Depot buprenorphine injections for opioid use disorder: Patient information needs and preferences

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Abstract

Introduction and Aims. There has been significant recent investment in new medications for opioid use disorder, including buprenorphine depot injections. Patients and professionals need good quality, independent information on medications to help them make informed treatment decisions. This paper aims to understand patients’ information needs and preferences in relation to buprenorphine depot injections. Design and Methods. Semi-structured qualitative interviews were conducted with 36 people using opioids (26 men, 10 women; 24–63 years). Twelve participants were currently prescribed daily oral methadone; 12 were currently prescribed daily oral buprenorphine; and 12 were using heroin and not in treatment. Interviews were transcribed, coded and analysed via Iterative Categorisation. Results. Participants asked many questions about depot buprenorphine injections. These related to: (i) medication purpose and availability; (ii) pharmacology; (iii) evidence base and effectiveness; (iv) safety and side effects; (v) administration and dosing; and (vi) reducing and ending treatment. Additionally, participants expressed their information preferences in terms of (i) ‘format’ and (ii) ‘source’. Specifically, they wanted printed, verbal and electronic materials provided by people in authority, particularly patients who had already had the medication. Discussion and Conclusions. All potential patients should be offered accessible information on depot buprenorphine to enable them to consider their options and participate meaningfully in treatment decision making. We recommend that further qualitative research is undertaken to produce informative video material that describes patient experiences of receiving depot buprenorphine. This should help to balance biomedical knowledge with lay knowledge, so facilitating more informed discussions when decisions about depot buprenorphine treatment are made. [Neale J, Tompkins CNE, Strang J. Depot buprenorphine injections for opioid use disorder: Patient information needs and preferences. Drug Alcohol Rev 2019;38:510–518]

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Introduction

‘Medication-assisted treatment’ (MAT) refers to the use of approved medications, combined with counseling and behavioural therapies, to provide a ‘whole-patient’ approach to the treatment of substance use disorders [1]. Medications used in MAT for opioid use disorder routinely include opioid agonists (e.g. methadone), partial agonists (e.g. buprenorphine) and opioid antagonists (e.g. naltrexone) [2]. Historically, these medications have almost always been taken daily, in liquid/linctus or tablet/film form, with injectables occasionally provided to patients who repeatedly fail to benefit from oral formulations [3]. Opioid agonist treatment is closely monitored by regulatory authorities and clinicians, and medication consumption is often physically supervised in a drug treatment or community pharmacy setting [4].

Research shows that MAT can decrease opioid use, increase retention in treatment, improve psychosocial treatment outcomes and reduce drug-related deaths [1,5,6]. Nonetheless, the use of medications for substance use disorder is not without challenges. Patients can become addicted to the agonists themselves, and there are risks associated with diversion, ‘using on top’ and missed doses [7]. In addition, patients have complained that the process of frequent dosing is stigmatising, restricts their freedom, and undermines their quality of life by making it difficult to work, take a holiday, and participate in other everyday activities [8–10]. Unsurprisingly, therefore, poor/non-adherence and treatment dropout are common in MAT [4].

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Global increases in opioid use, alongside poor adherence to existing medications, have latterly generated interest and investment in new types of MAT, including extended release formulations [11–14]. Over the last decade or so, buprenorphine depot injections have been developed for subcutaneous administration [15]. In November 2017, the first depot buprenorphine product Sublocade™ (RBP-6000) was approved by the US Food and Drug Administration (FDA) for monthly administration [16]. In November 2018, two additional products – Buvidal® Weekly and Buvidal® Monthly (CAM2038) – were approved by the European Medicines Agency (EMA) for use in Europe and by the Australian Therapeutic Goods Administration (TGA) for use in Australia [17,18]. Depot injections provide sustained medication release and bypass the need for daily dosing. This is expected to reduce the treatment burden for clinicians and patients, improve patient adherence, and remove the risk of diversion [7,11,12,19].

Medications containing buprenorphine partially activate the body’s opioid receptors but also attach themselves more strongly to those receptors than drugs such as heroin and morphine [7]. This should reduce opioid withdrawal symptoms and the desire to use opioids without causing the cycle of highs and lows associated with opioid use disorder [7,20]. When administered alone at high doses, buprenorphine is safer than pure opioid agonists, but will precipitate opioid withdrawal in individuals who are physically dependent on full opioid agonists [15,21]. In consequence, care must be taken when initiating buprenorphine treatment or when switching from methadone to buprenorphine; it is recommended that people should taper down their use of pure agonists prior to making the switch [22]. In addition, anyone making the transition should be in a state of moderate withdrawal before taking their first buprenorphine dose [21].

