## Guidance For The Use Of Buprenorphine Products For The Treatment Of Opioid Dependence In NHS Grampian

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<thead>
<tr>
<th>Co-ordinators:</th>
<th>Reviewer:</th>
<th>Approver:</th>
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<tbody>
<tr>
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<tr>
<th>Identifier:</th>
<th>Review Date:</th>
<th>Date Approved:</th>
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<tbody>
<tr>
<td>NHSG/Guid/Bup/MGPG1040</td>
<td>August 2022</td>
<td>August 2019</td>
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</table>

Uncontrolled when printed
Version 4

### Executive Sign-Off

This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature: [Signature]
Title: Guidance For The Use Of Buprenorphine Products For The Treatment Of Opioid Dependence In NHS Grampian

Unique Identifier: NHSG/Guid/Bup/MGPG1040

Replaces: NHSG/guid/bup/MGPG733, Version 3

Across NHS Boards: Yes

Organisation Wide: 

Directorate: 

Clinical Service: 

Sub Department Area: 

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Lead Author/Co-ordinator: Specialist Pharmacists in Substance Misuse

Subject (as per document registration categories): Clinical Guidance

Key word(s): Guidance, buprenorphine, naloxone, suboxone, subutex, opioid, dependence, OST

Process Document: Policy, Protocol, Procedure or Guideline

Document application: NHS Grampian

Purpose/description: This guidance advises all staff, involved in prescribing for substance misuse patients, on the appropriate use of buprenorphine products in managing opioid dependence.

Responsibilities for implementation:

Organisational: Management Teams

Departmental: Substance misuse management team

Area: General practitioner practices

Policy statement: It is the responsibility of all staff to ensure that they are working to the most up to date and relevant policies, protocols procedures.

Review: This guidance will be reviewed in three years or sooner if current treatment recommendations change.
This document is also available in large print and other formats and languages, upon request. Please call NHS Grampian Corporate Communications on (01224) 551116 or (01224) 552245.

Responsibilities for review of this document: Substance Misuse Pharmacists

Responsibilities for ensuring registration of this document on the NHS Grampian Information/Document Silo: Pharmacy and Medicines Directorate

Physical location of the original of this document: Substance Misuse Pharmacist Office, Fulton Clinic

Job/group title of those who have control over this document: Specialist Pharmacists in Substance Misuse

Responsibilities for disseminating document as per distribution list: Substance Misuse Pharmacists

Revision History:

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Previous Revision Date</th>
<th>Summary of Changes (Descriptive summary of the changes made)</th>
<th>Changes Marked* (Identify page numbers and section heading)</th>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Title simplified.</td>
<td>Throughout document</td>
</tr>
<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Removed reference to specific products.</td>
<td>Section 1, Page 2</td>
</tr>
<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Simplified who guidance is aimed at to clinicians with sufficient knowledge in the use of buprenorphine products.</td>
<td>Section 1, Page 2 and throughout document</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Reworded pharmacology to add clarity. No change to clinical intent bar mention of supra-lingual administration.</td>
<td>Section 2, Page 2-3</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Simplified sections on precipitated withdrawal.</td>
<td>Section 3, Page 3, Section 6.4, Page 6</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Renamed “Key Recommendations” “Choice of Opioid Substitution Therapy” and amended section in line with updated UK guidance ¹.</td>
<td>Section 4, Page 3-4</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Updated section to reflect change in available products.</td>
<td>Section 5, Pages 4-5</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Added information on safe prescribing.</td>
<td>Section 6.2, Page 5</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Updated hepatic advice in line with SmPCs.</td>
<td>Section 6.3, Page 5</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
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<td>Section 6.6, Page 8</td>
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<td>July 2019</td>
<td>April 2015</td>
<td>Updated frequency of review in line with UK Guidance.</td>
<td>Section 7.1, Page 9</td>
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<tr>
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<td>July 2019</td>
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<td>Added information on misuse, abuse and diversion.</td>
<td>Section 9, Page 10</td>
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<td>July 2019</td>
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<td>Updated advise on supervision in line with UK guidance.</td>
<td>Section 10, Page 10</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Updated section on missed doses in order to give more practical advice taking into account lower overdose risk.</td>
<td>Section 11, Page 11</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Added information on hospital admissions.</td>
<td>Section 12, Page 13</td>
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<td>July 2019</td>
<td>April 2015</td>
<td>Added information on driving.</td>
<td>Section 13, Page 13</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Removed age from contraindications section as covered in Section 4.</td>
<td>Section 14, Page 14</td>
</tr>
<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Updated pregnancy and breastfeeding sections in line with UK guidance.</td>
<td>Section 15, Page 14</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Revised consultation list to reflect new appointments and relevance to different healthcare settings, e.g. secondary care.</td>
<td>Section 17, Page 16</td>
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<tr>
<td>July 2019</td>
<td>April 2015</td>
<td>Added Clinical Opioid withdrawal scale.</td>
<td>Appendix 1, Page 18</td>
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<tr>
<td>Revision Date</td>
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<td>Summary of Changes (Descriptive summary of the changes made)</td>
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<tr>
<td>Sept 2019</td>
<td>April 2015</td>
<td>Proceeding changes made following feedback from MGPG.</td>
<td>See entries below</td>
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<tr>
<td>Sept 2019</td>
<td>April 2015</td>
<td>Added links to naloxone “take home” guidance and PGD documents.</td>
<td>Section 2, Page 3</td>
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<tr>
<td>Sept 2019</td>
<td>April 2015</td>
<td>Expanded information on prescribing for people with opioid analgesic dependence.</td>
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</tr>
<tr>
<td>Sept 2019</td>
<td>April 2015</td>
<td>Restructured and expanded section 6 in a bid to clarify guidance for initiation of products. Added table on initiation for different types of opioid dependence.</td>
<td>Section 6, Page 5</td>
</tr>
<tr>
<td>Sept 2019</td>
<td>April 2015</td>
<td>Reviewed information in 6.6 “Frequency of Administration”. Amended to “Less than daily dosing” in a bid to clarify.</td>
<td>Section 6.6, Page 8</td>
</tr>
<tr>
<td>Sept 2019</td>
<td>April 2015</td>
<td>Restructured section 11 on missed doses into tabular format in a bid to simplify.</td>
<td>Section 11, Page 11</td>
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* Changes marked should detail the section(s) of the document that have been amended, i.e. page number and section heading.
## Guidance For The Use Of Buprenorphine Products For The Treatment Of Opioid Dependence In Grampian

