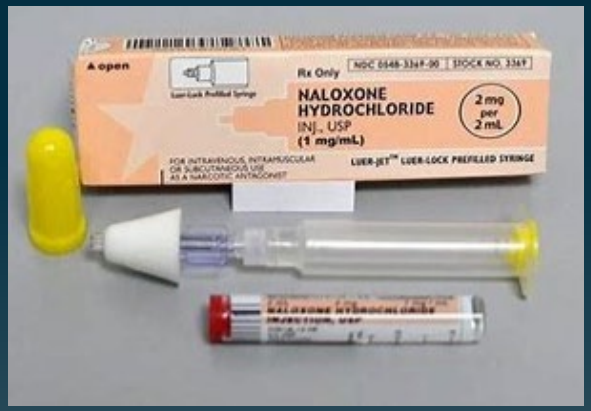
Questions we will answer

1. Discuss the place in therapy for long acting injectable buprenorphine in treatment of opioid use disorder.
2. Describe the administration of Sublocade
3. Explain the pharmacodynamics and pharmacokinetics of Sublocade
4. Describe the ways in which Sublocade can be acquired.
5. Evaluate the REMS program and safety considerations.

A Plug for Narcan

- People experiencing an opioid overdose are having a MEDICAL EMERGENCY
- Naloxone is a TOOL that anyone may use
- Think of it as a preliminary to administering CPR
- Prescribe it often
- Carry it
- Fast acting drug in the setting of long acting drugs of abuse



What is Long Acting Injectable Buprenorphine?

- Buprenorphine
- Injected into subcutaneou tissue
- Becomes a solid
- Dissolves over weeks

1 | SUBLOCADE Administration[1]

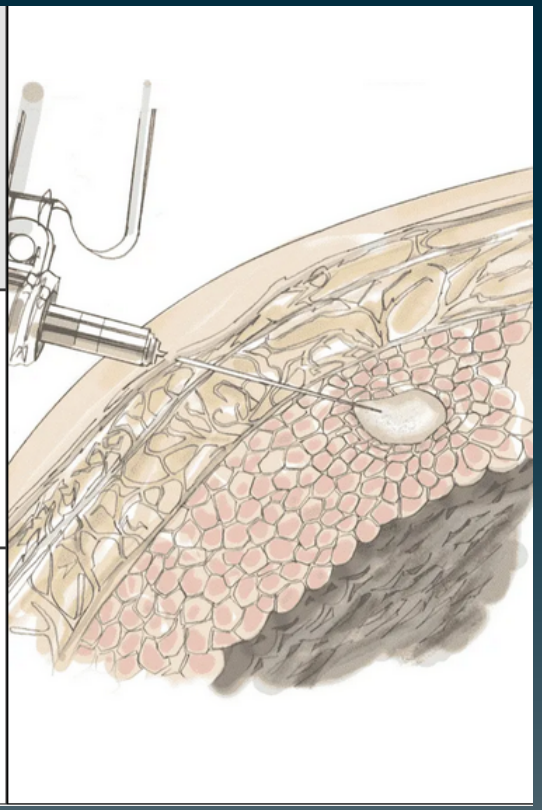
SUBLOCADE is administered as an injection into the abdominal subcutaneous tissue (total volume: 0.5 mL for 100 mg and 1.5 mL for 300 mg)

2 | Depot Formation[1]

SUBLOCADE is injected as a liquid, and upon contact with body fluids, the ATRIGEL® delivery system forms a solid depot containing buprenorphine

3 | Continuous Release[1]

After initial formation of the depot, buprenorphine is released via diffusion from, and the biodegradation of, the depot



Appropriate Candidates

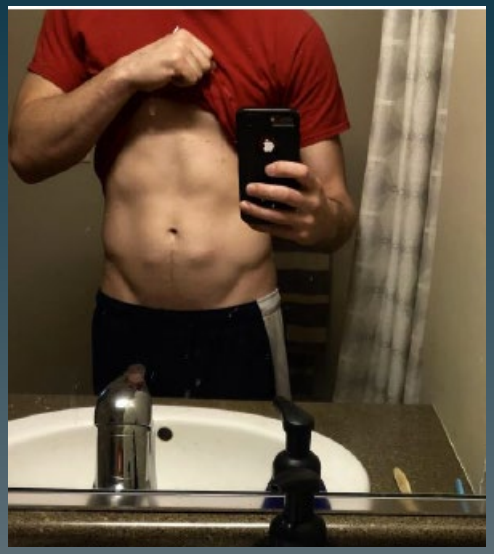
- Must tolerate 8-24 mg buprenorphine for a minimum of 7 days prior to first injection
- People struggling with recovery
- People who are stable
- Liver function
- Serotonin
- May prolong QTc

