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How to Prescribe Buprenorphine for Patients with Serious Illness

Buprenorphine can be used for the treatment of chronic pain, and is a gold standard treatment for Opioid Use Disorder (OUD). Buprenorphine is also a preferred opioid for the treatment of pain in older adults due to its unique safety profile and mechanism of action.[1,2]

Advantages of buprenorphine include decreased risk of overdose and reduced opioid side effects (e.g., depression, dysphoria, anxiety, sedation, respiratory depression, hyperalgesia, endocrine dysfunction, tolerance).[3]

Consider buprenorphine for patients with chronic pain who require around-the-clock treatment with opioid therapy. For comprehensive training, register for CAPC's virtual workshops, Managing Pain at the Intersection of Serious Illness, Chronic Pain, and Substance Use Disorder, and Navigating Prescribing Decisions for Patients with Chronic Pain and Serious Illness: Case Reviews.

Selecting a Buprenorphine Formulation[4,5]

Relevant Buprenorphine Formulations

Route of Administration	Transdermal (TD) Patch	Buccal Film	Sublingual (SL) Film
Formulations	Buprenorphine only (e.g. Butrans®)	Buprenorphine only (e.g. Belbuca®)	Buprenorphine/ naloxone (e.g. Suboxone®) Generic SL buprenorphine without naloxone
Indication	Pain	Pain	OUD and/or pain
Dosing Range	5-20 mcg	75-1800 mcg/day	2-32 mg/day
Dosing Frequency	Every 5-7 days	Daily to twice daily	Daily to four times/day
Common Dosing Schedule	Every 7 days	Twice a day	Daily for OUD; three times a day for pain
Steady State	3 days	4 days	7 days
Risk of Precipitated Withdrawal*	**No**	**Unlikely** (unless >450 mcg/day)	**Yes**

Precipitated withdrawal is the rapid development or acute worsening of opioid withdrawal shortly after administration of buprenorphine (typically doses > 2 mg) in someone who has recently used non-prescribed or prescribed opioids. To avoid precipitated withdrawal, follow the low-dose induction instructions on starting SL buprenorphine. The rate of precipitated withdrawal is 1-2% in the literature, and it is more common in people using high-dose synthetic opioids such as fentanyl.[6]

Approximate Equivalency Between Buprenorphine Formulations Based on Bioavailability**

Transdermal (TD) Patch	Buccal Film	Sublingual (SL) Film
5 mcg	75 mcg	0.25 mg (1/8th of a 2 mg film)
10 mcg	150 mcg	0.5 mg (1/4th of a 2 mg film)
15 mcg	300 mcg	0.75 mg (3/8th of a 2 mg film)
20 mcg	450 mcg	1 mg (1/2 of a 2mg film)

***Bioavailability represents systemic effect*

Treatment Indication(s)

	Transdermal (TD) Patch	Buccal Film	Sublingual (SL) Film
Chronic Pain and Opioid-Naïve	**Yes**	**Yes**	**No**
Chronic Pain and Opioid-Tolerant	**Yes** (often >10 mcg)	**Yes** (often >150 mcg)	**Yes** (often >1 mg)
Opioid Use Disorder	**No**	**No**	**Yes**

How to Start Buprenorphine

Determine the correct formulation based on mean morphine equivalent (MME) dose and presence of OUD. (Note that a combined buprenorphine/naloxone product is preferred for patients with OUD unless not tolerated.)

Opioid-naïve or using <100 mg MME/day (no OUD) ↓ Transdermal (TD) or buccal buprenorphine

Using >100 mg MME/day or OUD ↓ Low-dose initiation of sublingual (SL) buprenorphine (with or without naloxone)

Starting Buprenorphine (TD or Buccal): Start Low, Go Slow[7,8]

Baseline Daily MME	Starting TD Dose	Starting Buccal Dose
<30 mg	5 mcg/hour	75 mcg once a day on day 1, twice a day after that
30-100 mg	10 mcg/hour	150 mcg once a day on day 1, twice a day after that
100 mg-160 mg	Not recommended	300 mcg (once a day on day 1, twice a day after that); can titrate up to 450-900mcg twice daily
>160 mg	If patient is on >160 MME/day, use the low-dose initiation table below	

Low-Dose Initiation: The Recommended Approach for Transitioning Patients to Sublingual (SL) Buprenorphine[9,10,11]

Appropriate for most patients transitioning from opioid agonists to buprenorphine because it does not precipitate withdrawal symptoms.

