Buprenorphine Quick Facts

- Buprenorphine is a schedule III opioid with increasing use as an analgesic in patients with serious illness including those with comorbid opioid use disorder (OUD)
- With the recent elimination of the "DATA-Waiver Program" (also referred to as the "X" waiver) required to prescribe buprenorphine, all dosage forms, regardless of indication, may now be prescribed by any prescriber[1]
- The use and dosing of buprenorphine for pain is rapidly evolving and optimal practice has not been established[2]

BUPRENORPHINE VS. OTHER OPIOIDS

- Buprenorphine is a partial agonist at mu-opioid receptors and is an antagonist at kappa- and delta-opioid receptors
- Partial agonist activity at mu receptors **does not** equate to partial analgesia
- At equipotent doses, analgesia from buprenorphine is equivalent to full agonists (like morphine, oxycodone, fentanyl)
- Because buprenorphine does not occupy all the mu opioid receptors, the open receptors remain available for other full agonists (like hydromorphone or morphine) to provide analgesia for breakthrough pain
    - Hydromorphone, oxymorphone, and morphine are preferred for breakthrough pain due to their binding properties; oxycodone should be avoided
- Buprenorphine's partial agonist activity decreases the incidence of respiratory depression, constipation, euphoria, potential for misuse and overdose with buprenorphine vs. full mu agonists like morphine[3,4]
- Safe for use in mild to moderate liver failure and in renal failure
- High first pass hepatic metabolism results in poor (10-20%) oral bioavailability
    - For this reason, transdermal, sublingual, and buccal formulations are typically utilized
    - Buccal provides higher bioavailability than sublingual

PRODUCT QUICK FACTS

Prescribed for Pain

- FDA Labeled: Butrans® (transdermal patch), Belbuca® (buccal film)[5]
    - Butrans® and Belbuca® are the only buprenorphine products recommended for the opioid naïve[3]
    - Dosed in MICROgrams
- Off-Label: Subutex® (buprenorphine only, sublingual), Suboxone® (buprenorphine/naloxone, sublingual)
    - Prescribed at lower doses for pain than for OUD (e.g., buprenorphine 2mg SL BID for pain)[3]
    - The naloxone in Suboxone® does not block analgesic activity when administered sublingually, rather it prevents it from being abused parenterally[5,6]
    - Dosed in MILLIgrams
    - Should be avoided in patients with hepatic impairment

Buprenorphine Quick Facts

Prescribed for Opioid Use Disorder

- Labeled: Subutex® (buprenorphine only, sublingual), Suboxone® (buprenorphine/naloxone, sublingual)[5]

Product[5]	Strengths[5]	Common Frequency for Pain Indication	AWP* per 14-day Supply
Buprenorphine SL tablet(Subutex®)	2mg, 8 mg	Twice daily	$ - $$$
Buprenorphine-naloxone SL tablet (Suboxone®)	2mg/0.5mg; 8 mg/2 mg	Twice daily	$$-$$$
Buprenorphine-naloxone SL film (Suboxone®)	2mg/0.5mg, 4 mg/1 mg; 8 mg/2 mg; 12mg/3mg	Twice daily	$$-$$$$
Buprenorphine transdermal patch (Butrans®)	5, 7.5, 10, 15, 20 mcg/hr	Weekly	$$$-$$$$$
Belbuca® buccal film	75, 150, 300, 450, 600, 750, 900 mcg	Twice daily	$$$$-$$$$$
*AWP data obtained June 2023 from Enclara Pharmacia			

$	$0-$50
$$	$51-$100
$$$	$101-$200
$$$$	$201-$300
$$$$$	>$301

CLINICAL SCENARIOS

Switching *from* BUP *to* Full Agonist Opioid (e.g., Morphine)

