# Characteristics of Medications Useful for Opioid Use Disorder Treatment

| | Buprenorphine (monoproduct) SL tablet | Buprenorphine/ naloxone (bup/nx) SL tabs and filmstrips | Buprenorphine IV & IM | Buprenorphine depot (injectable and implantable) | Buprenorphine low dose buccal filmstrips | Buprenorphine Transdermal Patch | Naltrexone Oral and Depot Injectable | Methadone Oral |
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| **Brand Names** | "Subutex" | "Suboxone" (most common)<br><br>"Zubsolv" | "Buprenex" | "Sublocade" (subcutaneous)<br><br>Probuphine (implant) | "Belbuca" | "Butrans" | "Vivitrol" (depot IM Injectable)<br><br>"Depade" or "Revia" (oral) | "Dolophine"<br><br>"Methadose" |
| **Pharmacologic Action** | Partial agonist | Buprenorphine = Partial agonist<br>Naloxone = antagonist | Partial agonist | Partial agonist | Partial agonist | Partial agonist | Antagonist | Full Agonist |
| **Indications** | (1) Opioid withdrawal; (2) maintenance to prevent cravings or withdrawal; (3) acute or chronic pain management in opioid experienced patients.<br>**Note:** preferred agent in the ED or when beginning tx of OUD in hospital, as many patients with OUD fear naloxone in bup/nx | (1) Opioid withdrawal; (2) maintenance to prevent cravings or withdrawal; (3) chronic pain management in patients with OUD.<br>**Note:** the purpose of the bup/nx combination is strictly to deter misuse (crushing, snorting, injecting) – Bup is well absorbed SL, but Nx is poorly absorbed SL. This "combination" formulation is not necessary in a healthcare setting when administered by a nurse. | (1) FDA approved for pain management.<br>(2) However, can be useful formulation in treating patients with **complicated withdrawal** (e.g. patients with combined alcohol and opioid withdrawal, too confused to be able to keep a sublingual tablet under the tongue | Long-acting depot formulations for patients with OUD who struggle with managing prescriptions for SL tablets or filmstrips.<br><br>**"Sublocade"** depot injectable at 300mg is equivalent to 24mg/day, and can be very helpful for patients vulnerable to medication theft, or when not allowed to have SL formulations. | FDA approved for chronic pain management. However, the low dose options (as low as 75mcg) could provide a safer alternative to full mu agonists for opioid naïve patients, or patients less tolerant of opioids.<br>[Bup is a potent analgesic but at | FDA approved for chronic pain management. A very effective analgesic. Safer than other opioids, with less risk of misuse.<br>Used in other countries for Tx of OUD. | A powerful mu receptor blocker, antagonist. **Does not prevent cravings.** Tx of OUD, only after patient has completed opioid withdrawal. Usually started ~ 7 days after last dose of short half-life opioid in opioid | FDA approved for treatment of OUD – but only in specialized licensed clinics ("OTPs" – methadone clinics). Can also use in hospitals. Cannot be prescribed (to be filled at a pharmacy) for the Tx of OUD. |