An increase in MAT options is to be welcomed but will inevitably make treatment decision making more complicated [14]. Patients and professionals will need high quality, clear, independent information about depot buprenorphine to help them make informed choices. Licenses for new medications confirm the name of the medication, the health condition for which it should be used, the recommended dosage, wanted and unwanted effects, and information on using the medicine. Every licensed medicine also has a Summary of Product Characteristics (a legal document describing the product’s properties and the conditions attached to its use) and a patient information leaflet or PIL (which provides information on using the medicine safely) [23]. Beyond this, the availability of unbiased information on new medications tends to be limited, particularly for patients [24,25].

The pharmaceutical industry is widely considered incapable of providing non-promotional information on its products due to inherent financial conflicts of interest [26]. Reflecting this, direct-to-consumer advertising (DTCA) is permitted in only a very small number of countries and has been criticised for providing poor quality information and generating unnecessary medicine use [27]. Within the clinical encounter, meanwhile, power differentials between the doctor and patient, and the dominance of biomedical over lay knowledge, can prevent patients from articulating their questions and concerns about medications [24,28,29]. Illustrating this, a study of opioid treatment conducted in 10 European countries found that less than half of the people using opioids surveyed consulted physicians or pharmacists for information and most had limited knowledge of the available MAT options [30].

The aim of this paper is to better understand patients’ information needs and information preferences in relation to the new buprenorphine depot injection formulations. To this end, we address two specific questions: (i) What questions do potential patients have about depot buprenorphine? and (ii) How do potential patients want to receive information about depot buprenorphine? We then use the findings to consider ways of developing accessible information sources. We will report other important issues, such as potential patients’ personal willing to receive depot buprenorphine, separately [authors, in preparation].

Methods

Data were generated as part of a qualitative study exploring opioid users’ perceptions of, and willingness to receive, extended release depot buprenorphine. The research was funded by Camurus AB, the pharmaceutical company that has developed CAM2038/Buvidal®. Fieldwork was conducted in Greater London, UK, between June and October 2018 (just prior to the regulatory approvals of Buvidal® across Europe and Australia). Members of a specialist addiction Service User Research Group (SURG; https://www.kcl.ac.uk/ioppn/depts/addictions/research/surg/index.aspx) provided feedback to help shape the study design, and ethical approval was received from King’s College London University Research Ethics Committee with additional approvals granted from two voluntary sector services.

Recruitment sites included two alcohol and other drug treatment services, two homeless hostels, and an
alcohol and other drug peer support service. A quota sampling strategy was employed to recruit 12 people currently prescribed oral methadone; 12 people currently prescribed oral buprenorphine and 12 people who were using heroin daily but not currently in treatment. These criteria were chosen to include groups of people using opioids who might be eligible to have a depot buprenorphine injection; that is, ‘potential patients’. We anticipated that 36 participants would enable us to reach an adequate level of data saturation [31] whilst permitting tentative exploration of any differences between the three groups.

Recruitment processes varied slightly between the five sites to accommodate local service arrangements. However, they all followed the same basic protocol; that is, the study researcher (CT) briefed service staff on the aims and methods. Service staff then approached people whom they considered to be eligible, provided them with information about the study, and solicited permission to pass their contact details to CT. CT next contacted all interested people, described the study further, and completed a basic screening questionnaire to check eligibility. Several people who could not speak English were excluded at this point as there were no resources for interpreters. Otherwise, eligible people were invited to participate in a semi-structured interview at a time of their choosing.

Prior to interview, written informed consent was obtained. A topic guide was then used to explore participants’ personal circumstances; substance use and treatment history; views on depot buprenorphine; interest in receiving depot buprenorphine; factors that might encourage or discourage receipt of depot buprenorphine; and information needs and preferences in relation to depot buprenorphine. To facilitate discussion, participants received basic verbal information based on the concept of the depot buprenorphine product CAM2038/ Buvidal®. This information included how the medication would be injected under the skin; how it might release slowly over a period of 7 or 28 days; how it would be administered by a healthcare professional into the arm, thigh, stomach or buttock; how the dose would be determined by the patient and prescriber but could be ‘boosted’ if needed; and how side effects would be the same as for oral buprenorphine, although there might be some additional local discomfort from the injection. Participants were also shown a prototype depot injection prefilled syringe device that contained no active medication.