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Guidance For The Use of Buprenorphine Products For The Treatment Of Opioid Dependence In NHS Grampian

1. Introduction

This document is a guide to the prescribing and use of buprenorphine products in the management of opioid dependency. It is for use by all health care professionals in Grampian involved in managing this treatment. Buprenorphine should be initiated by prescribers with sufficient knowledge in its use or in collaboration with a specialist clinician in substance misuse.

2. Pharmacology

Buprenorphine:

- only partially activates opioid receptors producing a milder, less euphoric and less sedating effect than full opioid agonists such as heroin, morphine and methadone
- has a higher affinity for opioid receptors than heroin, methadone and many other opioid drugs. This means that:
  - buprenorphine can push other opioid drugs that are present in the body off the opioid receptors and take their place
  - at higher doses more opioid receptors will be occupied which can block or reduce the effect of other opioid drugs administered at the same time
  - patients may be less likely to use additional opioids on top of their buprenorphine prescription as they will gain little or no additional effect
  - if opioid pain relief is required the analgesic effect achieved can be significantly less than expected.
- has a ceiling effect. Continued dose increases will not result in a proportionate increase in effect
- possesses opioid activity which is usually enough to reduce cravings and prevent or alleviate opioid withdrawal in opioid dependent people despite only being a partial agonist of opioid receptors
Buprenorphine (continued):

- has a lower risk of overdose than full agonists if taken as prescribed. Overdose can still occur particularly with poly drug use. The impact of prescribing other CNS depressant drugs alongside buprenorphine should be considered. Adverse effects such as sedation and respiratory depression should be monitored for and information on opioid overdose and a supply of naloxone given. Refer to NHS Grampian “Take Home Naloxone” guidance for drug treatment services and patient group direction for other clinical services can be accessed by clicking on the links.
- has very little effect if swallowed thus tablets/wafers are either administered UNDER or ON the tongue depending on the product prescribed and administration guidance in the Summary of Product Characteristics (SmPC).

3. Precipitated Withdrawal

Because of its higher affinity buprenorphine has the potential to precipitate symptoms of opioid withdrawal when starting treatment.

This risk is higher when administered to patients that still have full opioid agonists in their systems. Buprenorphine pushes these full agonists off of opioid receptors leading to a drop in opioid effect which can precipitate symptoms of withdrawal in opioid-dependent patients.

To avoid precipitating withdrawal, the first dose of buprenorphine should be taken when the patient shows objective signs of opioid withdrawal. Use of a clinical opioid withdrawal scale can help assess the extent of withdrawal (see Appendix 1 or access via link below)

4. Choice Of Opioid Substitution Therapy

Drug Misuse and Dependence: UK Guidance on Clinical Management advises that methadone and buprenorphine are both effective medicines for maintenance treatment for heroin dependence, particularly when taken within the optimal dose range. There is insufficient evidence to support recommendation of one drug as more effective or safer than the other. The prescriber should provide the patient with a balanced view of the action of each medication to allow them to make an informed decision on their treatment choice.

