# Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder: A Randomized Clinical Trial[1]

camurus®

## Daily SL or oral buprenorphine for treating OUD is limited by:[2–4]

- Suboptimal adherence
- Diversion
- Intravenous misuse
- Unintended paediatric exposure

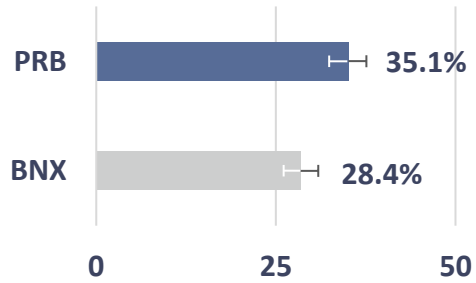
**Weekly or monthly PRB addresses some of these limitations**

**Adults diagnosed with and seeking treatment for moderate-to-severe OUD (N=428)**

R

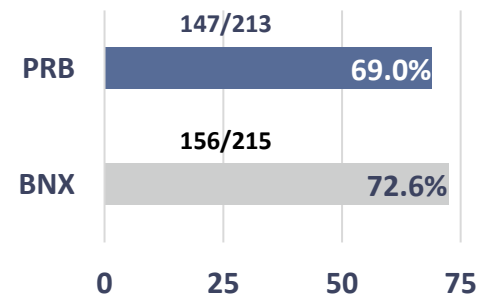
- n=213 → Titrated weekly/monthly PRB + placebo for 24 weeks
- n=215 → Titrated BNX + placebo injection for 24 weeks

## PRB and BNX offer comparable treatment outcomes and medication retention




**Primary endpoint: PRB non-inferior to BNX in proportion of opioid-negative urine samples from 1–24 weeks[a]**

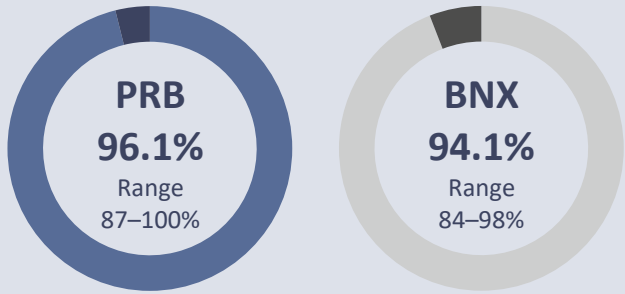
Secondary endpoint:
**PRB superior to BNX**
in proportion of opioid-negative urine samples from 4–24 weeks (CDF)[b]




**A similar proportion of patients completed 24 weeks of treatment**

**Opioid craving[c] and withdrawal[d] were suppressed from day 1 in both groups**

**High attendance at counselling during scheduled visits**




Most common AEs were:[e]

- Injection-site pain
- Headache
- Constipation
- Nausea
- Injection-site pruritus and erythema

| | PRB (n=213) | BNX (n=215) |
|---|---|---|
| Any AE, % | 60.1 | 55.3 |
| Non-fatal serious AE, % | 2.3 | 6.0 |
| Overdoses, % | 0 | 2.3[f] |
| Hospitalisations, % | 1.4 | 5.6 |
| Deaths, % | 0.5[g] | 0 |

All injection site reactions were mild or moderate in intensity

[a]European Medicines Agency endpoint; [b]Negative illicit opioid urine test results affirmed by self-report of no illicit opioid use; [c]Measured with a visual analogue scale; [d]Measured with the clinical opiate withdrawal scale; [e]See SmPC for complete AE profile; [f]Includes 4 accidental drug overdoses and 1 intentional overdose; [g]Owing to a traffic accident assessed as unlikely to be related to the study drug.

AE, adverse event; BNX, sublingual buprenorphine/naloxone; CDF, cumulative distribution function; OUD, opioid use disorder; PRB, subcutaneous prolonged-release buprenorphine; R, randomisation; SL, sublingual.

**1.** Lofwall MR, et al. *JAMA Intern Med* 2018;178:764–773; **2.** Lofwall MR, Walsh SL. *J Addict Med* 2014;8:315–326; **3.** Toce MS, et al. *Clin Toxicol (Phila)* 2017;55:12–17; **4.** Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep* 2013;62:56.