Interviews took place in private within the five participating services, were audio-recorded, and lasted between 37 and 100 min. Each participant was given a £20 shopping voucher at the end of their interview as a gesture of thanks. The 36 participants included 26 men and 10 women, aged 24–63 years (mean 45 years). Most (n = 24) were White British and over half (n = 21) reported that they were currently using heroin. A quarter (n = 9) said that they had ever received depot medication (contraception, antipsychotics or testosterone). Further participant details are shown in Table 1.

The audio-recordings were transcribed verbatim and the transcriptions were entered into the software programme MaxQDA v11 [32] for systematic coding. A coding frame was developed based on deductive codes derived from the interview guide and inductive codes emerging from the interview data. CT coded all the interview data line-by-line to the coding frame. For this paper, all data coded to the ‘information needs’ and ‘information preferences’ codes were exported into separate Word documents and analysed by JN via a process of Iterative Categorisation [33].

Analyses generated six categories of ‘information need’: (i) medication purpose and availability; (ii) pharmacology; (iii) evidence base and effectiveness; (iv) safety and side effects; (v) administration and dosing; and (vi) reducing and ending treatment. In addition, participants discussed their ‘information preferences’ in terms of: (i) ‘information format’ and (ii) ‘information source’. No notable differences between the three groups of participants (daily prescribed oral methadone, daily prescribed oral buprenorphine and daily heroin use) were evident. Findings are presented below using anonymised verbatim quotations to illustrate salient points.

Results

Information needs

Medication purpose and availability. Several participants asked why depot buprenorphine had been developed and questioned whether the intention was to provide patients with more medication choice or simply to replace another medication. As one female participant asked:

‘Are they going to stop the tablets and bring in an injection?’ (participant 9, buprenorphine, female, 55 years)

Other participants questioned whether buprenorphine depot injection was the same as buprenorphine tablets or film and, if not, how it compared with other buprenorphine products and with methadone. Some participants also wanted to know when depot injections would be available, how and where people could get one, and whether there would be dosing options besides...
7 and 28 days. Furthermore, one person asked whether people would be able to receive depot buprenorphine in prison; explaining that he had previously had a negative experience of withdrawal symptoms after his buprenorphine treatment had been stopped in police custody.

**Pharmacology.** Occasionally, participants requested clarification on what exactly was in the injection and whether the medication itself was in the form of an injectable tablet or a liquid. More frequently, they wanted to know whether it was mixed with an antagonist or ‘blocker’ (e.g. naloxone); whether it would interact with other drugs, including prescribed pain medications; or whether it contained sugar or other ingredients that might damage their teeth or health more generally:

‘Is there a lot of sugar in it? Is there stuff that can cause liver damage?... It’s still nice to know what you’re putting in you[rselves]’. (participant 25, methadone, male, 41 years)

In terms of the medication’s mode of action, participants queried how the injection delivered the amount of buprenorphine an individual patient needed; how it substituted for heroin; how it released the buprenorphine slowly; whether the buprenorphine stayed local to the injection site or was absorbed into the bloodstream; and how the medication was affected by temperature, exercise, health status or individual metabolism:

‘How does that work though? Because obviously people’s metabolism is different... Like some people will go through a medication quicker than other people’. (participant 19, buprenorphine, male, 46 years)

In addition, one or two participants mistakenly thought that the buprenorphine was dispersed into the body at certain times of the day and wanted to know if they would physically feel this occurring.

**Evidence base and effectiveness.** Few participants asked whether depot buprenorphine had been tested on animals or humans, or whether it had been approved in clinical trials or by regulatory authorities. Nonetheless, most wanted to know how effective it was, especially in terms of stopping heroin use, cravings and withdrawal symptoms:

‘Once it’s in you, does this take away the urge to use heroin?’ (participant 22, methadone, female, 50 years)
Some participants also queried if the medication would block the effects of any heroin taken; a few asked if it would stop alcohol seizures; and several were curious about how long the buprenorphine would take to have an effect once administered. Routinely, participants expressed concerns about what would happen if it did not work, ‘ran out early’, or was not effective for as long as the manufacturers promised:

‘I would want to know it will last that month… because that would be the main concern… I don’t want to get to say [day] 25, and on the 26th [day] I’m feeling rough because the stuff has worn out of your system’. (participant 3, heroin, male, 53 years)

Additionally, participants asked what would happen if people decided to use alcohol or other drugs ‘on top of’ the depot buprenorphine; particularly whether they would feel intoxicated, experience withdrawal symptoms or overdose.