A number of clinical factors can be taken into account to help the patient and the prescriber decide which medication is most appropriate. These include:

- a patient’s pre-existing preference for a particular medication
- previous substantial benefit from maintenance on a particular medication
- patient age and duration and extent of drug use. Buprenorphine has lesser opioid effects and may also reduce the risk of overdose. In patients with lower levels of drug dependence and in older patients more sensitive to sedative effects of opioids, buprenorphine may be safer
• specific safety concerns, e.g. methadone too sedating, diversion, poly drug and alcohol use, previous overdose, previous early disengagement from treatment, etc
• the potential value of rapid induction onto effective maintenance which is more achievable with buprenorphine
• likely need for strong opioids other than buprenorphine for acute pain management may make methadone more appropriate
• relevant drug interactions or co-morbidities should be taken into account. Examples include patients with respiratory disease, history of cardiac abnormalities, advanced heart disease, ischaemic heart disease, cardiac conduction problems, Long QT syndrome or those prescribed/taking drugs which prolong QTc, etc. Buprenorphine produces less respiratory depression and has less impact on QTc than methadone
• current treatment is no longer working, e.g. patient struggling to reduce further at lower doses of methadone. Some patients may find that at lower doses of methadone the dose might not provide cover for the full 24 hours. Buprenorphine has a longer half-life which might make dose reductions easier to tolerate
• in patients who have developed opioid analgesic dependence (prescribed or over the counter), buprenorphine may be an option however patients need to be assessed on a case by case basis to take into account ongoing requirements for pain management. The Faculty of Pain Medicine has developed the “Opioids Aware” website which provides a useful resource for prescribers.

5. Available Buprenorphine Products

Treatment is more likely to be successful when combined with psychological and/or social interventions tailored to the individual. Patients should be advised of this and encouraged to engage with the key worker providing these.

The choice of product should be made on an individual patient basis following assessment. For patients who require supervision, Espranor® oral lyophilisate (wafer) is the recommended product due to the speed at which it dissolves. This improves patient experience in the pharmacy and reduces opportunity for diversion.

5.1. Espranor® Oral Lyophilisate (Wafer) (Buprenorphine Hydrochloride)

Espranor® is a freeze dried wafer formulation of buprenorphine available as 2mg and 8mg lyophilisate wafers.

Wafers should be dissolved on top of the tongue. This differs from buprenorphine sublingual tablets which are administered under the tongue. It dissolves quickly which can be in as little as 15 seconds although this will be affected by individual circumstances such as how dry or moist the mouth is and how many wafers are being administered at the same time.

Espranor® is not interchangeable with other sublingual products due to differences in bioavailability (amount of drug which reaches the blood stream). Espranor® appears to have higher bioavailability than other sublingual buprenorphine products (see Section 6).
Advice on administration of Espranor oral lyophilisate can be found in Appendix 2

5.2. Buprenorphine and Naloxone Sublingual Tablets

- Generic buprenorphine and naloxone is available as 2mg/0.5mg and 8mg/2mg sublingual tablets.
- Suboxone® is available as 2mg/0.5mg, 8mg/2mg and 16mg/4mg sublingual tablets.

These formulations contain the opioid antagonist naloxone which is included purely as a deterrent for injecting where this is a concern. If tablets are injected naloxone will become active and is likely to produce symptoms of opioid withdrawal in opioid dependent patients. If taken as prescribed under the tongue the naloxone will have no effect as very little is absorbed from the mouth.

5.3. Buprenorphine Sublingual Tablets

- Generic buprenorphine is available as 0.4mg, 2mg and 8mg sublingual tablets.
- Temgesic® (buprenorphine) 200micrograms sublingual tablets do not have a licensed indication for treatment of opioid dependence therefore any prescribing for this indication is off-label.
- Generic buprenorphine is available in lower doses which may be helpful at the end of treatment or during detoxification.

For most formulations of sublingual tablets the active ingredient will generally be absorbed after 3-5 minutes however pulp may be present for 10-15 minutes after administration but will contain little buprenorphine. Again this can vary depending on how moist or dry the mouth is and the number of tablets administered at a time. To help this consider prescribing the lowest number of tablets to achieve the dose. Community pharmacies should offer water for the patient to moisten the mouth before administration of buprenorphine products.

6. Initiation Of Therapy

6.1. Opioid dependence must be diagnosed prior to starting treatment. A comprehensive assessment should be undertaken and include drug screening which is positive for opioid drugs. Drug screens should be interpreted alongside clinical information and should not be treated as definitive themselves.

6.2. Patients must be assessed on an individual basis by a health care professional with sufficient knowledge in the use of buprenorphine products to determine suitability of treatment. The patient’s medical history and other prescribed medicines should be considered for contraindications, cautions and interactions when determining if treatment is suitable (see also Sections 15 and 16)

6.3. Baseline liver function tests and documentation of viral hepatitis status is recommended prior to initiating treatment with buprenorphine.
Patients who have active viral hepatitis infection, are prescribed other medicines which interact with buprenorphine or have existing liver impairment are at risk of accelerated liver injury.

Regular monitoring of liver function is recommended in these patients.

Lower initial doses and careful dose titration in patients with mild to moderate hepatic impairment are recommended. Buprenorphine products are contraindicated in patients with severe hepatic impairment.

Both methadone and buprenorphine can accumulate in patients with hepatic impairment. Clinicians should weigh up the risk of continued illicit drug use versus the risks associated with the prescribed drug and monitor accordingly. With its ceiling effect, buprenorphine may present less of a risk of over sedation and overdose.

6.4. Precipitated withdrawal may occur when buprenorphine is first administered (see Section 3). If it happens, it typically begins within 1 to 3 hours after the first buprenorphine dose and peaks within 3 to 6 hours before improving. This should be discussed with all patients prior to commencing treatment with buprenorphine products and they should be reassured that, should they experience precipitated withdrawal, symptoms will improve.

