



Opioid dependence: buprenorphine prolonged- release injection (Buvidal)

Evidence summary

Published: 14 February 2019

www.nice.org.uk/guidance/es19

Key messages

The content of this evidence summary was up-to-date in February 2019. See summaries of product characteristics (SPCs), British national formulary (BNF), or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites for up-to-date information.

Buprenorphine prolonged-release injection (Buvidal, Camurus) is an opioid partial agonist/antagonist. It is administered as a weekly or monthly subcutaneous injection and must be given by a healthcare professional. It has a marketing authorisation for treating opioid dependence in adults and young people aged 16 years and over within a framework of medical, social and psychological treatment ([summary of product characteristics](#)).

Evidence was from 1 randomised controlled trial ([Lofwall et al. 2018](#), see the [evidence review](#) for details) in 428 adults diagnosed with, and seeking treatment for, moderate to

severe opioid use disorder. Overall, people using buprenorphine prolonged-release injection were no less likely to have opioid-negative urine samples or respond to treatment (defined as having no evidence of illicit opioid use at most assessments) compared with people using sublingual buprenorphine–naloxone.

Place in therapy

Buprenorphine prolonged-release injection may be an option where there is a risk of diversion of opioid substitution medicines or concerns about the safety of medicines stored at home. It may also be an option for people who have difficulties adhering to daily supervised opioid substitution medication, such as for people who are working or in education.

Buprenorphine prolonged-release injection may have a place in treating opioid dependence in people in custodial settings, where the risk of diversion and time needed for supervised consumption currently leads to challenges in supplying supervised medicines safely.

However, the higher drug acquisition cost of buprenorphine prolonged-release injection compared with other treatments for opioid dependence will need to be taken into account.

Factors for decision making

Effectiveness

Opioid-negative urine samples

Buprenorphine prolonged-release injection was non-inferior to sublingual buprenorphine–naloxone tablets for the mean percentage of opioid-negative urine samples during weeks 1 to 24:

- 35.1% for buprenorphine prolonged-release injection compared with 28.4% for sublingual buprenorphine–naloxone tablets; treatment difference 6.7%, 95% confidence interval (CI) –0.1% to 13.6%, $p < 0.001$ ([Lofwall et al. 2018](#)).

Responder rate

Buprenorphine prolonged-release injection was non-inferior to sublingual buprenorphine–naloxone tablets for the responder rate (a responder had no evidence of illicit opioid use at most assessments over 24 weeks):

- 17.4% for buprenorphine prolonged-release injection compared with 14.4% for sublingual buprenorphine–naloxone; treatment difference 3.0%, 95% CI –4.0% to 9.9%, $p < 0.001$ (Lofwall et al. 2018).

Safety

In Lofwall et al. (2018), the most common adverse events in the buprenorphine prolonged-release injection group were injection-site pain (8.9%), headache (7.5%), constipation (7.5%), nausea (7.0%), injection-site pruritus (6.1%) and injection-site erythema (5.6%). These were also the most common adverse events in the sublingual buprenorphine–naloxone (placebo injection) group, with similar proportions of participants experiencing these. Insomnia was reported by slightly more people in the buprenorphine prolonged-release injection group compared with the sublingual buprenorphine–naloxone group (5.6% compared with 2.8%). No statistical analyses were reported.

The summary of product characteristics states that deaths from respiratory depression have been reported in people having treatment with buprenorphine, particularly when used in combination with benzodiazepines. Deaths have also been reported when buprenorphine is used in combination with other depressants (such as alcohol), pregabalin and gabapentin, or other opioids.

Once administered, the prolonged-release injection dose cannot be removed. In the case of overdose, the long duration of action of buprenorphine along with the prolonged-release properties of the subcutaneous injection should be taken into account when determining length of treatment needed to reverse the effects of overdose ([summary of product characteristics](#)).

Limitations of the evidence

The chosen comparator (buprenorphine–naloxone sublingual tablets) in Lofwall et al. (2018) is not commonly prescribed for treating opioid dependence in the UK. The trial was

completed in US healthcare settings, and only 1 of the study sites was primary care based, which may limit the applicability to UK practice. However, the most common opioid misused by around 70% of participants at baseline was heroin, which reflects the UK population where heroin is the main problem drug of most adults who misuse drugs.

The primary outcomes of the trial were disease-orientated rather than patient-orientated outcomes. Important outcomes for patients, such as craving and withdrawal scores, were only investigated as exploratory outcomes.

Participants received expenses to attend study visits, which may have improved study retention rates and may not reflect treatment retention rates in a real-world setting. Participants received addiction counselling at scheduled weekly and monthly study visits and around 95% of people in each group attended scheduled sessions.

