

# 4

## Guidelines for the management of heroin withdrawal

### 4.1 Heroin withdrawal in context

#### Heroin withdrawal defined

Drug withdrawal is a substance-specific syndrome due to the cessation or reduction of heavy and prolonged drug use. This syndrome causes clinically significant distress and impairment in social, occupational, or other important areas of functioning. The characteristic features of heroin withdrawal are shown in table 6.

**TABLE 6: CLINICAL FEATURES OF THE HEROIN WITHDRAWAL SYNDROME**

<p><b>Increased sweating, lacrimation, rhinorrhoea, urinary frequency</b></p> <p><b>Diarrhoea, abdominal cramps, nausea, vomiting</b></p> <p><b>Muscle spasm leading to headaches, back aches, e.g. cramps, twitching, arthralgia</b></p> <p><b>Piloerection, pupillary dilatation, elevated blood pressure, tachycardia</b></p> <p><b>Anxiety, irritability, dysphoria, disturbed sleep, increased cravings for opioids</b></p>
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Physical symptoms generally commence 6 to 24 hours after last use, peak in severity during days two to four, and generally subside by day seven, while the psychological features of dysphoria, anxiety, sleep disturbances and increased cravings may continue for weeks or even months. Heroin withdrawal is unpleasant, though rarely, if ever, life-threatening in physically fit people. It can, however, significantly complicate concomitant medical or psychiatric conditions.

#### Objectives of withdrawal services

Heroin users present to withdrawal services for a range of reasons and motivations, and the goals of individual patients may vary considerably. Withdrawal services should not be seen as a stand-alone treatment that is likely to result in prolonged periods of abstinence, but instead as a transitional step on the long road to abstinence. Indeed, research suggests that withdrawal treatment alone has little, if any, long-term impact on levels of drug use (Mattick & Hall 1996; Vaillant 1988). Unfortunately, many patients, families, friends, and health and welfare professionals hold unrealistic expectations regarding the outcomes of withdrawal services. Many are disappointed when people in these programs either cannot give up their heroin use in the first place, or recommence regular heroin use soon after a withdrawal attempt.

<p><b>Set sensible withdrawal objectives with the patient and their carers</b></p>
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A realistic set of objectives for withdrawal services is as follows:

1. *To alleviate distress.* Palliation of the discomfort of heroin withdrawal symptoms is an important reason for patients presenting for treatment, and one of the primary aims of withdrawal services.
2. *To prevent severe withdrawal sequelae.* Although heroin withdrawal on its own is almost never life-threatening, withdrawal can present various serious problems:
  - Complication of concomitant medical or psychiatric conditions, e.g. precipitation of an acute psychotic episode in a patient with schizophrenia in remission, Wernicke's encephalopathy in alcoholics or dehydration in an individual with poor baseline nutritional status or diabetes.
  - Increased risk of overdose following withdrawal. This can occur with resumption of heroin use following the reduction in opioid tolerance that accompanies withdrawal, and due to the combined sedative effects of heroin use and medications used for the management of heroin withdrawal (e.g. benzodiazepines).
3. *To provide linkages to and enable engagement in ongoing treatment.* Withdrawal services are essentially acute services with short-term outcomes, whereas heroin dependence is a chronic relapsing condition, and positive long-term outcomes are more often associated with longer participation in treatment. Consequently, an important role of withdrawal services is to provide links with post-withdrawal services for those with other physical problems, or psychological or social needs. Optimally, they should have automatic access to drug treatment services, such as 'drug-free' counselling; naltrexone treatment; residential therapeutic communities; self-help programs; or substitution maintenance programs with methadone or buprenorphine. Managed withdrawal provides an opportunity to plan longer-term treatment and be linked to appropriate services. The boundaries between buprenorphine treatment to manage withdrawal and maintenance can be blurred — people who continue using heroin during withdrawal should be encouraged to consider transfer to maintenance treatment.
4. *To break a pattern of heavy and regular drug use.* Many patients want treatment to end their heroin use completely during the withdrawal episode, intending to stay off heroin for a set period of time afterwards. However, giving up entirely is not the goal of every patient.
5. *To get help with any other problems.* While some people will be unwilling or unable to continue in ongoing drug treatment programs, they may need — and be grateful for — contacts with welfare services (e.g. accommodation); general support and case management services (e.g. outreach workers); or primary or specialist health services.

