Buprenorphine/naloxone for opioid dependence

Important points to know about buprenorphine/naloxone(Suboxone®)

Background

Buprenorphine is an established maintenance treatment for people with opioid dependence that has been available in Australia for more than 10 years. It has similar effectiveness as methadone in reducing heroin or illicit morphine use, keeping people in treatment, improving health and social wellbeing, and reducing blood-borne virus transmission as well as criminal activity.

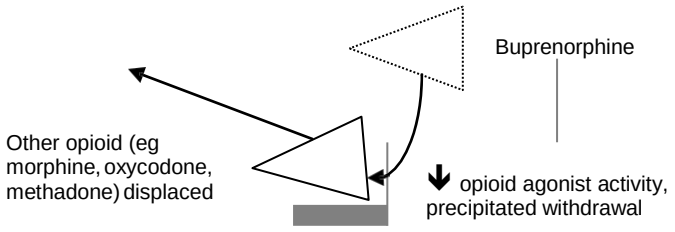
> Suboxone® is a combination of buprenorphine and naloxone, which has been available over the last few years. The naloxone is inactive orally but if the preparation is injected, the naloxone attenuates the effect of the buprenorphine and can precipitate withdrawal if the person is opioid dependent. It is taken sublingually.
> The 'film' formulation is the only formulation of buprenorphine/naloxone generally authorised in South Australia.

> Buprenorphine is a S8 or S100 drug. However buprenorphine is only a partial opioid agonist, which means that there is a ceiling to the cardio-respiratory and CNS depressant effects of buprenorphine so it is inherently safer than other S8 opioids.

> Despite this ceiling effect, buprenorphine is an opioid agonist so people on buprenorphine will experience tolerance to opioids and will experience withdrawal if it is stopped. It is also an effective analgesic.

> Risk of precipitated withdrawal. The major risk associated with commencing buprenorphine is precipitated withdrawal. This happens if the patient still has a significant amount of opioid in his or her system that is occupying the mu-opioid receptors. If a patient is given buprenorphine in this situation, the buprenorphine, which has higher receptor affinity but lower intrinsic activity, displaces the other opioid from the receptors resulting in lower opioid agonist activity and precipitating withdrawal.

Understanding precipitated withdrawal



> The typical dosage range for opioid dependence is 12-16mg daily. Most patients become stable on 12-24mg per day but some need a higher dose. Maximum daily dose is 32mg per day. Occasionally people might become stable on 8mg per day.

> The drug is taken sublingually at the pharmacy as a supervised daily dose. Once the patient is stable, the dose can be doubled and they can then change to second daily dosing. (eg 16mg daily would be 32mg every second day).

> Effect onset at 30 to 60 minutes. Its peak effect is at one to four hours. Effect duration is short at low dose (eg 4mg) but the effects of doses of more than 16mg can last from 24 to 72 hours, which allows for alternate day dosing.

Criteria for opioid dependence

Presence of three or more in last 12 months

> Tolerance (marked increase in amount; marked decrease in effect).

> Characteristic withdrawal symptoms; substance taken to relieve withdrawal.

> Opioids taken in larger amount and for longer period than intended.

> Persistent desire or repeated unsuccessful attempt to quit.

> Much time/activity to obtain, use, recover.

> Important social, occupational, or recreational activities given up or reduced.

> Use continues despite knowledge of adverse consequences (eg failure to fulfil role obligation, use when physically hazardous).

New patients - starting buprenorphine – the first week

1. Check you have not reached the maximum allowable number of patients (10x). If not sure, contact the Drugs of Dependence Unit on 1300 652 584
2. Patients may expect immediate commencement of treatment, but the process can take time and a planned approach is best. Make initial appointments for assessment on Monday – Friday between 9am - 4.30pm when the Drugs of Dependence Unit is available to grant authorities.
3. Establish that the patient is opioid dependent. Three of the features of dependence need to have been present in the last 12 months to make the diagnosis. Common features include tolerance, withdrawal if the drug is ceased abruptly and continued use despite awareness of harm. See criteria for dependence on page 1.
4. If the patient is pregnant, refer to DASSA for further management.
5. If there are concurrent alcohol or benzodiazepine related problems, refer to DASSA for further management.

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6. Only start the patient on Suboxone® film when he or she is actively withdrawing. Signs of withdrawal include:
   - dilated pupils (eg >4mm diameter)
   - pulse >90
   - BP > 140/90
   - Piloerection [goosebumps]
   - sweatiness and sometimes sniffing, yawning and watery eyes.
   - anxiety.

   Not all of these might be present during withdrawal.

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7. You need to get an authority from the Drugs of Dependence Unit just like you do for all S8s. The only difference is that Suboxone® film / buprenorphine-naloxone is S100 and you need an authority immediately before you start the patient, not after two months. Phone 1300 652 584 to have a copy of the application form faxed to you.

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8. Complete the authority application form and fax back to the Drugs of Dependence Unit on 1300 658 447.

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9. Phone the Drugs of Dependence Unit on 1300 652 584 and obtain a verbal authority number.

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10. Ring the prospective pharmacy and check it is open seven days per week. Note its opening hours. If suitable, check that they will take on the patient and the weekly cost for opioid pharmacotherapy patients. Available pharmacy information can be obtained from the Alcohol and Drug Information Service on 1300 13 1340.

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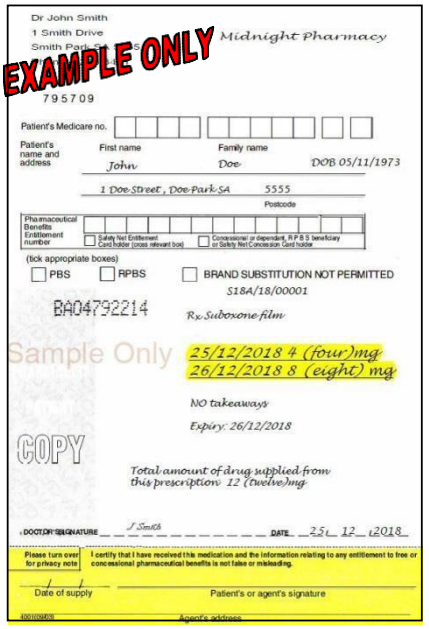
11. Make sure the patient knows the payment cost.
12. Write a prescription for Suboxone® film with the usual patient and prescriber identifiers and include:
    - the designated pharmacy (script only valid at this pharmacy)
    - the authority number
    - the dose to be dispensed daily, underlined and highlighted (in numerals and words
    - the expiry date (use this to make sure the patient comes back to see you at the appointed time)
    - the number of unsupervised doses (see right. Nil at the start)
    - total amount of the drug supplied from the prescription, eg 16mg of Suboxone® for 30 days = 480mg (in numerals and words)



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13. Inform the patient that they should not drive during the first week of stabilisation. Once their dose has been stable for a few days, they can drive. You may wish to use a patient agreement to record this advice.

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14. See the patient on days one and two and then day six or seven, to check progress. Ring the pharmacist each time to instruct re dosing.

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15. Doses:
    - **Day 1**: 4mg. The patient could come back four hours later for another 4mg dose.
      - **DO NOT INCREASE DOSE IF SEDATED**
      - **IF MAIN DRUG WAS CODEINE, TOLERANCE MAY NOT BE AS HIGH. START ON HALF THE SUGGESTED DOSES BUT MAY NEED FULL DOSES AS DESCRIBED.**
    - **Day 2**: increase on day 1 by 4mg. ∴8mg or 12mg.
    - **Day 3**: may increase by 2-4mg and then for the next week maintain at 12-16mg/d.

    Suboxone® comes in 2mg and 8mg films, which cannot be broken down into smaller dose increments.

After the first week

See the patient weekly for the first month, then monthly.