Safety and side effects. Repeatedly, participants asked if depot buprenorphine was ‘safe’. For example, they queried whether too much buprenorphine could be released at once, whether patients could accidentally overdose on it, or whether it could be wrongly administered into a vein:

‘If it went into the vein, which it shouldn’t be in the vein, what’s the repercussions?’ (participant 32, heroin, male, 47 years)

Relatedly, participants questioned whether depot buprenorphine was addictive or would cause unwanted side effects. In this regard, they asked about scarring, itching, pain, lumping or redness at the injection site, but also nausea, headaches, constipation, mood changes, dizziness, daytime tiredness, liver problems and hair loss. Participants additionally expressed concerns about potential changes in their weight, libido, heart rate, blood pressure, clarity of thought, fertility, appetite, and sleep, and one person wondered if patients would be legally allowed to drive if they had had a depot buprenorphine injection. Others asked what would happen if patients had a bad reaction after receiving an injection, and whether there was another drug that could be administered to counter any unintended negative effects:

‘Is there any way… it can be reversed?… Like when people have overdoses, and then they reverse it. Are there any ways, if any error were to happen… that that can be [reversed]?’ (participant 2, buprenorphine, male, 45 years)

Administration and dosing. Although participants had been told that the medication would be administered by a healthcare professional, some still wanted to know if it could be self-administered. Others queried how the initial dose would be calculated; how much dose would be released each day; and how patients would feel at different times of the day, and from day to day, including whether they would experience ‘a buzz’, withdrawal symptoms, or mood swings:

‘Are you going to have mood swings because it might not release as much that day as it did the day before?’ (participant 25, methadone, male, 41 years)

Participants additionally questioned how the dose could be changed if patients felt they were receiving too much medication or not enough, and how long would it take for any change in dosage to have an effect. They also asked whether the dose received would spike on the day after the injection and diminish towards the end of the injection period, potentially leaving them feeling unwell:

‘When it’s running out, do you feel like shit, a couple of days before you have to get your next injection?’ (participant 4, heroin, male, 53 years)

Reducing and ending treatment. Several participants wanted to know whether depot buprenorphine was intended as a maintenance medication and, if not, for how long patients were expected to receive it. Others asked how patients would ‘come off’ depot buprenorphine, including how long coming off would take:

‘I would want to know about how you would reduce, how they go about reducing you’. (participant 22, methadone, female, 50 years)

Participants were also keen to know how severe the withdrawal symptoms would be when a patient stopped having depot buprenorphine injections, and whether patients would crave more for opioids after coming off depot medication because they would be accustomed to having a constant dose of buprenorphine in their body. Additionally, they wondered whether, and if so for how long, the buprenorphine would remain in their system after the injection had officially ended:

‘And when it comes to the end of 7 days, it’s going to still be in your blood… Is that not right?’ (participant 20, buprenorphine, male, 56 years)
Information preferences

Format. Participants frequently emphasised that it would be necessary to have access to information on depot buprenorphine in a range of formats because patients have diverse needs and preferences. Reflecting this, they described the importance of having printed, verbal and electronic materials, and of enabling people to access as little or as much information as they wanted:

‘You’ve got to have a package... Some people [want] video, some people are for leaflets, some people are for oral... Some people can’t read... some people can’t write. Some people would like to watch something... You would have to... do it in all different ways to suit everybody’. (participant 6, heroin, female, 42 years)

In terms of printed materials, participants expressed a desire for leaflets, factsheets, newsletters and posters. Whilst some liked the idea of receiving a written letter, others said that they would prefer to read published academic research. Some participants thought that printed written material would be best as it could be taken away, so enabling them to digest it, refer back to it, and use it to make considered decisions about whether depot buprenorphine was right for them personally. Others explained that they struggled to read written materials due to poor eyesight or limited literacy, or argued that written materials were old-fashioned and could be dull and hard to follow:

‘Sometimes reading can be hard going, especially if it’s not particularly what you want to hear, or you’re not interested in it’. (participant 11, methadone, female, 40 years)

Many participants explained that they would want verbal information on buprenorphine depot injections because it would be easier to ask questions. Moreover, they thought that they would understand the medication better if somebody explained it to them in person. Others liked the idea of participating in a group or seminar where professionals and patients who had already had depot buprenorphine told them about the medication:

‘The right way to go would be maybe a small group, five, ten people. Someone like yourself [researcher] and then someone like myself. But I would have to have... done so many months of it [depot buprenorphine], so I know what I’m talking about’. (participant 3, heroin, male, 53 years)

Although some participants cautioned that people in opioid treatment do not tend to have computers, others emphasised that the Internet is an important source of information. Indeed, several participants explained that they already used medical websites, pharmaceutical websites, YouTube videos, and academic websites to research pharmaceutical drugs and treatment. These participants said that they would want to find out about depot buprenorphine by gathering information online. Others expressed interest in watching videos/DVDs of people who had had depot buprenorphine talking about their experiences:

‘I mean maybe watching a video on someone that’s actually done six months on it’. (participant 18, buprenorphine, male, 57 years)

Source. Participants consistently argued that information on depot buprenorphine should come from people who had ‘authority’ and could be ‘trusted’ because they knew the medication. In this regard, they referred to doctors, nurses, drug workers, counsellors, researchers and pharmaceutical companies; although some felt that pharmaceutical company information might be biased and unreliable. Repeatedly, however, participants emphasised that the best information source would be people who had already had the medication and could therefore speak from personal experience. Participants argued that these individuals would be easier to talk to, more independent/truthful, and better able to answer their questions. This, they said, would inspire and reassure them if they were considering depot buprenorphine for the first time:

‘I think you would get a better straight answer from someone who’s been through it... They could give you the bonuses... they could give you the disadvantages... they can give you some idea as to what to expect if they’ve been through it themselves’. (participant 26, methadone, male, 44 years).

Discussion

People using opioids (both in and out of treatment) had many questions about depot buprenorphine injections. For example, they wanted information on the purpose and technology behind depot injections (including why they had been developed and how they worked) as well as on how depot MAT would personally affect people who received it (by, for example, reducing and stopping heroin use, craving and withdrawal symptoms). These numerous questions are
unsurprising given that opioid agonists are complex multivalent drugs [34,35]; depot injections are multifaceted bio-delivery systems with uncertain outcomes [19]; and extended release medications are a very new way of providing MAT [20].

Participants’ requests for information on the availability of depot buprenorphine suggested that they were potentially interested in receiving MAT via this new delivery system. Nonetheless, questions relating to safety, side effects and efficacy were prevalent. Some questions (e.g. whether the medication contained sugar or an antagonist) could be addressed relatively easily within the standard patient information leaflet; others (e.g. whether the medication would have long-term side effects) might be difficult to answer with confidence until further research has been completed. Additionally, participants raised issues that drug manufacturers might never be able to answer with certainty (e.g. whether someone would be able to receive depot buprenorphine in prison and how individuals would feel from day to day).

Participants also wanted to know how depot buprenorphine would compare with other forms of MAT, thus indicating that they would want to weigh up the pros and cons against more traditional options [14]. Other participants asked how the buprenorphine dose could be increased or decreased if their circumstances altered and, importantly, when and how patients would be able to reduce and come off depot treatment. In many ways, these findings are unremarkable and parallel wider literature on being prescribed drugs for chronic conditions; that is, patients who take medication long-term worry about side effects, the adverse impact on other aspects of their lives, and feelings of loss of control [36–38]. Equally, the findings are consistent with prior research that has shown how trust, perceptions of efficacy, empowerment and control affect the uptake and use of biomedical HIV prevention products [39] and how lack of information and poor understanding can deter people who inject drugs from engaging with hepatitis C treatments [40].

The concept of the ‘informed patient’ has been widely used in recent years and is underpinned by an assumption that patients take responsibility for their health and actively seek out medical information, often by the Internet [29,41,42]. Consistent with this idea, participants in the study wanted information in a range of formats and some said that they would proactively look for information online. Nonetheless, others referred to limited ability to read, little interest in long documents, and poor access to computers. Furthermore, most wanted and expected information to be provided ‘to them’. Socio-demographic factors (e.g. limited education, low income and poor health) impede proactive health information seeking [43] and are also common amongst people who use non-prescribed opioids [44,45]. It is therefore important that accessible information is routinely ‘offered to’ all potential depot injection patients to avoid compounding any pre-existing knowledge inequalities.