## 4.2 Non-pharmacological aspects in the management of heroin withdrawal

As well as the use of medications (pharmacotherapy) the delivery of withdrawal services entails:

- assessment,
- treatment-matching,
- planning for withdrawal,
- supportive care, and
- linkages to services for further treatment and support.

The assessment of patients presenting for treatment was discussed in Section 2.2.

## Treatment selection

Treatment selection is a synthesis of:

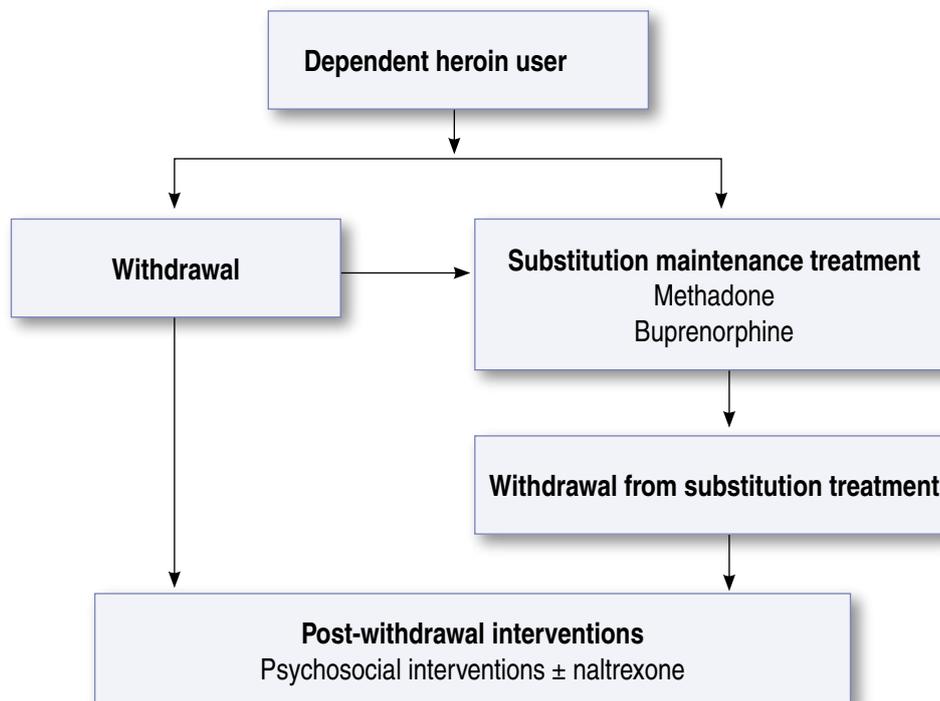
- assessment of the patient;
- examination of the available treatment options and likely outcomes; and
- negotiation with the patient around a suitable treatment pathway.

In considering possible modalities, it is important to remember that many people come for treatment with misconceptions and/or inadequate information about the two major options available. These treatment pathways for dependent heroin users are set out in Figure 2.

In general, withdrawal treatment is appropriate for those who are considering abstinence-oriented, post-withdrawal treatment (such as naltrexone, residential rehabilitation programs, counselling or 12-step programs), or for those who are not interested in longer-term treatment, and merely want a 'break' from dependent heroin use.

However, maintenance substitution treatment (with methadone or buprenorphine) may be more appropriate for those with significant heroin dependence who will not accept residential rehabilitation or naltrexone treatment, but nevertheless want to stop or permanently reduce their heroin use and all the damage it is causing them.

