October 2026

# Emergency Department Direct-to-Inject (DTI) Buprenorphine

This is the recommended starting protocol for most EDs and new programs. This algorithm initiates weekly long-acting injectable buprenorphine (XR bup) without a sublingual (SL) lead-in for patients with opioid use disorder (OUD). The Clinical Opiate Withdrawal Scale (COWS) and time since last opioid use help determine readiness for XR bup dosing.

**OUD and interested in long-acting injectable bup**

NO → See below for SL bup protocols

YES

COWS ≥ 4 and last opioid use >6h*

NO → See below for SL bup protocols

YES

XR bup 24 mg weekly

**XR bup requires the same timely follow-up engagement and ongoing support after discharge as other formulations.

Discharge with return precautions.
Follow up with outpatient within 3-5 days for next dose.**

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*Reassure patients plasma levels will continue to rise for 24 hrs. However, if breakthrough withdrawal symptoms persist after 24 hrs, consider SL bup 8 mg TID PRN.****

**Starting bup may be delayed or modified if there are complicating factors.**

***Complicating factors:**

- Altered mental status, delirium, intoxication.
- Long-term methadone maintenance.

*** Consider avoiding supplemental SL bup in first 24hrs to decrease risk of precipitated withdrawal.

*The only absolute contraindication is a true buprenorphine allergy, which is exceedingly rare.*

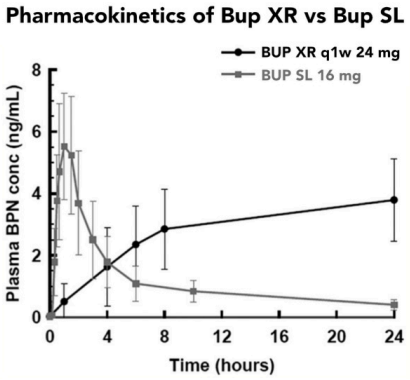
**DTI bup is OK in pregnancy and breastfeeding.**

***COWS ≥ 8 + 2 objective signs of withdrawal***

OK for high dose start.
See "Emergency Department Buprenorphine Quick Start."

***COWS < 4***

Low dose initiation.
See "Buprenorphine Hospital Start: Low-Dose Bup Initiation with Opioid Continuation."




**Return Precautions:**

1. Overshoot: Sedation, nausea, headache
2. Undershoot: Progressing or under-treated withdrawal
3. Buprenorphine induced withdrawal (precipitated withdrawal)
4. Injection site: Bump ok; red, warm, tender not ok

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*Emerging Practice: Direct-to-Inject (DTI) Buprenorphine*

# 1st Dose in No or Low Withdrawal

This emerging practice accommodates patients who are in no or low withdrawal in ED or clinic settings.

**OUD and interested in long-acting injectable bup**

NO → See page 1 for SL bup protocols

YES ↓

**COWS ≥ 4 and last opioid use >6h***

NO → **XR bup 8 mg weekly**

YES ↓

**XR bup 24 mg weekly**

Discharge with return precautions.
Follow up with outpatient within 3-5 days for next dose.**

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*Reassure patients plasma levels will continue to rise for 24 hrs. However, if breakthrough withdrawal symptoms persist after 24 hrs, consider SL bup 8 mg TID PRN.****

**Starting bup may be delayed or modified if there are complicating factors.**

***Complicating factors:**

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**XR bup requires the same timely follow-up engagement and ongoing support after discharge as other formulations.

**Return Precautions:**

1. Overshoot: Sedation, nausea, headache
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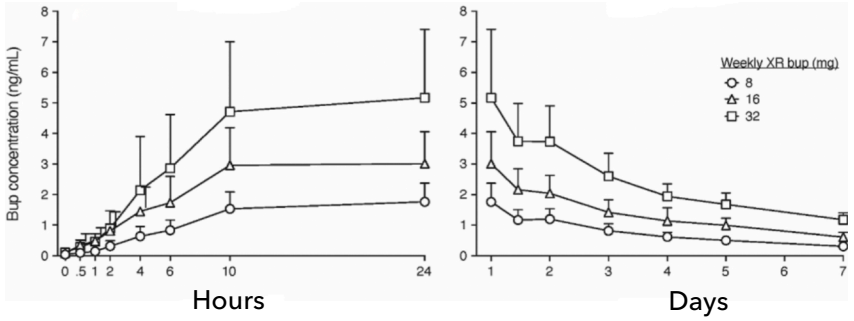
**Pharmacokinetics of Weekly XR Bup**

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# *Emerging Practice: Direct-to-Inject (DTI) Buprenorphine*
# Routes to XR Bup Monthly

This emerging practice supports patients who receive their 1st dose in the ED or clinic and 2nd dose in a clinic setting.