Pros

- Medication management
- Therapeutically superior
- Allows “breaking up” with hand-to-mouth
- Therapeutic window
- Side effects same as SL buprenorphine

Cons

- Cost
- Injection
- Risks of injection
- Cannot be removed after 14 days
- Mostly anecdotal guidance for tapering



Sublocade Dosing

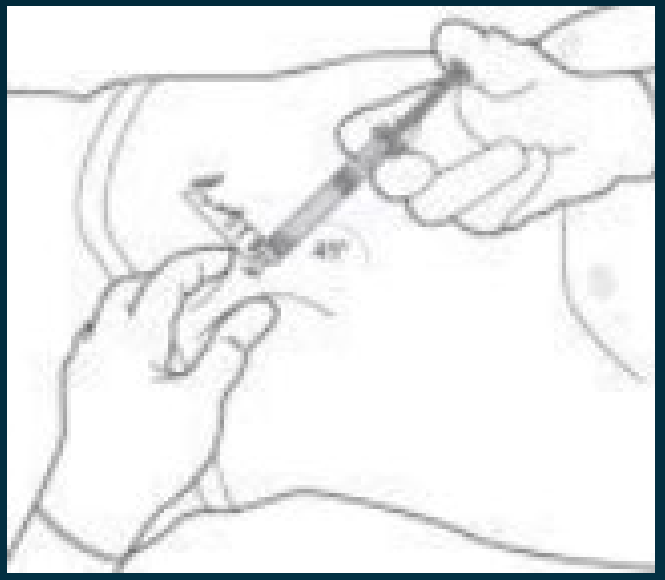
- Appropriate candidates have been on 8 mg buprenorphine SL daily for at least 7 days prior to initial injection
- Your patient may dose SL buprenorphine the day of injection
- First 2 months are 300 mg loading doses (1.5 mL each)
- Month 3 and beyond are 100 mg maintenance doses
- STOP doing the math
- There is freedom to remain on 300 mg or alternate dosing (cost is the same). Base this on patient response.
- The goal is complete or near complete blockade of the mu receptors

Making the Sale to the Patient

- Conversation should be direct and honest and include the pros and cons to the patient.
- “The only bad thing is that it’s an injection.”
- “This is not a comfy shot, but I have ways to make it much more comfortable if that worries you.”
- Patients should understand about the bump that is formed. Many are worried that it never goes away.
- Many people ask for the reassurance that they may go back onto SL medication if desired. Try to get a 3-4 month buy-in from patients to not abandon ship too soon.

The Injection

- This is a subcutaneous injection
- Avoid subdermal injection!!
- 18 G needle
- Medication is THICK
- Injection is uncomfortable
- Use of local anesthetic and speed of injection
- Injection only approved for abdominal tissue
- Rotate sites
- Ice pack post injection if needed



