Use of long-acting injectable buprenorphine for opioid substitution therapy position statement: Consultation report

COMMENTS RECEIVED FROM EXTERNAL REFEREES AND OTHERS

All reviewers submitted declarations of interests which were viewed prior to the addressing of comments.

Section numbers in the leftmost column refer to numbering in the consultation draft, while section numbers in the responses refer to both the consultation draft and the final published version.

Invited reviewers			**Type of response and declared interests**
BM	Mr Brian Martin	Addictions Advanced Nurse Practitioner, East Ayrshire Addiction Services	*Individual response.* Declaration of no interest submitted.
DW	Ms Diane Watson	Advanced Clinical Pharmacist, NHS Greater Glasgow and Clyde	*Individual response.* Declaration of no interest submitted.
HMcN	Ms Helen McNally	Service Manager Community Forensic Mental Health Team, Holywell Hospital (Northern Ireland)	*Individual response.* Declaration of no interest submitted.
IM	Mr Ian Morrison	Advanced Nurse Prescriber, NHS South Ayrshire Addiction Services, Ayr	*Individual response.* Declaration of no interest submitted.
KMcG	Mr Kevin McGinley	Community Mental Health Nurse, The Edinburgh Access Practice, Edinburgh	*Individual response.* Declaration of no interest submitted.
LW	Dr Lars Williams	Consultant in Anaesthesia and Pain Management, NHS Greater Glasgow and Clyde	*Individual response.* Declaration of no interest submitted.
SMC		Ms Pauline McGuire, Principal Pharmacist – commenting on behalf of Scottish Medicines Consortium	*Group response.* Declaration of no interest submitted.
TE	Dr Tim Elworthy	Consultant Psychiatrist – Addictions, NHS Tayside.	*Individual response.* Declaration of no interest submitted.

Open consultation			Type of response and declared interests
MB	Dr Michael Basler	Consultant in Pain Medicine and Anaesthesia, Glasgow Royal Infirmary	*Individual response.* *Non-financial personal interests eg research projects* - A colleague is on the group but the view are all my own I have published a few letters on the topic of medication opioids and pain.
NHS24		Mr Martin Carragher, Senior Charge Nurse Mental Health Hub, NHS 24 – commenting on behalf of NHS 24	*Group response.* *Nature and purpose of your group or organisation* – NHS Services. *How might the information in the draft Healthcare Improvement Scotland position statement impact on your organisation's functions/status/productivity?* - Draft information will have no discernible impact on the function of our organisation as not directly providing this specialised treatment. No declarations.
SMacF	Ms Sarah MacFarlane	Specialist Pharmacist, Substance Use, NHS Fife	*Individual response.* Declaration of no interest submitted.
SS	Dr Susan Smith	Consultant Anaesthetist, Glasgow Royal Infirmary	*Individual response.* Declaration of no interest submitted.

Section	Reviewer	Comments received	Development group response
General			
	BM	I have managed to read through the guideline a few times now. Each time I have been left with a view that this is a very comprehensive document offering a wealth of appropriate, clear and concise information to the various relevant groups including service users, prescribers and clinicians who will be administering to and supporting individuals receiving Buvidal. I find the tone, language and addition of images and tables to be appropriate and well balanced allowing those with little or no previous understanding or knowledge of Buvidal to become informed to a good standard but also to serve as a reminder, prompt and good practice guide to those that already have a working knowledge of Buvidal. I do not have anything to specifically add or comment on with regards to areas of concern or gaps in the information provided and would be happy for this document to become a working document for my own use and for me to be able to recommend its use to both colleagues and service users alike. Lastly I would like to thank the contributors on the working group for their time and efforts and commend them for the excellent work.	Noted. Thank you.
Section 1			
	SS	Long acting injectable form	No response required
	HMcN	Clearly set out, providing an overview of the product alongside a visual aide.	Noted. Thank you.
	NHS24	Product description is clear and simple to understand.	Noted. Thank you.
Section 2			
	IM	Patients should be given more choice and information regarding the choice of OST, allowing them to make a more informed choice if agreed within prescribing.	Agreed. In section 2.1 (now section 3.1), the position statement points out that “In Scotland, long-acting injectable buprenorphine is indicated for use in people for whom methadone is not suitable and buprenorphine is considered appropriate” and notes that individuals may hold strong views about the use of either of these drugs. The position statement

