

Prescribing Guideline for medicines used in the treatment of opioid dependence.

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1. PURPOSE AND SCOPE

The purpose of this document is to provide guidance on the management of Opiate Substitution Therapy (OST) in patients in NHS Dumfries and Galloway in line with current best practice.

Scope: Management of all patients with opiate dependency, primarily via (but not exclusive to) NHS Dumfries and Galloway Specialist Drug and Alcohol Services (SDAS).

2. DOCUMENT AIMS

To provide guidance on the prescribing of opiate substitution therapy in NHS Dumfries and Galloway in line with current best practice.

All service users are supported to make an informed choice on what medication to use for Medication Assisted Treatment (MAT) and the appropriate dose.

Service users will decide which medication they would like to be prescribed and the most suitable dose options after a discussion with their healthcare practitioner about the effects and side effects.

Service users will be able to change their decision as circumstances change.

There should be a discussion about dispensing arrangements and this should be reviewed regularly.

Your responsibility as a prescriber:

This guidance is not intended to replace clinical judgement; it does not take away a prescriber's right to determine what is clinically most appropriate for their patient, nor their responsibility for that decision.

Information changes over time. Prescribers are advised to seek the most current information on medicines such as the latest Summary of Product Characteristics, or British National Formulary.

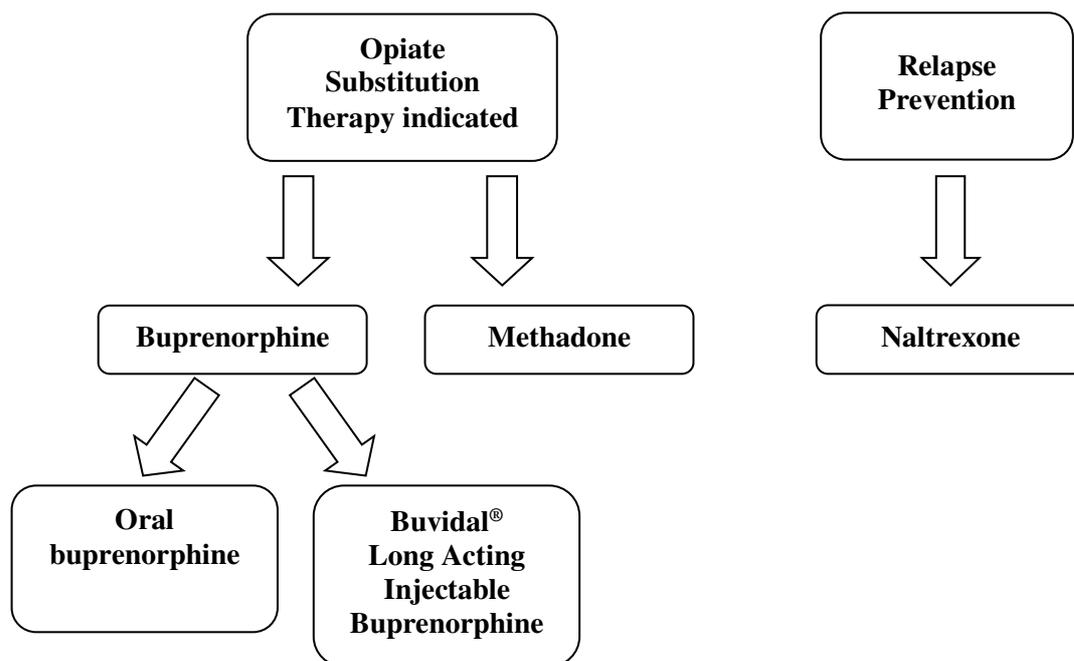
3 Opiate Substitution Therapy (OST) Guidance.

3.1. Introduction:

OST with methadone and buprenorphine, are commonly used for the treatment of opiate dependence. They work by binding to opioid receptors in the brain. They help to prevent opiate withdrawals and reduce illicit opiate use which results in an improvement in quality of life and increase in survival rates.¹ The goal of treatment with OST is to reduce harms associated with dependence to illicit opiates and thereby improve health. OST should be considered if the patient is taking opiates on a regular basis and there is convincing evidence of dependence.^(1 & 2)

Naltrexone is an '**opioid antagonist**' and works by blocking the opioid receptors which stops the effects of any opiates or opioids. This is a treatment option for relapse prevention, once a patient has stopped taking opiates.³

A patient information leaflet on medicines used in the treatment of opioid dependence will be given to the patient at initial assessment and they will be involved in making a joint decision around their treatment along with the health care professional (see appendix 1). Treatment with OST is not contingent on uptake of other interventions or abstinence from other drugs. This is in line with the Medication Assisted Treatment (MAT) Standards⁴.



Espranor® has been identified as the recommended buprenorphine formulation of choice in NHS D&G due to a comparatively lower supervision time and reduced ability to divert medication, thus potential for both increased safety and cost effectiveness.

*Suboxone® (Buprenorphine and Naloxone), Subutex® and generic buprenorphine sublingual tablets are equally effective to Espranor® as OST.^(1&5)

3.2 Buprenorphine

Buprenorphine is a mixed opiate agonist / antagonist; it partially activates opioid receptors, producing relatively lower opioid receptor related side effects, such as sedation, compared to full agonists like heroin and methadone. The agonistic action of buprenorphine reduces cravings and prevents withdrawal symptoms.¹

Although only partially activating, it has a higher affinity for the receptor than other opiates and so can push other opiates off the receptor; blocking their effect and making it less likely that service users will use illicit opiates on top of buprenorphine. The risk of overdose with buprenorphine is consequently lower than for heroin or methadone, although still possible especially with poly drug use. Buprenorphine has less of a respiratory depressant effect than methadone and less effect on cardiac conduction which contributes to a better safety profile than methadone as an OST choice.⁶

Titration to a therapeutic maintenance dose is much quicker with buprenorphine compared to methadone; making treatment more comfortable for many service users.⁶

Understanding the pharmacology is necessary to manage transition on and off buprenorphine. It also has a profile that assists opiate dependent persons to detoxify off other opiates such as heroin, methadone and prescription opioids. Buprenorphine has a longer half life than methadone and therefore effects are felt for longer, making reductions of dose more tolerable. ^(1 & 6)

Buprenorphine is the first line treatment choice for opiate dependence in NHS Dumfries and Galloway due to its safer profile; unless the patient has a strong preference for methadone, has had failed attempts with buprenorphine in the past or takes long term opiates for chronic pain.