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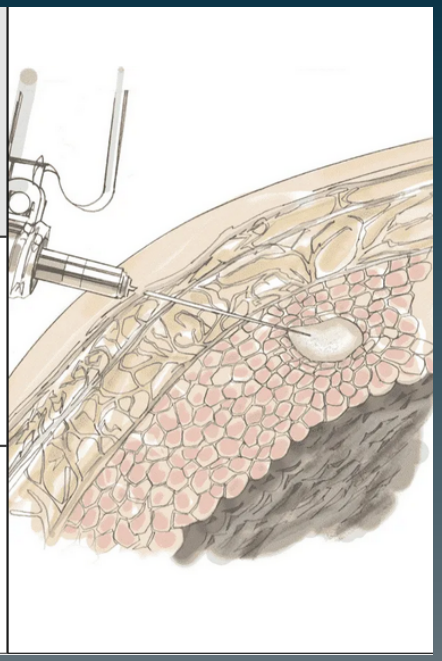
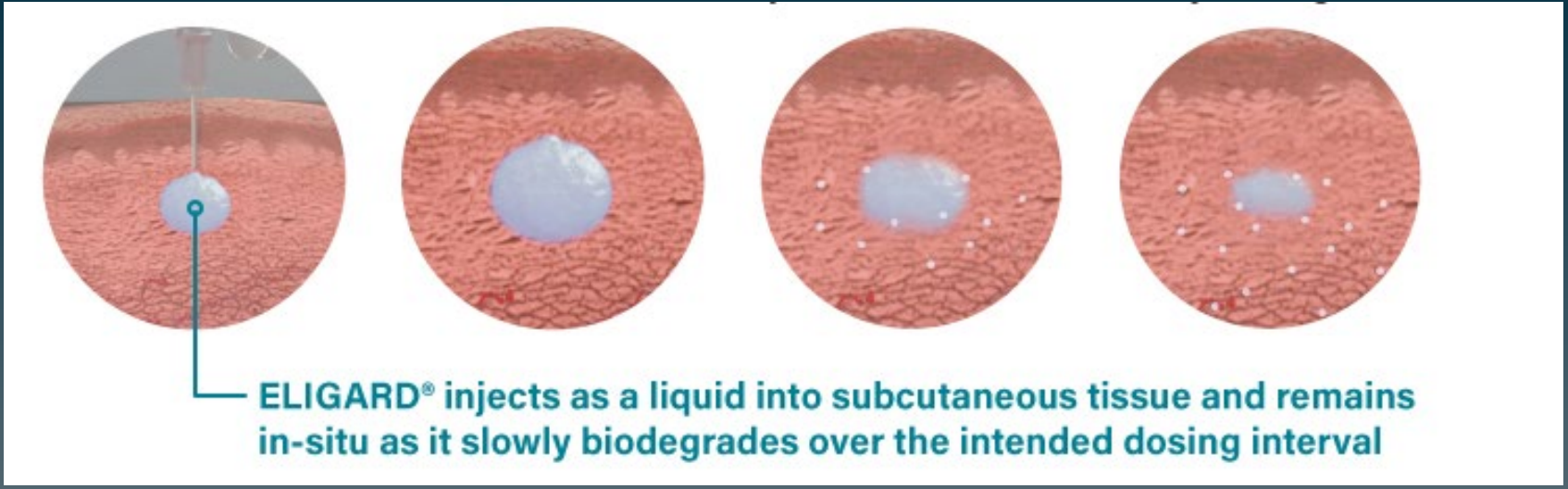


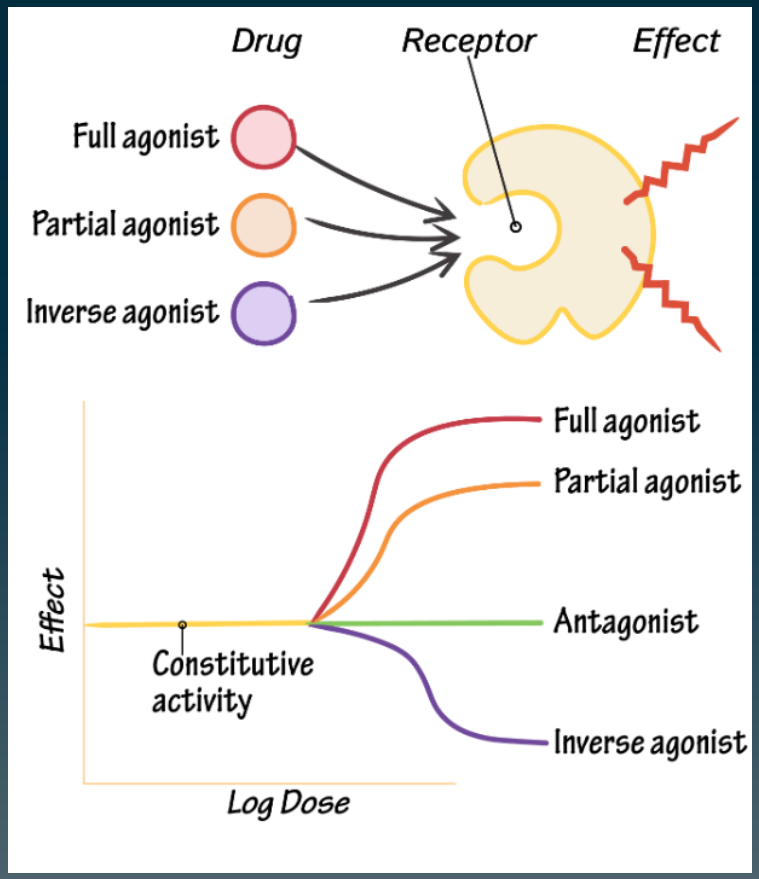
Drug Delivery System

- Atrigel delivery system
  - Biodegradable polymer that breaks down over time
- Allows for prolonged release