Participants received 7-day and 4-week supplies of take-home buprenorphine–naloxone (the comparator treatment) during the first and second 12 weeks of the trial respectively. This does not reflect UK practice where people would receive no more than 1 week of take-home doses in a single instalment. Adherence to sublingual buprenorphine–naloxone was not assessed in Lofwall et al. (2018), therefore it is not possible to say if people in the sublingual buprenorphine–naloxone group adhered to their treatment.

Person-related factors

Buprenorphine prolonged-release injection is administered by a healthcare professional and removes the need for regular attendance (most commonly daily) for dispensing or supervised administration of opioid substitution medicine.

Some people may not want to use an injectable form of opioid substitution therapy and may prefer an oral therapy. Injection-site reactions can happen after the injection is given and around 17% of people in the trial experienced these.

Buprenorphine prolonged-release injection is recommended up to a weekly maximum dose of 32 mg or monthly maximum dose of 128 mg, which is approximately equivalent to 18 mg to 24 mg daily of sublingual buprenorphine. Therefore it may not be suitable for people with opioid substitution requirements greater than this. A maximum of 1 additional 8-mg dose can be given between regular weekly or monthly injections if needed, based on an individual person's temporary needs.

Resource implications

A 30-day supply of buprenorphine prolonged-release injection costs £239.70 (excluding VAT) irrespective of the strength prescribed (Camurus: personal communication 2018). A 30-day supply of methadone oral solution at usual doses costs around £15 to £30 (excluding VAT; Drug Tariff, February 2019). A 30-day supply of sublingual buprenorphine tablets at usual doses costs around £140 to £250 (excluding VAT; Drug Tariff, February 2019). See the [evidence review](#) for costs of other medicines for opioid dependence.

Additional costs of using buprenorphine prolonged-release injection include healthcare professional time and appropriate facilities to administer the injections. The increased drug acquisition cost compared with other treatments for opioid dependence, and additional administration costs of buprenorphine prolonged-release injection might be partially offset against savings made through removal of the need for dispensing and supervised consumption of medication.

Implications in practice

- Specialists from a range of backgrounds and settings including mental health, pharmacy, medicines management, and health and justice were asked for their views on using buprenorphine prolonged-release injection in practice.
- Buprenorphine prolonged-release injection was viewed as an option by some of the specialists for people:
 - where there is a risk of diversion of opioid substitution medicines or concerns about the safety of medicines stored at home
 - who have difficulties adhering to daily supervised opioid substitution medication (such as if they are working or in education)
 - who are stable on a therapeutic dose of sublingual buprenorphine
 - who live in rural areas without easy access to a community pharmacy.
- Some specialists thought buprenorphine prolonged-release injection would only be used second line if current first-line therapies were unsuitable.
- Suggested barriers to using buprenorphine prolonged-release injection included:

- cost of the injection (particularly for local authority commissioned services)
 - provision of training and support to clinicians, and additional staff resource to administer the injection
 - secure storage of the injection at sites
 - lack of clarity around who would most benefit from this approach to treatment
 - lack of clarity around treating overdose
 - lack of clinician familiarity with the product
 - service user preference.
- Weekly or monthly dosing and potential cost savings through the removal of daily supervised administration of medicines were thought to be levers for using buprenorphine prolonged-release injection. However, some specialists considered that the cost savings would be insufficient to cover the increased drug acquisition cost compared with some other treatments.
 - Because it is a controlled drug, supply and storage of the injection was considered to be a specific issue for commissioning and procurement, with the need for controlled drug cabinets and standard operating procedures. If buprenorphine prolonged-release injection was prescribed on FP10, the question was raised around who would collect this; the service user or service staff?
 - Suggested advantages for people using buprenorphine prolonged-release injection included:
 - service user convenience and preference
 - reduced accidental poisonings through not needing to store the medicine in the home
 - increased flexibility to engage in work or study.
 - Suggested disadvantages for people using buprenorphine prolonged-release injection included:
 - implications for pain management
 - limitations for a quick response to, for example, a request for a residential or

community detoxification

- the need to attend a clinic for the injection to be given (especially for a person who could manage an oral dose that they self-administer)
 - reduced potential to promptly identify issues with the service user's health or treatment because of a reduction in pharmacy interaction.
- In the health and justice system, buprenorphine was viewed as a possible option for a limited group of people, such as those in open category D sites who go out to work during the week or are released regularly on licence for short periods, and who could not attend usual daily supervised consumption sessions. It was considered that a significant change to the care pathway would be needed if buprenorphine prolonged-release injection was used instead of sublingual buprenorphine. This was because of the need to escort people to a treatment room for administration by a nurse rather than supervision by a registered healthcare professional (nurse, pharmacist or pharmacy technician) in the house block or wing.

This evidence summary was commissioned by Public Health England.

ISBN: 978-1-4731-3246-7