1. Start your patients on low-dose buprenorphine while continuing their current opioids, including breakthrough/PRN dosing.
2. Increase the buprenorphine dose gradually over 6 days.
3. Depending on pain level, at a dose of 8 mg daily of buprenorphine, reduce the long-acting opioid dose by 50%.
4. Once at a dose of 12 mg daily of buprenorphine, stop the long-acting opioid.
5. Patient should be seen in follow-up for an evaluation within the week following the transition.

Other Considerations

- Assess pain intensity and impact of pain on function.
- Discuss and document the benefits and risks of opioid therapy with the patient.
- Evaluate for OUD using DSM criteria: **tinyurl.com/52dcwutc**.
- Insurance is more likely to cover the combined buprenorphine/naloxone product.
  - Insurance plans may have a preference for either a film or a tablet, but both are effective and dosing guidance is the same.
  - Add "opioid dependence, uncomplicated" as a diagnosis (F11.20 code).
- Provide naloxone and education on opioid overdose.
- Review state prescription drug monitoring program (PDMP) before prescribing.

How to Initiate

Day	Buprenorphine/naloxone (2 mg film or tablet)	Full agonist (prescribed or not prescribed)
1	0.5 mg twice a day (1/4 film or tab)	Full dose
2	1 mg twice a day (1/2 film or tab)	Full dose
3	1 mg three times a day (1/2 film or tab)	Full dose
4	2 mg three times a day (1 film or tab)	2/3 dose
5	4 mg three times a day (2 films or tabs)	None
6 and onward	Adjust buprenorphine dose further. Typical OUD doses range from 12-24 mg/day. Lower doses may be adequate for pain.	None

Note: For patients who present in opioid withdrawal or wish to rotate to buprenorphine faster, the Traditional Buprenorphine Initiation Method (that requires opioid discontinuation and experiencing mild to moderate opioid withdrawal symptoms) can be considered. For information on this method, visit: **tinyurl.com/aywkb6x5**

What to Tell Patients about Buprenorphine

Patch

- Apply to a hairless part of the body (upper outer arm, upper chest, upper back, or side of the chest).
- Rotate application sites and counsel as usual with other transdermal systems (e.g., no direct heat).
- **Change patch every 7 days**. If end-of-dose failure, you may consider dosing every 5 days.
- It is okay to swim and shower with patch applied.
- Topical reaction occurs in approximately 10-35% of patients but rarely requires stopping treatment.[12]
- If localized skin irritation occurs, patients can apply one squirt of over the counter fluticasone nasal spray to the skin, and let it dry completely before applying the patch (off-label use).

Buccal/Sublingual

- Film/tablet is sensitive to moisture; make sure hands are dry when handling and applying.
- Do not swallow; take a sip of water before applying, and then do not eat or drink until the film/tab dissolves (usually 30-40 minutes).
- It may take several days/weeks to adjust; patient may use as-needed opioid agonists for poorly-controlled pain.
- It is okay to cut or split films or tablets.[13]
- Encourage good dental hygiene to avoid irritation.

For additional buprenorphine prescribing resources, visit: tinyurl.com/3n64s2zp

For references, visit: capc.org/buprenorphine-references

This document does not replace clinical judgment for treatment of an individual patient. This material is the result of work led by Katie Fitzgerald Jones supported with resources and the use of facilities at the Veterans Affairs Boston Healthcare Center and the New England Geriatric Research Education and Clinical Center. The content is the responsibility of the authors and does not represent the views of the VA, academic affiliates, or U.S. government.