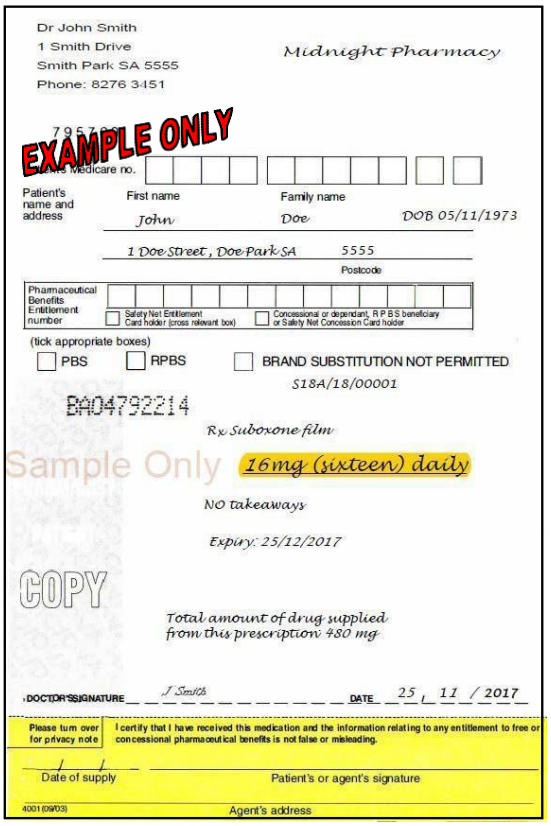
Note that the script needs to be current for the patient to be dosed at the pharmacy.

After the first week, the patient can increase the dose by 4mg per week until they are stable. Remember the maximum dose is 32mg per day.

A prescription for ongoing Suboxone® would look like this.

Please note the following need to be included:

> the designated pharmacy (script only valid at this pharmacy)
> the authority number
> the expiry date (use this to make sure the patient comes back to see you at the appointed time)
> the number of unsupervised doses (see right. Nil at the start)
> total amount of the drug supplied from the prescription, eg 16mg of Suboxone® for 30 days = 480g (in numerals and words).



Once the patient is stable (or patients being transferred once stabilised)

> Generally, most patients become stable within a few weeks. The idea behind maintenance treatment is to get the physical aspects of the chemical dependence under control so they can function normally and you can then work with the patient in sorting out other problems. Opioid dependence is a DSM 4/ICD 10 diagnosis so the mental health related MBS item numbers and referral options can be used with people with this diagnosis.

> Doses needed vary but most patients require daily buprenorphine doses in the range 12-24mg to achieve stabilisation, although some patients require higher (eg up to 32mg/day) or lower (4-8 mg/day) doses to achieve their treatment goals.

> Patients can stay on Suboxone® for as long as they need to remain stable. They should be encouraged to stay on maintenance at least a year. The longer someone has been dependent before seeking help, the longer the duration of the maintenance. The patient might want to think about coming off maintenance if they have been stable for six or 12 months and if they have relative stability in their personal lives that will support this action. Indicators of stability are detailed below. See below for advice on ceasing treatment.

Regular reviews

Once patients are stable they should be reviewed every two to three months.

At each appointment:

- **Ask** the patient about their recent substance use. Quantity and frequency; look at alcohol, opioids, stimulants such as methamphetamine, cannabis and benzodiazepines.
- **Ask** whether the patient is thinking about using drugs, and how strong these thoughts are.
- **Ask** about their general social functioning: work, relationships, family, voluntary work and community participation
- **Ask** them about their mental health.
- **Look** at whether they seem comfortable, are anxious, or agitated.
- **Look** for signs of intoxication or withdrawal
- **Look** for signs of recent injecting drug use such as track marks.
- **Obtain** a urine sample for a urine drugscreen.

If drug use continues, or resumes, then talk through the reasons with the patient. Often there are ongoing stressors such as relationships, legal matters, Family Court, finances and accommodation that trigger resumption or continuation of drug use, despite treatment. Sometimes an increase in dose can be effective, but in addition work with the patient to seek other help with these other issues.