			acknowledges that there is no simple formula that can be recommended to determine the clinical suitability of either methadone or buprenorphine but emphasises that clinicians should discuss treatment choices when obtaining informed consent for their treatment so that patients are empowered to make their own decision, taking account of the reasonable informed advice of the prescriber, which also helps the patient to take account of their own personal circumstances. Also, in section 2 (now section 3), there is a link to Annex 1 where the MAT standards are listed, including Standard 2 - All people are supported to make an informed choice on what medication to use for MAT, and the appropriate dose.
	KMcG	Good clear detail for suitable patient treatment.	Noted. Thank you.
	MB	With time these guidelines will be eroded in the community as over pressure services deal with the complex and chaotic healthcare issues that occur with users. Expect death to occur from polypharmacy when users on monthly injections attend other services, give inadequate information, obtain prescription meds by deception etc. This will work in the ideal world where there are resources and good links between services. In the real world there are often issues with IT, poor information and pressurised healthcare and social care professionals and there will undoubtedly be issues in patients taking long acting meds that can interact with a variety of substances. The SCOTTISH EXEC / SIGN are still not differentiating between EFFICACY - some benefit in highly observed and small groups versus EFFECTIVENESS which is that fact that a treatment works in the vernalised population warts and all. I would suggest that it is unethical to put this treatment into the population without rigorous monitoring as it will affect several areas for which Scotland has a poor record e.g. drug deaths, drug diversion and illicit degrading of the drug itself, crime issues, polypharmacy, mental health, acute care pressures including issues with acute pain management as well as chronic pain	We agree that there is a difference between efficacy, as shown in the controlled conditions of a clinical trial and effectiveness as shown in the population and context in which the product is used. The position statement working group recognises the paucity of evidence and for this reason there are no recommendations in this document. The working group strongly disagrees with the suggestion that the use of long-acting injectable buprenorphine is unethical. The evidence, as with much of medicine, is imperfect but there is evidence of clear benefit for some patients. There is no evidence of significant harms at a level above oral OST.
	LW	Is any consideration being given to using this in opioid weaning for patients with chronic pain and prescribed opioid dependency? Weaning is often extremely difficult in these patients, particularly in the absence of inpatient detox facilities.	This topic was not included in published source guidelines or in statutory advice. We are not aware of evidence on this topic. A consensus statement on

			general principles of chronic pain management is included in section 10.2 The working group acknowledges that this is an interesting, but specialist, area and falls outside of the scope of this position statement. A sentence has been added to the Introduction to clarify that management of dependency on prescribed opioids is not within the remit of this document and long-acting injectable buprenorphine is not licensed for use in detoxification (see section 1.5).
	NHS24	Section on patient selection appears to be based on robust evidence in field that supports this treatment being targeted at those patients likely to receive most benefit.	Noted. Thank you.
2.1	IM	If attending pharmacy is an issue due to distance, peer influences and begin vulnerable. Also for those working this may be a better choice.	We do not fully understand this statement, although agree that long-acting injectable buprenorphine may be particularly appropriate for individuals who struggle to attend regular treatment appointments, for example due to work commitments. The position statement notes that long-acting injectable buprenorphine *[offers] greater convenience for service users who would no longer be required to attend treatment sites for frequent supervised administration of treatment. Weekly or monthly appointments would be more convenient for service users who:* • *travel abroad* • *have work or study commitments* • *have mobility issues* • *live in rural areas where access to community pharmacies will be difficult* • *have regular release from custody on license for short periods.*
	KMcG	Information provided on other medication choices for OST.	This was not included in the scope of this position statement.
	MB	The section on acute and chronic pain here needs to be changed, There is a very real risk that there will be significant issues with a depot drug and acute	The challenges regarding acute and chronic pain management are recognised by the working group.