**OUD and interested in long-acting injectable bup**

NO → See page 1 for SL bup protocols

YES

**COWS ≥ 4 and last opioid use >6h***

NO → **XR bup 8 mg weekly injection**

YES

**XR bup 24 mg weekly injection**

1-5 days

1-3 days

**XR bup 128 mg OR 300 mg monthly injection**

**Starting bup may be delayed or modified if there are complicating factors.**

***Complicating factors:**

- Altered mental status, delirium, intoxication.
- Long-term methadone maintenance.

*** Consider avoiding supplemental SL bup in first 24hrs to decrease risk of precipitated withdrawal.

*The only absolute contraindication is a true buprenorphine allergy, which is exceedingly rare.*

**DTI bup is OK in pregnancy and breastfeeding.**

**Return Precautions:**

1. Overshoot: Sedation, nausea, headache
2. Undershoot: Progressing or under-treated withdrawal
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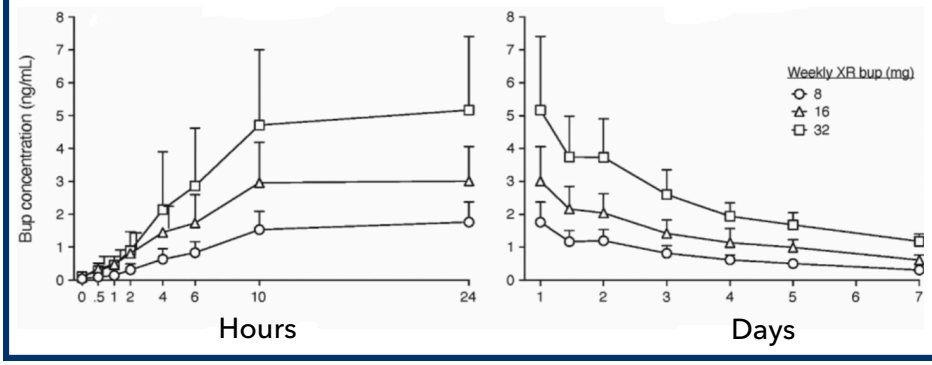
**Pharmacokinetics of Weekly XR Bup**

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# DTI Adjuncts, Management of Bup Precipitated Withdrawal, and Currently Available XR Formulations

**May consider symptom targeted treatments for breakthrough withdrawal during XR initiation, including:**

**Restlessness, sweating, tachycardia**

- **Clonidine** 0.1-0.3 mg q6-8h prn sweating/racing heart/chills/hot flashes/anxiety, #28 *onset in 30-60 min* or **Lofexidine** 0.18 mg 3-4 tabs q6h sweating/chills/anxiety, #112 *onset in 30-60 min* or **Tizanidine** 4 mg q6h prn muscle aches/restlessness/anxiety, #28 *onset in 30-60 min* or **Guanfacine** ER 4mg daily prn anxiety/restlessness/sweating, #7 *onset in 2-4 hrs*
- **Ketamine** 16 mg troche [or 16 mg/ml syrup] 8–16 mg sublingual q8-12h prn withdrawal symptoms, max 48 mg/day, #8 troches [or 8 ml].

