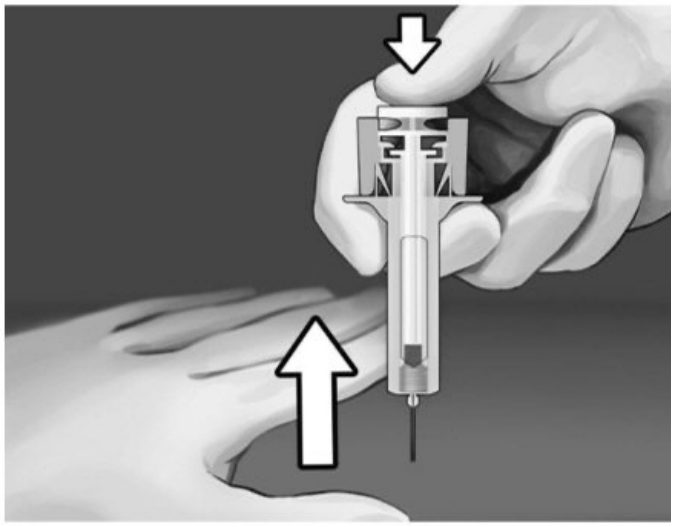
Long-Acting injectable (LAI) buprenorphine



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Overview

- What is LAI bupe
- LAI bupe evidence
- LAI bupe initiation and discontinuation
- LAI bupe counseling points
- Cases
- Logistics
- Resources
- Q&A

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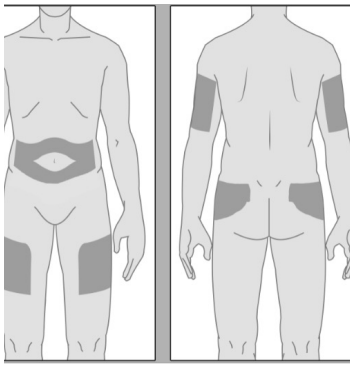
What is LAI bupe?

- Depot medication: SC injection
  - Extended-release
    - Slow onset= Good for initiation in fentanyl era
    - Consistent plasma concentrations
- Weekly and Monthly dosing options
- Two formulations: Sublocade & Brixadi



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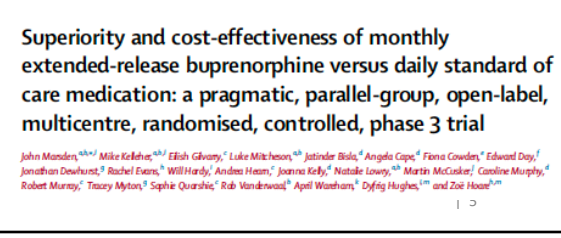
What is the evidence for LAI bupe?

- Effectiveness of LAI bupe vs. SL bupe
  - Non-inferior to daily sublingual (N=428 pts w/mod-severe OUD) (Lofwall 2018)
  - Superior to daily sublingual (N=341 pts w/Mod-severe OUD) (Mardsen 2023)

JAMA Internal Medicine | Original Investigation

Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder
A Randomized Clinical Trial

Michelle R. Lofwall, MD; Sharon L. Walsh, PhD; Edward V. Nunes, MD; Genie L. Bailey, MD; Stacey C. Sigmon, PhD; Kyle M. Kampman, MD; Michael Frost, MD; Fredrik Tiberg, PhD; Margareta Linden, PhD; Behshad Sheldon, BS; Sonia Oosman, BS; Stefan Peterson, PhD; Michael Chen, PhD; Sonnie Kim, PharmD



Superiority and cost-effectiveness of monthly extended-release buprenorphine versus daily standard of care medication: a pragmatic, parallel-group, open-label, multicentre, randomised, controlled, phase 3 trial

John Marsden, Mike Kelleher, Elish Gilvarry, Luke Mitcheson, Jatinder Bisla, Angela Cape, Fiona Cowden, Edward Day, Jonathan Dewhurst, Rachel Evans, Will Hardy, Andrea Hearn, Joanna Kelly, Natalie Lowry, Martin McCusker, Caroline Murphy, Robert Murray, Tracey Myton, Sophie Quarshie, Rob Vanderwaal, April Wareham, Dyfrig Hughes, and Zoë Hoare

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What is the evidence for LAI bupe?