**FIGURE 2: TREATMENT PATHWAYS FOR DEPENDENT HEROIN USERS**



Clinical decision-making should have an evidentiary basis, and patients should be presented with the relative evidence, i.e. the merits and the limitations of treatment outcomes associated with each approach. Within such a framework, there is widespread evidence suggesting that maintenance substitution remains the 'gold standard' treatment for most people with chronic heroin dependence, by virtue of its success in keeping patients in treatment, and reducing drug-related harms.

Once it is established that withdrawal is to be attempted, consideration must be given to the services needed to achieve the best outcome. An optimal setting and adequate supports should be found for each patient, and monitoring arranged for their personal requirements and medication needs.

## The optimal setting for withdrawal

Withdrawal can occur in a continuum of settings, ranging from intensive residential (e.g. inpatient withdrawal unit or hospital) to outpatient (e.g. ambulatory or home-based withdrawal services). Most heroin withdrawal attempts can occur in outpatient settings, usually with the assistance of a general practitioner, alcohol and drug worker, or other health professional. However, there are circumstances where a residential setting is indicated (see Table 7).

Some patients may wish to persevere with an outpatient withdrawal, despite unsuitable home environments or having repeatedly 'failed' as outpatients before. Such attempts at outpatient withdrawal may still be appropriate, however clinicians should first negotiate with their patient some mutually agreed criterion of failure (e.g. no significant progress within a week) at which point consideration of a switch will be made to an alternative treatment pathway.

**TABLE 7: COMPLEX PRESENTATIONS REQUIRING RESIDENTIAL WITHDRAWAL SERVICES**

<b>Criteria for intensive residential settings (e.g. inpatient withdrawal unit)</b>
<ul style="list-style-type: none"> <li>• Unstable medical / psychiatric condition;</li> <li>• Polydrug dependence and withdrawal from multiple drugs;</li> <li>• History of medical or psychiatric conditions, or past drug use, uncertain or indicate a need for close monitoring.</li> </ul>
<b>Criteria for supported residential setting (e.g. community withdrawal unit)</b>
<ul style="list-style-type: none"> <li>• Unsupportive home environment, such as with other drug users, or without anyone reliable to supervise and support the patient;</li> <li>• Repeated failure at outpatient withdrawal.</li> </ul>

## Getting organised for withdrawal

Residential withdrawal settings generally provide the full range of services needed for a withdrawal episode. They set out to be drug-free, with support available from staff and fellow patients, and the capacity for continuous monitoring. They usually have access to medical staff and medications. Patients on a waiting-list may need short-term support in the interim.

Commencing an outpatient withdrawal requires planning, and the mobilisation of the necessary supports and services. Patients should prepare themselves and their environment in advance, to maximise their chance of 'success'. For example, it is very hard to get through withdrawal in the company of others still using heroin.

**A safe environment should be organised at the beginning of the withdrawal episode.**

A 'safe' place is one where there won't be any drugs easily accessible, and where patients will not be confronted by other drug users. It is important to have caring people to support a patient during withdrawal, and these support people themselves need guidance and information about the process, and suggestions as to what they can reasonably do to help.

## Supportive care

Patients need information regarding:

- the nature and duration of withdrawal symptoms;
- strategies for coping with symptoms and cravings;
- strategies to remove high-risk situations;
- the role of medication.

Patients often have limited concentration during withdrawal, and information may have to be repeated, perhaps even re-phrased, to be fully understood and absorbed. Written information is valuable in these circumstances, and is also recommended to support patients and their relatives people (contact the local drug and alcohol authority for relevant literature).

Counselling during the withdrawal episode should be aimed specifically at supporting the patient through problems associated with withdrawal and in facilitating post-withdrawal links.