**Nausea/Vomiting**

- **Ondansetron** 4 mg 1-2 ODT q6h prn nausea/vomiting, max 6 tabs/24h, #28
- **Metoclopramide** 5 mg 1-2 PO q6h, prn nausea/vomiting, max 9 tabs/24h, #42

**Diarrhea**

- **Loperamide** 2 mg q8h prn diarrhea, #21
- **Dicyclomine** 10 mg 1-2 q6h prn diarrhea/abdominal cramping, #40

**General anxiety**

- **Gabapentin** 600-800 mg q8h prn anxiety, #21
- **Baclofen** 10 mg q8h prn muscle cramps, #21
- **Hydroxyzine** 25 mg 1-2 q6h prn anxiety/agitation/insomnia, #50

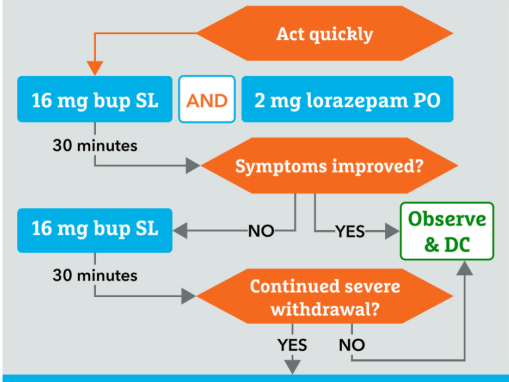
**Insomnia**

- **Quetiapine** 50 mg q8h prn anxiety/insomnia, #21
- **Trazodone** 50-100 mg qHS prn insomnia, #20

**In the event of buprenorphine precipitated withdrawal (sudden severe worsening of withdrawal symptoms, e.g., abrupt COWS score increase of >5):**

**Treatment of bup precipitated withdrawal**

(Sudden, significant worsening of withdrawal soon after bup administration.)




**Adjuvants:**
OK but should not delay or replace bup. Use sparingly with appropriate caution.

**Benzodiazepines:**
- Lorazepam 2 mg PO/IV

**Antipsychotics:**
- Olanzapine 5 mg PO/IM

**Alpha-agonists:**
- Clonidine 0.1-0.3 mg PO

**D2/D3 agonists:**
- Pramipexole 0.25 mg PO

**Gabapentinoids:**
- Pregabalin 150 mg PO

**Escalate level of care to manage potential moderate to deep sedation including cardiac, pulse oximetry, and end tidal $CO_2$ monitoring:**

1. Ketamine (0.3 mg/kg IV slow push q 15 minutes and/or infusion).
2. Fentanyl 200 mcg IV q10 minutes. Total dose of > 2000 mcg has been reported.

**After clinical resolution, observe and discharge with bup Rx and/or XR-bup**

*Source: CA Bridge's "Emergency Department Buprenorphine Quick Start"*

For refractory precipitated withdrawl not responding to bup / fentanyl / ketamine, consider dexmedetomidine. Typically need higher dosing, e.g., starting at 1-1.5 mcg/kg/hr and titrating up as needed.

**Pain, muscle aches**

- **Ibuprofen** 400 mg 1-2 q6h prn pain, #40
- **Acetaminophen** 500 mg 1-2 q6h prn pain, #40

**Restlessness**

- **Pramipexole** 0.25 mg 1-2 q8h prn restless legs, #21

## Available formulations of long acting injectable buprenorphine (XR bup)

| Generation | Formulation | US Brand Name | Dosage Form | Doses | Injection Volumes | Median Time to Max Concentration (Tmax) | Mean Half Life (T1/2) |
|---|---|---|---|---|---|---|---|
| 2nd | XR bup weekly (50 mg/mL) | Brixadi Weekly | Pre-filled syringe | 8 mg, 16 mg, 24 mg, 32 mg | 0.16 mL, 0.32 mL, 0.48 mL, 0.64 mL | 24 h | 5 d |
| 2nd | XR bup monthly (356 mg/mL) | Brixadi Monthly | Pre-filled syringe | 64 mg, 96 mg, 128 mg | 0.18 mL, 0.27 mL, 0.36 mL | 6-10 h | 19-25 d |
| 1st | XR bup monthly (200 mg/mL) | Sublocade | Pre-filled syringe | 300 mg, 100 mg | 1.5 mL, 0.5 mL | 24 h | 45-60 d |

This protocol was designed by addiction medicine experts across the United States through an interactive, collaborative process led by the Bridge Center.

***Please scan the QR code or use the link below for a list of contributors and references.***

https://bridgetotreatment.org/DTI-Contributors-and-References

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