		pain management. This may or may not be an issue but the data is still poor. The research question of whether high dose buprenorphine will interfere with acute pain management is yet to be properly answered. All the assumptions come from audit data and it is often based on "it does not seem to be a problem in our unit." The objective evidence is based on small studies. Also these patients frequently need primary and secondary care and often have complex comorbidity and are at risk of trauma. To introduce this without a clear plan as to how to deal with this is poor medicine. Addicts also have cancer and there is no mention of palliative care or cancer pain management. It looks like the gatekeepers of opioids are chronic pain clinics which a) do not use opioids regularly - see the opioid crisis - and b) have very, very limited resources to deal with these complex patients. Active drug abuse and severe mental health issues are usually a contraindication to referral to pain clinics in some services. Moreover there are NO specialised clinics in my area which has the biggest problems despite colleagues trying to set one up for 5 years. Secondary care Pain clinics are very poorly resourced compared to addiction, psychiatric and even pall care services. It is a nonsense to think they will be able to deal with any issues on this medication in a timely manner. Addicts change and they be on the medication doing fine and suddenly get a co morbid medical issue that needs pain relief. What and where then ?	Buprenorphine is a partial agonist and adds complexity to pain management. Long-acting injectable buprenorphine may add to this complexity. This will require careful joint working between pain service/GP/Drug and alcohol treatment service/palliative care team to manage and plan. Section 10.1 on acute pain management is reproduced from the SmPC and therefore is the regulatory position. In the absence of direct evidence for chronic pain management in people using long-acting injectable buprenorphine, the group has developed a consensus statement on the general principles of chronic pain extrapolated from other evidence-based sources (eg SIGN 136). More specific development of pain services and the complex issues involved in them is beyond the scope of the position statement. The Faculty of Pain Medicine of the Royal College of Anaesthetists provides information on pain management in palliative care for individuals with recognised drug problems. It notes that “The principles of analgesic practice in substance misusers are fundamentally no different from those for other adult patients needing palliative care.” This information has been added to section 10.2
	HMcN	Easy to read and follow.	Noted. Thank you.
	NHS24	This section appears clear and supported by evidence.	Noted. Thank you.
	SMC	Paragraph 1 - Suggest removing “subcutaneous implant” from the list in brackets. At the time of the 2017 UK Drug Misuse guideline, only oral and sublingual formulations of buprenorphine were available in the UK. Although the 2017 Guideline refers to the subcutaneous implant, this is to note that it was not available in the UK or Europe.	Agreed – brackets have been edited as suggested

		Paragraph 2 - "*Both are cost-effective and recommended, for example, by NICE, for the treatment and prevention of withdrawals …*" This paragraph isn't referenced but assuming this is referring to the NICE MTA which has a status in Scotland as it has been endorsed by HIS. NICE TA 114 (2007) covered methadone and **oral** formulations of buprenorphine so could possibly be a bit misleading and suggest that NICE considered Buvidal cost effective. NICE has not carried out a cost-effectiveness evaluation of Buvidal, but has published an Evidence Summary in February 2019 that notes that Buvidal "may have a place ,for example in custodial settings… but that the high acquisition cost compared with other treatments should be taken into account."	This is adapted from the 2017 UK Drug Misuse guideline which does not provide a reference for the statement. We have revised the text in the position statement to clarify that the cost effectiveness claim refers directly to oral formulations. "The UK Drug Misuse Guideline states that oral methadone and oral buprenorphine are both effective at achieving positive outcomes in opioid-dependent individuals."
2.2	IM	Oral medication is the least intrusive however injectable should be an option.	Agreed. This product is an option for people who prefer the injectable option compared with oral methadone or buprenorphine. Buprenorphine is available in sublingual/oral lyophilisate formulations and long-acting injectable form. The mechanism for delivery of buprenorphine should be a patient-centred decision.
	KMcG	Basic information provision which will require updating regular as information becomes available.	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	TE	Scottish Government guidance for the use of Buvidal for opiate substitution treatment in prisons during the COVID-19 pandemic[14] further notes that the following groups in custody should not be considered for transfer to long-acting injectable buprenorphine: • those on remand • those with less than 6 months of their sentence left to serve. I do not see the need to include this in the SIGN guidance. The basis for these recommendations from the Scottish Government were not clear at the time, other than to reduce financial impact. The acute phase of the COVID pandemic has passed and in any case, in the prison we are not abiding by this guidance as it prevents patients accessing treatment that would be beneficial to them. I continue to see no justification for the recommendations from Scot Gov on this matter.	Agreed. The working group acknowledges that although published in 2020, the advice from Scottish Government has now been superseded by the implementation of the MAT Standards, published in 2021. In Scotland, funding was provided to support the implementation of Buvidal® in the prison setting, because at the start of the pandemic, Buvidal® was not incorporated to most health boards' formulary and therefore required a commitment that treatment would continue on release. Given the more widespread availability of Buvidal® and increased likelihood that long-acting injectable buprenorphine which is started in prison will be continued in a community setting, this paragraph has been removed.

