Buprenorphine Cross-Tapering using a Low-dose (microdosing) Strategy

Background: Buprenorphine is a mu opioid receptor partial agonist that is indicated for pain management and the treatment of opioid use disorder (OUD). Traditional induction for patients with OUD requires a patient to experience opioid withdrawal (measured via COWS scores) prior to buprenorphine initiation. This is necessary because high doses of buprenorphine, a partial opioid agonist, may cause precipitated withdrawal when used in the setting of a full opioid agonist. Low dose induction (microdosing) of buprenorphine uses the buprenorphine buccal films (Belbuca®), which are dosed in micrograms, allowing buprenorphine initiation without requiring withdrawal with a minimal risk of precipitated withdrawal. Doses are increased over 3-4 days to achieve full maintenance dosing. Case reports and case series have generally demonstrated success with this approach in hospital settings using a variety of different dosing approaches.

Intent: For use as an alternative to traditional buprenorphine induction strategies

Intended Patient Population

1. Patients requesting buprenorphine treatment who have a history of illicit opioid use (e.g. fenta**NYL**) AND who wish to avoid the need for moderate withdrawal symptoms prior to induction with standard starting doses of buprenorphine. UDS confirmation is not necessary.
   - For example, patients stabilized on full agonist and transitioning to buprenorphine:
     - From methadone
     - Who have experienced prior precipitated withdrawal
     - Without significant withdrawal symptoms at initiation

OR

2. Patients on full opioid agonist for treatment of pain AND who wish to initiate buprenorphine
   - For example:
     - Patients admitted with acute pain and comorbid OUD, requiring opioids for analgesia
     - Patients on chronic opioids for analgesia

3. This approach may also be used in pregnant patients (SAMHSA 2018).

Procedure:

1. **Full Opioid Agonist**

   Prior to buprenorphine micro-dosing induction, establish scheduled regimen of oxy**CODONE**, **HYDRO**morphone, fenta**NYL**, morphine, or methadone that is effective for pain, withdrawal, and cravings per patient report.

   - **Recommended full opioid agonist regimens:**
     - Long acting options - Oxycodone ER 40mg PO TID or Methadone 40mg PO daily PLUS
     - Short acting options – Oxycodone IR 20mg PO q4h or hydromorphone IR 8mg PO q4h

2. **Clinical Opioid Withdrawal Scale (COWS) Monitoring**

- COWS should be documented throughout the induction process to monitor for withdrawal at least every 12 hours (e.g. with every other buprenorphine administration) and as needed based on withdrawal (eg. nausea/diarrhea, cravings).
- If COWS scores rise, encourage patients to continue low dose (microdose) induction pathway. Offer non-opioid adjuvants or higher doses of full-agonist opioids for withdrawal symptoms. If patients prefer not to continue, pause buprenorphine, continue full-agonist opioids, and consider psychiatry consult.

Discharge Considerations:

- Ensure early discharge planning for follow-up with buprenorphine provider and for OUD care
- Provide Narcan® – utilize MyPennPharmacy for discharge prescription if available.

Low Dose (microdosing) induction regimen using Belbuca® and Suboxone® (Buprenorphine/naloxone)

- On Day 1, while continuing full-agonist opioids, use buccal buprenorphine 300mcg or 150 mcg per the chart below
- After Day 2 or 3, consolidate total daily dose into once daily dosing as Suboxone® (buprenorphine/naloxone) once on a stable dose post-titration and prior to discharge.
- If needing assistance at any point during this titration, please contact the Opioid Stewardship Pharmacist (HUP only). If unavailable, reach out to Psychiatry.