Pharmacodynamics – Buprenorphine

- Partial agonist of the μ-opioid receptor
- High receptor binding
- Low dissociation kinetics
- Long half-life
  - SL ~38 hours



https://www.drawittoknowit.com/course/pharmacology/glossary/pharmacology/pharmacologic-agonists

Pharmacodynamics

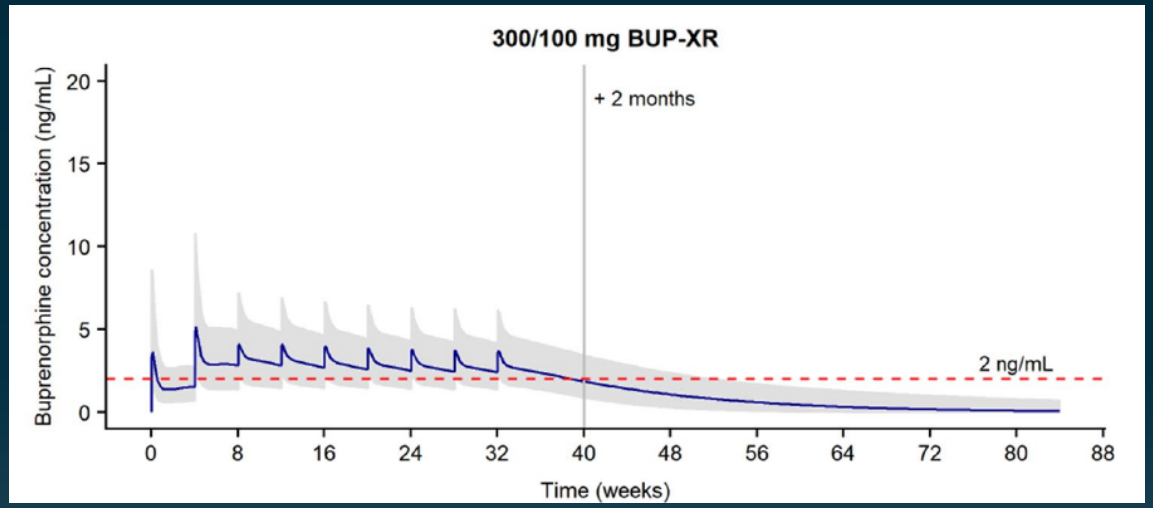
- Higher buprenorphine serum concentration has been associated with diminished response to full agonist opioids
  - Nasser *et al* evaluated the effects of sustained release buprenorphine on response to 18 mg hydromorphone
    - Subjective effects from study participants (VAS Score)
  - 1.9 ng/mL serum concentration was associated with non-inferiority on VAS score
  - 3.0 ng/mL serum concentration was associated with a near zero VAS score
- Study was sponsored by Indivior