- Evidence for LAI bupe in Real-world settings:
  - Bridge clinics:
    - 70% retained at 6 mo (N=118) (Heil 2023)
    - 65% retained (N=40) (Pekham 2021)
  - VA: 81% received 6+ injections (N=26) (Cotton 2021)
  - Post-incarceration: 69% LAI bupe vs. 35% sublingual be retained at 8 weeks (N=52) (Lee 2021)
  - MOUD tx in Canada: 7% lower risk for non-fatal OD among pts receiving LAI bupe compared to pts receiving SL bupe (N=379) (Lee 2023)

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How do patients start LAI bupe?

- **Sublocade:** Monthly injections
  - Already on SL?
    - 300 mg, 300 mg, 100 mg– OR – 300 mg, 300 mg, 300 mg
    - First 2 injections are 1 week apart
  - Not on SL bupe?
    - Per Label, 1 dose of SL before receiving injection
- **Brixadi**: Weekly and monthly
  - Already on SL? Straightforward conversion from SL to monthly LAI
  - Not on SL bupe?
    - Per Label, 1 dose of SL before receiving injection
    - One weekly injection before starting monthly

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

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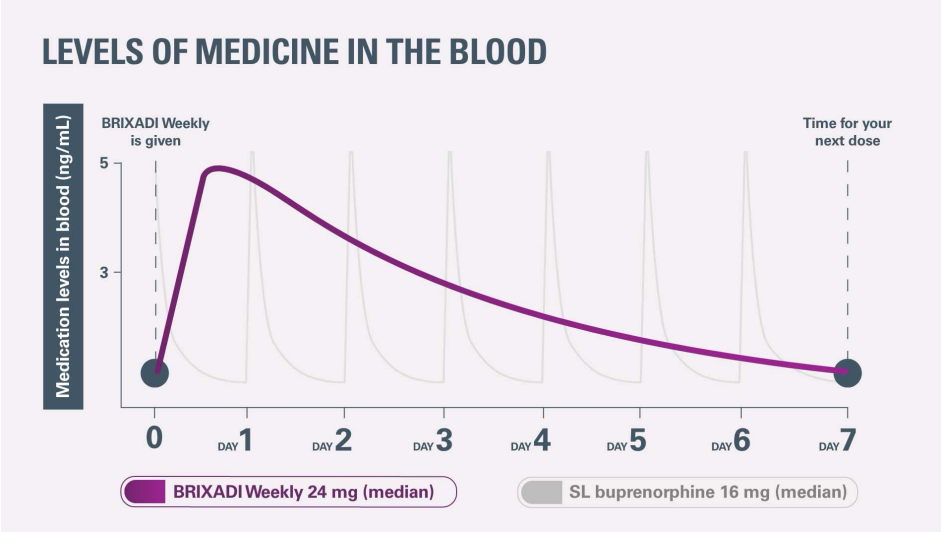
How do patients start LAI bupe



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How do patients start LAI bupe?

- **Rapid LAIB initiation**
  - Off-label
  - For patients not already on SL bupe and no to mild withdrawal sx
  - Administer Brixadi weekly BEFORE sublingual is administered
  - Patients continue opioid use x 24 hours

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Rapid LAIB data

- Case series of rapid LAIB (N=13 patients) (Brady & O'Conor 2025)
  - 10 patients had mild withdrawal sx
  - 2 patients had no withdrawal sx
  - 1 patient had precip withdrawal (received SLB within 24 hours after injection)
- For comparison:
  - 1/17 reported "it felt very rough" in rapid LAIB case series (Rosenwohl-Mack 2025)
  - 11.5% of patients initiating bupe in hospital experienced precip withdrawal (Thakrar 2025)

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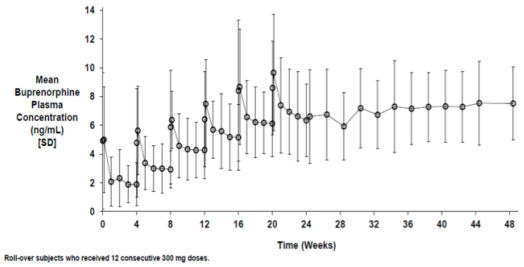
Continuing LAI bupe

- 4-6 injections until steady state is reached
- Windows for injections
  - Weekly (+/- 2 days)
  - Monthly (+/- 7 days)
  - *Even longer once at steady state*



Roll-over subjects who received 12 consecutive 300 mg doses.

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Discontinuing LAI bupe

- Little data
- Unlikely to experience any withdrawal if stopping after steady state is reached (4+ injections)
- Case reports of discontinuing after single injection with minimal withdrawal

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What should I tell patients about LAI bupe?