6.5. Initial Dosing Schedules

To minimise the risk of precipitated withdrawal, and ensure successful induction, the first dose of buprenorphine should not be given until the patient has been assessed and displays objective signs of mild opioid withdrawal (see Table 1.) Use of a clinical opioid withdrawal scale provides objective and subjective measures for assessing symptoms of withdrawal (Appendix 1).

During the initiation of treatment, daily supervision of dosing is recommended (see Section 10) to ensure proper placement of the product in the mouth and to observe patient response to treatment as a guide to effective dose titration.

The clinician should contact the community pharmacist to discuss and agree initial dosage instructions and alert them that the patient needs to be displaying mild symptoms of opioid withdrawal before they give the first self-administered dose. This also allows the pharmacy time to order the product/make sure it is in stock. The pharmacy team can provide support and reassurance to the patient while they stabilise on the treatment.

If the clinician is not able to assess the patient in person prior to giving the first dose on day 1:

- There should be a clear plan agreed between the clinician and community pharmacist as to how the assessment of opioid withdrawal symptoms will take place. The clinical opioid withdrawal scale can be used to measure this.
- This could be a phone consultation between clinician and patient to see how they are and the pharmacist would assess the patient in person for signs of withdrawal providing they are competent to undertake this.
• Clinicians should record in the patient’s clinical notes whether it was themselves or the pharmacy which undertook the assessment of opioid withdrawal.
• If the pharmacy undertook this assessment they should record this in the patient’s pharmacy records.

To reduce the severity and duration of precipitated withdrawal (should it occur) it is recommended that the dose for day 1 is split regardless of the formulation. Following treatment induction on day 1, the patient should be stabilised to a maintenance dose during the next few days by progressively adjusting the dose according to the clinical effect of the individual patient.

Patients should be advised that they may experience mild symptoms of withdrawal during the first 24 hours of treatment but this should resolve thereafter. The clinical opioid withdrawal scale should be used to support assessment during induction. Where precipitated withdrawal occurs, delay the next dose until symptoms start to ease.

Table 1. Induction from full opioid agonists

<table>
<thead>
<tr>
<th>Type of full agonist</th>
<th>Current dose of full agonist</th>
<th>Point of induction</th>
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<tbody>
<tr>
<td><strong>Heroin</strong></td>
<td>Any dose, any route of administration</td>
<td>When objective and clear signs of withdrawal appear (at least 6 hours from the last use of heroin).</td>
</tr>
<tr>
<td><strong>Methadone</strong></td>
<td>Reduce to 30mg daily or lower prior to transfer. Higher doses may lead to precipitated withdrawal or treatment failure where the opioid effect experienced is not enough to cover withdrawal symptoms from cessation of full agonist opioids.</td>
<td>When objective and clear signs of withdrawal appear (at least 24 hours from the last use of methadone).</td>
</tr>
<tr>
<td><strong>Opioid Analgesics</strong></td>
<td>Any dose, any route of administration</td>
<td>When objective and clear signs of withdrawal appear (time will depend on choice of opioid used).</td>
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Table 2. Dosing during induction

<table>
<thead>
<tr>
<th>Product</th>
<th>Buprenorphine and buprenorphine plus naloxone sublingual tablets</th>
<th>Espranor® Oral Lyophilisate</th>
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<tbody>
<tr>
<td><strong>Day 1</strong></td>
<td>4mg of buprenorphine followed later in the day by a further 4mg based on individual need. Maximum dose on Day 1 = 8mg in divided doses</td>
<td>2mg of buprenorphine followed by a further 2mg to 4mg later in the day based on individual need. Maximum dose on Day 1 = 6mg in divided doses.</td>
</tr>
<tr>
<td><strong>Day 2</strong></td>
<td>The dose can be titrated up to a maximum of 16mg daily on day 2. From day 2 doses should be prescribed as a single daily dose. Titrate dose in steps of 2-8mg buprenorphine guided by assessment of the clinical and psychological status of the patient until the effective maintenance dose is achieved.</td>
<td>The dose can be titrated up to a maximum of 12mg daily on day 2. From day 2 doses should be prescribed as a single daily dose. Titrate dose in steps of 2-6mg buprenorphine guided by assessment of the clinical and psychological status of the patient until the effective maintenance dose is achieved.</td>
</tr>
<tr>
<td><strong>Maximum Daily dose</strong></td>
<td>Doses above 16mg are rarely indicated due to ceiling effect. Assess that administration/sublingual placement of tablet is correct in the first instance as this may affect absorption. Maximum daily doses: - Buprenorphine plus naloxone = 24mg/6mg. - Buprenorphine sublingual tablets = 32mg</td>
<td>Titrate to a maximum dose of 18mg daily according to patient need.</td>
</tr>
</tbody>
</table>

### 6.6. Less than daily dosing

Less than daily dosing is not commonly used in practice but may be of benefit to some patients, particularly in the later stages of dose reductions.

