Buprenorphine (Bup) Hospital Quick Start

- Any prescriber can order Bup in the hospital, even without an x-waiver.
- Bup is a high-affinity, partial agonist opioid that is safe and highly effective for treating opioid use disorder.
- If patient is stable on methadone or prefers methadone, recommend continuation of methadone as first-line treatment.

Uncomplicated* opioid withdrawal?**

- YES (stop other opioids)
- Administer 8mg Bup SL

1 Hour

Withdrawal symptoms improved?

- NO
- Start Bup after withdrawal
  Supportive meds prn, stop other opioids

- YES
- Administer 2nd dose
  Inpatient: 8mg. Subsequent days, titrate from 16mg with additional 4-8mg pm cravings.
  ED: 8-24mg. Consider discharge with higher loading dose.

Maintenance Treatment
16 mg Bup SL/day
Titrated to suppress cravings; Usual total dose 16-32mg/day

Discharge
- Document Opioid Withdrawal and/or Opioid Use Disorder as a diagnosis.
- If no X-waiver: Use loading dose up to 32mg for long effect and give rapid follow up.
- If X-waiver: Check CURES (not required in Emergency Department if ≤7 day prescription), prescribe sufficient Bup/Nx until follow-up.

Buprenorphine Dosing
- Either Bup or Bup/Nx (buprenorphine/naloxone) films or tab sublingual (SL) are OK.
- If unable to take oral/SL, try Bup 0.3mg IV/IM.
- OK to start with lower initial dose: Bup 2-4mg SL.
- Total initial daily dose above 16mg may increase duration of action beyond 24 hrs.
- Bup SL onset 15 min, peak 1 hr, steady state 7 days
- May dose qday or if co-existing chronic pain split dosing TID/QID.

*Complicating Factors
- Altered mental status, delirium, intoxication
- Severe acute pain, trauma or planned large surgeries
- Organ failure or other severe medical illness
- Recent methadone use

**Diagnosing Opioid Withdrawal

Subjective symptoms AND one objective sign

Subjective: Patient reports feeling “bad” due to withdrawal (nausea, stomach cramps, body aches, restlessness, hot and cold, stuffy nose)

Objective: [at least one] restlessness, sweating, rhinorhea, dilated pupils, watery eyes, tachycardia, yawning, goose bumps, vomiting, diarrhea, tremor

Typical withdrawal onset:
- ≥ 12 hrs after short acting opioid
- ≥ 24 hrs after long acting opioid
- ≥ 48 hrs after methadone (can be >72 hrs)

If unsure, use COWS (clinical opioid withdrawal scale). Start if COWS ≥ 8 AND one objective sign.

If Completed Withdrawal:
- Typically >72 hrs since last short-acting opioid, may be longer for methadone. Start Bup 4mg q4h pm cravings, usual dose 16-32mg/day. Subsequent days, OK to decrease frequency to qday

Opioid Analgesics
- Pause opioid pain relievers when starting Bup.
- OK to introduce opioid pain relievers after Bup is started for breakthrough pain. Do not use methadone with Bup.

Supportive Medications
- Can be used as needed while waiting for withdrawal or during induction process.

Pregnancy
- Bup monoprodact or Bup/Nx OK in pregnancy.
- Consider referencing buprenorphine in pregnancy guide.

Overdose Education Naloxone Kit
Naloxone 4mg/0.1ml intranasal spray

The CA Bridge Program disseminates resources developed by an interdisciplinary team based on published evidence and medical expertise. These resources are not a substitute for clinical judgment or medical advice. Adherence to the guidance in these resources will not ensure successful patient treatments. Current best practices may change. Providers are responsible for assessing the care and needs of individual patients.

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REFERENCES


Starting Buprenorphine Immediately after Reversal of Opioid Overdose with Naloxone


Heroin or Fentanyl* overdose reversed with naloxone

*or other short-acting opioid

Are any patient exclusion criteria present?

