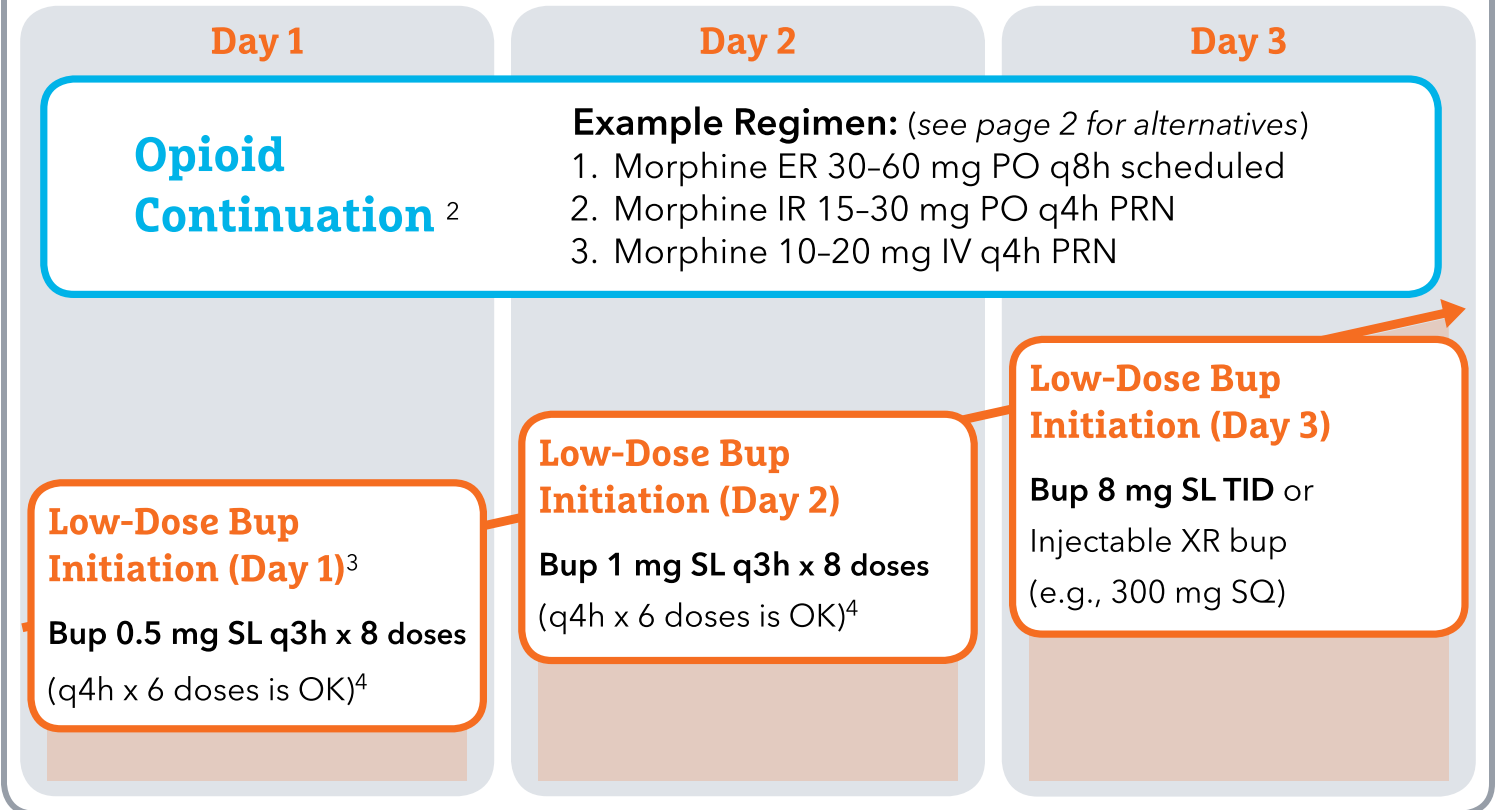


## Treatment Bundle Over Three Days<sup>1</sup>

Maximize pain control & withdrawal treatment with opioid analgesics throughout bup initiation