Many patients will want to deal with a range of personal, emotional or relationship problems during the withdrawal episode, but they should be persuaded to defer all this until later. Attempting to work through such issues will almost certainly be emotionally painful and anxiety-provoking, which just intensifies cravings and withdrawal and puts the whole withdrawal program in jeopardy. Furthermore, patients in withdrawal tend to be irritable, agitated, tired and run-down; they can suffer from mood swings and poor sleep patterns, as well as having difficulty in concentrating. This is definitely not the optimal frame of mind in which to try to solve significant, long-standing life problems. Assure your patients that you understand that they have many important issues to work through to get their lives together again, but it is best to take one step at a time. There will be opportunities for these wider problems to be addressed as part of their ongoing rehabilitation after they get through withdrawal. On the other hand, crisis intervention may be required during a withdrawal episode to ensure adequate accommodation, food or other urgent welfare issues.

In addition to supportive counselling from health professionals and the support of family, friends and peer workers, heroin users may also benefit from 24-hour telephone counselling services for help when others are unavailable. Each state in Australia has telephone alcohol and drug services (see Appendix 2).

## Monitoring

An important part of withdrawal services is regular and frequent monitoring, to check:

- general progress;
- drug use;
- response to the medication(s);
- severity of withdrawal symptoms (which can be facilitated by the use of withdrawal scales);
- complications or difficulties;
- ongoing motivation levels.

Doses of medication can then be adjusted according to the patient's progress. It is recommended that patients undergoing outpatient withdrawal be reviewed by a health professional (e.g. alcohol and drug worker, general practitioner, or experienced pharmacist) **at least daily** during the first few days of treatment.

## Scales for assessing opioid withdrawal

There are various opioid withdrawal scales available to refer to. Subjective scales are far more sensitive to changes in withdrawal severity, and are better predictors of patient outcomes. Objective scales are not only less sensitive, but usually need to be administered by a health professional. They may nevertheless be useful in corroborating subjective ratings, particularly in individuals who are thought to be over- or under-rating their withdrawal severity. Copies of several scales that are commonly used in Australia and overseas are provided in Appendix 3.

## 4.3 Overview of buprenorphine in the management of heroin withdrawal

### Efficacy of buprenorphine compared to other withdrawal medication regimes

A systematic (Cochrane) review (Gowing *et al.* 2006) of controlled trials found that:

- buprenorphine is more effective than clonidine in ameliorating withdrawal signs and symptoms, and is associated with a significantly higher rate of completion of treatment;
- there appears to be no significant difference between buprenorphine and tapered methadone in terms of completion of treatment, but withdrawal symptoms may resolve more quickly with buprenorphine.

These conclusions applied to both inpatient and outpatient settings.

### Buprenorphine for the management of withdrawal in the medically ill

Uncontrolled studies have reported favourably on the use of buprenorphine for the management of heroin withdrawal in medically-ill patients (Parran *et al.* 1994). One randomised controlled trial found buprenorphine to be as effective as clonidine and methadone for the short-term management of withdrawal in heroin-dependent HIV-infected patients hospitalized for medical reasons on an inpatient AIDS unit (Umbricht *et al.* 2003). These studies suggest buprenorphine is of potential value in the management of withdrawal in the medically ill. Furthermore, the sublingual preparation is well suited to individuals who cannot tolerate oral medications. Caution should be used in using buprenorphine or other opioids in individuals with certain medical conditions (see Section 2.1).

### The role of buprenorphine in withdrawal

The aim of medication in withdrawal is the reduction of withdrawal symptoms and cravings; it is not the complete removal of all symptoms. The clinician should discuss patients' expectations of the medication with them, and address any misconceptions.

In particular, the following principles regarding doses should be understood by the patient:

- Buprenorphine doses that are too high can result in increased rebound withdrawal, prolonged duration of symptoms, increased side-effects, and increased cost of the medication.
- Alternatively, use of doses that are too low can result in unnecessary withdrawal discomfort, continued heroin use and treatment drop-out.