Benefits

- Not having to think about daily medication
- No risk of loss or theft
- Ease of travel
- Consistent medication levels
- Higher serum levels at max dosing than max SL dosing
- Less withdrawal when initiating with LAI than with SL
- Generally, little-no withdrawal when stopping→ease of tapering
- Window for receiving

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What should I tell patients about LAI bupe?

Risks

- Must be prepared for long-acting opioid blockade
- Withdrawal when starting if not already on SL bupe
- SE:
  - Pain, redness, itching at injection site.
  - Potential for sedation after first injection (Sublocade)
  - HA (also for SL)
  - Insomnia (more for Brixadi; also for SL)
  - Otherwise, same side effects as sublingual
  - No LT side effects

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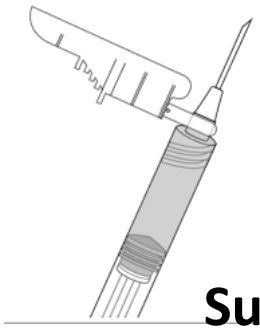

Sublocade vs. Brixadi

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	Sublocade	Brixadi
Active Ingredient	Buprenorphine (same active ingredient as Suboxone ® or Subutex®)	Buprenorphine (same active ingredient as Suboxone ® or Subutex®)
Any naloxone in it?	No	No
Needle size	⅝ inch long Thicker needle	½ inch long Thinner needle
How painful is it?	Everyone is different. We can use ice and numbing medication to reduce pain.	
Where is it injected?	Stomach, back of arm, buttock, thigh (in fat just below skin)	
Injection area	Leaves a lump you can see	Lump not noticeable
How often do I get it?	Monthly	Monthly Weekly (optional)
Medication doses	Monthly doses 300 mg 100 mg	Monthly doses 128 mg 96 mg 64 mg Weekly doses 32 mg 24 mg 16 mg 8 mg

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	Sublocade	Brixadi
How does the dose compare to Suboxone® or Subutex ® ?	At highest dose, is even higher than 32 mg Suboxone® or Subutex® daily	At highest dose, is about the same as 24 mg Suboxone® or Subutex® daily
Common Side Effects	Pain, redness, itching at injection site	Pain, redness, itching at injection site
Less Common Side Effects	Fatigue after first injection Headache Constipation — Nausea	— Headache Constipation Insomnia Nausea
Drug Interactions	Blocks other opioids	Blocks other opioids

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What should I tell patients about LAI bupe?

- What will the withdrawal be like?
  - If switching over from SL
    - Most likely little to none
    - Takes 4-6 injections until steady state. Until then, may experience some “wearing off” before end of the month
      - Treat with supplemental SL bupe, get next injection early
  - If newly initiating bupe:
    - 24-48 hours
    - Message: we will support you during this time!
    - Takes 4-6 injections until steady state. Until then, may experience some “wearing off” before end of the month
      - Treat with supplemental SL bupe, get next injection early

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What should I tell patients about LAI bupe?

Other patient questions:

- What if I am in the hospital and need pain medications?
- What if I don't like it?
- Other?

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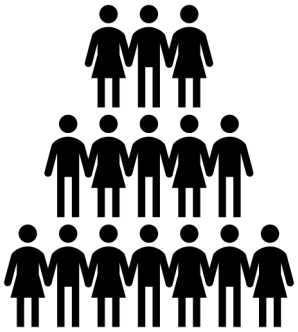
Who should I talk to about LAI-bupe?

- Everyone!
  - Not everyone will want it, but patients should be aware.
  - .BUPESTABLENEW



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Why did patients start?

- Case 1: 73 year old man, stable on SL bupe for years. Tired of taking a daily medication, tired of dealing with stress of pharmacies
- Case 2: 44 year old woman, stable on bupe, interested in LAI bupe for bupe discontinuation
- Case 3: 37 year old woman, previously did well on bupe, has not been able to start SL despite repeated efforts
- Case 4: 43 year old woman, struggles to take bupe given chaotic substance use and social circumstances. Also taking LAI PrEP

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Case #1: Switching over from non-prescribed SL bupe

- 52 year old man, long-term bupe tx out of state until returning to NY when resumed using heroin
- Presented to resume bupe treatment. Taking 8 mg SL daily (buying). Wanted to start Brixadi.
- Received 64 mg Brixadi monthly plus 14, 8 mg strips supplemental bupe
- 2 weeks after injection: Had cravings, used up strips
- 3 weeks after injection: Return for 2nd injection. Received 96 mg injection.
- Continues to receive 96 mg injection monthly

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

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Case #2: Rapid LAIB

- 40 year old man with hx of OUD, cocaine use, 6-12 bags of heroin daily, chaotic use→ loss of employment.
- Last heroin use right before appointment.
- Highly motivated to receive injection right away. Risk/Benefits counseling.
- Brixadi 32mg weekly given. Supportive medications provided. Advised to use own supply ~24h
- One week later: no withdrawal, and dramatically reduced use of heroin. Received Brixadi 128mg.
- He continues to be engaged in care and has started his new job.