# Prescribing Information for Buvidal (buprenorphine prolonged-release solution for injection)

## Please refer to the Summary of Product Characteristics (SmPC) before prescribing

Weekly/Monthly Buvidal® BUPRENORPHINE PROLONGED-RELEASE SOLUTION FOR INJECTION

**Active ingredient:** Buprenorphine. Prolonged-release solution for injection in pre-filled syringes. Weekly injection (8 mg, 16 mg, 24 mg, 32 mg) or monthly injection (64 mg, 96 mg, 128 mg, 160 mg).

**Indication:** Treatment of opioid dependence within a framework of medical, social and psychological treatment. Treatment is intended for use in adults and adolescents aged 16 years or over.

**Dosage:** To avoid precipitated withdrawal, initiate when objective and clear signs of mild to moderate withdrawal are evident, considering the duration of action of the opioid, time since last dose and degree of opioid dependence. Do not start until ≥6 hours after last heroin or short-acting opioid. Reduce methadone to ≤30 mg/day and start Buvidal® ≥24 hours after the last methadone dose. Buvidal® may trigger withdrawal symptoms in methadone-dependent patients. *Initiation in patients not already receiving buprenorphine:* Patients not previously exposed to buprenorphine, administer 4 mg sublingual buprenorphine and observe for an hour to confirm tolerability. Recommended starting dose of Buvidal® is 16 mg, with one or two additional 8 mg doses at least 1 day apart (target dose of 24 mg or 32 mg during the first week). The dose for the second week is the total dose administered during the first week. May transfer to monthly Buvidal® after four weeks and once stabilised. *Switching from sublingual buprenorphine*: Switch directly to weekly or monthly Buvidal®, starting on the day after the last sublingual buprenorphine dose. See SmPC for dose recommendations. *Maintenance:* Weekly or monthly as needed. One supplemental Buvidal® 8 mg dose may be administered between regular weekly or monthly doses (except 160mg). The maximum dose is 32 mg weekly, with an additional 8 mg dose, or 160mg monthly. *W*eekly doses may be administered up to 2 days before or after the weekly time point, and monthly doses may be administered up to 1 week before or after the monthly time point. If a dose is missed, administer the next dose as soon as practical. *Termination*: Consider prolonged-release characteristics and any withdrawal symptoms. If switching to sublingual buprenorphine, do so one week after the last weekly dose or one month after the last monthly dose of Buvidal®. *Elderly:* No dosing recommendations over 65 years. Consider renal and hepatic function.

**Administration**: Administration of Buvidal® is restricted to healthcare professionals only. For subcutaneous administration only. Inject slowly and completely into sufficient subcutaneous tissue of the buttock, thigh, abdomen, or upper arm area. Do not re-inject the same injection site for at least 8 weeks (each area can have multiple injection sites).

**Contraindications:** Hypersensitivity to buprenorphine or excipients. Severe respiratory insufficiency. Severe hepatic impairment. Acute alcoholism or *delirium tremens.*