After a satisfactory stabilisation has been achieved the frequency of dosing may be decreased to dosing every other day at twice the individually titrated daily dose. For example, a patient stabilised to receive a daily dose of 8mg buprenorphine may be given 16mg buprenorphine on alternate days, with no dose on the intervening days. This may be further decreased to 3 times a week (for example on Monday, Wednesday and Friday). The dose on Monday and Wednesday should be twice the individually titrated daily dose, and the dose on Friday should be three times the individually titrated daily dose, with no dose on the intervening days. The dose given on any one day should not exceed the product’s maximum dose. Patients requiring a titrated daily dose >8mg buprenorphine/day may not find this regimen adequate.
6.7. Transferring patients from a sublingual buprenorphine product to Espranor®

The bioavailability of Espranor® oral lyophilisate (wafer) is around 25-30% higher than sublingual tablets which has potential to result in symptoms such as over-sedation if transferred from a sub-lingual product at the same daily dose. The dose of Espranor® oral lyophilisate (wafer) should therefore be initiated according to the following table and titrated according to patient response which may vary.

Table 3. Suggested Espranor® conversions

<table>
<thead>
<tr>
<th>Current Daily Dose Buprenorphine Sublingual tablets</th>
<th>Suggested Buprenorphine Dose Reduction</th>
<th>New Daily Dose Espranor® oral lyophilisate (wafer)</th>
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<tbody>
<tr>
<td>24 - 32mg</td>
<td>6 - 14mg</td>
<td>18mg - consider if appropriate</td>
</tr>
<tr>
<td>20 - 24mg</td>
<td>2 - 6mg</td>
<td>18mg</td>
</tr>
<tr>
<td>10 - 18mg</td>
<td>2mg</td>
<td>8 - 16mg</td>
</tr>
<tr>
<td>2 - 8mg</td>
<td>0mg</td>
<td>2 - 8mg</td>
</tr>
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</table>

7. Maintenance

7.1. Patients prescribed opioid substitution therapy should be seen more frequently (at least fortnightly) initially and when stable, less frequently, such as once a month. Depending on local service arrangements and other support available, prescribers may feel their patient can be reviewed as little as every three months.

7.2. Co-existing physical, emotional social and legal problems as well as drug and alcohol misuse should be addressed. Third sector agencies may be able to provide this additional support and patients should be signposted or referred accordingly.

7.3. Drug testing can be used to monitor patient concordance with prescribed medication and detect ongoing illicit drug use. Urine or oral fluid tests for drugs of misuse should be undertaken according to each individual patient’s progress.

7.4. Presence of an illicit drug in a sample should be used to guide treatment. Drug testing when a patient in treatment has already admitted to using, is generally not worthwhile except when the testing is being used to assess non-compliance with prescribed medication.

NB: In Grampian, current laboratory urine screening does not identify buprenorphine (July 2019). Where available, point of care testing may identify buprenorphine.

8. Dosage Reduction

8.1. Patient response and ability to cope/continue with dose reduction is key. If the patient begins to struggle with the rate of reduction, support the patient to stabilise on a dose where they feel comfortable and review treatment plan.
8.2. Buprenorphine doses can be reduced initially by 2mg every two weeks or so, with final reductions being around 400micrograms. Reducing frequency of administration to alternate days is another option that might work for some patients.

8.3. Patients can experience withdrawal symptoms at the end of treatment irrespective of the speed of reduction and should be advised/supported accordingly.

8.4. For detoxification regimens, more rapid reductions are possible with buprenorphine however the patient’s motivation, ability to cope and support structure should be carefully assessed. The risk of relapse and overdose due to loss of tolerance are increased. **Rapid reductions are only recommended for use by specialist clinicians in substance misuse in the in-patient setting and are not recommended in community settings.**

8.5. A discussion with the patient around the feasibility of naltrexone post reduction may be introduced at this time. See NHS Grampian guidance.

9. Misuse, Abuse And Diversion

As with other opioid drugs buprenorphine can be misused or abused. Risks include overdose, spread of blood borne viruses and infections, respiratory depression and hepatic injury. Risk may be increased by either the patient or other people where diversion, bullying or theft occurs.

Prescribing sub-optimal doses of buprenorphine may also result in medicine misuse by the patient which in turn can lead to overdose or treatment dropout. A patient who is under-dosed with a buprenorphine product may self-medicate with opioids, alcohol or other sedative-hypnotics such as benzodiazepines.

To minimise the risk prescribers should take appropriate precautions when prescribing and dispensing buprenorphine, such as use of supervised administration, avoiding prescribing large quantities of medication on a “take home” basis and ensuring that clinical monitoring is appropriate to the patient's needs.

Intravenous or intranasal misuse of combined buprenorphine/naloxone products are expected to be less likely than buprenorphine alone as naloxone can precipitate withdrawal in individuals dependent on heroin, methadone, or other opioid agonists.