3.2.1. Oral Buprenorphine

Espranor[®] is a formulation of buprenorphine that comes in a dispersible film that dissolves on top of the tongue. Espranor[®] dissolves much quicker, usually within 15 seconds, compared to generic buprenorphine sublingual tablets which take approximately 5 minutes to dissolve. This makes the supervision process easier for the service user and the pharmacy staff supervising the dose and reduces the risk of diversion when compared to the sublingual tablet form.

Espranor[®] contains gelatine⁷. Those whose dietary or religious beliefs would prevent them from having Espranor[®] should be offered sublingual buprenorphine tablets.

Prior to initiating treatment:

1. Opioid dependence must be diagnosed prior to starting treatment. A comprehensive assessment should be undertaken, including drug screening to confirm the presence of opiates. Drug screens should not be used as a definitive tool for diagnosis but should be interpreted alongside other clinical information.
2. The routine work up for new patients includes LFT's, FBC, U&E's and BBV screening. Obtaining these blood tests should however not delay starting OST. Buprenorphine can cause accelerated liver injury if the service user already has hepatic impairment or viral hepatitis. Regular monitoring of liver function is recommended in these people. Buprenorphine can be prescribed for patients with mild to moderate liver impairment but it is suggested that it is initiated and titrated at a slower rate for people with severe liver impairment.
3. The service user's medical history, allergies and other prescribed or over the counter (OTC) medicines should be considered for contraindications, cautions and interactions when determining if treatment with buprenorphine is appropriate.
4. Precipitated withdrawal may occur when initiating buprenorphine treatment. If this happens, it typically starts within 1-3 hours after the first dose and peaks within 3-6 hours before improving. This should be discussed with the service user prior to initiating treatment and

they should be reassured that should they experience precipitated withdrawal, the symptoms will improve.⁸

5. The service user should be offered overdose awareness training and a naloxone supply.
6. The service user should be advised of side effects and the effect on driving (DVLA guidance⁹).
7. Contraceptive advice should also be given if the service user is a female of child bearing potential and referral to sexual health completed if needed.

Preparations available:

Espranor® - Buprenorphine lyophilisate wafer (available in 2mg and 8mg strengths)

Generic buprenorphine sublingual tablets (available in 0.4mg, 2mg and 8mg strengths)

There is a slight difference in bioavailability between Espranor and generic buprenorphine and therefore a difference in usual maintenance dose and maximum licensed dose.

Dosage regime:

Induction from Heroin to Buprenorphine:

Ideally, the individual will be free of Heroin for at least 12 hours.

Amount of Heroin: 0.1g - 0.2g (Average cost £10) per day smoking

Day 1 0.4mg CUS 4mg away

Day 2 4mg CUS 2mg away

Day 3 8mg CUS

Can then be increased / reduced by 2mg daily as needed.

Amount of Heroin: 0.2g - 0.4g + (Average cost £20) per day or more

Day 1 0.4mg CUS 6mg away

Day 2 8mg CUS 4mg away

Day 3 16mg CUS

Can then be increased / reduced by 2mg daily as needed.

Espranor usual maintenance dose: 8-16mg daily (Max dose 18 mg per day)

Generic buprenorphine usual maintenance dose: 12-24mg daily (Max dose 32mg per day)⁵

Monitoring:

Service users should be seen regularly when initiating treatment. Once stable this can be gradually reduced to up to 3 monthly based on risk assessment. Co-existing physical, emotional, social and legal problems should be addressed as well as drug and alcohol use. Service users should be signposted or referred to additional services where appropriate.

Drug testing can be used to measure concordance and detect ongoing illicit drug use. This should be used only to guide treatment or assess for non-compliance if this is suspected.

Reduction regime:

Doses of buprenorphine can be reduced by 2mg every 2 weeks until the patient reaches 2 - 4mg daily.

Thereafter, doses should be reduced by 0.4mg every 1-2 weeks.

Quicker reductions can be offered if appropriate.

Missed Doses:

If 1 - 4 days of buprenorphine are missed, the service user should be assessed for opiate use in these days. If no opiates have been used then they can continue the prescription at the same dose.

If 5+ days of buprenorphine are missed, and the daily dose is 8mg or less it may be possible to continue on the existing prescription, as long as no opiates have been consumed in this time.

If the daily dose is >8mg then they will need to re-commence from 8mg if no opiates have been consumed in this time.⁸

If opiates have been consumed, the patient would need to be re-titrated.

Transitioning from methadone to oral buprenorphine

Traditionally patients would have to reduce their methadone dose gradually until they were on 30mg of methadone daily or less and then stop their methadone for 24 - 72 hours until they were in moderate withdrawal before commencing buprenorphine. This is still an option if the patient would prefer to transition this way and they would just commence buprenorphine as per the dosage regime stated on the previous page.

In contrast to this traditional method, the process of micro-dosing allows patients to continue their use of their methadone until a therapeutic dose of buprenorphine has been achieved. At that point, the full agonist is discontinued.

Overall, this process will normally take one - three weeks.

Small doses of buprenorphine administered during the early stages of micro-induction stay below the threshold to displace the full opioid agonist enough to induce withdrawal. Studies have shown that doses of 0.2mg to 1mg will likely only displace a small percentage of opioid receptor occupancy.

Prior to initiating micro-induction:

- i) The patient must be informed of the rationale and process of micro-induction and provided with the microdosing patient information leaflet (see appendix 2).
- ii) The patient must be made aware of risks and benefits of the micro-induction process.
- iii) The patient needs to give informed consent to go ahead with micro-induction.
- iv) The patient should be made aware of the off-label nature of the process and this discussion should be documented in the patient's notes after completing a treatment agreement (see appendix 3).
- v) On the agreed date to commence micro-induction, the patient should continue to be in receipt of their current prescription of methadone. The dose of methadone will remain constant through the initial phases of the introduction of buprenorphine. Buprenorphine will be introduced in small increasing doses, increasing daily.
- vi) The patient should be given a copy of the micro-dosing regime (see appendix 4). The patient should have a consultation with the prescriber and/or designated practitioner at least weekly.
- vii) In the mid to late stages of the micro-introduction regime, patients may experience some discomfort. Medication for symptomatic relief of the symptoms should be explained and provided to the patient. See section 3.4 on managing withdrawal symptoms.

Micro-induction should only be carried out under the direct care of the Specialist Drug and Alcohol Service (SDAS) and will be prescribed using the local Prescription process (HBPA or HEPMA).

The patient should remain on their usual dispensing for methadone during this period. Weekly dispensing without the need for supervised consumption is appropriate for buprenorphine, unless there are any concerns regarding risk associated with this.

