Clinical Resource Guide: Transitioning to Buprenorphine for Pain

INTRODUCTION

Refractory pain not responsive traditional opioids and pain management strategies can be difficult to manage. Escalating doses or a transition to subcutaneous or intravenous route of administration can result in variable responses and may require changes in routine or even patient care setting, adding burden to the patient and considerable additional therapy cost to care. The burgeoning awareness of the pain-relieving benefits of buprenorphine resulting from the 2022 updated CDC Clinical Practice Guideline for Prescribing Opioids for Pain have led some clinicians to consider the drug in the hospice setting for patients experiencing uncontrolled pain. This Pharmacist Corner was created to serve as a resource to hospice administrators and clinicians by providing guidance on the following:

Pharmacist Corner Objectives

1. Provide a general overview of buprenorphine for plan
2. Describe patient-specific factors when considering a transition to buprenorphine for pain
3. Determine the appropriate buprenorphine transition strategy based on patient's current opioid regimen

BUPRENORPHINE FOR PAIN MANAGEMENT

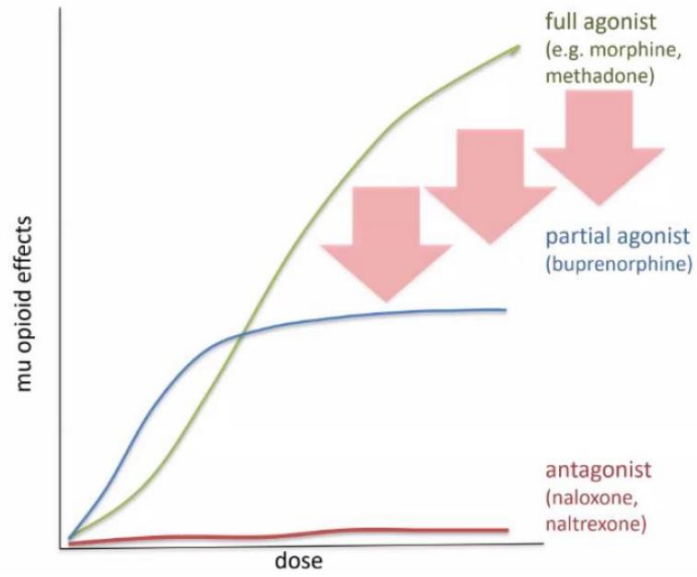
Prior to considering whether a transition to buprenorphine may be appropriate for a patient with refractory pain, it is essential to have at least a basic understanding of buprenorphine and available products.

While buprenorphine is often associated with treatment of opioid use disorder, the low dose buprenorphine formulations (*Butrans®* transdermal patches and *Belbuca®* buccal films) as well as the IV formulation (*Buprenex®*) are FDA-approved for pain. While buprenorphine sublingual tablets and buprenorphine/naloxone sublingual tablets and films are only FDA-approved for opioid use disorder, these formulations have been used off-label for treatment of pain, often in patients with severe pain where *Butrans®* or *Belbuca®* were not found to be effective or patients required > 90mg of morphine or an equivalent dose of another full-agonist opioid.

Brand Name	Formulation	Strengths	FDA Indication
Buprenex®	IV/IM	0.3mg/ml	Pain
Butrans®	Transdermal	5,7.5,10,15,20mcg/hr	Pain
Belbuca®	Buccal film	75,150,300,450,600,750,900mcg	Pain
Subutex®	Sublingual tablet	2mg, 8mg	OUD*
Suboxone® Zubsolv® (buprenorphine/naloxone)	Sublingual film Sublingual tablet	2/0.5mg, 4/1mg, 8/2mg, 12/3mg 2/0.5mg, 8/2mg	OUD*
Sublocade® Brixadi®	Subcut injection	100mg, 300mg 8mg, 24mg, 64mg	OUD

**Off-label use for pain management*

Pharmacologically, the pain-relieving effect of buprenorphine results from its partial agonism of mu-opioid receptors. However, this does not mean the patient experiences only partial pain. The term is used to describe the specific activation of the receptor and specific proteins responsible for analgesia as compared to full agonists, like morphine or oxycodone. The partial activation of the mu-opioid receptor in combination with antagonist effect at the kappa and delta opioid receptors, may explain how it provides analgesia with a more favorable adverse effect profile, including less withdrawal, less tolerance, and a ceiling effect on respiratory depression that serves to lower the risk of overdose with use (see image below).