	MB	Anything that cannot be chemically manipulated by addicts to abuse the constituent products is the key...I remember the days of Temgesic	No response required
	HMcN	I agree that those on remand and with short sentences should not be excluded.	As above. The position statement has been revised to remove the statement on exclusions in prison settings.
	NHS24	This section is detailed and is informative and a clear explanation is provided with rationale for prescribing.	Noted. Thank you.
Section 3			
	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	HMcN	Clear and easy to follow.	Noted. Thank you.
	NHS24	Clear guidance and appropriate rationale provided.	Noted. Thank you.
3.1	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	TE	Consideration needs to be given to use in prison where we often retoxify people who have been detoxified unnecessarily in prison and are at high risk of relapse/overdose, especially on liberation. Additionally, opiate use in prison is often low severity due to lack of access to drugs, but will escalate on liberation or if drugs are introduced into the prison. For the above reasons therefore, we do not expect patients to be exhibiting opiate withdrawal symptoms prior to initiation on to Opioid substitution therapy, as they are either not physically tolerant, or have very low tolerance. Instead we rely on a good history, drug screens and a cautious dose titration schedule to ensure safe and appropriate commencement of OST.	This section is derived from the Summary of Product Characteristics (SmPC) which contains no reference to retoxification (or specific use in prisons). The Scottish Government guidance for the use of Buvidal for Opiate Substitution Treatment in Prisons during the COVID-19 Pandemic also does not refer to retoxification. The working group acknowledges the importance of this issue and notes that it explains why some people may be started on OST even when they may not be suitable if following conventional guidance. Although 'retoxification' may not be a widely used term, it is a practice which reduces the risk of overdose on liberation. Long-acting injectable buprenorphine may offer additional value as it gives the community services time to catch up and

			organise reviews. At present there is insufficient evidence to support guidance in this area but acknowledge there are some variations in clinical practice and it could be a topic where consensus statements are developed in future revisions of this position statement.
	MB	Again it likely that whatever is put here will be slightly "bent" to fit pressures and needs. Currently many services are under extreme pressure	Noted. This position statement is provided to NHS boards and other stakeholders for information only. Local adaptation to suit regional priorities and capacity is encouraged.
	NHS24	Clear guidance.	Noted. Thank you.
3.2	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	TE	Acute alcoholism needs to be defined better. Do you mean high risk alcohol consumption, harmful use of alcohol, alcohol dependence but currently drinking, or any form of alcohol dependence whether they are drinking or not?	This section is derived verbatim from the SmPC. The working group acknowledges the difficulties caused by a lack of specificity, however notes that the more general term may be helpful in this context as it allows for clinical judgement. While the term 'acute alcoholism' is rarely used, the DVLA guidelines uses the terms 'alcohol misuse' and 'alcohol dependency', which are also not further defined.
	MB	Again it likely that whatever is put her will be slightly "bent" to fit pressures and needs. Currently many services are under extreme pressure See section on pain	Noted. This position statement is provided to NHS boards and other stakeholders for information only. Local adaptation to suit regional priorities and capacity is encouraged.
	NHS24	Clinical information supported by evidence form studies OF OST.	Noted. Thank you.
3.3	KMcG	Very clear easy to follow information	Noted. Thank you.
	NHS24	Well-structured section outlines the recommended route of administration and good practice re rotating subcutaneous injection sites.	Noted. Thank you.
3.4	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are

			listed in section 13.4
	TE	Are there different dose equivalencies for Espranor? When Espranor was brought out the drug company recommended dose reduction when converting from generic buprenorphine. I believe they have provided our health board with different dose equivalencies between Buvidal and Espranor, than between Buvidal and buprenorphine. However, this was 2 years ago and they may have further evidence to say this is not necessary. So worth checking with them I think.	Espranor® has a 25–30% higher bioavailability compared with other sublingual buprenorphine products such as Subutex®. The manufacturer of Buvidal® has run simulations for the switching from Espranor® to Buvidal® and provided the recommended corresponding doses of weekly and monthly Buvidal® which have been added to Table 1. The SmPC for Espranor® (oral lyophilisate formulation) notes that *"Espranor® is not interchangeable with other buprenorphine products. Different buprenorphine products have different bioavailability. Therefore, the dose in mg can differ between products. Once the appropriate dose has been identified for a patient with a certain product (brand), the product cannot readily be exchanged with another product."*
	NHS24	This section appears to be clear about safe initiation, also covering issues such as patient preference and safety as well as prescribers responsibilities.	Noted. Thank you.
3.5	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	NHS24	Support the advice in this section.	Noted. Thank you.
Section 4			
	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	NHS24	Support the evidence based approach.	Noted. Thank you.
4.1	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	TE	Dose reduction if elevated LFTs -- this is too simplistic a response. There may be other causes for elevated LFTs that require investigation and rectifying. Then, if LFTs remain elevated a risk/benefit decision has to be made as to	Agreed. If LFTs are elevated further investigation is required and may require clinical judgement about the risks/benefits of treatment and need for closer