Discontinuing micro-dosing

Stop buprenorphine and re-titrate methadone dose from the dose the patient is currently on. The methadone dose can be increased by 5-10mg after 3 days and then by further 5-10mg weekly thereafter.

3.2.2. Long acting injectable buprenorphine (LAIB)

This formulation of buprenorphine (brand name Buvidal[®]) is a prolonged release subcutaneous depot injection which can be administered weekly or monthly.¹⁰ Buvidal[®] has many benefits including:

- It is long acting and effects are felt for a week or month depending on which formulation is used.
- It takes away the need for daily supervised consumption, making it more acceptable to the patient and eliminating time at the community pharmacy.
- The licence states that it can be administered up to 2 days in advance or after the due date for weekly injections and 1 week in advance or after the due date for the monthly injection reducing the risk of missing doses¹⁰
- There is evidence that it supports people back into employment and reduces stigma
- It makes it easier for patients travelling abroad as they do not need to carry medication in their luggage
- It has a positive impact on quality of life for the service user, which has been evidenced through our local pilot study
- It reduces the clinical burden on the service
- Improves adherence and reduces diversion
- Prevents potential access by children

Preparations available:

Buvidal prolonged release solution for injection

(weekly doses: 16mg, 24mg & 32mg; monthly doses 64mg, 96mg, 128mg & 160mg; top up 8mg)⁵

Dosage regime:

To minimise the risk of precipitated withdrawal, and ensure successful induction, the patient should be commenced on to oral buprenorphine as per the micro-induction process. Once the patient is on a stable oral buprenorphine dose, Buvidal can be commenced the day after the last oral dose.

First week: conversion of oral daily dose to weekly depot + 1 x 8mg top up throughout the first week (at least 1 day apart)

Second week onwards: Total daily dose administered during the previous week¹⁰

In some cases individuals who have previously been treated with Buprenorphine may be re-started directly on to Buvidal.

The recommended starting dose of Buvidal is 16mg, with one or two additional 8mg doses at least 1 day apart. The dose for the second week is the total dose administered during the first week. At the prescribers' discretion, individuals may start on 24mg weekly if re-starting directly on to Buvidal.

Maintenance:

Individuals can be switched to monthly LAIB once stable on weekly dose (weekly dose x 4 = monthly dose). Three weekly doses are preferred to gain steady state before switching to monthly Buvidal.

The monthly LAIB dose can be increased / decreased following a discussion between key worker, patient and prescriber.

To avoid missed doses, the licence states that the weekly dose can be given up to 2 days before or after due date and monthly dose can be given up to 1 week before or after the due date.¹⁰ It has been agreed locally, after reviewing evidence from our initial service evaluation, that if the patient has been stable on the same monthly dose for 3 months, they can be administered their next monthly dose up to 28 days after the due date.

The maximum monthly dose is 160mg.¹⁰ If an individual is administered a 160mg dose, the next administration must be after the full 28 days. The 160mg dose cannot be administered early.

A maximum of one supplemental 8mg LAIB injection may be administered at an unscheduled visit between regular weekly and monthly doses (apart from 160mg monthly dose)¹⁰, based on the service user's needs. If a 8mg injection has been administered, the monthly dose can be given up to 7 days before its administration due date if the individual is still in a state of withdrawal.

Co-existing physical, emotional, social and legal problems should be addressed as well as drug and alcohol use. Service users should be signposted or referred to additional services where appropriate.

Drug testing can be used to measure concordance and detect ongoing illicit drug use. This should be used only to guide treatment.

Switching from buprenorphine to LAIB¹⁰

| Daily Espranor* Dose (mg) | Daily SL Subutex or generic buprenorphine Dose (mg) | Weekly SC Bupival Dose (mg) | Monthly SC Bupival Dose (mg) |
|------------------------------|---|--------------------------------|---------------------------------|
| 2 – 4 | 2 – 6 | 8 | - |
| 6 – 8 | 8 – 10 | 16 | 64 |
| 10 – 12 | 12 – 16 | 24 | 96 |
| 14 – 18 | 18 – 24 | 32 | 128 |
| - | 26 – 32 | - | 160 |

*25-30% higher bioavailability for Espranor than for SL buprenorphine tablet¹¹.

Switching from methadone to LAIB: Follow micro-induction process and then convert to Bupival as per table above.

The SDAS depot administration chart should be used for each individual patient (see appendix 5). This counts as the legal prescription (“kardex”) as well as the administration chart and should be scanned and saved in the patient’s notes.

Discontinuing treatment

If the individual is to be switched to another opiate then a period of at least 1 week should be left if using the weekly dose of Bupival, or a period of 1 month should be left if using the monthly dose of Bupival.¹⁰ See methadone section if switching back to methadone.

Detox from Bupival

The preferred detox schedule is 3 months at each step down. For example, if an individual has been stable for at least 3 months on the 128mg monthly dose, this can be stepped down to 96mg monthly for three months then reduced further to 64mg monthly for three months. Bupival provides a slow and gentle taper detox with few reported withdrawal symptoms due to its prolonged release characteristics, long half-life and gradual ‘wear off’ time.

The individual should remain open to SDAS for 8 weeks after last injection. Following this period, the individual should receive information signposting them to the Focus & Recovery Hub, 3rd sector support from With You and ADS, in addition to information around how to contact us if they are feeling vulnerable in the future. Individuals should understand the risk of opioid naive overdose once Bupival has reduced in their system should they return to opioid use.

3.3 Methadone

Methadone hydrochloride is an opioid receptor agonist, which activates all opioid receptors with dull effect.

Methadone has a long duration of action; an optimal dose will exert clinical effects for 24-36 hours, however at lower doses the duration of clinical effects may be shorter. Methadone takes between 4 to 5 days for plasma levels to stabilise and can take up to 10 days to reach steady state. Once stabilised, methadone has a long elimination half-life (usually 13-47 hours, mean 25 hours), which allows for a once-daily dosing schedule^{5&12}. It may take two to four weeks (or more) to achieve an optimal dose with methadone.