10. Supervision of Consumption

10.1. As a minimum, it is recommended that doses of buprenorphine containing products should be supervised whilst titrating and stabilising the dose. This provides the patient with additional support and monitoring from the community pharmacy team, ensures that the patient is administering the product correctly and helps the initial stages of treatment run smoothly. Patients who are being switched from a “take home” methadone prescription may benefit from a short period of supervision for the same reasons.
NHSG Community Pharmacy guidance can be accessed via the following link. https://www.communitypharmacy.scot.nhs.uk/nhs-grampian-pharmacy-services/addiction-support/

10.2. Changes to supervised consumption should be considered on an individual patient basis following assessment of risk and reviewed regularly. Factors which may influence the need for supervision include but are not limited to:

- concordance with treatment and other elements of the care plan
- likelihood of diversion
- changes in substance use
- ability to manage medicines, e.g. with children in the household
- patients who have significant psychiatric diagnoses or are at risk of self-harm
- periods of instability
- work or educational commitments

As the health care professional in most regular contact with patients, the community pharmacist should be contacted to discuss patient presentation and potential risks in making changes to the level of supervision prior to making the change.

10.3. It is recommended that each instalment consists of no more than one week supply of buprenorphine to minimise risk to patients in possession of large quantities of controlled drugs. This might include risk of coercion/bullying to divert medication. Twice or three times a week dispensing should be considered as a first step.

11. Missed Doses

The risk of overdose when restarting buprenorphine following missed doses is lower than with methadone. If the patient has been using full opioid agonists such as heroin or methadone in the period of missed buprenorphine doses, there may be a risk of precipitated withdrawal if buprenorphine is re-introduced. The patient’s use of other opioids in the days since last buprenorphine dose should therefore be considered by the pharmacist and prescriber alike when deciding which action to take.

The community pharmacist should gather as much information as possible from the patient, e.g. experiencing symptoms of opioid withdrawal/intoxication, use of any other opioids, alternative drugs and/ or alcohol. This will help determine action. Where the patient does not return to the pharmacy and there are concerns for patient safety, the pharmacist should contact the prescriber to alert them. The pharmacist should record any interventions on the patient clinical care record.
Table 4. Advice for missed doses

<table>
<thead>
<tr>
<th>Number of days missed</th>
<th>Advice for community pharmacist</th>
<th>Advice for prescriber</th>
</tr>
</thead>
</table>
| **Less than 3 days buprenorphine missed** | If there are no additional concerns/patient rarely misses doses:  
- continue to dispense the prescription as stated  
- ask patient about reasons for non attendance | The pharmacist will not contact the prescriber if less than 3 days have been missed unless there are additional concerns.  
Additional concerns such as:  
- non-attendance is out of character  
- regular missing doses  
- patient attending intoxicated  
Dose may be dispensed however prescriber should also be contacted to highlight concerns | Review patient to ensure that buprenorphine:  
- remains the most appropriate treatment.  
- the dose remains appropriate  
Consider patient’s.  
- reason(s) for missing doses.  
- treatment goals.  
E.g. Continued opioid craving / use on top of the prescription check dose is sufficient/ correct administration? |

| **3 or 4 days buprenorphine missed** | - Assess the patient’s use of opioids in the days since last buprenorphine dose.  
- Where there has been no opioid use or where the patient is experiencing symptoms of opioid withdrawal, the prescription may be continued at the same dose. | - Record details of pharmacist contact in patient’s clinical records.  
- Discuss missed doses with patient at next consultation. |

| Pharmacist assesses that it is appropriate to continue at the current dose:  
- continue to dispense the prescription as stated  
- contact the prescriber to inform them of missed doses and action taken  
- record details in patient clinical care record | - Consider available information.  
- Determine whether it is necessary to review the patient in person.  
- Consider need for re-titration versus continuation of dose.  
- Advise pharmacist of action.  
- Generate new prescription if re-titration is required. |

| 5 or more days buprenorphine missed | - Contact the prescriber to advise that 5 days have been missed to agree how to proceed. | - Consider the dose of buprenorphine currently prescribed and reason for missing doses.  
-For daily dose of 8mg daily or lower it may be possible to continue using existing prescription so long as this remains clinically appropriate.  
- For daily doses greater than 8mg re-titratre as described in Section 6 (initiation). |
12. Emergency/Planned Admission to Hospital

The high affinity of buprenorphine for opioid receptors may impact on the management of acute pain during hospital admissions. For planned admissions this can be minimised by:

- ensuring that the patient is aware of this effect when starting buprenorphine
- contacting the hospital ward ahead of admission to alert them and where possible agree a plan.

There are a number of strategies which can be used to manage pain which include but are not limited to:

- Prescribing non-opioid analgesia and/or use of anaesthesia
- Using higher doses of full opioid agonists
- Splitting the dose of buprenorphine across the day.

Involving the specialist pain management team and anaesthetist can help optimise pain control where available.

Acute Pain Service: Bleep 2864 or ASCOM 52590
Woodend Acute Pain Service: Bleep 4379

On admission ward staff should contact the community pharmacist and community prescriber to make them aware of the admission and ask them to put a hold on dispensing instalment prescriptions until otherwise informed.

The community prescriber should be contacted at an early stage for discharge planning. If the buprenorphine product has been temporarily reduced or stopped in hospital where clinically appropriate this should be re-titrated before discharge. Where ongoing treatment with an opioid analgesic is required following discharge a plan should be agreed including information on when and how to reduce and stop the opioid analgesic and re-titrato/reintroduce the agreed opioid substitute.