Features to determine whether patient is stable/dose is adequate:

- No longer constantly thinking about using opioids (heroin, morphine). These intrusive thoughts about substance use are called cravings.
- No longer actually using opioids other than the Suboxone®/buprenorphine-naloxone. This can be established through:
  - Patient's history
  - Presence of fresh track marks
  - Urine drug screens (you can do up to 22 tests per year under Medicare for monitoring a patient in treatment). Request a urine screen for drugs of dependence/abuse. Write that the patient is on Suboxone®. If they are not using any additional opioids the result will come back buprenorphine only.
- Whether they are working, engaged in education, active parenting.
- Whether they are attending for dosing every day. The pharmacist will ring you if your patient misses more than three doses in a row. You should see the patient and talk about why they missed their doses.
- How they present to the pharmacist (eg always tidy, courteous, payments are on time, not intoxicated).

Ceasing treatment

When patients have been stable for an extended period of time and wish to come off treatment, planning can for this can start. Patients do best when they have had an extended period of time with little or no drug use.

They also do best when treatment cessation is planned and the patient is in control of the rate of dosage reduction. If there are crises along the way, then slow or stop the reduction (or even increase the dose) and then, once stable, talk through future plans with the patient.

It is important to consider:

- the patient's environment, whether they now operate in a drug free social environment
- what relationships they are in that give them resilience
- whether they have ongoing legal, financial, accommodation or family issues that are stressful
- whether there are ongoing unresolved or untreated mental health problems..

Consider reductions of 2mg every three-to-four weeks and monitor withdrawal effects with the patient. Often patients can cease from 2mg but at times they can experience significant withdrawal. If this is the case either use symptomatic medications or contact the Drug and Alcohol Clinical Advisory Service for further advice (see below).

Ceasing from doses higher than 2mg is not recommended. Withdrawal is significant and relapse into using illicit opioids is likely.

Unsupervised doses

Unsupervised doses or 'take-aways' increase flexibility for the patient and reward them for progress. Indicators of progress are listed above in the section 'Features to determine whether patient is stable/dose is adequate'.

Refer to the SA Health Drugs of Dependence 'Guidelines for prescribing take away doses' at http://www.sahealth.sa.gov.au/drugsofdependence under Forms and Resources.

In summary:

- Patients can start to have unsupervised doses after the first two months of treatment, as long as opiate use and injecting has ceased (check urine drug screens and injecting sites). If drug screens are positive for amphetamines or opiates, then unsupervised doses should not be allowed. Prescribers are encouraged to use the risk assessment tool (PDF 155KB) (opens in a new window) to assist their assessment of, and to document the risk of allowing a patient to have unsupervised doses.
- The maximum number of unsupervised doses per week is five for Suboxone®. Patients should gradually build up to this level after 18 months of treatment. Generally up to six/month up to first nine months, then three/week to 18 months.
- Beyond 18 months the number of unsupervised doses is based on a judgement regarding diversion risk, and the risk of patients using medications up ahead of schedule. Increases in unsupervised doses should be incremental with further increases based on evidence of continued high level functioning.

Interpreting urine drug screens

For details on the use of urine drug screens in the context of monitoring opioid dependence, please refer to the fact sheet called 'Urine drug screening: its use in determining patient' progress'.

Missed doses

Missed doses may indicate that the patient is experiencing problems and may be becoming unstable. Pharmacists will let you know if the patient misses more than three consecutive doses, or more than 10 in one month. This may indicate reduced stability, plus there is the risk of reduced tolerance when the Suboxone® has not been taken for a few days. This increases the risk of toxicity when the patient resumes dosing. Therefore when there have been missed doses:

- Talk with the patient about the circumstances and if there are other stressors that need to be addressed, then assist the patient with these.
- Assess their current substance use (self-report, urine drug screen, examination for sedation, track marks, talk with pharmacist about how the patient has been presenting).
- If up to three doses missed, resume normal dosing.
- If four or five days missed, halve the dose. Resume previous dose over two-to-three days after daily. assessment. (increases by up to 8mg per day to previous dose).
- If more than five days missed, resume stabilisation as if the patient were starting afresh (see above).