- Continued heroin use or cravings may not be due to inadequate doses of medication. For example, patients who continue to associate with other heroin users, and are present when others are acquiring or using heroin, can expect to have cravings regardless of their dose of buprenorphine.
- Buprenorphine will not reduce symptoms of withdrawal, or cravings, related to the use of non-opioid drugs.

## Preventing precipitated withdrawal on commencing buprenorphine

Buprenorphine can precipitate opioid withdrawal in someone who has recently used heroin (within the past 6 hours), slow-release oral morphine (within the past 12 hours) or higher doses of methadone (See Section 3.2). Buprenorphine-precipitated withdrawal typically commences one to four hours after the first buprenorphine dose, is generally mild to moderate in severity, and lasts for up to 12 hours. Patients experiencing severe discomfort may benefit from symptomatic withdrawal medication (e.g. clonidine 0.1mg, 3 to 4 hourly as required), and should be directed to see their prescribing doctor.

Patients should not receive the first dose of buprenorphine if they are experiencing heroin effects. It is preferable to withhold the first dose until the patient is beginning to experience the early features of withdrawal. Typically this will occur six hours or more after their last use of heroin. If there are doubts or concerns, the patient should be asked to come back for dosing later in the day, or alternatively, a lower initial dose can be dispensed (e.g. 2 or 4 mg) as it is less likely to precipitate significant withdrawal than a high initial dose.

### Preventing precipitated withdrawal on commencing buprenorphine

**No heroin for at least 6 hours: severe discomfort may need palliation.**

**No methadone for at least 24 hours.**

**No buprenorphine if there are obvious heroin effects: wait for early withdrawal signs, or send away to return next day.**

## Use of ancillary medications in conjunction with buprenorphine

Buprenorphine provides general relief of withdrawal symptoms, so that other symptomatic medications for opioid withdrawal are not routinely required. An exception is when patients experience difficulty sleeping during withdrawal, and may benefit from the limited use of benzodiazepines as a hypnotic. Benzodiazepines should not be used routinely from the outset of the withdrawal episode. Where sleep is a problem, it is safer to increase the dose of buprenorphine than to prescribe benzodiazepines, with non-pharmacological approaches being encouraged (sleep hygiene strategies). Non-pharmacological methods may not have an instant effect on sleep, but if continued for days to weeks such strategies will help establish normal sleep patterns.

## Continued use of heroin and other drugs

Patients who keep on using heroin during buprenorphine treatment may have difficulty stabilising on the medication, and may continue to experience features of precipitated withdrawal after each dose.

Persistent features of precipitated withdrawal discomfort may be grounds for transfer to methadone, or other withdrawal medications.

**The unsupervised use of other sedative drugs, such as benzodiazepines, alcohol, other opioids, tricyclic antidepressants, and sedative antipsychotics in combination with buprenorphine, can be extremely dangerous, resulting in respiratory depression, coma and death.**

All patients should be informed verbally and in writing of these risks, and this advice documented in the clinical records. Intoxicated patients should not be dosed with buprenorphine or sedative medications.

## 4.4 Buprenorphine regimens in outpatient withdrawal settings

Buprenorphine is long-acting, and so is well suited to outpatient withdrawal settings, allowing for once-a-day supervised dosing.

**Take-away doses are not recommended during the initial treatment period, and are subject to jurisdictional regulations.**

Patients unable to attend an authorised pharmacy daily for supervised dispensing should consider alternative withdrawal medications.

There is no conclusive evidence of an optimal buprenorphine dosing regime for heroin withdrawal. In general, daily buprenorphine doses of 4 to 16 mg appear to be most effective in reducing withdrawal severity and heroin use (Gowing *et al.* 2006).

Induction onto buprenorphine for the purposes of detoxification should follow the same principles as for buprenorphine maintenance. Reductions of the buprenorphine dose should not be commenced until the patient has received a dose that virtually abolishes withdrawal symptoms for 24 hours.