**Special warnings and precautions for use:** Must not be administered intravenously, intramuscularly or intradermally. Monitor for any attempts to remove the depot. Some precautions associated with buprenorphine class. *Prolonged-release properties* of the product should be considered during treatment. Patients with concomitant medicines and/or co-morbidities should be monitored for signs and symptoms of toxicity, overdose or withdrawal. *Respiratory depression:* Deaths reported with buprenorphine. Care in respiratory insufficiency. *CNS depression:* Buprenorphine may cause drowsiness. *Dependence:* Chronic administration of buprenorphine can produce opioid dependence. *Serotonin syndrome:* Concomitant serotonergic agents (e.g. monoamine oxidase inhibitors, selective serotonin re-uptake inhibitors, serotonin and noradrenaline re-uptake inhibitors or tricyclic antidepressants) may result in serotonin syndrome, a potentially life-threatening condition - if clinically warranted, observe carefully, particularly during initiation and dose increases and consider reducing or discontinuing therapy if serotonin syndrome is suspected. *Hepatitis, hepatic events and hepatic impairment:* Recording of baseline liver function tests and viral hepatitis status recommended. Hepatic injury reported with buprenorphine. Caution with buprenorphine in moderate hepatic impairment – monitor for signs and symptoms of opioid withdrawal, toxicity and overdose. Monitor hepatic function regularly. *Drug withdrawal syndrome (GB):* Before starting any opioids, discuss withdrawal strategy with the patient. Dose tapering over weeks or months may be required. Risk of neonatal withdrawal syndrome following use in pregnancy. *Precipitation of opioid withdrawal syndrome:* Buprenorphine products have precipitated withdrawal symptoms in opioid-dependent patients when administered before the agonist effects from recent opioid use or misuse have subsided. *Renal impairment:* Caution in severe renal impairment. *QT-prolongation:* Caution with other medicines that prolong the QT interval and in patients with a history of long QT syndrome or other risk factors for QT prolongation. *Acute pain management:* A combination of opioids with high mu-opioid receptor affinity, non-opioid analgesics and regional anaesthesia might be necessary. Monitor and titrate, considering potential risk of overdose and/or death. *Sleep-related breathing disorders:* Opioids can cause sleep-related breathing disorders. *Opioid class effects:* See SmPC for details. *Interactions*: See SmPC for buprenorphine interactions. *Pregnancy and lactation*: Caution – see SmPC for details. *Driving and operating machines:* Minor to moderate influence, including drowsiness, dizziness or impaired thinking – likely to be pronounced by alcohol or CNS depressants. See SmPC for details of what individual patients should be told by the prescriber.

**Undesirable effects:** *Very common:* insomnia, headache, nausea, hyperhidrosis, drug withdrawal syndrome, pain. *Common:* infection, influenza, pharyngitis, rhinitis, lymphadenopathy, hypersensitivity, decreased appetite, anxiety, agitation, depression, hostility, nervousness, abnormal thinking, paranoia, medical dependence, somnolence, dizziness, migraine, paraesthesia, syncope, tremor, hypertonia, speech disorders, lacrimal disorder, mydriasis, miosis, palpitations, vasodilation, hypotension, cough, dyspnoea, yawning, asthma, bronchitis, constipation, vomiting, abdominal pain, flatulence, dyspepsia, dry mouth, diarrhoea, gastrointestinal disorder, rash, pruritus, urticaria, arthralgia, back pain, myalgia, muscle spasms, neck pain, bone pain, dysmenorrhea, injection site reactions (pain, pruritus, erythema, swelling, reaction, induration, mass), peripheral oedema, asthenia, malaise, pyrexia, chills, neonatal withdrawal syndrome, chest pain, abnormal liver function tests. *Other:* urinary retention, injection site reactions (abscess, ulceration and necrosis). See SmPC for further details.

**Overdose:** Apply general supportive measures, closely monitoring and treating respiratory and cardiac status. Consider long duration of action of buprenorphine and prolonged release from the depot.

**Package quantities and UK net price:** 1 pre-filled syringe per pack. Weekly injection (8 mg (0.16 ml), 16 mg (0.32 ml), 24 mg (0.48 ml), 32 mg (0.64 ml)): £55.93. Monthly injection (64 mg (0.18 ml), 96 mg (0.27 ml), 128 mg (0.36 ml), 160 mg (0.45 ml)): £239.70. **Marketing authorisation numbers:** *GB:* PLGB 42800/0001, PLGB 42800/0003-9. **ROI and NI:** EU/1/18/1336/001-7, EU/1/18/1336/009. **Legal category:** POM. **Marketing authorisation holder:** Camurus AB, Ideon Science Park, SE-223 70 Lund, Sweden. Email: Camurus.uk@camurus.com Additional information available on request.

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**Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard (or search for MHRA Yellow Card in the Google Play or Apple App Store) for the UK and http://www.hpra.ie/homepage/about-us/report-an-issue for Ireland. Adverse events should also be reported to Camurus AB via email: safety@camurus.com**

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