Other considerations

> Depression and anxiety. It is best to stabilise the opioid dependence with maintenance treatment before treating the patient's mental health problems. In many cases the mental health problems can improve just by being on maintenance treatment. If mental health problems are ongoing, targeted psychological therapies or pharmacological approaches may be indicated.

> Hepatitis C if the patient has been injecting. Hepatitis C can be treated with Direct Acting Antiviral agents. Treatment can in most situations be provided through general practice. Information can be obtained from the South Australian Hepatitis SA website; https://hepsa.asn.au/about-hepatitis/hepatitis-c/treatment-hcv information can be obtained at https://www.nps.org.au/australian-prescriber/articles/managing-hepatitis-c-in-general-practice

> If pregnancy occurs during treatment, seek advice from the Drug and Alcohol Clinical Advisory Service (DACAS) on 7087 1742.

It is best for patients to stay on their maintenance treatment while pregnant.

Concurrent alcohol or benzodiazepine dependence problems. Problems with alcohol or benzodiazepine dependence can become more evident once the patient is being maintained on Suboxone®/buprenorphine-naloxone. There is an increased risk of opioid toxicity if these other substances are used as well. Information on referrals in these situations can be made via the Alcohol and Drug Information Service (1300 13 1340), the duty doctor at DASSA Central on 7425 5000 during work hours or from the 24-hour Drug and Alcohol Clinical Advisory Service on 7087 1742.

- There are only a few clinically important drug interactions with Suboxone®/buprenorphine-naloxone. Sedative effects with alcohol, benzodiazepines and other sedatives are cumulative. Suboxone® at maintenance doses will block most opioids at normal doses. Taking additional opioids when on maintenance will NOT cause a precipitated withdrawal; they just won't work very well because the μ-receptors are tightly occupied by the buprenorphine. If you have concerns about a patient's ongoing use of opioids advice can be sought from the duty doctor at DASSA Central Clinic on 8130 7500 during work hours
  or the 24-hour Drug and Alcohol Clinical Advisory Service (7087 1742 or 1300 13 1340).

- Pain problems. Suboxone®/buprenorphine-naloxone acts as a medium potency opioid. It is an effective analgesic and will often help with pre-existing pain. NSAIDs and paracetamol can be used in addition. In circumstances where additional acute pain relief is required, contact the Drug and Alcohol Clinical Advisory Service for advice on 7087 1742 or 1300 13 1340.

Other resources for advice/assistance

Drug and Alcohol Clinical Advisory Service
Tel: 7087 1742

For clinical advice from senior DASSA clinicians 24 hours a day, seven days a week.

Drugs of Dependence Unit (DDU)
Tel: 1300 652 584
Fax: 1300 658 447

(The DDU 'Guidelines for prescribing take away doses' at http://www.sahealth.sa.gov.au/drugsofdependence Under forms and resources)

DASSA Central Services
Tel: 7425 5000 (ask for Duty Doctor or Nurse), 9:00am – 5:00pm, Monday – Friday.

DASSA Northern Service
Tel: 08 7485 4600 (ask for Duty Doctor or Nurse), 9:00am – 5:00pm, Monday – Friday.

DASSA Southern Service
Tel: 8325 8111 (ask for Duty Doctor or Nurse), 9:00am – 5:00pm, Monday – Friday.

DASSA Buprenorphine/Naloxone (Suboxone®) Information

Information on understanding Suboxone® prescribing is available from the GP Program-Medication assisted treatment of opioid dependence page of the SA Health website

(To access this go to the home page of the SA Health website
→Clinical Resources
→Clinical Programs
→Drug and alcohol programs
→GP Program (Medication Assisted Treatment for Opioid Dependence).

The National Guidelines for Medication Assisted Treatment for Opioid Dependence are available on the home page of the National Drug Strategy website.

Alcohol and Drug Information Service
Tel: 1300 13 1340
8.30am to 10pm every day. Confidential telephone counsellingand information.

Hepatitis SA
Tel: 8362 8443 or 1300 437 222 (regional callers)
www.hepatitissa.asn.au/

Government of South Australia
SA Health

DRUG and ALCOHOL SERVICES SOUTH AUSTRALIA