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| | combination medication. | Some patients with OUD fear this formulation (believing the Nx precipitates withdrawal).<br>Some patients complain of significant headaches with the bup/nx combo formulation. | until it is absorbed. | Administered in clinics, but also some inpatient units, and some EDs.<br><br>**"Probuphine"** implantable rods last 6 months, but only available at a lower dose (8mg/day SL equivalent). Requires an office procedure. Use is limited. | even traditional "low doses" (1-2mg SL) can cause prolonged nausea and/or sleepiness in opioid naïve patients.]<br><br>150mcg buccal as analgesic ~ = 7.5mg hydrocodone. | | dependent patients.<br>May have to wait longer after patients weaned off of buprenorphine or methadone.<br><br>For Tx of OUD, used in some residential programs, correctional facilities, and some outpt settings. | Can be prescribed for Tx of pain (but with caution). |
| **Route of Administration** | **<u>Sublingual</u>**<br><br>**DO NOT swallow** – oral/gastric absorption of Bup is poor. | **<u>Sublingual</u>**<br><br>**DO NOT swallow** – oral/gastric absorption of Bup is poor (and Nx absorption increases with swallowing) | IV or deep IM | <u>Subcutaneous</u>: injection of ~ 1.5ml in the abdominal wall.<br><br>Implants: placed in the medial arm. | Buccal mucosa film | Transdermal Patch | <u>For treating OUD, must plan to use depot IM injectable</u>.<br>Oral to test patient response, and for daily dosing in residential setting. | Oral: Methadone clinics usually use a liquid formulation. Prescriptions for pain are usually tablets. |
| **Dosing/ Time of Onset/ Duration** | 2-32 mg per day – daily or in divided BID or TID.<br>Onset 15-30 minutes, peaks @60 minutes.<br><br>Half-life: 16-60 hours | Nx has minimal SL absorption.<br>"Suboxone" dosed per Bup component (same as the monoproduct – "Subutex").<br>2/0.5mg – to 32/8mg per day, dosed daily or divided BID or TID. | 0.3mg/ ml vials.<br><br>As an analgesic, 0.3mg IV ~ = 10mg IV morphine.<br><br>For Tx of complicated opioid | **Sublocade**: 300 mg sq in abdominal area given monthly. May opt after 2 months to decrease to 100 mg monthly maintenance. Gradual onset, peaks in 8-12 hours.<br><br>**Probuphine:** 74.2 mg buprenorphine, 4 | 150mcg to 900mcg buccal filmstrip formulations.<br><br>[150mcg buccal as analgesic ~ = 7.5mg hydrocodone.] | Dose range: 5mcg/hr to 20mcg/hr patches.<br><br>Patches are changed Q 7 days.<br><br>Effect onset ~ 1 hour, peaks in ~ 2 days. | Oral 25--100 mg/daily. [Usually test at 25mg/day, then increase to 50-100mg].<br><br>*Depot IM Injectable* = 380 mg/~ 2 | For treatment of OUD, doses begin at ~ 10-30mg/day and are gradually titrated up to therapeutic doses which very patient specific, ranging from |

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| | **ED Dose** usually begins with 8mg SL (unless complicating factors).<br>Some patients may need higher doses for acute withdrawal management.<br>Some facilities initiate at 16mg SL | Onset, peak, duration same as the monoproduct.<br><br>"Zubzolv" has a higher bioavailability, so equivalent formulations are 2.1mg/0.3mg, 4.2mg/0.7mg,6.3 mg/1 mg.<br>Onset ~30 minutes; peaks @ 2.5-3 hours; Duration: 24-27 hours | withdrawal, dose ~ 0.3 to 0.6mg Q 15-60 minutes until relief. Then Q 2-8 hours. [switch to SL as soon as patient able].<br>Onset ~ 5 minutes, peaks ~ 30-60 minutes, duration ~ 6+ hours. | implant (Rods) subdermally in medial arm/peaks within 24 hours/delivers continuous stable blood levels/6 months | Onset in ~ 30 minutes, peak in 3 hours.<br><br>Duration ~ 12 hours. | | hours/~ 4 weeks/ | ~ 20 to 200+ mg/day, depending on patients' opioid tolerance and need.<br>For OUD usually dosed once daily.<br>For pain management, dose is usually divided to 2x or 3x per day. |
| **Bioavailability** | ~ 20-40% **sublingual**<br><br>[oral ~ 5- 10%] | Bup ~20-40% **sublingual.** Nx SL absorption is ~minimal.<br>Do not give orally.<br>Nx has high bioavailability IN, IV, IM, SQ. | 100% | "Sublocade": ~ 100%<br><br>"Probuphine": ~ 100% | 45% to 65% | 15% | *Oral*=5-40%<br><br>*Injectable* =100% | >80% of oral liquid. Less for tablet formulations. |
| **Common Side Effects** | Headache, nausea, sweating, rhinitis, constipation. | Headache, nausea, sweating, rhinitis, constipation, insomnia, vertigo.<br>Reported side effects (particularly headaches) are reported more commonly with the Bup/Nx combo-product than the mono-product. | Nausea, headache, constipation. | Headache, nausea, sweating, rhinitis, constipation<br><br>Pain/pruritis at injection/insertion site | Nausea, headache, constipation. However, adverse effects reduced with this lower dose formulation. | Headache, nausea, sweating, rhinitis, constipation | Nausea, vomiting, headache, insomnia, elevated liver enzymes, and depressed mood<br>**Injectable: Pain at injection site** | Constipation, nausea, vomiting, headache, stomach pain<br><br>*QT prolongation |
| **Contra-indications** (other than | **Patients must be in (or completing)** | **Patients must be in (or completing) opioid** | Caution in patients with hemodynamic | Patients should be stabilized and tolerating shorter | IF patient has OUD or has physical opioid | Patients are usually stabilized on SL | Patients must have cleared | Methadone is a long half-life full mu |

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| allergies to buprenorphine or other components of the formulations). | **opioid withdrawal to <u>begin</u> Bup**. Assess carefully for complicating factors before administering, and if present, consider reducing dose. | **withdrawal to <u>begin</u> Bup/Nx**. Assess carefully for complicating factors before administering, and if present, consider reducing dose. | instability (e.g. sepsis) – titrate more slowly. | acting buprenorphine (usually SL bup) before administering depot injectable or an implantable formulation. | dependence, as with other bup formulations, must be in opioid withdrawal before administering first dose. | formulations before beginning Butrans Patch. If beginning after full mu agonist opioids, be sure wearing off (and consider waiting for withdrawal Sx) before applying "Butrans" Patch | metabolism of all opioids, and fully completed course of withdrawal. Otherwise, naltrexone will precipitate opioid withdrawal. | agonist. Caution with other sedating medications or other QT prolonging medications. |
| **Pregnancy Concerns** (primary objective is to avoid precipitating withdrawal – which may cause fetal distress, and pre-term labor). | Safe in Pregnancy, (<u>preferred over bup/nx combo-product</u>). However, must avoid precipitating withdrawal. Do not delay in pregnant patient clearly in moderate to severe withdrawal. | Appears to be safe in pregnancy. However, must avoid precipitating withdrawal. Although mono-product preferred in pregnancy, may use bup/nx if mono-product not available, or if patient misuses mono-product. | Safe in pregnancy (but must take precautions to avoid precipitating withdrawal). | Safe in pregnancy (but must take precautions to avoid precipitating withdrawal). | Safe in pregnancy (but must take precautions to avoid precipitating withdrawal). | Safe in pregnancy (but must take precautions to avoid precipitating withdrawal). | Should <u>not initiate</u> during pregnancy – as high risk for precipitating withdrawal. | Safe in pregnancy, but dose schedule must be adjusted in 3rd trimester. |
| **Accessibility** | Any provider may order for patient in hospital. In New Mexico, no pre-authorization required for Medicaid patients, but commercial payors may require | Any provider may order for patient in hospital. In New Mexico, no pre-authorization required for Medicaid patients, but commercial payors may require. | Only administered in a healthcare setting, typically in the OR for pain management, or in the ED or ICU for complicated opioid withdrawal management. Any provider can order in hospital. | Any provider may order "Sublocade" injectable for patient in hospital (if indicated). Both the injectable and implantable will require pre-authorization outpatient ($$$$). | Any provider may order for patient in hospital. But as outpatient, a pre-authorization probably required ($$$). | Any provider may order for patient in hospital. But as outpatient, a pre-authorization probably required ($$). | Not a controlled substance. Oral form very inexpensive. The depot injectable ("Vivitrol") is low cost if administered in hospital. But as out-patient, a pre- | Any provider may order for patient in hospital. But for outpatient treatment of OUD – only available in specialized licensed clinics ("OTPs" – methadone clinics). |

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| | | | | | | | authorization may be required ($$$). | Cannot be prescribed (to be filled at a pharmacy) for the Tx of OUD. |
| **Regulatory Concerns** | Provider must have x-waiver to prescribe for OUD.<br><br>[Any provider with a DEA license can prescribe for "pain"]. | Provider must have x-waiver to prescribe for OUD.<br><br>[Any provider with a DEA license can prescribe for "pain"]. | Treatment of complicated opioid withdrawal is an off-label use. But as medication is generic, and relatively low cost, unlikely to get FDA approval for Tx of withdrawal. | Providers must have X-waiver to prescribe as an outpatient.<br><br>Probuphine is only available through a Probuphine Risk Evaluation and Mitigation Strategy (REMS) Program | FDA Indication is for pain management.<br><br>Thus, any provider with a DEA license can prescribe for "pain." | FDA Indication is for pain management.<br><br>Thus, any provider with a DEA license can prescribe for "pain." | No regulatory issues.<br>Not a controlled substance. | For treatment of OUD – only available in specialized clinics.<br>Because (for OUD) not obtained at a pharmacy, methadone treatment is not visible on Board of Pharmacy PDMP Reports. |
| | **Buprenorphine (monoproduct) SL tablet** | **Buprenorphine/ naloxone (bup/nx) SL tabs and filmstrips** | **Buprenorphine IV & IM** | **Buprenorphine depot (injectable and implantable)** | **Buprenorphine low dose buccal filmstrips** | **Buprenorphine Transdermal Patch** | **Naltrexone Oral and Depot Injectable** | **Methadone** |

DEA: Drug Enforcement Administration, Source: Reference 25, Substance Abuse: Research and Treatment. Doi: 10.4137/SART.S5452

**NOTE: This document is not intended to be all-inclusive of the topic All patients should be carefully assessed for the appropriate treatment.**