Using health information can, meanwhile, empower members of marginalised communities as it enables them to discuss their treatment options within the doctor/patient encounter and even challenge medical opinion [29,41–43]. Study participants expressed a desire for information provided by healthcare professionals, scientists, and drug developers; even though there was some skepticism about the independence of information provided by pharmaceutical companies. Importantly, however, participants consistently wanted to hear the views and experiences of people with lived experience of depot buprenorphine; in other words, they often prioritised ‘lay knowledge’ over more formal ‘biomedical knowledge’ [41,46]. Providing people who use opioids with access to information based on the lived experience of people receiving depot buprenorphine could help potential patients engage more fully in discussions about this new medication. Moreover, patient-centred care and shared decision making might increase if doctors were also able to listen to, and learn from, the personal accounts of actual patients [14,47].

Limitations

The analyses presented derive from qualitative interviews conducted with 36 people using opioids from one UK city. Discussions were largely based around the concept of two depot buprenorphine products (CAM2038/ Buvdal® Weekly and Buvdal® Monthly); non-English speakers were not interviewed; and those who agreed to participate were a self-selecting group who may have had a particular interest in buprenorphine depot injections (we note that nine of 36 had already had a depot injection). As such, we cannot draw any empirical generalisations from our findings. Despite this, the frequency with which participants reported similar questions and opinions on information formats and sources suggests that these findings are likely to be replicated in other opioid using samples and with respect to other depot buprenorphine products. We did not identify any notable differences between the three groups (people prescribed methadone daily, people prescribed buprenorphine daily, and people using heroin daily), but this might relate to the relatively small number of study participants. Additionally, information needs
and preferences might vary more significantly according to other socio-demographic characteristics (e.g. sex, age, race, education, housing status) and this could be explored in a future larger study.

**Conclusion**

People who use opioids are likely to have many questions about new depot buprenorphine injection formulations and will want authoritative information in a range of formats (and languages). As with any medication, it will be difficult to predict which questions any individual patient may have and impossible to answer all questions definitively. That said, potential patients will almost certainly want to know how the medication compares with alternative medications, how it delivers buprenorphine, how it can help those with opioid use disorder, whether it is safe and has side effects, how they can access it, how it will make them feel, and when and how they can come off it.

Despite increasing global use of the Internet and electronic media, simple leaflets and verbal explanations still appear to be essential information sources for people who use opioids. A leaflet that includes basic factual information, personal accounts of patients who have had depot buprenorphine, and links to more comprehensive scientific research would enable people to access as much or as little information as they wanted. We also recommend that an independent prospective, longitudinal, qualitative study exploring how patients experience depot buprenorphine injections over a period of months and years is needed. Findings from this research should be published in academic journals but additionally turned into an accessible online video resource (precedents for this include: http://www.healthtalk.org/ and https://www.livesofsubstance.org/). Potential patients could then be signposted to watch the video material at home and invited to view it in treatment services. Equally, it could function as a training tool for doctors. The patient-focused nature of the content would help to balance biomedical knowledge with lay knowledge, so facilitating more informed discussions when decisions about depot buprenorphine treatment are made [14,46,47].

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**Conflict of Interest**

JN has received honoraria and research grants from pharmaceutical companies: Camurus AB and Mundipharma International Ltd. JS is a researcher and clinician who has worked with a range of types of treatment and rehabilitation service-providers. He has also worked with a range of governmental and non-governmental organisations, and with pharmaceutical companies to seek to identify new or improved treatments from whom he and his employer (King’s College London) have received honoraria, travel costs and/or consultancy payments. This has included discussions with Camurus AB, Indivior and Molteni Farma (all three of whom have developed ultra-long-acting buprenorphine formulations) and also an oversight role for the UK part of a safety trial of CAM2038/Buvidal®; the product discussed in this paper. For a fuller account, see John Strang’s webpage at: http://www.kcl.ac.uk/ioppn/depts/addictions/people/hod.aspx. Charlotte Tompkins received salary support from Camurus AB whilst undertaking this study.

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