Day	Buprenorphine
Day 1	*Buprenorphine (Belbuca®) 300 mcg buccal q4h OR Buprenorphine 150 mcg q3h *May consider either dosing schedule based on patient's risk or fear of precipitated withdrawal and to allow for patient choice. Consider nursing staff capabilities in choosing the frequency of administration.
Day 2	Buprenorphine /naloxone 2 mg SL q6h
Day 3	Buprenorphine/ naloxone 4mg SL q6h (alternatively 8mg q12h if preferred)
Day 4	Full dose Buprenorphine /naloxone 16-24mg daily (may be split up BID or TID)
Full Opioid Agonist	
• Full agonists should be continued during this induction and may be tapered starting on Day 2 of induction OR discontinued once patients reach 16-24mg of buprenorphine/naloxone daily. The approach should be agreed upon with the patient. • Full agonist therapy may also be continued after you reach the goal buprenorphine dose for pain or continued symptoms of withdrawal. Work with the patient to develop a taper plan that is reasonable and to optimize non-opioids for symptom management while tapering full agonist opioids. • For transitions from methadone: For buprenorphine induction in patients on methadone doses of ≥80 mg daily it is recommended to seek expert consultation. Give the final dose of methadone on Day 1 and follow buprenorphine 150 mcg dosing titration protocol above. On day 2, you may give an additional 30 mg of methadone orally daily for persistent withdrawal symptoms.	
For patients not tolerating anything in the oral cavity: Can use IV buprenorphine 300 mcg q6h on day 1; 600 mcg IV q6h on day 2; and 1200 mcg (1 gram) IV q6h on day 3	
Approximate Buprenorphine Equivalencies: 1 mg sublingual buprenorphine ≈ 450 mcg buccal buprenorphine ≈ 250 mcg IV buprenorphine	

****A NOTE on TAPERING:** All tapering should be done with shared-decision making with the patient. Optimize nonopioids to increase chances of success. See additional considerations in table above.

Patients on chronic opioids:

- On day 1 of buprenorphine low dose (microdose) induction, maintain full agonist therapy. Day 2, decrease full agonist by 30-50% and then 25% every 2-3 days thereafter or as indicated based on expected acute/chronic pain trajectory.

  For example: Baseline regimen: Oxy**CODONE** ER 40 mg PO q12h and oxy**CODONE** 10 mg PO q6h (total daily oxy**CODONE** = 120 mg = oral morphine equivalent (OME) 180 mg) → Decrease 50% to oxy**CODONE** ER 20 mg PO q12h x 2 days and oxy**CODONE** 5 mg PO q6h

x 2 days; then oxy**CODONE** 10 mg ER PO q12h and oxy**CODONE** 10 mg PO q8h x 2 days; then discontinue oxy**CODONE** ER and decrease to oxy**CODONE** 10 mg PO q12 h x 2 days, then stop all oxy**CODONE**.

Patients on opioids for acute pain:

- If patients are having refractory pain on full dose buprenorphine/naloxone (16 mg/d), consider lowering the buprenorphine/naloxone dose to 8 or 12 mg daily and giving in split q6-8h dosing (i.e. 4 mg SL q8h or q12h) until the need for full opioid agonist for acute pain management resolves at which time the buprenorphine/naloxone dose should be increased back up to the 16 mg total daily dose.
- Provide PRN opioid analgesic. Provide rapid taper (over 3-5 days) as acute pain resolves.
  For example: Baseline regimen: Oxy**CODONE** 10 mg PO q4h → Decrease 30% (Day 1) oxy**CODONE** 10 mg PO q6 x 2 days; then oxy**CODONE** 10 mg PO q12h x 2 days; then oxy**CODONE** 5 mg PO q12h x 2 days, then stop if full agonist is no longer needed.

References

Antoine D, Huhn AS, Strain EC, Turner G, Jardot J, et al. Method for successfully inducting individuals who use illicit fentanyl onto buprenorphine/naloxone. Am J Addict. 2020, 00:00-00.

Brar R, Fairbairn N, Sutherland C, Nolan S. Use of a novel prescribing approach for the treatment of opioid use disorder: Buprenorphine/naloxone microdosing – a case series. Drug Alcohol Rev 2020;39:588-594.

Klaire S, Zivanovic R, Barbic SP, Sandhu R, Mathew N, Asar P. Rapid micro-induction of buprenorphine/naloxone for opioid use disorder in an inpatient setting: A case series. Am J Addict 2019;28:262-265.

Rozylo J, Mitchell K, Nikoo M, Durante SE, Barbic SP, et al. Case report: Successful induction of buprenorphine/naloxone using microdosing schedule and assertive outreach. Addict Sci Clin Pract. 2020;15:2: https://doi.org/10.1186/s13722-020-0177-x.

Substance Abuse and Mental Health Services Administration. *Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants*. HHS Publication No. (SMA) 18-5054. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2018.

Weimer MB, Guerra M, Morrow G, Adams K. Hospital-based Buprenorphine Microdose Initiation. J Addict Med. 2020; 00:00-00: 10.1097/ADM.0000000000000745.

Updated by: Emily Casey; additional input from Ashish Thakrar, Jeanmarie Perrone, Maggie Lowenstein, Navid Roder

Reviewed by: PPMC, PAH, PMPC, CCH, HUP, Oct 2023