Some flexibility in doses is allowable to accommodate a range of factors, such as amount of heroin use and psychological condition, which may impact on each patient's individual dosing requirements and withdrawal severity.

Review by a trained health professional is recommended on a daily basis during the first few days of the withdrawal regime. This is important so that doses can be adjusted, if necessary, and any difficulties being experienced on the medication can be addressed. It is also needed to ensure provision of appropriate support, care and monitoring.

**Buprenorphine doses should be titrated against severity of withdrawal features and cravings for heroin use, actual use of heroin or other drugs, and occurrence of side-effects and intoxication.**

Doctors may choose to prescribe a fixed daily dose (e.g. Day 1: 6 mg, Day 2: 8 mg, Day 3: 10 mg etc) or, alternatively, prescribe a flexible regime with upper and lower limits on any particular day and instructions for the pharmacist or withdrawal worker regarding dose titration (e.g. Day 1: 6 mg, Day 2: 6–10 mg; Day 3: 8–12 mg etc).

The planned duration of withdrawal treatment should be guided by the patient. Most commonly the duration of buprenorphine administration will be between five and 20 days.

Longer-term reduction regimes (over 2 to 3 weeks) permit more time for relapse prevention and after-care planning, but there are good reasons for preferring a short-term withdrawal regime (4 to 5 days) and not prolonging buprenorphine treatment:

- Administration of buprenorphine for more than several days may be associated with rebound withdrawal when ceased (Lintzeris 2002). Such rebound withdrawal typically starts one to three days after the last dose of buprenorphine, and peaks two to five days after the last dose, with some symptoms persisting for several weeks.
- Prolonged, probably unsuccessful, attempts at withdrawal can be demoralising for the patient, resulting in lowered capability, self-esteem, and/or confidence in the treatment provider. For this reason, a limit on the time spent on a gradual reduction regime should be discussed with the patient early in the program.

A formal review of progress should be scheduled partway through an outpatient withdrawal program. At the time of the review, those patients who remain ambivalent about long-term post-withdrawal treatment, and who have not been able to cease their heroin use, may need referral to an inpatient supervised withdrawal program. Alternatively, an extension of the withdrawal regime over several weeks may be warranted.

Longer-term maintenance substitution treatment (with buprenorphine or methadone) should be recommended to patients who:

- cannot stop, or markedly reduce, their heroin use during the withdrawal episode;
- relapse into regular heroin use as the dose of buprenorphine is reduced or ceased;
- do not feel confident about maintaining abstinence but do not want to relapse to dependent heroin use and the associated harms.

It is recommended that such patients stabilise on a maintenance substitution medication for a longer period of time before coming off their maintenance treatment, to give them the opportunity to first distance themselves from heroin use and possibly to address any problematic psychological and social issues which may be affecting them.

## 4.5 Buprenorphine for heroin withdrawal in residential settings

Buprenorphine is well suited to use in inpatient withdrawal settings, given its ability to alleviate the discomfort of withdrawal symptoms without significantly prolonging their duration.

**It is recommended that an interval of at least two to three days be available from the time of the last buprenorphine dose to the time of planned discharge**

Duration of dosing will be determined by the length of admission available. e.g. in a 7-day admission, treatment will be limited to the first 4–5 days.

Approaches to dispensing in inpatient settings will depend on the level of supervision and staffing available. Titration regimes generally require nursing staff who can administer withdrawal scales and S8 medications, so places with limited access to nursing staff may be better suited to fixed regimes with the option of additional ‘rescue’ doses as required.

The additional rescue doses should only be administered :

- at least 4 hours after the earlier dose; and
- if the patient is experiencing moderate or severe withdrawal discomfort.

Buprenorphine doses in inpatient settings can generally be lower:

- outpatient regimes must accommodate higher cravings and exert blockade effects;
- outpatient regimes are generally limited to once-a-day dosing.

