Buprenorphine Resource Guide

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QIN-QIO Quality Innovation Network - Quality Improvement Organizations
CENTERS FOR MEDICARE & MEDICAID SERVICES iQUALITY IMPROVEMENT & INNOVATION GROUP

Formulations for Opioid Use Disorder (OUD)

Name	Dosage Form/Strengths	Dosing
Suboxone® **Buprenorphine/naloxone** (generic) (film) 	Sublingual **contains naloxone** 2 mg/0.5 mg, 4 mg/1 mg, 8mg/2 mg, 12mg/3 mg	**Day 1**: 12–48 hours after last opioid dose, patient should be experiencing at least one objective sign of withdrawal with a Clinical Opiate Withdrawal Scale (COWS) score >11. Give 2-4 mg initially, if still in withdrawal after 60–90 minutes, may increase in increments of 2-4 mg every 1-2 hours until stable, max 16 mg. **Day 2:** Start total Day 1 dose or less if patient is sedated. Follow similar protocol until patient is stable. **Subsequent initiation days:** Start total Day 2. Follow similar protocol. Usual final dose is 8–16 mg daily. **Dose Conversion** Suboxone® | Zubsolv® 2mg/0.5mg | 1.4mg/0.36mg 4mg/1mg | 2.9mg/0.71mg 8mg/2mg | 5.7mg/1.4mg 12mg/3mg | 8.6mg/2.1mg
Buprenorphine/naloxone (generic) (tablet) 	2 mg/0.5 mg, 8 mg/2 mg	
Zubsolv® buprenorphine/naloxone (sublingual tablet) 	0.7 mg/0.18 mg, 1.4 mg/0.36 mg, 2.9 mg/0.71 mg, 5.7 mg/1.4 mg, 8.6 mg/2.1 mg, 11.4 mg/2.9 mg	
Buprenorphine (sublingual tablet) 	2 mg 8 mg	**dosing based on buprenorphine component** Same as above. The buprenorphine mono product without naloxone (Subutex®) is no longer preferred over buprenorphine/naloxone (Suboxone® etc.) for the treatment of OUD in pregnancy as, the mono product carries a higher risk for misuse and buprenorphine/naloxone has not been found to cause an increased risk.[5-7] Similarly, and in general, the buprenorphine mono product (Subutex®) should be avoided for the treatment of any patients with opioid use disorder.
Sublocade® buprenorphine (Extended release injection) 	100 mg/0.5 mL 300 mg/1.5 mL	Initiate treatment with 8–24 mg of SL product for at least 7 days, then 300 mg SQ monthly x 2 months, then 100 mg SQ monthly for maintenance, may be increased to 300 mg SQ monthly for patients without satisfactory clinical response. Doses must be given 26 days or more apart.

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   Published June, 2022. Accessed March 15, 2023.

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   American Journal of Obstetrics & Gynecology MFM. 2020;2(3):100179. doi:10.1016/j.ajogmf.2020.100179

7. Kanervo MM, Tupola SJ, Nikkola EM, Rantakari KM, Kahila HK.
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   Acta Obstetricia et Gynecologica Scandinavica. 2022;102(3):313-322. doi:10.1111/aogs.14497

8. **Sublocade** [package insert]. Indivior UK Limited.
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   Published August 2022. Accessed March 15, 2023.

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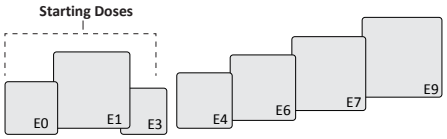
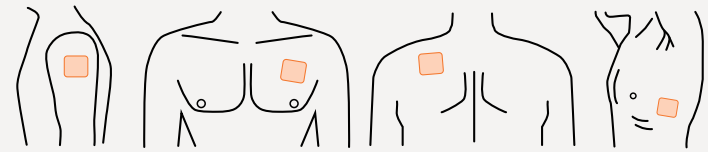
Formulations for Pain Management

Brand Name	Dosage Form/ Strengths	Dosing	
Buprenex® (generic)	Injection 0.3 mg/mL	IM & IV: 0.3 mg Q 6 hours prn, may be repeated x 1 after 30-60 minutes	Moderate to severe pain; Used in the institutional setting
Belbuca® 	Buccal film 75 mcg 150 mcg 300 mcg 450 mcg 600 mcg 750 mcg 900 mcg	Opioid-naïve: 75 mcg daily, then if tolerated Q 12 hours, after 4 days may increase to 150 mcg every 12 hours Experienced: taper current opioid to 30 MEDD or less, initiate dosing next day based on MEDD prior to taper as follows: MEDD < 30: 75 mcg daily or every 12 hours MEDD 30 – 89: 150 mcg every 12 hours MEDD 90 – 160: 300 mcg every 12 hours MEDD >160: consider alternative agent Max dose: 900 mcg every 12 hours Titrate dose as needed every 4 days *The films come in different sizes that do not correspond with dose. Make sure to double-check that the appropriate dose is given.*	Chronic moderate to severe pain
Butrans® (generic) 	Transdermal Patch 5 mcg/hr 7.5 mcg/hr 10 mcg/hr 15 mcg/hr 20 mgh/hr	Opioid-naïve: 5 mcg/hr every 7 days Opioid-experienced: taper as above. Initiate dosing next day based on MEDD prior to taper as follows: MEDD < 30: 5 mcg/hr every 7 days MEDD 30 – 80: 10 mcg/hr every 7 days MEDD > 80: 20 mcg/hr every 7 days and consider alternative agent May increase dose every 3 days, using no more than 2 patches Max dose: 20 mcg/hr every 7 days Titrate dose as needed every 72 hours	Chronic moderate to severe pain

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1. **Buprenex** [package insert]. Hull, England: Reckitt Benckiser Healthcare (UK) Ltd. https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=b086772e-d15a-4d13-b1a2-38bfbde1f18c&type=pdf Published June 2022. Accessed March 15, 2023.
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4. **Buprenorphine** [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc. https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=593c2a50-de4f-6bf8-e053-2a91aa0ae306&type=pdf Published June 2017. Accessed March 15, 2023

History of Buprenorphine

1966: Buprenorphine is discovered at the labs of Reckitt & Colman.