Specific Scenario	Dosing Guidance
FROM Subutex® SL tabs or Suboxone® SL tabs/film **TO Full agonist opioid** *Subutex® and Suboxone® are dosed in MILLIgrams*	There is no established conversion from sublingual or transmucosal buprenorphine to other opioids. It is best to discontinue buprenorphine and begin a PRN short-acting opioid with opioid-naïve dosing and monitor use over a few days to determine daily long-acting needs. Rotating a patient from buprenorphine to a full agonist opioid requires close monitoring, as the full agonist opioid has a higher risk of respiratory depression.[7] Starting the full agonist opioid as a PRN and at opioid-naïve dosing reduces this risk.
FROM Belbuca® film **TO Full agonist opioid** *Belbuca® is dosed in MICROgrams*	
FROM Butrans® **TO Full agonist opioid** *Butrans® is dosed in MICROgrams/hr*	The 1:75 (mg to mg) ratio is commonly seen in literature, however only applicable to buprenorphine transdermal to oral morphine equivalent (OME) conversions[8] • Convert buprenorphine transdermal from MICROgrams/Hour to MILLIgrams/Day • Use the ratio above to convert to OME

Switching *from* full agonist opioid *to* Butrans® patch

Specific Scenario	Dosing Guidance		
FROM Full agonist opioid TO Butrans® patch[3,5] *Butrans® is dosed in MICROgrams/hr*	OME < 30mg	At the next dosage interval, begin 5mcg/hour transdermally every 7 days	Doses may be titrated at ≥ 72 hours after patch placement Titrate dose in 5, 7.5 or 10mcg/hour increments by using no more than 2 patches of the 5, 7.5, or 10mcg/hour systems as needed to achieve adequate analgesia. Do not exceed a dose of 20mcg/hour
	OME 30mg-80mg	Taper the current around-the-clock opioid for up to 7 days to no more than 30mg/day OME before beginning Butrans® At the next dosage interval, begin 10mcg/hour transdermally every 7 days	
	OME > 80mg	Consider the use of an alternate analgesic. The 20mcg/hour transdermal buprenorphine may not provide adequate analgesia.	

Switching *from* full agonist opioid *to* Belbuca® film

FROM Full agonist opioid TO Belbuca® film[3,5] *Belbuca® is dosed in MICROgrams*	*OME < 30mg*	*75mcg transmucosally once daily, or every 12 hours if tolerated* *After 4 days, increase dosage to 150mcg every 12 hours*	*Titrate in increments of 150mcg every 12 hours no more frequently than every 4 days to provide adequate analgesia* *Maximum: 900mcg every 12 hours* *Do not exceed 900mcg every 12 hours due to the potential for QT prolongation*
	OME 30mg-89mg	Taper the current ATC opioid to no more than 30mg OME/day before beginning Belbuca® Initiate 150mcg transmucosally every 12 hours	
	OME > 90mg-160mg	Taper the current ATC opioid to no more than 30mg of OME/day before beginning Belbuca® Initiate 300mcg transmucosally every 12 hours	
	OME > 160 mg	Consider the use of an alternate analgesic. The buccal/ transmucosal film may not provide adequate analgesia.	

Switching *from* full agonist opioid *to* buprenorphine SL

Specific Scenario	Dosing Guidance
FROM Full agonist opioid TO Subutex® SL tablets or Suboxone® SL tablets/film *Subutex® and Suboxone® are dosed in MILLIgrams*	**Buprenorphine SL is used off label for analgesia and not recommended for those taking < 160mg OME; consider Butrans® or Belbuca® for these patients**. **There is no established conversion factor between full agonist opioids and sublingual buprenorphine dosed in MILLIgrams**. Rotating from a full agonist opioid requires significant planning to minimize opioid withdrawal and/or worsening pain.[7] For additional guidance, consult your Enclara Pharmacia pharmacist.
Initial Indication for BUP is OUD - Patient Now Needs Pain Management Too	Divide the total daily buprenorphine dose every 6 to 8 hours to enhance analgesic effects • Long half-life and high receptor affinity allows once-daily dosing for OUD, but analgesic effect may only last 6 hours; this approach allows for a continued stable buprenorphine dose. • More buprenorphine can be added to maintenance dosing for pain in those taking < 32mg SL daily[9] • Initiate short-acting full agonist opioid (hydromorphone, morphine are preferred) for breakthrough analgesia

Buprenorphine-Naloxone (Suboxone®) - Place in Therapy of Pain

Use of this product should be limited to patients at risk for opioid diversion or opioid abuse. The naloxone component prevents users from abusing this product parenterally.[3]

REFERENCES

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