### Footnotes

- A rapid three-day bup up-titration schedule is presented here** that may not be appropriate for some patients such as patients receiving high-dose (e.g., ≥100 mg daily) methadone. Extend initiation schedule by lengthening the dose interval to q4h, q6h, or q8h+ and/or increasing the number of doses to be given at each step prior to advancing. **Example:** bup 0.5 mg SL q4h for 12 doses. (See page 2 for Example Five Day and Eight Day Ramp schedules.)
- Opioid Analgesic (full agonist) Dosing:** The doses presented here assume a very high opioid tolerance. Use clinical judgment to tailor opioid dose to match expected level of opioid tolerance. Morphine doses are presented as a guide for conversion to preferred opioid. (See page 2 for Alternative Full Agonist Opioids.) Combine opioids with a multimodal analgesic strategy for optimized comfort and pain control (e.g., NSAIDs, ketamine, and regional anesthesia. (See [CA Bridge Acute Pain Management](#) guide.)
- Bup Dosing:** SL film doses are presented here as a guide for conversion to preferred bup formulation. If bup 0.5mg SL (quartering a 2 mg SL film) is a pharmacy barrier, most patients will tolerate bup 1 mg SL or an alternative formulation can be used. **Example:** bup buccal film 300 mcg, or bup 0.15 mg IV. (See page 2 for Alternative Bup Formulations.)
- Bup Frequency:** It is OK to hold doses for sleep. Continue dosing when awake. If nursing capacity limits q3h dosing intervals increasing to q4h or q6h is generally well tolerated. Most patients will tolerate 1-2 missed doses per step.

# Tailoring the Guide to Your Hospital and Your Patient

## Troubleshooting When Pain and Withdrawal Increases

**Is the full agonist opioid dose too low?** If a patient displays worsening pain and withdrawal after bup administration, additional full agonist opioid is the first line treatment. Consider rapid up-titration of short-acting PRN opioid and increase the scheduled long-acting opioid as indicated.

**Is the rate of bup increase too rapid?** Bup dosing can be paused for 2-4 hours then restarted and/or bup up-titration can be lengthened to five, eight, or more days by decreasing the bup dose and/or increasing the dose interval period.

**Is multimodal analgesia optimized?** Consider non-steroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, and ketamine. Particularly, **ketamine (bolus 0.3 mg/kg IV over 15 minutes or infusion of 0.3-0.5 mg/kg/h)** may reduce pain and discomfort.

**Are adjuvant treatments of withdrawal optimized?** Consider symptom-targeted clonidine 0.1-0.3 mg PO, pramipexole (D2/D3 agonist) 0.25 mg PO, ondansetron 4 mg PO, and/or lorazepam 1-2 mg PO (or equivalent).

**Should high-dose bup be started?** When severe and/or precipitated withdrawal develops, consider transition to high-dose bup. See Emergency Department Quick Start Guide.

## Example Five Day Low-Dose Initiation Schedule

**Day 1-2:** Bup 0.5 mg SL q6h for 8 doses

**Day 3-4:** Bup 1 mg SL q6h for 8 doses

**Day 5:** Bup 8 mg SL TID or injectable XR bup

## Example Eight Day Low-Dose Initiation Schedule\*

**Day 1:** Bup 0.5 mg (¼ of 2 mg strip) SL once

**Day 2:** Bup 0.5 mg SL BID

**Day 3:** Bup 1 mg (½ of 2 mg strip) SL BID

**Day 4:** Bup 2 mg SL BID

**Day 5:** Bup 3 mg (1+½ of 2 mg strip) SL BID

**Day 6:** Bup 4 mg (2 of 2 mg strip) SL BID

**Day 7:** Bup 6 mg (3 of 2 mg strip) SL BID

**Day 8:** Bup 8 mg SL TID or injectable XR bup

\* May be considered for high-dose methadone transitions to bup. Continue full dose methadone through day 7 then stop.