- Benzodiazepine, other sedative or intoxicant suspected
- Altered mental status, depressed level of consciousness, or delirium
- Unable to comprehend potential risks and benefits for any reason
- Severe medical illness such as sepsis, respiratory distress, organ failure present or suspected
- Report of methadone use
- Not a candidate for buprenorphine maintenance treatment for any reason

NO TO ALL

Is the patient awake with signs of opioid withdrawal? (i.e. COWS >4)

NO

YES

Is the patient agreeable to treatment with buprenorphine?

NO

YES

16mg SL Buprenorphine

Administered as a single dose or in divided doses over 1-2 hours. (Start with 0.3mg IV if unable to tolerate SL.)

Observe in ED until patient shows no clinical signs of excessive sedation or withdrawal (typically 2 hours).

OK to administer additional doses of Bup up to 32mg. Engage, use motivational interviewing, and link to ongoing care.

YES TO ANY

Provide supportive care, observe and reevaluate.
Buprenorphine After Opioid Overdose (ODNaloxoneBup)

The minimum inclusion criteria for ODNaloxoneBup is an otherwise healthy patient with no suspected co-ingestions and no recent methadone use with a normal level of consciousness, normal mental status, and the ability to provide informed consent. Administration of buprenorphine (Bup) to patients intoxicated with alcohol, benzodiazepines or other sedative can result in potentially dangerous respiratory depression. Patients with acute illness or severe chronic illness such as infection, heart failure, liver failure, respiratory failure or acute renal failure can experience unpredictable sedation and respiratory depression. Patients with altered mental status are not able to provide a reliable history or adequately consider the risks and benefits to provide informed consent. Patients taking methadone should be supported to continue methadone treatment; overdose is not an indication to switch to buprenorphine and may disrupt care. Additionally, the interaction with buprenorphine and methadone is not well understood and potentially adverse antagonistic (withdrawal) interactions can occur.

**Be prepared**  There are two “worst case scenario” adverse events possible with ODNaloxoneBup: 1) additive sedation with respiratory depression and 2) precipitated withdrawal. While neither of these has been reported at this time, any ED should be prepared and willing to adequately manage these potential complications. Reversal of buprenorphine is accomplished with high-dose naloxone (2-3mg IV push followed by 4mg/hr infusion) (9,10). Precipitated withdrawal is treated with empirically titrated with a multimodal approach that may include: benzodiazepines, alpha-2 agonists (clonidine, dexmedetomidine, lofexidine), high affinity full agonist opioids (hydromorphone), ketamine, and dopamine antagonists (e.g. metoclopramide or haloperidol).

**Why this works**  Once naloxone has reversed opioid overdose (regardless of whether withdrawal signs/symptoms have been precipitated), initiation of buprenorphine should yield a relative increase in mu-opioid receptor (MOR) agonism and be experienced as stabilization or withdrawal relief. *In vitro* (+NaCl), naloxone exhibits 5-fold higher MOR affinity than morphine and comparable MOR affinity as sufentanil and, under these same physiological conditions, buprenorphine exhibits 6-fold higher MOR affinity than naloxone. Following naloxone displacement and reversal of opioid overdose, buprenorphine is therefore expected to displace naloxone from available MORs (and residual naloxone effect should wash out rapidly due to its pharmacokinetics; see figure below). Once bound to MORs, buprenorphine’s high-affinity, longer-acting MOR occupancy should effectively prevent return of full agonist toxicity (provide opioid blockade) even if relatively high concentrations of full agonist remain in the circulation. The positive treatment responses we have observed suggest the possibility that as naloxone is metabolized and/or displaced from MORs a mixed state of buprenorphine partial agonism and full opioid agonism (from the residual opioid that caused the overdose) occur, thereby avoiding an abrupt transition from full to partial agonism that would have been experienced as precipitated withdrawal.

References:


