The Medical Letter®
on Drugs and Therapeutics
Adapted for Canada

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Comparison Table: Some Drugs for Maintenance Treatment of Opioid Use Disorder

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Drug	Some Available Formulations	Target Maintenance Dosage	Adverse Effects	Drug Interactions	Pregnancy/Lactation	Comments	US Cost[2]	CAN Cost[5]
Buprenorphine – generic	2, 8 mg sublingual tabs	16 mg once/d	▸ Sedation/respiratory depression (less than methadone), headache, abdominal pain, constipation, nausea, vomiting, insomnia, sweating ▸ *Probuphine*: implant-site pain, pruritus, and erythema; insertion and removal of drug-eluting implants has been associated with nerve injury and implant migration and extrusion ▸ *Sublocade*: injection-site reactions ▸ *Bunavail*: oral mucosal erythema	▸ Coadministration of benzodiazepines or other sedating drugs can be dangerous ▸ Inducers of CYP3A4 can reduce buprenorphine levels, and inhibitors of CYP3A4 can increase them ▸ Concurrent use of other serotonergic drugs can result in serotonin syndrome ▸ May interfere with analgesic activity of full opioid agonists	▸ Considered safe and effective for use in pregnant or breast-feeding women	▸ Buprenorphine is a schedule I controlled substance in Canada; federal authorization is not required to prescribe buprenorphine/naloxone ▸ Buprenorphine is a schedule III controlled substances in US; can be prescribed in outpatient setting ▸ Generally considered the maintenance treatment of choice; similar in efficacy to methadone at higher doses	$1083.60[7]	N.A.C.
Probuphine (Braeburn)	74.2 mg subdermal implant	4 implants for 6 mos					4950.00[7]	N.A.C.
Sublocade (Indivior)	100 mg/0.5 mL, 300 mg/1.5 mL prefilled syringes for subcutaneous injection	100 mg once/mo (300 mg first 2 mos; increase to 300 mg once/mo if clinical response is inadequate)					9480.00[7]	N.A.C.
Buprenorphine/Naloxone – generic	2/0.5, 8/2 mg sublingual tabs	16/4 mg once/d			▸ Generally considered safe in pregnant women, but efficacy data are limited; buprenorphine without naloxone is preferred ▸ Formulations without naloxone are preferred for use in breastfeeding women	▸ *Probuphine*: approved in US for 6 or 12 months' treatment in patients stabilized on ≤8 mg/d of buprenorphine; drug levels are similar to those with 8 mg/d of sublingual buprenorphine; REMS certification is required for prescribers ▸ *Sublocade*: approved for treatment of patients who have received transmucosal buprenorphine for ≥7 days with dose adjustment to 8-24 mg/d of buprenorphine sublingual tabs or equivalent; refrigerate during storage (discard if left at room tem for >7 days; steady state buprenorphine levels with target dosage ~10% higher than those with 24 mg/d of sublingual tabs ▸ *Cassipa*: approved for use after induction and stabilization of the patient, and titration to a dose of 16 mg of buprenorphine using another product ▸ Efficacy of naloxone-containing formulations may be reduced in patients with severe hepatic impairment ▸ *Bunavail* 4.2/0.7 mg and *Zubsolv* 5.7/1.4 mg produce systemic buprenorphine levels equivalent to those seen with 8 mg of other buprenorphine formulations	2339.10[7]	$425.80[8]
Bunavail (BioDelivery Sciences)	2.1/0.3, 4.2/0.7, 6.3/1 mg buccal films	8.4/1.4 mg once/d					2793.60[7]	N.A.C.
Cassipa (Teva)	16/4 mg sublingual films	16/4 mg once/d					N.C.	N.A.C.
Suboxone (Indivior UK; Indivior in US)	2/0.5, 8/2 mg sublingual tabs[6]	16/4 mg once/d					2933.30[7]	1769.50[8]
Zubsolv (Orexo)	0.7/0.18, 1.4/0.36, 2.9/0.71, 5.7/1.4, 8.6/2.1, 11.4/2.9 mg sublingual tabs	11.4/2.8 mg once/d					2989.40[7]	N.A.C.

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Drug	Some Available Formulations	Target Maintenance Dosage	Adverse Effects	Drug Interactions	Pregnancy/Lactation	Comments	US Cost[2]	CAN Cost[5]
Methadone – generic	5, 10 mg tabs; 5, 10 mg/5 mL oral solution; 10 mg/mL oral concentrate; 40 mg tabs for oral suspension[3]	80-120 mg once/d (some rapid metabolizers may require more frequent dosing)	▸ Sedation/respiratory depression, constipation, lightheadedness, dizziness, sedation, nausea, vomiting, sweating, QT-interval prolongation and (rarely) arrhythmias such as torsades de pointes	▸ Coadministration of benzodiazepines or other sedating drugs can be dangerous ▸ Inducers of CYP3A4 or 2B6 can reduce methadone levels, and inhibitors of CYP3A4 or 2B6 can increase them ▸ Concurrent use of other serotonergic drugs can result in serotonin syndrome ▸ Concurrent use of other QT interval-prolonging drugs can cause arrhythmias such as torsades de pointes	▸ Generally considered safe and effective for use in pregnant or breastfeeding women	▸ Schedule I controlled substance in Canada; provincial guidelines for prescribing in BC, ON, QC, SK; other provinces follow Health Canada guidelines ▸ Schedule II controlled substance in US; only available for treatment of opioid use disorder through opioid treatment programs with supervised dosing ▸ Shown to reduce mortality in clinical trials; should be used when buprenorphine is unavailable or ineffective and in patients who would benefit from supervised dosing ▸ Drug accumulates for 4-7 days during induction; respiratory depressant effect peaks later and lasts longer than analgesic effect ▸ US federal law prohibits initial doses >30 mg or first daily doses >40 mg	$73.50[4]	N.A.C.
Dolophine (Roxane)	5, 10 mg tabs[3]						850.80	N.A.C.
Metadol (Paladin)	1, 5, 10, 25 mg tabs; 1 mg/mL oral solution; 10 mg/mL oral concentrate						N.A.	$15.80[5]
Naltrexone – generic *Revia* (Teva; Duramed in US)	50 mg tabs	50 mg once/d	▸ Generally well tolerated; nasopharyngitis, insomnia, headache, nausea, and toothache are most commonly reported ▸ Rarely: depressed mood/suicidality (cause and effect not established), hepatotoxicity (occurs frequently in opioid- and alcohol-dependent patients) ▸ *Vivitrol*: injection-site reactions	▸ Blocks effects of usual doses of opioids, including antidiarrheals and antitussives ▸ Can precipitate severe withdrawal in patients with physiological opioid dependence; patients should be free of dependence for ≥7 days before initiation ▸ Discontinue 72 hours (oral formulation) or 30 days (IM formulation) before elective surgery	▸ Data on safety and efficacy in pregnancy are limited; women at high risk for relapse who become pregnant can generally continue treatment ▸ Women taking naltrexone should not breastfeed; the drug passes into breast milk to a clinically significant extent	▸ Not a controlled substance ▸ ER naltrexone is an alternative for highly motivated patients who do not have access to buprenorphine or methadone, or do not want to take an opioid, and for those who also have alcohol use disorder ▸ Adherence is poor with oral naltrexone; it has generally only been effective in patients who were legally required to take the drug ▸ Has not been shown to reduce mortality ▸ *Vivitrol*: must be refrigerated; use within 7 days of removing from refrigerator (do not expose to temperatures >77°F)	371.00 1648.90	1314.50 1314.50
extended-release microspheres – *Vivitrol* (Alkermes)	380 mg ER suspension for injection	380 mg IM in alternating buttocks q4 wks or once/mo					7854.00	N.A.C.

N.A.C. = Not available in Canada; N.A. = Not available in US; N.C. = Cost not yet available

1. Drugs for opioid use disorder. Med Lett Drugs Ther 2017; 59:89.
2. Approximate WAC for 6 months' treatment at the lowest target maintenance dosage. WAC = wholesaler acquisition cost, or manufacturer's published price to wholesalers; WAC represents published catalogue or list prices and may not represent an actual transactional price. Source: AnalySource® Monthly. May 5, 2017. Reprinted with permission by First Databank, Inc. All rights reserved. ©2017. www.fdbhealth.com/policies/drug-pricing-policy. www.fdbhealth.com/policies/drug-pricing-policy.
3. To reduce the risk of drug diversion, the liquid formulation, diluted in colored water or juice, is generally used in treatment programs.
4. Cost of oral concentrate.
5. Approximate WAC for 6 months' treatment at the lowest target maintenance dosage, based on price from a national wholesaler (prices in Ontario, May 2017).
6. In the US, *Suboxone* is available as 2/0.5 mg, 4/1 mg, 8/2mg, and 12/3 mg sublingual films.
7. Approximate WAC for 6 months' treatment at the target maintenance dosage. Source: AnalySource® Monthly. February 5, 2018.
8. Approximate WAC for 6 months' treatment at the target maintenance dosage, based on price from a national wholesaler (prices in Ontario, February 2018).