Methadone may cause QTc prolongation in particular with doses in excess of 100mg and in combination with medicines that prolong QTc.¹²

Prior to initiation:

1. Opioid dependence must be diagnosed prior to starting treatment. A comprehensive assessment should be undertaken including drug screening to confirm the presence of opiates. Drug screens should not be used as a definitive tool for diagnosis but should be interpreted alongside other clinical information.
2. The service user's medical history, allergies and other prescribed or OTC medicines should be considered for contraindications, cautions and interactions when determining if treatment with methadone is appropriate.
3. Carry out an ECG if risk factors:
 - a. Heart or liver disease (family history of sudden death)
 - b. Electrolyte abnormalities
 - c. Concomitant treatment with CYP3A4 inhibitors e.g. clarithromycin, ketoconazole, itraconazole and many HIV treatments.
 - d. Concomitant treatment with other medicines that have the potential to cause QT interval prolongation e.g. Quetiapine
4. Offer overdose awareness training and naloxone supply to the service user and significant others.
5. The service user should be advised on side effects and the effect on driving (DVLA guidance⁹).
6. Contraceptive advice should also be given if the service user is a female of child bearing potential and referral to sexual health completed if needed.

Preparations available:

Methadone mixture 1mg per 1ml

Methadone mixture 1mg per 1ml (sugar-free)

Methadone 5mg tablets. Not licensed for drug treatment but may be considered off-label for supporting periods of travel etc.⁵

Dosage regime:

Initial dose: 10-30mg daily

In the community setting, doses should be titrated at no more than 10mg increments every 5-7 days as necessary until there is no sign of withdrawal or intoxication.

Maintenance:

Service users should be seen fortnightly when initiating treatment. Once stable this can be gradually reduced to up to 3 monthly based on risk assessment.

The normal maintenance dose is 60-120mg methadone daily. Maintenance doses are dependent on the person's response; in some circumstances the maintenance dose required may be out with this range.

Due to the long half-life of methadone, once daily administration dosing should provide a steady state for most individuals once an adequate dose is established. Some individuals may wish to 'split' their dosing, this should be discussed with the MDT and prescriber on an individual case basis.

An ECG should be taken at any time another medication with QTc prolongation potential is added on alongside methadone and should be repeated following dose increases of either of the medications with QT prolonging potential (methadone or other). Ideally carry out the ECG within 2 weeks following such a change.

An ECG should be repeated annually if taking > 100mg methadone per day, or pre-existing cardiac risk factors.

QTc is prolonged if > 440ms in men or > 460ms in women.

QTc > 500 is associated with an increased risk of torsades de pointes¹³.

For QTc intervals > 500ms, possible actions - reduce methadone dose, eliminating other contributing factors (discuss stimulant/alcohol use), alternative treatment such as buprenorphine, or discontinue methadone treatment.

Patients with evidence of polysubstance use with benzodiazepines or gabapentinoids are at increased risk of accidental overdose. A reduction of methadone to a lower, safer level should be considered. NHS D&G SDAS recommend that this is especially relevant for service users on a dose of 60mg methadone or more.

Reduction regime:

Doses can be reduced in consultation with the service user and should not be more than 10mg decrements at at-least weekly intervals.

Missed doses:

Regular missed doses can be associated with loss of opiate tolerance.

Pharmacies are required to inform the specialist service, using the NEO360 Missed Dose function to report by email, if a patient has missed 3 or more doses and place the patient's prescription on hold. In this instance the patient should be reviewed by their named practitioner and advice sought on an individual basis with the prescribing team.

If 3-5 days are missed:

- Patient presents in withdrawal and/ or denies opiate use in their days missed they will require to be re-titrated, reducing their dose by 50% for 3 days and increasing in 10mg increments weekly until stable.
- Patient presents without withdrawal symptoms and reports opiate use in their days missed, it may be appropriate to continue their prescription at their current dose.
 - If normal dose is up to 50mg daily, then they can continue as normal
 - If normal dose is >50mg daily, then reduce by 25% for 3 days and then increase by 10mg weekly until stable

If >5 days are missed then the patient should be re-titrated from 30mg.

Switching back to Methadone from Buprenorphine:

The patient should be switched back to oral buprenorphine on the day that they are due their next Buprenorphine injection. They should remain on this dose for 1 week and then can be switched to methadone as per induction.

3.4 Treatment of opiate withdrawal symptoms – short term and to be reviewed every 24 hours

| Symptom | Recommended treatment |
|----------------------------|--|
| Diarrhoea | Loperamide 4mg initially followed by 2mg after each loose stool |
| Nausea/Vomiting | Prochlorperazine 3mg buccal tablet twice daily when required |
| Stomach cramps | Mebeverine 135mg 3 times daily |
| Sleeplessness | Zopiclone 3.75- 7.5mg at night when required (Max duration of 14 days) |
| Muscular pains / headaches | Paracetamol / Ibuprofen dose as per BNF |

Treatments for symptomatic relief are available from community pharmacy via Pharmacy First or via GP.

3.5 Relapse Prevention - Naltrexone

Naltrexone is an opioid antagonist which can be used once the service user is abstinent from opiates. It works by blocking the mu opioid receptors, preventing other opiates from binding and therefore preventing the pleasurable effects of consuming opiates.^(3&14)

Prior to initiation:

- The service user's medical history and other prescribed or OTC medicines should be considered for contraindications, cautions and interactions when determining if treatment with naltrexone is appropriate.
- Baseline LFTs should be repeated if more than 2 months since last check.
- Opioid abstinence must be confirmed prior to starting treatment. A comprehensive assessment should be undertaken including drug screening to confirm there is no presence of opiates.
- Service users must be completely withdrawn and abstinent from opiates for 7 days (short acting opiates) to 10 days (long acting opiates) before starting naltrexone. This can be confirmed using a Point of Care Test.
- Patient Treatment Agreement should be completed (see appendix 6).
- Patients should be warned against the concomitant use of opioids (e.g. opioids in cough medication, opioids in symptomatic medication for the treatment of common colds, or opioids contained in anti diarrhoeal agents, etc.) during Naltrexone treatment. During treatment with Naltrexone, painful conditions should be treated with non-opioid analgesia only.^{5 & 14}

Preparation available:

Naltrexone 50mg tablets

Dosage regime:

Initially 25 mg daily on day 1, then increased to 50 mg daily from day 2 onwards.⁵ Total weekly dose may be divided and given on 3 days of the week for improved compliance (e.g. 100 mg on Monday and Wednesday, and 150 mg on Friday); maximum 350 mg per week.

Discontinuation:

No tapering is necessary on discontinuation and continuing need should be reviewed after 1 year.³

Monitoring

- LFT, GGT, AST & ALT should be checked on weeks 1 and 3 after starting treatment

- LFT, GGT, AST & ALT repeated monthly for the next 3 months
- LFT, GGT & AST & ALT every 6 months thereafter for duration of treatment
- Ongoing requirement assessed and confirmed every 6 months (normally by GP). There is no limit to the length of treatment if it is beneficial.