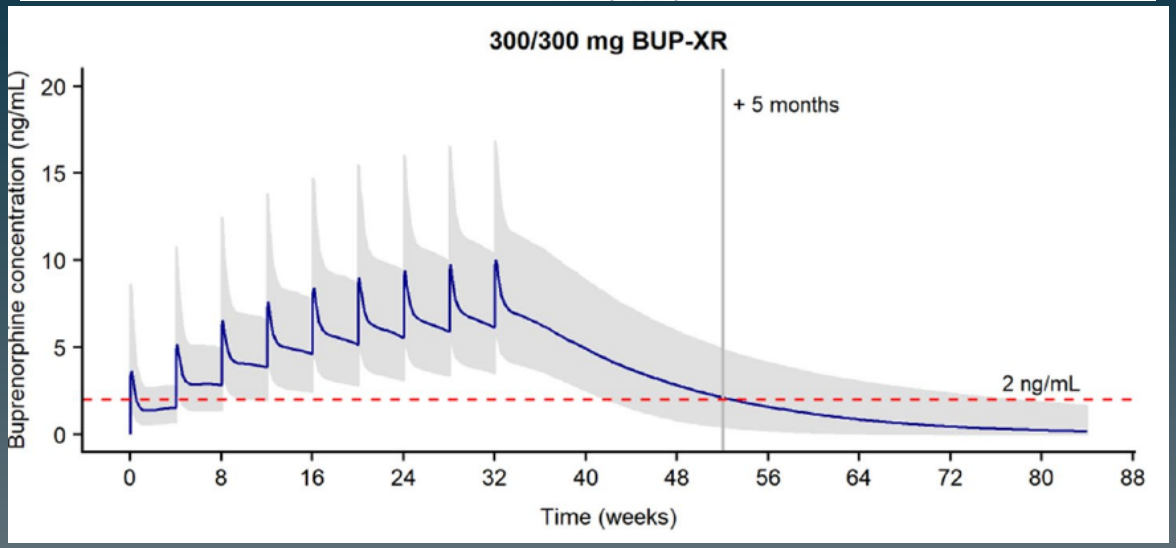
Pharmacokinetics

Pharmacokinetic Parameters	Transmucosal Buprenorphine		XL Injectable Buprenorphine		
Dose	12 mg daily	24 mg daily	300 mg after 1st injection	100 mg monthly at steady state	300 mg monthly at steady state
Average Plasma Concentration at steady state(ng/mL)	1.71	2.91	2.19	3.21	6.54
Max Plasma Concentration at Steady State (ng/mL)	5.35	8.27	5.37	4.88	10.12
Min Plasma Concentration at Steady State (ng/mL)	0.81	1.54	1.42	2.48	5.01

Sublocade Prescribing Information

Sustained Buprenorphine Concentration after Discontinuation of Treatment





A Jones *et al*. Population PK of a Monthly BNP Depot Injection

Special Populations - Pregnancy

- Animal studies involving pregnant rats and rabbits who were administered Sublocade during organogenesis caused embryolethality, reduced fetal body weights, and visceral and skeletal malformations
  - Administered 38 and 15 times the max recommended human dose (300 mg)
  - Believed to be partially related to Atrigel solvent (N-methyl-2-pyrrolidone)
- MOMs study is currently evaluating the safety of a new ER buprenorphine formulation that dose not contain N-methyl-2-pyrrolidone

Risk Evaluation Mitigation Strategies Program

- Purpose: manage potential risks associated with Sublocade as required by the Food and Drug Administration
- Restricted distribution of Sublocade to limit serious harm or death that may be cause by intravenous injection

REMS Program Requirements
❖ All healthcare settings and pharmacies that dispense Sublocade must be certified in the Sublocade REMS program
❖ Healthcare providers and pharmacies must obtain Sublocade through a restricted distribution program
❖ **Sublocade should never be dispensed directly to a patient**

Ways to Acquire Sublocade

Acquire Through a REMS Certified Pharmacy

Becomes a REMS Certified Dispenser

Ordering from a REMS Certified Pharmacy

- This method does not require you to become REMS certified
- A prescription is sent to a REMS certified pharmacy
  - Pharmacy will bill the patient's insurance
  - May require a prior authorization
- Prescription will then be sent directly to the clinic for administration
- Pros: some billing structures in FQHCs limit ability to directly bill for Sublocade
- Cons: Can cause a delay in treatment, drug can only be used for the patient it was prescribed to

Becoming a REMS Certified Dispenser

- Requires your site to become certified with the REMS program
- Order Sublocade through an authorized distributer
- Clinic can keep Sublocade on hand and administer to patients
  - No prescription involved
- Depending on how your organization bills for encounters, you may not be able to bill for Sublocade
- Store in a locked room and/or refrigerator
- Pros: Can initiate patients quicker and greater control over inventory
- Cons: Some organization won't be able to bill Medicare/Medicaid for the cost of the drug

How to become Certified in the Sublocade REMS Program

- Designate an authorized representative
  - The authorized representative will make sure that each dispensing site meets requirements to purchase, receive, and dispense Sublocade
- Complete "Sublocade REMS Program Healthcare Setting and Pharmacy Enrollment Form"
- Establish processes and procedures to verify that Sublocade is dispensed directly to health care provider for administration to a patient
- Be sure to have a secure (locked) fridge to store Sublocade

Tapering

- No official guidance on tapering this drug
- It is LONG ACTING and the drug is still present 1 year after discontinuation!
- Patient 1: “I kept waking up wondering if today was the day I would withdraw.”
- Patient 2: “I think they were putting buprenorphine in the water supply.”
- Patient 3: An official tapering using the medication

Connecting Patients to this Treatment

- Buy and bill vs. specialty pharmacy
- Currently covered by Maine Care
- Most private insurances are covering
- In Support
- Waterville infusion clinic
- Stay tuned for this in Bangor

Brixadi

- Another ER subcutaneous formulation of buprenorphine, not yet FDA approved
- If approved will be available as
  - Weekly Injections (8 mg, 16 mg, 24 mg, 32 mg)
  - Monthly Injections (64 mg, 96 mg, 128 mg)
- FDA rejected 1st new drug application in 2020 and 2021 due to deficiencies in 3rd party manufacturing facilities
- May be able to have alternative injection sites
- Might be able to be used with more confidence in pregnancy

Questions