		whether to reduce/withdraw buprenorphine, recognising that relapse carries its own risks. Close monitoring of LFTs may be necessary if treatment continues. If the elevated LFTs are a reaction to Buvidal may not be a dose dependent phenomena anyway, in which case reducing dose may not help.	monitoring. A new paragraph has been added after the consensus statement: *"Individuals who develop abnormal liver function test results whilst on long-acting injectable buprenorphine should have these appropriately investigated and other causes excluded. Consideration should be given to the balance of risks and benefits of continuing treatment and additional monitoring should be considered if continuing."*
	HMcN	Clear and concise.	Noted. Thank you.
	NHS24	Good practical guide for clinicians.	Noted. Thank you.
4.2	KMcG	Clear information	Noted. Thank you.
	NHS24	Support this section as vulnerable population with complex lifestyles means this may be a challenge, explanation of grace period.	Noted. Thank you.
4.3	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	This will likely occur for several reasons but the reason of relapse will be unlikely to be communicated to many of the other services, e.g pain clinic, hepatology that may be looking after said individuals. This time is a risk for death in addicts in my opinion.	Noted. Thank you. The working group believes that the SmPC here is referring more to planned than unplanned ending of treatment. Relapse is not referred to in this paragraph, and treatment termination with Buvidal® may be for a number of reasons, including no longer requiring OST, and transfer to other formulations.
	NHS24	Advice appropriate.	Noted. Thank you.
Section 5			
	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	HMcN	Clear and concise.	Noted. Thank you.
	NHS24	Section is clear.	Noted. Thank you.
5.1	KMcG	Clear information	Noted. Thank you.

	SS	I have concerns about perioperative management of patients on long acting injections with respect to general anaesthetic drug interactions and cost op pain management. Will there be a SOP for planned and emergency surgery?	No specific cautions or contraindications are listed in SmPC for this situation. None of the published guidelines which provide information on long-acting injectable buprenorphine contain advice for individuals who are taking Buvidal® and undergoing surgery and/or general anaesthesia, therefore it has not been possible to develop consensus statements on this topic. For elective procedures, it is possible to convert individuals using injectable formulations to oral buprenorphine.
	NHS24	Emphasis on this is important for non-specialist as likely to encounter these situations in out of hours periods	Noted. Thank you.
5.2	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	Do we really have ANY evidence about this in the real complex cohorts e.g. patients with polypharmacy, mental health issues and other complex medical problems e.g. liver failure, HIV	These data are derived from the SmPC and likely to be based on safety data supplied by the manufacturer. No further evidence has been identified. In the clinical experience of the working group it is better for patients with polypharmacy. The group is not aware of deterioration of complex mental health issues, and most patients prefer the clarity of mind.
	HMcN	Clear.	Noted. Thank you.
	NHS24	Section is robust.	Noted. Thank you.
5.3	KMcG	Clear information	Noted. Thank you.
	MB	The amount of patients who are on a sedating polypharmacy that drive is high. The regular use of cannabis with this polypharmacy is common. The current system of doctors warning patients to self report if they feel not fit to drive is not fit for purpose. I have been able to address prescription medication abuse on more than one occasion by informing a patient that I could not support them driving,	Noted. This section lays out the legal responsibilities of the prescriber under the Road Traffic Act 1988. It is beyond the scope of this document to comment on the appropriateness of this legislation.

	HMcN	Clear.	Noted. Thank you.
	NHS24	Helpful guide to clinicians.	Noted. Thank you.
5.4	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	NHS24	Robust section outlining the benefits versus risks.	Noted. Thank you.
5.5	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	Will be an issue. Expect some improvement initially but then a fall in the gains made over the years.	No response required
	HMcN	Underlines in detail what practitioners should be mindful to.	Noted. Thank you.
	NHS24	Clear informative and factual.	Noted. Thank you.
Section 6			
	KMcG	A possible game changer for persons requiring OST, enabling persons to live their life with less restrictions, opens up a potential for persons to be less reliant on traditional model services.	Noted. Thank you.
	MB	Needs resources, monitoring and staff - none of which are likely to happen in the current environment.	The working group notes that Scottish Government is allocating significant resources to the implementation of the MAT standards.
Section 7			
	KmcG	Licensing, storage, cost, training, not enough evidence from trials and studies as yet.	Noted. Thank you. The current indications for use of long-acting injectable buprenorphine are included in this document, with verbatim reproduction of the SmPC. Section 11 includes a discussion of training issues and a consensus statement. Regarding storage, the SmPC notes that long-acting injectable buprenorphine should not be refrigerated or frozen. The British National Formulary notes that, as a Schedule 3 (CD no register) controlled drug, it should be stored and supplied in line with the Misuse