TRANSITION CONSIDERATIONS

Opioid Withdrawal

Buprenorphine also has a higher binding affinity to the mu-opioid receptor than any of the traditional full agonist opioids. This results in buprenorphine preferentially occupying the opioid receptors and replacing opioids with a lower binding affinity. This effect is responsible for the risk of precipitated opioid withdrawal if a patient is transitioned to buprenorphine too aggressively or rapidly. This can result in severe GI side effects and an initial increase in pain experienced.

Patient Compliance

To minimize the risk of opioid withdrawal, a multi-step transition is often required involving a three-to-five-day buprenorphine titration while continuing therapy with the full opioid agonists. If the patient, caregivers and/or care setting is not able to support these efforts, a transition to buprenorphine may not be in the best interest of the patient, as it may subject them to unnecessary burden in the form of opioid withdrawal symptoms or increased pain.

Cost

A one-month supply of buprenorphine or buprenorphine/naloxone sublingual tablets can range from $60-400/month, which is significantly more expensive than treating a patient with methadone or most morphine SR formulations. However, if a patient with refractory pain is using an opioid infusion, Oxycontin or a high dose fentanyl patch, buprenorphine may result in a lower monthly therapy cost

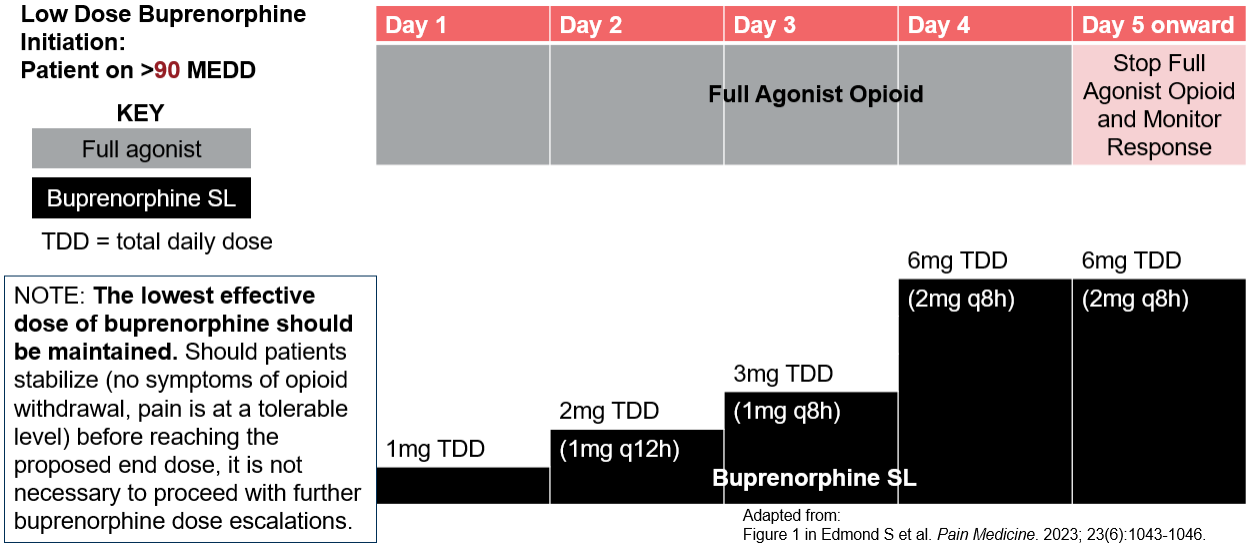
STRATEGIES FOR TRANSITIONING TO BUPRENORPHINE

STEP 1	Calculate the opioid morphine equivalent of current opioid regimen
STEP 2	Based on calculation above, select the appropriate titration plan below:

Less than 50mg/day	50-90mg/day	More than 90mg/day

• **< 30mg/day**
  ○ Patch is preferred
  ○ Select 5mcg/hr
  ○ Take last dose of full opioid agonist at time of patch placement
• **30-49mg/day**
  ○ Patch is preferred
  ○ Select 10mcg/hr
  ○ May consider overlapping dosing of full opioid agonist with patch placement for first 24-48 hours or until assessment reveals efficacy of the patch
	• **50-70mg/day**
	  ○ Buccal film preferred
	  ○ 150mcg q12h
	  ○ Recommend continuing immediate-release opioid therapy on a q4-6h prn basis. Titrate if patch dose by 50-100% if patient continues to experience pain not at goal
	• **71-90mg/day**
	  ○ Buccal film preferred
	  ○ 300mcg q12h
	  ○ Recommend continuation of immediate-release opioid as noted above
		Recommend initiation of buprenorphine or buprenorphine/naloxone sublingual tablet
		• Early emphasis on reducing risk of withdrawal and patient discomfort
		• Patients with previously uncontrolled pain may stabilize on lower doses of buprenorphine than expected.
		• Continue full agonist opioid days 1-4 after initiating buprenorphine
		• **Buprenorphine Dosing**
		  ○ Day 1: 1mg/day (1/2 tab)
		  ○ Day 2: 1mg q12h
		  ○ Day 3: 1mg q8h
		  ○ Day 4: 2mg q8h
		  ○ Day 5: Continue /Titrate

The image below provides a visual for the low dose buprenorphine initiation method outlined for patients on more than 90mg of morphine equivalent per day at the time of transition



Adapted from:
Figure 1 in Edmond S et al. *Pain Medicine*. 2023; 23(6):1043-1046.

If the patient continues to experience uncontrolled pain or opioid withdrawal symptoms after full agonist opioids are stopped on day five, it would be appropriate to continue to titrate buprenorphine dose by 2mg/dose every 24-48 hours until resolution of symptoms or patient experiences undesirable side effects.

SUMMARY

Transitioning from full opioid agonists to buprenorphine in patients with uncontrolled pain or opioid-induced side effect can be done in the hospice setting, but it requires close monitoring, the ability to adhere to a buprenorphine titration regimen, and the possibility of multiple modifications to the buprenorphine regimen until a safe and effective dose is determined. For questions regarding patient-specific clinical scenarios, please call BetterRX for support with a Clinical Pharmacy Consultation.

References

1.) Gudin J, Fudin J. A narrative pharmacological review of buprenorphine: a unique opioid for the treatment of chronic pain. Pain Ther 2020; 9:41-54.
2.) Khanna IK, Pillarisetti S. Buprenorphine- an attractive opioid with underutilized potential in treatment of chronic pain. J Pain Research 2015; 8:859-70.
3.) Daitch J, Frey M, Silver D et al. Conversion of chronic pain patients from full-opioid agonists to sublingual buprenorphine. Pain Phys 2012;15:ES 59-66.
4.) Mailinoff HL, Barkin RL, Wilson G. Sublingual buprenorphine is effective in the treatment of chronic pain syndrome. AM J Ther 2005; 12: 379-84.
5.) Bertland DW, Mailinoff HL, Weiner MA et al. When opioids fail in chronic pain management: the role for buprenorphine and hospitalization. Am J Ther 2013: 20: 316-21.
6.) Daitch D, Daitch J Novinson D et al. Conversion from high dose full-opioid agonists to sublingual buprenorphine reduces pain scores and improves quality of life for chronic pain patients. Pain Med 2014; 15: 2087-94.
7.) Schmidt-Hansen M, Bromham N, Taubert M et al. Buprenorphine for treating cancer pain (review). Cochrane Database Syst Rev 2015 Mar 31;(3): CD009596
8.) Edmond S, Currie S, Gehrke A et al. Optimizing Interdisciplinary Virtual Pain Care and Buprenorphine Initiation During Covid-19: A Quality Improvement Study