## Alternative Full Agonist Opioids

In contrast to general practice where opioid sparing is a best practice, during bup dose up-titration the aim is to safely **maximize** full agonist opioids for optimized comfort and prevent treatment disengagement such as leaving against medical advice (AMA).

**Do not aim to decrease the full agonist during bup dose up-titration.** Simultaneous bup up-titration and full agonist weaning may abruptly reduce total opioid activation resulting in pain and withdrawal.

### Alternative to Morphine ER 60 mg PO q8h:

Oxycodone ER 40 mg PO q8h **or**

Methadone 10 mg PO q8h

### Alternative to Morphine IR 30 mg PO q4h PRN:

Oxycodone IR 20 mg PO q4h PRN **or**

Hydromorphone 6-8 mg PO q4h PRN

### Alternative Morphine IV 20 mg q4h PRN:

Hydromorphone 4 mg IV q4h PRN **or**

Fentanyl 200 mcg IV q4h PRN

## Bup Plasma Concentrations with Low-Dose Initiation

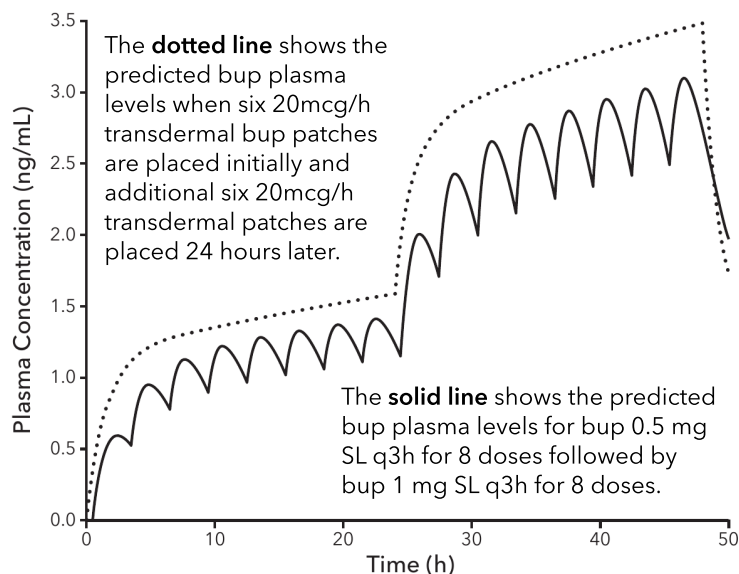


Figure Source: Azar, Pouya, et al. "48-hour Induction of Transdermal buprenorphine to Sublingual buprenorphine/Naloxone: The IPPAS Method." *Journal of Addiction Medicine* (2022): 10-1097.

## Alternative Bup Formulations

Alternatives that approximate a bup 0.5 mg SL dose:

- Bup IV\* ~ 0.15 mg IV
- Bup buccal film 300 mcg\*\*
- Bup oral (PO) - swallowing a bup 2 mg SL tablet (absorption is variable, estimate 0.5-0.8 mg SL)
- Bup transdermal patch 20mcg/hr\*\* ~ bup 0.5 mg SL over 24hrs. (See figure for additional dosing details)

\*\* FDA Approved for pain management only

## Further Reading

Weimer, M. B., Herring, A. A., Kawasaki, S. S., Meyer, M., Kleykamp, B. A., & Ramsey, K. S. (2023). ASAM clinical considerations: bup treatment of opioid use disorder for individuals using high-potency synthetic opioids. *Journal of addiction medicine*, 17(6), 632-639.

\* Methadone transition

Terasaki, Dale, Christopher Smith, and Susan L. Calcaterra.

"Transitioning hospitalized patients..." *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* 39.10 (2019): 1023-1029.