			of Drugs (Safe Custody) Regulations 1973. The relevant advice for Prisons in Scotland is found in Guidance On The Safe Management Of Controlled Drugs In The Scottish Prison Service: Standard operating procedure. Since the updated Responsible Pharmacist Regulations were published in 2013, standard operating procedures for the management of controlled drugs, are required in registered pharmacies, including an accountable officer who is responsible for the safe and secure handling of controlled drugs. Each NHS health board has a policy for safe and secure handling of medicines.
	MB	Resources and links between services	Noted. Thank you.
	NHS24	Section is appropriate.	Noted. Thank you.
7.1	KMcG	Very clear information	Noted. Thank you.
	MB	How can we consent someone if we are not monitoring the long term effects of this intervention in a high risk group? Are we going to consent and say that we do not know if you have an accident whether or get cancer whether your pain killers will be effective?	Although the position statement includes guidance about important points to consent patients on when starting long-acting injectable buprenorphine, it is beyond the scope of this document to list all such points. These may be addressed in local guidelines, for example discussion of opioid blockade and that other opioid analgesia may be less effective in the context of long-acting injectable buprenorphine use. These can be discussed with patients who can take a capacitous decision to choose to accept this as a risk within treatment. The position statement notes "*As part of the process of gathering consent patients should understand the implications of different treatment options, including potential risks and benefits, side effects, financial and other commitments."*
	NHS24	Support this section as based on principles of partnership working and patient choice.	Noted. Thank you.
7.2	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are

			listed in section 13.4
	MB	Should not be given to non-engagers but will likely happen	The working group notes that Buvidal® may be a catalyst for engagement and may provide a good option for people who regularly miss doses, have reduced tolerance and have to be re-titrated which is a risky time for overdose. It can only be administered to individuals who engage with services for treatment.
	NHS24	Clear alternatives draft section appropriate.	Noted. Thank you.
7.3	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	Will likely be prescribed anyway at points when they "seem to be engaging" and continued when they fall back into addiction. See the number of drug dates that occur with methadone being present as well as a variety of prescribed and non-prescribed substances	The working group notes that addiction is often a relapsing condition and recovery is now accepted as progress towards improved health and wellbeing. Buvidal® may be protective when there are lapses. As above, individuals must engage to receive treatment. Just as with other forms of OST it would not be stopped if someone were to relapse into illicit opioid use. This is a clear decision that services take, as OST is evidenced as protective against overdose. The reviewer is correct that this protection sadly does not prevent all deaths due to overdose, though buprenorphine is more likely to be protective than methadone due to the receptor blockade effects.
	NHS24	Good rationale of this issue.	Noted. Thank you.
Section 8			
	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	Will likely be poor due to the poor access to addiction records in secondary care and the chaotic lifestyle of many addicts.	Poor access to records between services is an issue in many areas, but beyond the scope of this document, which is describing best practice.

		This is a very key issue. In my experience some addicts go elsewhere when doors are closed to them due to non-engagement.	
	NHS24	More specific worked examples or scenarios may be helpful.	The working group acknowledges this request, however flexibility of approach is important to support access to effective treatment. Addictions services are used to transferring patients as they move to other areas, this document includes a minimum dataset of information to include (see Section 9). The optimal configuration of services to deliver the high-level principles in this position statement may be determined locally to align with local resources and service structures.
Section 9			
	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	The belief that there is a well-established and resourced system to deal with these issues is a nonsense. There is an excuse pain team for SURGICAL wards only in my Hospital. There are some protocols for methadone and some that seem less robust for buprenorphine. The evidence for these are based on ad hoc experience audits and a little bit of research. There is NO pain team for the MEDICAL wards. I cannot comment on the Pall Care / Cancer service. There is no desire to see these patients in the chronic pain clinics without Substantial extra resource. Many of these patients have complex and intractable issues and often medication is the last thing that can solve their pain issues. Despite 20 year of educating individuals I have still come across senior clinicians who view the WHO ladder (initially made by 8 people in a room in the 1980's) as a mechanism of treating all chronic pain. This is nonsense and has caused the opioid crisis. As tough as treating addiction is, multiply by 10 to treat many types if chronic pain in an addict.	Thank you. The position statement does not report such a belief. This is a position statement on the use of long-acting buprenorphine for opioid substitution therapy. There are some established pain and addictions clinics across Scotland. This is a resource issue and out of the scope of the position statement.
	NHS24	No issues with this section.	Noted. Thank you.
	SMC	Page 26 *"Long-acting injectable buprenorphine is used for opioid substitution therapy, and not pain management".* That is currently true, however, the company has	Noted. The consensus statement was developed with this information available to group members, and influenced the wording. The group noted that