1978: Buprenorphine is launched in the UK as an intravenous opioid analgesic.

1981: The FDA approves injectable buprenorphine (Buprenex®); buprenorphine is classified as a Schedule II opioid.

2002: The FDA approves sublingual buprenorphine and naloxone (Suboxone®) and sublingual buprenorphine (Subutex®); buprenorphine is classified as a Schedule III opioid.

2010: The FDA approves buprenorphine transdermal system (Butrans®) for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate.

2015: The FDA approves buprenorphine buccal film (Belbuca®) for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate.

Buprenorphine was originally developed as an analgesic and was subsequently used for OUD before novel delivery systems allowed for approval in chronic pain management.
FDA=Food and Drug Administration; OUD=opioid use disorder.

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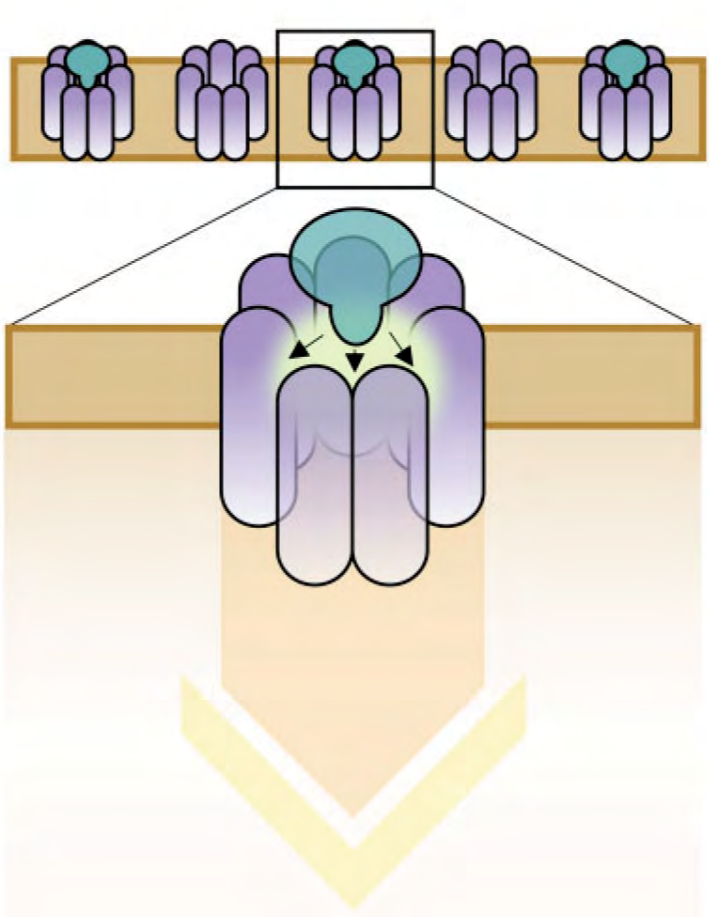
Buprenorphine Analgesia

1. Potency
The relationship between drug dose or concentration and specified response intensity.

2. Affinity
The attraction between a molecule and its receptor, quantified as a binding constant.

3. Partial agonist
A compound that displays less intrinsic activity than a full-agonist reference agent displays; depends on 3D structure.*

4. Intrinsic activity
The capacity of bioactive agents to activate specific receptors to promote downstream signaling responses.



1. Buprenorphine has high potency and a slow dissociation rate, allowing for effective long-lasting analgesia at low doses.

2. Buprenorphine has a very high binding affinity at the μ-OR (i.e., higher attraction than most full μ-OR agonists).

3. As a partial agonist, buprenorphine has lower μ-OR signaling than full μ-OR agonists, which may contribute to fewer opioid-related adverse events.

4. Buprenorphine has lower intrinsic activity than full μ-OR agonists (potentially limiting negative effects) but enough activity to be an effective analgesic.

Figure 2. Receptor/ligand definitions and applications to buprenorphine at the μ-opioid receptor. *Definition of a partial agonist: a compound with an intermediate intrinsic activity that at full receptor saturation produces less than the maximal effect obtainable with full agonists in some specified set of in vitro or clinical circumstances [25]. Buprenorphine is a potent Schedule III opioid with high binding affinity at the μ-opioid receptor that behaves as a partial agonist on the basis of in vitro studies [7, 14, 26]. Although buprenorphine has less total intrinsic activity (capacity to activate a receptor to induce multiple signaling pathways) than full μ-opioid receptor agonists, it still effectively stimulates the analgesic signaling pathway from the μ-opioid receptor. 3D=three dimensional; OR=opioid receptor.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7139205/pdf/pnz356.pdf

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