An evening dose (between 5pm and 10pm) is recommended, to allow relief of withdrawal symptoms until the morning. Note: buprenorphine should not be administered if there are any features of intoxication or sedation.

The following regime (Lintzeris 2002) is recommended for an admission time of approximately one week, and can be tailored accordingly:

**TABLE 8: PROPOSED INPATIENT WITHDRAWAL REGIME**

Day	Buprenorphine S/L tablet regime	Total daily dose
Day 1	4 mg at onset of withdrawal, & additional 2 to 4 mg evening dose prn	4 to 8 mg
Day 2	4 mg mane, with additional 2 to 4 mg evening dose prn	4 to 8 mg
Day 3	4 mg mane, with additional 2 mg evening dose prn	4 to 6 mg
Day 4	2 mg mane prn; 2 mg evening prn	0 to 4 mg
Day 5	2 mg prn	0 to 2 mg
Day 6	no dose	
Day 7	no dose	
	Total proposed dose	12 to 28 mg

This regime serves as a guide only, and considerable individual variation in withdrawal severity and medication requirements should be expected.

Post-withdrawal options should be explored prior to discharge (see next section).

- Naltrexone: Patients commencing naltrexone treatment should do so during their admission.
- Buprenorphine: Patients wishing to commence buprenorphine maintenance treatment should continue their buprenorphine as inpatients until transfer to a community-based provider can be organised.

## 4.6 Transition to post-withdrawal treatment

### Naltrexone treatment

This section considers commencement of naltrexone after a short period of use of buprenorphine (less than 10 days) to manage withdrawal from heroin. Commencement of naltrexone after cessation of buprenorphine maintenance treatment is discussed in section 3.10. Refer to the clinical guidelines on the use of naltrexone (Bell *et al.* 2003) for treatment of opioid dependence for information on patient selection, and management once on naltrexone.

The simplest approach is to wait five to seven days after last dose of buprenorphine before commencing naltrexone. Precipitation of withdrawal by naltrexone is unlikely following a 7-day opioid-free period (Bell *et al.* 2003). However, the pharmacology of buprenorphine does enable the commencement of naltrexone earlier than this (Umbricht *et al.* 1999). Naltrexone commenced early in the course of heroin withdrawal managed with buprenorphine (day 2 or 3 after cessation of heroin while buprenorphine still being prescribed) will result in increased severity of withdrawal on the day of the first dose of naltrexone, but may reduce the duration of withdrawal. This approach is best undertaken in an inpatient or intensive day-care setting that is able to respond to serious withdrawal symptoms if they occur.

A third option is to commence naltrexone 2 to 5 days after cessation of a brief course of buprenorphine for management of heroin withdrawal. This is likely to be associated with mild to moderate precipitated withdrawal. It is best undertaken in an inpatient or day care setting with the ability to respond to severe withdrawal if it were to occur.

### Which procedure is best?

Administration of naltrexone within five days of stopping buprenorphine use is likely to result in opioid withdrawal following the first dose of naltrexone. This typically commences 90 minutes to 4 hours after the first naltrexone dose, peaks around 3 to 6 hours after the naltrexone dose, and generally subsides in severity within 12 to 24 hours. The withdrawal is frequently experienced as moderate to severe at its peak. Subsequent doses of naltrexone produce considerably less severe withdrawal discomfort.

Most patients undergoing this procedure request symptomatic medication, and clonidine (0.1–0.15 mg every 3 to 4 hours as required) and a benzodiazepine (e.g. diazepam 5mg, 3 to 4 hourly, maximum of 30 mg in a day, as required) should be prescribed.

Most patients find either procedure tolerable. All patients need supervision and access to the prescribing doctor.

#### PREPARE THE PATIENT IN ADVANCE

**for the increase in withdrawal severity, the role of medications,  
and the risks of using heroin to overcome the withdrawal symptoms.**

