Buprenorphine (Bup) Hospital Start: Low-Dose Bup Initiation with Opioid Continuation

Treatment Bundle Over Three Days[1]

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

Day 1	Day 2	Day 3
Opioid Continuation[2]	**Example Regimen:** (*see page 2 for alternatives*) 1. Morphine ER 30–60 mg PO q8h scheduled 2. Morphine IR 15–30 mg PO q4h PRN 3. Morphine 10–20 mg IV q4h PRN	
Low-Dose Bup Initiation (Day 1)[3] **Bup 0.5 mg SL q3h x 8 doses** (q4h x 6 doses is OK)[4]	**Low-Dose Bup Initiation (Day 2)** **Bup 1 mg SL q3h x 8 doses** (q4h x 6 doses is OK)[4]	**Low-Dose Bup Initiation (Day 3)** **Bup 8 mg SL TID** or Injectable XR bup (e.g., 300 mg SQ)

Footnotes

1. **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.)*

2. **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.)

3. **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.)*

4. **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.

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January 2026

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.

Bup Plasma Concentrations with Low-Dose Initiation

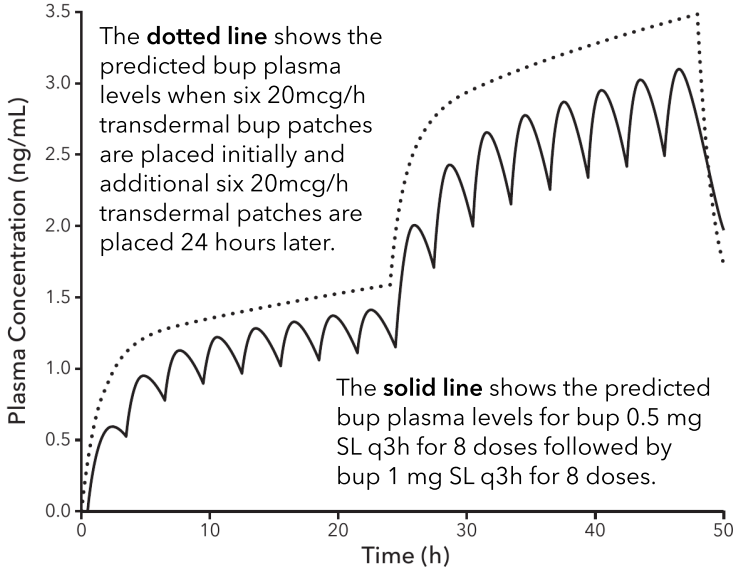

Figure Source: Azar, Pouya, et al. "48-hour Induction of Transdermal buprenorphine to Sublingual buprenorphine/Naloxone: The IPPAS Method." *Journal of Addiction Medicine* (2022): 10-1097.

Alternative 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

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.