13. Driving

It is the responsibility of the patient to inform the DVLA of their current medical status. Doctors and other healthcare professionals should:

- advise the individual on the impact of their medical condition for safe driving ability
- advise the individual on their legal requirement to notify the DVLA of any relevant condition
- treat, manage and monitor the individual’s condition with ongoing consideration of their fitness to drive
- notify the DVLA when fitness to drive requires notification but an individual cannot or will not notify the DVLA themselves.
For buprenorphine (oral) [DVLA guidance](https://www.medicines.org.uk/emc; www.medicinescomplete.com/mc/bnf/current/) for health care professionals states that application for a Group 1 license (car and motorcycle) may be considered when all of the following conditions can be met:

- stable on the programme for a minimum of 1 year
- the treatment programme is supervised by a consultant or specialist GP
- the treatment is for management of opiate dependence
- oral treatment only (not parenteral) but naltrexone implants may be considered
- there has been compliance with the programme (adherence to prescription and appointments, and toxicology testing with sustained stability)
- no non-prescribed psychoactive drug use during the programme or extra use of prescribed drugs such as methadone, buprenorphine, benzodiazepines
- there is no toxicological evidence of drug misuse
- there is no adverse effect from treatment likely to affect safe driving
- there is no alcohol misuse or dependence.

14. Contraindications To Use Of Buprenorphine Containing Products

A full list of contraindications, cautions and adverse effects can be found in the Summary of product characteristics or the British National Formulary.


- Severe respiratory insufficiency
- Severe hepatic insufficiency
- Acute alcoholism or delirium tremens
- Hypersensitivity to buprenorphine, naloxone or to any of the excipients.
- Patients suffering chronic pain for which additional opioid analgesia is frequently required.

15. Precautions for Buprenorphine Containing Products

15.1. Pregnancy

Specialist support should be sought when treating this patient group. UK clinical guidance states that: "Research evidence demonstrates no difference in adverse effects between methadone and buprenorphine with both having no adverse effects on the pregnancy or neonatal outcomes, with incidence of Neonatal Abstinence Syndrome (NAS) similar to methadone exposure (Blandthorn, Forster & Love 2011, Jones et al 2010). However, there is some evidence that buprenorphine use results in NAS of lower severity.

Therefore, in a pregnant woman who is informed of the risks it is reasonable to allow her to remain on methadone or buprenorphine. Transfer to buprenorphine during pregnancy is not advised because of the risk of precipitated withdrawal and the risk of inducing withdrawal in the foetus. If detoxification is unsuccessful and the patient’s drug use becomes uncontrolled at any stage of pregnancy, reduction should be stopped or the opioid dose increased until stability is regained."
The impact of buprenorphine on pain management plans during labour should be considered (See Section 12).

15.2. Breastfeeding

For mothers stabilised on a buprenorphine product who wish to breastfeed, an individual risk-benefit analysis to inform decision making should be undertaken. Due to the lack of evidence of the effects of these drugs on breastfed infants, manufacturers’ advice is to avoid, although expert consensus opinion states that the effects of these medications on the breastfed infants is likely to be minimal and that breastfeeding is not contraindicated.

UK Guidance states “Breastfeeding should be encouraged, even if the mother continues to use drugs, except where she uses cocaine or crack cocaine, or a very high dose of benzodiazepines. Specialist advice should be sought if she is HIV positive. Hepatitis C is not a contraindication to breast feeding (HIS 2013). Methadone or buprenorphine treatment is not a contraindication to breastfeeding and breastfeeding may reduce the intensity and length of neonatal abstinence syndrome and has been shown to improve outcomes (Mayet et al 2008)”

15.3. Liver function (see Section 6.3).

15.4. Overdose

Buprenorphine is reported to be safer in overdose than full agonists, such as methadone\(^3\), causing less respiratory depression. This being said, drug related deaths involving buprenorphine have been reported particularly when taken in combination with other sedative drugs such as alcohol or benzodiazepines.

In the event of overdose, medical advice should be sought. Standard procedures for reversing opioid-induced respiratory depression should be followed. It may be necessary to use more than the normal amount of naloxone.

15.5. Concomitant use of CNS depressants

As with methadone, concomitant use of buprenorphine with benzodiazepines, alcohol and other CNS depressant drugs may result in fatal overdose. Caution should be employed when initiating buprenorphine containing products in poly drug users. Consideration should be given to the potential illicit use of CNS depressants before initiating treatment.

16. Adverse Effects

A full list of side effects and cautions can be found in the Summary of product characteristics or the British National Formulary.
https://www.medicines.org.uk/emc
https://www.medicinescomplete.com/mc/bnf/current/
The most common side effects of buprenorphine products include: constipation, headaches, sleeplessness, sickness and sweating. It should be noted that patients often report a “clear head” with buprenorphine containing products as opposed to the “clouding” effect often experienced with methadone or heroin.