Daily dose of sublingual buprenorphine	BRIXADI (weekly)	BRIXADI (monthly)
≤ 6 mg	8 mg	--
8-10 mg	16 mg	64 mg
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18-24 mg	32 mg	128 mg

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Case #3: Tapering

- 44 year old woman
  - On SL bupe 2 mg BID-TID, interested in LAI bupe for bupe discontinuation
  - Titrated up on SL to 8 mg
  - 7/1: Brixadi 64 mg injection given
  - 7/31: Brixadi 64 mg injection given
  - 11/4: had a couple weeks of mild withdrawal sx, now feeling good

Table 1: Daily doses of sublingual buprenorphine (Subutex, Suboxone, or generic product equivalents) and suggested corresponding BRIXADI (weekly) or BRIXADI (monthly) doses

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

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Why do people stop LAI bupe?

- Tapering off all bupe
- Didn't suppress cravings (Sublocade could be an option)
- Undertreated withdrawal sx
- SE (insomnia)

(Lee 2022)

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Logistics

- What everyone should know:
  - Can refer to Add Med fellows clinic for counseling, initiations, injections
  - Most LPNs have been trained in giving Brixadi
  - Medicaid covers all bupe formulations

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Logistics

- If you are interested in doing more:
  - Ordering
    - Medicaid patients: Order medication to Genoa pharmacy
      - BUPELAI**RX**
    - Medicare/Commercial: Email *staff member* and cc *staff members* for help
    - **Important!** Specialty pharmacy will only ship to the address on ordering provider's DEA license
  - Storage- Narcotics cabinet
  - Administration
    - Orders in Epic for Brixadi and Sublocade

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Protocol & SmartPhrases

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SmartPhrases

- BUPESTABLENEW
- **.BUPELAI…**
  - BUPELAI**COUNSELING**
  - BUPELAI**PATIENTHANDOUT**
  - BUPELAI**PATIENTHANDOUTSPANISH**
  - BUPELAI**RX**
  - BUPELAI**BRIXADISTART**
  - BUPELAI**RAPIDHX**
  - BUPELAI**ADMIN**
  - BUPELAI**AP**

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Take-home points

- LAI bupe can be a good option for both new and existing bupe patients
- Talk to all your patients about LAI-B
- Add med clinic and providers are here to help

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Questions?

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Extra slides

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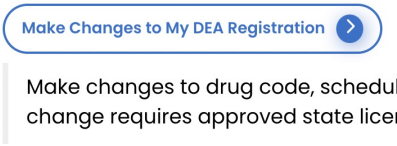
Prescribing Logistics

1. Google “change DEA address”
2. Click on: DEA Forms & Applications-Diversion Control Division
3. Click on:



4. Info you need:
   - DEA address Zip code
   - Month/Year expiration

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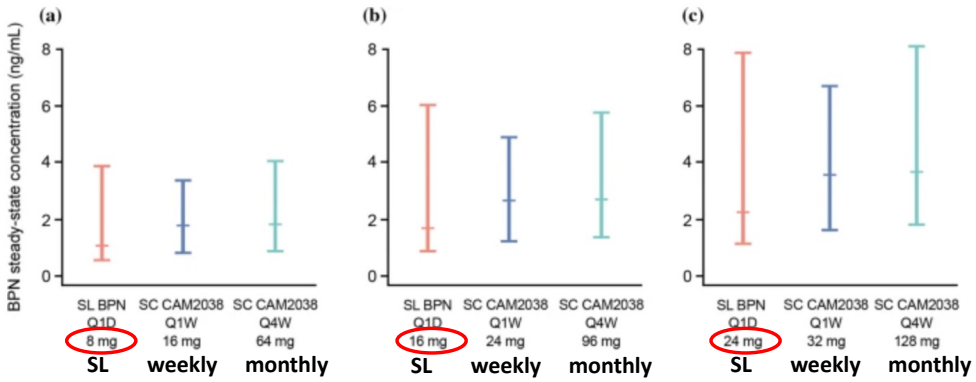
Pharmacology: Comparing bupe levels: daily SL bupe vs. Brixadi



(Bjornsson et al., *Clinical Pharmacokinetics,* 2023)

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