4 Monitoring:

OST medicines governance working group (answerable to MHD SMT) are responsible for the monitoring of compliance with this guideline through case review and datix reporting, and clinical outcome measures until such time as the Mental Health Prescribing Governance Subcommittee (answerable to ADTC) is established.

5 Equality & Diversity:

Impact assessment completed 5th June 2020

Outcomes: Positive or no impact in all areas except as outlined below.

| Impact Area | Option | Explanation and action to be taken |
|--|-----------------|------------------------------------|
| | (a), (b) or (c) | No negative impact expected |
| Updated 2022: guidance is anticipated to reduce inequalities further by offering more patient focussed treatments in line with new national Medication Assisted Treatment standards. | | |

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7 Document Control

7.1 Document Status:

| | |
|---------------------------|---|
| Title | Opiate Substitution Therapy (OST) Prescribing Guideline |
| Author | Samantha Nairn, Advanced Specialist Pharmacist; SDAS OST Working Group |
| Approver | ADTC |
| Document reference | MH19-002 |
| Version No. | 3.1 |

7.2 Document Amendment History:

| Version | Section(s) | Reason for update |
|---------|------------|---|
| 1.0 | All | No current NHS D&G guidelines in place |
| 1.8 | 3.2.2 | Information on gelatine content in Espranor following IIA |
| 2.0 | Various | Minor adjustments on language and formatting |
| | | Change to dosing guidance on Espranor v Sublingual conversion in line with local agreement |
| | | Addition of Buprenorphine long acting injection: Buvidal |
| | | Addition of micro-induction process |
| | | Link to national Medication Assisted Treatment Standards |
| 2.1 | Various | Language and formatting changes |
| | | Minor inaccuracies corrected |
| | | Updated IIA comment |
| 2.2 | Scope | As result of comments from MHD SMT Exclude HMP Dumfries; agreed to create alternative guidance that fits with SPS working patterns |
| | P10/11 | Addition to clarify inclusive of Midpark hospital inpatients |
| | Whole | Remove minor inaccuracies/clarification Prescribing responsibility disclaimer added |
| 2.7 | Various | Updated micro dosing scheme and section to refer to appendix |

| | | |
|------------|-----------------------|---|
| 2.8 | Microdosing protocols | Update to 10-30mg protocol to be in line with others. Update to 60-90mg protocol to be for doses of methadone 60mg and over with no upper limit |
| 2.9 | Added leaflet | Inserted leaflet appendix 10.1 |
| 3.0 | All | Minor adjustment by SDAS review group Addition of comparison table between generic sublingual buprenorphine and Espranor Addition of text around stopping micro-dosing. Change of medication for withdrawal from promethazine to zopiclone. Update of information leaflets in appendices. |
| 3.1 | Various | Added naltrexone to introduction. Update QTC information. Amended buprenorphine initiation doses. Addition of Detox from Buvidal section. Amended timeframe for missed doses. |

7.3 Distribution:

| Name | Responsibility | Version Number |
|---------------------|---|-----------------------|
| Communications team | Add to Beacon | 3.1 |
| Management team | SDAS Dissemination to SDAS staff, including sessional prescribers | 3.1 |
| OST Working group | Dissemination to GPs with addictions interest | 3.1 |
| Management team | SDAS dissemination to Area Drug Partnership | 3.1 |

7.4 Associated Documents: See references section

7.5 Action plan for implementation

| Action: | Lead Officer: | Timeframe: |
|---------------------------|----------------------|-------------------|
| Disseminate to SDAS staff | S Nairn | Nov 2024 |
| Training implementation | S Nairn | Nov 2024 |

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9. Glossary

OST Opiate substitution therapy: A medication prescribed to alleviate opiate withdrawals and aid in abstinence from other (often illicit, sometimes prescribed) opiates

SDAS Specialist Drug and Alcohol Service

10. Appendices

Appendix 1. Medicines used in the treatment of opioid dependence- Patient Information Leaflet. Medicines used in the treatment of opioid dependence



Information for Patients/Family/Friends/Carers

This leaflet provides information on the medicines used in the treatment of opioid dependence by the NHS Dumfries & Galloway Specialist Drug and Alcohol Service.

What are opiates and opioids?

Opiates are drugs made from the opium found in poppy plants, for example heroin.

Opioids are manufactured drugs NOT made from opium, for example methadone, oxycodone or fentanyl.

What do opiates and opioids do?

Opiates and opioids relieve pain, relax the body and cause feelings of warmth, well-being, high or euphoria. Over time with continued use, more of the drug (opiate or opioid) is needed to achieve the same effect. This is known as **tolerance** and continued use will lead to **dependence**, which means opiates/opioids will need to be taken to avoid withdrawal symptoms.

Opiates and opioids act on the Central Nervous System (CNS; what the body does without thinking) and slow it down. This means actions such as a person's breathing and heart rate are slower, ability to think is slower and reaction times are slower.

What causes withdrawal symptoms?

Opiates and opioids attach to **opioid receptors** in the brain. When the receptor is stimulated it generates the "feel-good" sensation. If the opiate/opioids are stopped suddenly, the receptors empty and this is what causes **withdrawal symptoms**. Withdrawal symptoms include:

- Hot and cold sweats
- Joint aches
- Runny nose and eyes
- Nausea and/or vomiting
- Stomach cramps and/or diarrhoea
- Difficulty sleeping

What are the medication options for opioid dependence?

The main options available for opioid dependence are:

- **Buprenorphine**
- **Methadone**
- **Naltrexone**

Buprenorphine and methadone are from a group of medicines called **Opiate Substitution Treatment** or **OST** for short, which are used to help people get off opiates/opioids.

Naltrexone is an opioid antagonist and is used by people who have successfully reduced and stopped taking opiates/opioids who are looking for support to stay abstinent and prevent relapse.

How does the medication work?

Buprenorphine and methadone work similarly. They bind to the opioid receptors in the brain and stop the withdrawal symptoms and cravings. These medications act as a replacement for opiates/opioids, such as heroin. If a person has become dependent on heroin (a short acting opiate) withdrawal symptoms will usually start approximately 6-8 hours after last use. Buprenorphine and methadone are long acting opioids and last for approximately 24 hours.

Methadone is a '**full agonist**' at the opioid receptors in the brain. Methadone binds to the receptors and stimulates them in a similar, but not the same, way as heroin. It has a less intense but longer lasting effect.

Buprenorphine is a '**partial agonist**' at the opioid receptors in the brain. This means that it partially blocks opioid receptors, but also partially stimulates them. Buprenorphine, therefore, blocks the effects of any opioids taken but because it stimulates the receptors a bit it stops withdrawal effects. It also puts a 'ceiling' on how much effect you can get from any other opioids taken.