17. Consultation

The document was sent to the following individuals/groups for consultation:

Seonaid Anderson  Consultant Psychiatrist, Integrated Alcohol Service
Steve Beason  Psychiatrist, NHSG Substance Misuse Service
Carol Buchanan  GP with Special Interest in Substance Misuse
Karen Cranfield  Consultant Anaesthetist, Acute Pain Service, ARI
Lynne Crighton  Specialist Pharmacist, Gastroenterology
Bruce Davidson  Clinical Lead NHSG Substance Misuse Service
Susanne Duncan  Pharmacist Independent Prescriber, Buchanhaven Pharmacy
Angela MacManus  Principal Pharmacist, Royal Cornhill Hospital
Andrew McKechnie  Pharmacist, Aberdeenshire Drug and Alcohol Service
Steve Hay  Consultant Psychiatrist NHSG Substance Misuse Service
Richard Legg  GP with Special Interest in Substance Misuse
CPN Clinical Leads  NHSG Substance Misuse Service
David Taylor  Nurse Manager, Aberdeenshire Drug and Alcohol Service

18. References


Appendix 1 – Clinical Opiate Withdrawal Scale

Clinical Opiate Withdrawal Scale

Introduction

The Clinical Opiate Withdrawal Scale (COWS) is an 11-item scale designed to be administered by a clinician. This tool can be used in both inpatient and outpatient settings to reproducibly rate common signs and symptoms of opiate withdrawal and monitor these symptoms over time. The summed score for the complete scale can be used to help clinicians determine the stage or severity of opiate withdrawal and assess the level of physical dependence on opioids. Practitioners sometimes express concern about the objectivity of the items in the COWS; however, the symptoms of opioid withdrawal have been likened to a severe influenza infection (e.g., nausea, vomiting, sweating, joint aches, agitation, tremor), and patients should not exceed the lowest score in most categories without exhibiting some observable sign or symptom of withdrawal.

http://www.drugabuse.gov/nidamed-medical-health-professionals
# APPENDIX 1

## Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient’s signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

<table>
<thead>
<tr>
<th>Reason for this assessment:</th>
<th>Date and Time <em><strong>/</strong></em>/____</th>
</tr>
</thead>
</table>

### Resting Pulse Rate
- **beats/minute**
  - Measured after patient is sitting or lying for one minute
  - 0 pulse rate 80 or below
  - 1 pulse rate 81-100
  - 2 pulse rate 101-120
  - 4 pulse rate greater than 120

### GI Upset
- over last 1/2 hour
  - 0 no GI symptoms
  - 1 stomach cramps
  - 2 nausea or loose stool
  - 3 vomiting or diarrhea
  - 5 multiple episodes of diarrhea or vomiting

### Sweating
- over past 1/2 hour not accounted for by room temperature or patient activity.
  - 0 no report of chills or flushing
  - 1 subjective report of chills or flushing
  - 2 flushed or observable moistness on face
  - 3 beads of sweat on brow or face
  - 4 sweat streaming off face

### Tremor
- Observation of outstretched hands
  - 0 no tremor
  - 1 tremor can be felt, but not observed
  - 2 slight tremor observable
  - 4 gross tremor or muscle twitching

### Restlessness
- Observation during assessment
  - 0 able to sit still
  - 1 reports difficulty sitting still, but is able to do so
  - 2 frequent shifting or extraneous movements of legs/arms
  - 3 unable to sit still for more than a few seconds

### Yawning
- Observation during assessment
  - 0 no yawning
  - 1 yawning once or twice during assessment
  - 2 yawning three or more times during assessment
  - 4 yawning several times/minute

### Pupil size
- 0 pupils pinned or normal size for room light
- 1 pupils possibly larger than normal for room light
- 2 pupils moderately dilated
- 3 pupils so dilated that only the rim of the iris is visible

### Anxiety or Irritability
- 0 none
- 1 patient reports increasing irritability or anxiousness
- 2 patient obviously irritable or anxious
- 4 patient so irritable or anxious that participation in the assessment is difficult

### Bone or Joint aches
- If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored
  - 0 not present
  - 1 mild diffuse discomfort
  - 2 patient reports severe diffuse aching of joints/muscles
  - 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort

### Gooseflesh skin
- 0 skin is smooth
- 3 piloerection of skin can be felt or hairs standing up on arms
- 5 prominent piloerection

### Runny nose or tearing
- Not accounted for by cold symptoms or allergies
  - 0 not present
  - 1 nasal stuffiness or unusually moist eyes
  - 2 nose running or tearing
  - 4 nose constantly running or tears streaming down cheeks

## Source
Appendix 2 – How To Administer Espranor

How to Administer Espranor

Espranor is sensitive to moisture.

Make sure your hands are dry before handling the wafer.

1. Tear a square off the blister pack along the perforated lines.

2. The foil is easily peelable.

Do not force the wafer through the foil as it is fragile and can easily break. Instead, fold back the foil and then peel it off.

3. Remove the wafer carefully from the foil and take out from the packaging immediately.

4. Place the wafer on the tongue and close your mouth. Allow it to remain there for a few seconds until it has dissolved.

Try to avoid swallowing during the first 2 minutes.

Do not eat or drink for at least 5 minutes.