		submitted a licence extension to the European Medicines Agency to extend the licence to include the treatment of chronic pain. Still uncertain but could become available in the UK later this year. Might be worth re-wording this sentence to future proof.	there was no guarantee that the company submission would be approved and progress to the stage of a change in marketing authorisation. Even if it did, the timescale for this was not predictable. Therefore the decision was made to ensure that the document was fully in line with the current regulatory definitions at time of publication and the document could be updated in future if, and when, any changes were made to the licensing status of long-acting injectable buprenorphine. A sentence has been added to note this submission.
9.1	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4 and see above.
	DW	The SPC for Buvidal recommends 'a combination of use of opioids with high mu-opioid receptor affinity (eg fentanyl)' It should be noted that short acting fentanyl (lozenges) are licenced only for breakthrough cancer pain and not all acute pain. Furthermore, fentanyl patches are licenced only for severe chronic stable pain, therefore should not be used in acute pain.	Noted. Thank you. A paragraph has been added to clarify these issues. *"The working group suggests caution in the use of fentanyl lozenges for acute pain management which are highly addictive due to their potency. Transdermal fentanyl patches are licensed only for use in chronic pain management."*
	SS	See previous point (5.1) - we need some kind of SOP for managing planned and emergency surgical care and pain management	Noted. This may be developed locally to reflect the availability of local resources and local processes. It is outwith the scope of this document.
	MB	See above. Is the evidence there? Are the resources there? Is the link between services there? Is the monitoring of patients there?	This section is reproduced from the SmPC.
	NHS24	Informative and clear.	Noted. Thank you.
9.2	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	Will be an issue for all the reasons above In the light of the issues with Gabepentinoids , Opiates, Addiction Poverty and Chronic Pain and illicit substances, the fact that Scotland has poorly coordinated services and has done nothing about this in the face of horrendous	Noted. This document aims to describe good practice and commenting on the real world limitations and resource issues is not within its scope.

		mortality is a poor reflection of Scottish Healthcare.	
	LW	See earlier comment (Section 2) about potential use in weaning patients with prescribed opioid dependency	This topic was not included in published source guidelines or in statutory advice.
	NHS24	Informative and clear.	Noted. Thank you.
Section 10			
	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	Training about what? If it is only in the addiction service you may be leaving other searches e.g. surgical teams, cancer units flying blind	As long-acting injectable buprenorphine may be administered by a range of professionals depending on the clinical setting, the position statement does not specify who should receive training although notes that *"The professional regulatory bodies (such as the Health and Care Professions Council, the General Medical Council, the General Pharmaceutical Council and the Nursing and Midwifery Council) are responsible for setting the standards of behaviour, competence and education of regulated healthcare professionals"* The consensus statement includes *"NHS organisations and contracted services must ensure appropriate staff are trained and competent to deliver medicines, including as subcutaneous injections…"*
	NHS24	National standards for training.	Noted. Thank you.
Section 11			
	KMcG	Good clear informative information	Noted. Thank you.
	TE	'The treatment offers more protection from the risk of accidental overdose than either methadone or oral buprenorphine' ---> is this an evidenced based statement, especially when comparing with oral buprenorphine? Similarly for the following statement (especially comparing to oral buprenorphine) 'Buvidal is more protective than methadone, and more protective than oral buprenorphine, however it won't protect you from overdose at all costs. It helps people that may have an accidental overdose, but it is not clear what would	These statements were adapted from a patient information leaflet developed by a UK not-for-profit substance misuse service provider and cannot be assumed to be evidence based. We have revised the statements to be more balanced, noting that Buvidal® may be more protective in an opiate overdose however this benefit is reduced if other depressant drugs such as benzodiazepines or gabapentinoids are taken. We have also removed the statement that it is more protective than oral

		happen if someone was determined to see how much they could take before they overdose' 'What happens if I miss my injection?' ---> In practice we are giving patients there doses even if they are later than 2 days (weekly) or 7 days (monthly). Duration of treatment is often an important factor in clinical decision making around these missed doses. 'If I have been on Buvidal for and want to come off, what's the process?' --> Emerging evidence from Glasgow and locally that reducing monthly dose to lowest dose and then stopping after 3 months with no further OST results in effective detox.	buprenorphine or methadone. Noted. This statement matches advice from the SmPC – *"To avoid missed doses, the weekly dose may be administered up to 2 days before or after the weekly time point, and the monthly dose may be administered up to 1 week before or after the monthly time point.* *If a dose is missed, the next dose should be administered as soon as practically possible."* The working group agrees with this point, however notes that Buvidal® is not licensed for detoxification. The wording of this Q&A has been revised to include dose reduction to the lowest monthly dose.
	MB	Will you be brave enough to tell patients there is much we do not know about this drug and that they may be at risk of death - QT interaction	The working group notes that oral buprenorphine has been licensed for use as OST since 1995. This is a new formulation not a new drug.
	NHS24	This section was clear and well written.	Noted. Thank you.
	SMC	*Typo Pg 29 - "What happens if I'm still feel like I'm in withdrawal after my first injection?"* *Typo Pg 34 - If I have been on Buvidal for and want to come off, what's the process?*	Thank you. The text has been revised to remove these typos.
11.1	KMcG	Requires bigger clinical trials, studies and peer reporting	Noted. However this section refers to sources of further patient information.
	MB	As far as I can see the evidence is limited to little silos and thus may not reflect the real world Efficacy v Effectiveness	Noted. However this section refers to sources of further patient information.
Section 12			
	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	Limited	We agree that the volume of evidence available on long-acting injectable buprenorphine is currently

			limited.
	NHS24	The evidence base for long-acting injectable buprenorphine is strengthened by evidence for OST in general.	Noted. This section highlights that the evidence base for this position statement was drawn from *"guidelines (of any quality) which contained directly relevant information on the use of the product, or robust evidence-based guidelines containing information on management of opioid dependence which could be extrapolated to the population of interest"*
12.1	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	A little bit of evidence is a little bit of evidence however you dress it up	Noted. Thank you.
	NHS24	Evidence of rigour in the systematic literature review.	Noted. Thank you.
12.2	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you. Some of the circumstances which may prompt an update to this position statement are listed in section 13.4
	MB	Limited	We agree that the quality of evidence available on long-acting injectable buprenorphine is currently limited.
	NHS24	High quality of evidence.	Noted. Thank you.
Section 13			
	KMcG	Good information but will require regular updating as more information becomes available	This section describes the methodology used to develop this position statement and will be updated if the process used to support future iterations.
	MB	Good	Noted. Thank you.
	NHS24	Methodology appears to have credibility.	Noted. Thank you.
13.1	KMcG	Good information but will require regular updating as more information becomes available	The update process is described in this section (now section 13.4).
13.2	KMcG	Good information but will require regular updating as more information becomes available	This section describes the membership of the working group that developed this position statement and will be updated in line with future iterations of the document, as required (now section 13.5).

	MB	I am sure it is balanced but there needs to be thoughts about all care cancer	The working group acknowledges the importance of this issue but it was not included in the remit of this document. The progressive development of the evidence base and increasing experience with Buvidal® may support the development of consensus advice in future iterations of this position statement.
	NHS24	Representative of best knowledge available across the field.	Noted. Thank you.
13.3	KMcG	Good information but will require regular updating as more information becomes available	This section describes the individuals that provided peer review feedback for the draft position statement and will be updated in line with future iterations of the document, as required (now section 13.6).
	NHS24	Representative of best knowledge available across the field.	Noted. Thank you.
13.4	KMcG	Good information but will require regular updating as more information becomes available	Not appropriate.
Useful resources			
	KMcG	Good information but will require regular updating as more information becomes available	Noted. Thank you.
	NHS24	Helpful list of resources.	Noted. Thank you.
Annex 1			
	SMacF	I feel there is an important model of delivery not sufficiently reflected in Annex 1. We are currently utilising 'Community- Model 2', whereby our patients receive their Buvidal at our static sites (of which we have three) without a HO licence. We are using named-patient medication. We operate satellite clinics from a number of other sites (variety of buildings such as GP practices or council buildings for example). Due to the rural geography in Fife, it is very difficult for many of our patients to attend an appointment at a static site. We are moving towards a model where Buvidal will be administered in satellite clinics in order to provide equitable access in Fife, in line with MAT standards. As such, this model is similar to Model 4 but, crucially, is without a HO license. We will instead use named-patient Buvidal dispensed from our acute sites or from community pharmacy. I wanted to highlight this important model of delivery given the difficulty in	Agreed. A further model (Model 5) has been added to the Annex to combine the features of Model 4 in the context of operation without a Home Office license (now Annex 2).

		obtaining HO licences. I hope this information is useful. If I can answer any further questions, please do not hesitate to contact me.	
	NHS24	This section is appropriate.	Noted. Thank you.
Annex 2			
	NHS24	This section is appropriate.	Noted. Thank you.
Annex 3			
	NHS24	This section is appropriate.	Noted. Thank you.
References			
	KmcG	Requires broader referencing as information becomes available	The references in this position statement reflect the guidelines from which the draft consensus statements were adapted and developed, statutory guidance from SmPC and the Scottish Medicines Consortium and other sources of supporting material.
	NHS24	References are valid and credible, while there is no large base of evidence on buvidal the large amount of evidence on the benefits of OST treatment generally are transferable to this treatment option.	Noted. Thank you.