Naltrexone is an '**opioid antagonist**' and works by blocking the opioid receptors which stops the effects of any opiates or opioids.

Once on the correct dose, oral medication is taken once per day and the long-acting injection of buprenorphine (Buvidal®) is administered once per week or once per month.

Medicines used to help treat opioid dependence prevent the feelings of withdrawal, provide a stable feeling and prevent cravings. These medicines reduce the need to find money through a variety of avenues including criminal activity. They also reduce the risk of experiencing withdrawal symptoms, catching a Blood Borne Virus (BBV) like Hepatitis C and HIV, having an overdose and police arrest.

Assessment and medication:

At your first face to face appointment at the Specialist Drug and Alcohol Service, you will be seen by a practitioner who will discuss with you the treatment options available and in collaboration with you agree on the most suitable treatment. They will gather some basic information with the view to starting a treatment plan as soon as possible. This may or may not include medication. Ideally, medication will be started on the same day, however, if not as soon as possible thereafter. You will then be allocated a named practitioner who will offer a further appointment for a more detailed assessment where you will discuss personal goals and how you can be supported to achieve them whilst working with the service.

Starting medication:

In the early stages of treatment, your medication will normally be dispensed daily with supervised consumption at a community pharmacy. As you progress through your treatment plan, decisions about dispensing will be discussed with you and amended as appropriate. It is important to discuss with your practitioner any issues that might make it difficult for you to stay in treatment (for example work, education, health conditions) so they can support you as best they can.

Achieving the right medication dose:

Research shows that when people on OST receive between 60mg-120mg of methadone a day or 12mg-18mg of buprenorphine a day, they do better in terms of staying in treatment and stopping use of other drugs. Keep giving feedback to your practitioner until you are receiving a dose which is high enough to prevent your withdrawal symptoms and your cravings to take other opioids. If you find that your medication is not lasting 24 hours, it is important you speak with your practitioner as the dose can be adjusted. The agreed dose should support you to complete your daily routine in comfort. The type of opioid, quantity, frequency and by what route it's usually taken informs the dose needed for OST. This could be less than the average range. Your personal dose can best be worked out in discussion with your practitioner.

Pharmacy and supervised consumption:

Your community pharmacy is there to support you and make sure you are safe to receive your medicine. Make sure you know when they are open and what services they can provide. Supervised consumption is where the pharmacy witnesses you taking your medication to support you with the daily dose of prescribed OST and to ensure your safety. Attending the pharmacy daily provides regular structure and supports you to achieve positive change. Relaxed dispensing can be discussed with your practitioner once stability has been evidenced.

Factors that affect access to take home doses:

- Not missing any doses
- Supportive family life
- Engagement with other forms of support offered
- Urine or saliva test results showing no opioid use or other overdose risks
- Being able to safely store your medication in a locked cupboard or box to stop children or other adults accessing the medication
- Having a stable home environment
- Positive progress with work or education
- No recent history of selling or giving medication to anybody else

Missed doses:

For their safety, if a person misses three or more daily doses of their OST they will require a review. The daily dose of OST may be temporarily reduced as tolerance may be lowered and overdose may be a risk.

Types of Medication: (Please see table below)

| Type of medication | Buprenorphine (Espranor®) | Long Acting Injectable Buprenorphine (Buvidal®) | Methadone | Naltrexone |
|----------------------------------|---|---|---|---|
| What form does it come in? | Oral wafer – dissolved on top of tongue Sublingual tablet - dissolved under tongue | Injection | 1mg/1ml Oral Solution (Liquid) | 50mg Tablet |
| How often is it taken? | Once per day | Once per week until stable then once per month | Once per day | Once per day |
| Starting treatment | There is a risk of precipitated withdrawals if taken too soon after last opiate | An oral test dose of buprenorphine is needed to confirm suitability if not had buprenorphine before | Should be taken at least 8 hours after the last dose of heroin. Other opiates may require a longer period | A minimum of 7-10 days opiate free are needed before starting |
| What is the usual starting dose? | Initially 0.4 mg daily, followed by 2–4 mg if required on day one. Micro-dosing follows a medication regimen chart | Usually 3 weekly injections. Doses available -Weekly:16mg, 24mg, 32mg | Starting dose is between 10mg-30mg daily (depending on use of opiates) | Starting dose is usually ½ tablet (25mg) on day 1 |
| Rate of dose increases | Can be quickly increased to appropriate dose. Doses are adjusted in steps of 2-8mg daily. Most patients will fall between 8mg and 16mg daily. Strengths available: 0.4mg, 2mg 8mg | Progress to monthly injection once stability has been achieved. Doses available – Monthly: 64mg, 96mg, 128mg, 160mg Top up: 8mg | Dose is increased slowly as needed, with no more than 10mg weekly increases with regular reviews. It can take 3 days to feel the full effect of the increased dose. It may take a few weeks to reach appropriate dose. Optimal dose is usually between 60mg-120mg daily | Dose is increased to 50mg daily thereafter. |
| What does it feel like? | Gives a clear headed feeling. Provides strong stability and consistency through each day | Gives a clear headed feeling. Provides strong stability and consistency through each day / week/ month | Gives a cloudy headed and drowsy feeling. Provides stability and consistency when dose is taken as prescribed at the same time each day | You will have a clear head. There will be no opioids in your body |
| Using other substances | At higher daily doses of buprenorphine opiates/ opioids will have little effect on top due to blocking action | Strong blocking effect. Greatly reduces risk of overdose from opiates/ opioids | Higher doses of methadone flood the opiate receptors leaving little room for heroin. Greater risk of overdose if higher than normal dose taken or if used with other substances | No effect from opioids due to complete blocking action |
| Stopping treatment | Good option for detoxing allowing for a planned reduction | You are committed to take Buprenorphine for the duration of the injection (week or month). Reducing the dose of the monthly injection can be used to facilitate a detox | Methadone can be reduced gradually, however some people prefer a switch to buprenorphine at lower doses | |

Common Side Effects to OST and Tips for Managing Them:

It is important to remember as with many other medications, you may experience side effects. These can be managed and usually lessen in time as your body adjusts to the medication. If you do experience side effects, speak to your practitioner who will offer you support to manage them.

Common side effects include:

| | |
|---|--|
| <ul style="list-style-type: none">• Tiredness or drowsiness | Discuss with your practitioner |
| <ul style="list-style-type: none">• Sweating a lot | Ensure that you drink enough. Discuss with your practitioner if this does not improve |
| <ul style="list-style-type: none">• Constipation | Ensure diet contains fruit and vegetables; drink plenty of water or other drinks; daily exercise. Discuss with your practitioner if this continues. |
| <ul style="list-style-type: none">• Nausea or lack of appetite | Drink plenty of water/fluids and eat small amounts of food often. This usually wears off over a week or two. |
| <ul style="list-style-type: none">• Dental issues | Opioids can cause a dry mouth leaving teeth susceptible to decay. Rinse your mouth with water after you have taken methadone. Clean your teeth and drink water. |
| <ul style="list-style-type: none">• Lowered sex drive | Talk to your practitioner if this is causing problems. There are lots of possible causes and they might be able to help. |
| <ul style="list-style-type: none">• Serious side effects are rare | These can include chest pain, shallow breathing, abnormal heartbeat, fainting, getting confused or having hallucinations. Discuss any of these with your practitioner or with your GP. |

DISCLAIMER:

This leaflet is to help you understand about some of the medications offered by the NHS Specialist Drug and Alcohol Service. If you are started on any of these medications, your allocated worker will explain the medication in more detail. It is advisable that you also read the manufacturer's Patient Information Leaflet (PIL) in full (see <http://www.medicines.org.uk/emc/>). You may find more information on the internet, but beware as internet-based information is not always accurate.

Further information about the different types of medication and how they are used can be found on the Choice and Medications website: <http://www.choiceandmedication.org/nhs24/printable-leaflets>

Produced by NHS Dumfries and Galloway Specialist Drug and Alcohol Service (Sept 2024, v3).
Review date Jan 2027.

Appendix 2. Microdosing patient information leaflet.

Micro-dosing Methadone to Buprenorphine

Patient information leaflet

What is micro-dosing?

Micro-dosing allows patients currently prescribed methadone to gradually transfer to buprenorphine without needing a period of opioid withdrawal.

Standard initiation of buprenorphine requires patients to reduce their dose of methadone to 30mg/day and go through moderate opioid withdrawals to avoid precipitated withdrawal, making the transition from methadone to buprenorphine challenging for many patients. The micro-dosing process gradually introduces buprenorphine and slowly replaces methadone. This reduces the risk of patients relapsing and minimises withdrawal effects that may be experienced.

What to expect:

The micro-dosing period will normally take between 15 – 28 days. Doses of buprenorphine will progressively be titrated up whilst your methadone dose is maintained. You will have appointments with your practitioner at regular intervals. Once stable on the expected dose of buprenorphine, the methadone is reduced then discontinued.

The micro-dosing process uses two buprenorphine products available in different strengths; Buprenorphine 0.4mg sublingual tablets and Espranor[®] (buprenorphine) 2mg and 8mg oral lyophilisate (wafer).

You will remain on the same methadone pharmacy dispensing intervals during the micro-dosing period. Dispensing of oral buprenorphine will be weekly in most cases.

How to take your medicine:

Buprenorphine 0.4mg tablets are **SUBLINGUAL (Dissolve **UNDER** the tongue)**

Espranor[®] 2mg & 8mg wafers are **ORAL (Dissolve **ON** the tongue)**

Tablets and wafers should not be chewed, crushed or swallowed whole. Do not eat or drink for at least 5 minutes after taking this medicine.

Other important things to know:

- All medicines can cause side effects. The most common side effects are; stomach pain, diarrhoea, muscle aches, anxiety and sweating.
- Do not take other medicines or substances that make you sleepy. It is dangerous to mix opioid substitution medication with other opiates (e.g. heroin, methadone, or codeine), sleeping tablets (including benzodiazepines) or alcohol. It can lead to overdose, which can be fatal.
- Keep your medicines in a safe place. Medicines must only be taken by the person it is prescribed for. Store medication securely out of reach from children and other adults.

Produced by Specialist Drug & Alcohol Service (v1) 2022 Review due Jan 2027

Appendix 3. Micro-dosing Patient Treatment Agreement.

Micro-dosing Patient Treatment Agreement

| | |
|------------------|-------------|
| Name of patient: | CHI number: |
|------------------|-------------|

| | Patient to initial to confirm |
|--|-------------------------------|
| I understand that micro-dosing is an off label process. | |
| I confirm that I have received the patient information leaflet "Micro-dosing from methadone to buprenorphine" and that I have read and understood the information leaflet. | |
| I will report any side effects to my Named Nurse or Doctor. | |

| | |
|--------------------------------|-------|
| Signature of Patient: | Date: |
| Named Healthcare Professional: | Date: |

Appendix 4. Micro-dosing schedules

Micro-dosing regime for Methadone 1mg/ml Oral Solution dose 10mg – 30mg

Patient Name:

CHI:

Buprenorphine 0.4mg tablets are **SUBLINGUAL (Dissolve **UNDER** the tongue)**
Espranor Wafer 2mg & 8mg doses **ORAL (Dissolve **ON** the Tongue)**

| | Dose | Consumption instructions | Methadone Dose |
|---|-------|------------------------------------|------------------------|
| Day 1 | 0.4mg | 1 x 0.4mg tablet | Current Dose |
| Day 2 | 0.8mg | 2 x 0.4mg tablets | Current Dose |
| Day 3 | 1.2mg | 3 x 0.4mg tablets | Current Dose |
| Day 4 | 2mg | 1 x 2mg wafer | Current Dose |
| Day 5 | 2.8mg | 1 x 2mg wafer 2 x 0.4mg tablets | 2/3 rd Dose |
| Day 6 | 4mg | 2 x 2mg wafers | 2/3 rd Dose |
| Day 7 | 4mg | 2 x 2mg wafers | 2/3 rd Dose |
| Day 8 | 4mg | 2 x 2mg wafers | 2/3 rd Dose |
| Day 9 | 6mg | 3 x 2mg wafers | 1/3 rd Dose |
| Day 10 | 6mg | 3 x 2mg wafers | 1/3 rd Dose |
| Day 11 | 8mg | 1 x 8mg wafer | 1/3 rd Dose |
| Day 12 | 8mg | 1 x 8mg wafer | 1/3 rd Dose |
| Day 13 Named nurse to offer ongoing reviews (+/- every 2-3 days) which can be done by phone and adjust the dose upwards in 2mg increments if required. | 8mg | 1 x 8mg wafer | STOP METHADONE |

Micro-dosing regime for Methadone dose 31mg -60mg

Patient Name:

CHI:

Buprenorphine 0.4mg tablets are **SUBLINGUAL (Dissolve **UNDER** the tongue)**

Espranor Wafer 2mg & 8mg doses **ORAL (Dissolve **ON** the Tongue)**

| | Dose | Consumption instructions | Methadone Dose |
|--------------------|-------|-----------------------------------|--|
| Day 1 16/09/24 | 0.4mg | 1 x 0.4mg tablet | Current dose 50mg |
| Day 2 17/09/24 | 0.8mg | 2 x 0.4mg tablets | Current dose 50mg |
| Day 3 18/09/24 | 1.2mg | 3 x 0.4mg tablets | Current dose 50mg |
| Day 4 19/09/24 | 2mg | 1x 2mg wafer | Current dose 50mg |
| Day 5 20/09/24 | 2.8mg | 1x 2mg wafer 2 x 0.4mg tablets | Current dose 50mg |
| Day 6 21/09/24 | 4mg | 2 x 2mg wafers | Current dose 50mg |
| Day 7 22/09/24 | 4mg | 2 x 2mg wafers | Current dose 50mg |
| Day 8 23/09/24 | 4mg | 2 x 2mg wafers | Current dose 50mg |
| Day 9 24/09/24 | 6mg | 3 x 2mg wafers | 2/3 rd current dose 33mg |
| Day 10 25/09/24 | 6mg | 3 x 2mg wafers | 2/3 rd current dose 33mg |
| Day 11 26/09/24 | 8mg | 1 x 8mg wafer | 2/3 rd Current dose 33mg |

| | | | |
|--------------------|------|---------------------------------|--|
| Day 12 27/09/24 | 8mg | 1 x 8mg wafer | 2/3 rd Current dose 33mg |
| Day 13 28/09/24 | 10mg | 1 x 8mg wafer 1 x 2mg wafer | 1/3 rd Current dose 17mg |
| Day 14 29/09/24 | 12mg | 1 x 8mg wafer 2 x 2mg wafers | 1/3 rd Current dose 17mg |
| Day 15 30/09/24 | 14mg | 1 x 8mg wafer 3 x 2mg wafers | 1/3 rd Current dose 17mg |
| Day 16 01/10/24 | 14mg | 1 x 8mg wafer 3 x 2mg wafers | 1/3 rd Current dose 17mg |
| Day 17 02/10/24 | 16mg | 2 x 8mg wafers | Stop methadone |
| Day 18 03/10/24 | 16mg | 2 x 8mg wafers | |
| Day 19 04/10/24 | 16mg | 2 x 8mg wafers | |
| Day 20 05/10/24 | 16mg | 2 x 8mg wafers | |
| Day 21 06/10/24 | 16mg | 2 x 8mg wafers | |

Micro-dosing regime for Methadone dose 61mg +

Patient Name:

CHI:

Buprenorphine 0.4mg tablets are **SUBLINGUAL (Dissolve **UNDER** the tongue)**

Espranor Wafer 2mg & 8mg doses **ORAL (Dissolve **ON** the Tongue)**

| | Dose | Consumption instructions | Methadone Dose |
|--------|-------|----------------------------------|-----------------------------------|
| Day 1 | 0.4mg | 1 x 0.4mg tablet | Current Dose |
| Day 2 | 0.8mg | 2 x 0.4mg tablets | Current Dose |
| Day 3 | 1.2mg | 3 x 0.4mg tablets | Current Dose |
| Day 4 | 2mg | 1 x 2mg wafer | Current Dose |
| Day 5 | 2.8mg | 1x 2mg wafer 2 x 0.4mg tablet | Current Dose |
| Day 6 | 4mg | 2 x 2mg wafers | Current Dose |
| Day 7 | 4mg | 2 x 2mg wafers | Current Dose |
| Day 8 | 4mg | 2 x 2mg wafers | Current Dose |
| Day 9 | 6mg | 3 x 2mg wafers | 2/3 rd of Current Dose |
| Day 10 | 6mg | 3 x 2mg wafers | 2/3 rd of Current Dose |
| Day 11 | 6mg | 3 x 2mg wafers | 2/3 rd of Current Dose |

| | | | |
|--------|------|---------------------------------|-----------------------------------|
| Day 12 | 8mg | 1 x 8mg wafer | 2/3 rd of Current Dose |
| Day 13 | 8mg | 1 x 8mg wafer | 2/3 rd of Current Dose |
| Day 14 | 8mg | 1 x 8mg wafer | 2/3 rd of Current Dose |
| Day 15 | 10mg | 1 x 8mg wafer 1 x 2mg wafer | 1/3 rd of Current Dose |
| Day 16 | 10mg | 1 x 8mg wafer 1 x 2mg wafer | 1/3 rd of Current Dose |
| Day 17 | 12mg | 1 x 8mg wafer 2 x 2mg wafers | 1/3 rd of Current Dose |
| Day 18 | 12mg | 1 x 8mg wafer 2 x 2mg wafers | 1/3 rd of Current Dose |
| Day 19 | 14mg | 1 x 8mg wafer 3 x 2mg wafers | 1/3 rd of Current Dose |
| Day 20 | 14mg | 1 x 8mg wafer 3 x 2mg wafers | 1/3 rd of Current Dose |
| Day 21 | 16mg | 2 x 8mg wafers | Stop methadone |

Appendix 5. SDAS Depot administration chart.

| | | | | | |
|--|--|-------------------------------|------------------|---|--------------------------------------|
| Name | | CHI Number | | Consultant | |
| Address | | SDAS contact | | GP | |
| | | Other medication taken | | Allergies - Drug & Reaction / NKDA | |
| Drug | | Dose | Frequency | | Site of injection |
| Signature | | Name: | Date: | Current dose started | Stopped Date Signature |
| Additional instructions / comments / pharmacy | | | | | Reason: |

Prescription valid for 1 year from signature (unless otherwise specified) any changes require a new prescription

| | | | | | | | | | | | |
|----------------------|--|--|--|--|--|--|--|--|--|--|--|
| Date | | | | | | | | | | | |
| Dose (mg) | | | | | | | | | | | |
| Lot / batch | | | | | | | | | | | |
| Expiry | | | | | | | | | | | |
| Given by INIT | | | | | | | | | | | |
| Site | | | | | | | | | | | |
| Date next due | | | | | | | | | | | |

Appendix 6. Naltrexone patient treatment agreement.

Naltrexone Patient Treatment Agreement

Patient Name:

Address:

DOB:

CHI:

I would like to start on a Naltrexone programme. The purpose of Naltrexone and the dangers of trying to override the opiate blockade have been fully explained to me. I understand that I will have a reaction to the tablet if I have used any opiates (heroin or codeine within the last 7 days or methadone within the last 10 days).

Patient Signature.....

Named Nurse Signature.....

Date: