Substance Withdrawal Management

Guidelines for medical and nursing practitioners in primary health, specialist addiction, custodial and general hospital settings
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in primary health, specialist addiction,
custodial and general hospital settings
Acknowledgements

The main authors of this guideline were Ashley Koning, Michelle Fowler, Moira Gilmour and Vanessa Caldwell. Contributions by the members of the Matua Raḵi team and the Withdrawal Management Reference Group were greatly appreciated.

The Substance Withdrawal Management Guidelines for medical and nursing practitioners in primary health, specialist addiction, custodial and general hospital settings have in large part been based on the New South Wales Department of Health’s: Drug and Alcohol Withdrawal Clinical Practice Guidelines. Matua Raḵi is grateful for the generosity of the NSW Department of Health in allowing their original material to be adapted for use in the New Zealand context. Matua Raḵi is also grateful to Dr Fraser Todd and the Ministry of Health for permission to use a substantial excerpt from Te Ariari o te Oranga: the Assessment and Management of People with Co-existing Mental Health and Substance Use Problems, Todd 2010.

This guideline is one of a series that have been developed to provide information about safer withdrawal management. Each set of guidelines is tailored to the information needs of a particular audience. They have been designed to provide readily accessible and appropriate information for the specialist addiction sector, the general addiction and allied workforces or for people who use substances and their family, whānau and support people.

This guideline was developed with support from the New Zealand Ministry of Health and funding from the Methamphetamine Action Plan following the Cabinet Briefing paper 2009.

Disclaimer

The opinions expressed herein are the views of the authors and do not necessarily reflect the official position of the Ministry of Health.

The guidelines in this document should not be considered exhaustive, exclusive or substitutes for individualised care and treatment decisions.

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Foreword

Tēnā koutou, Kia orana, Fakaalofa lahi atu, Taloha ni, Talofa lava, Malo e lelei, Ni sa bula vinaka, Nameste, Talofa.

I am pleased to endorse the Substance Withdrawal Management: Guidelines for medical and nursing practitioners in primary health, specialist addiction, custodial and general hospital settings.

The Ministry requested that Matua Raķi provide this guidance document in order to promote safe care for people who experience withdrawal from a range of substances. This development has also been in response to calls for practical withdrawal management guidelines tailored to the New Zealand context. The formation of these guidelines has drawn from a range of similar material from Australia and the United States as well current New Zealand research.

This document has been developed for use in a range of settings where clinicians and practitioners work with people who are likely to suffer from voluntary or involuntary withdrawal symptoms after cessation of substance use.

I believe these guidelines will be an important and useful resource for frontline workers, including those in Mental Health Services, the New Zealand Police, Department of Corrections, Emergency Departments and other hospital wards and units, General Practitioners, Primary Health care workers and the specialist addiction treatment sector of Aotearoa New Zealand.

Dr David Chaplow
Director of Mental Health
Ministry of Health
July 2011
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Withdrawal Management

In the context of addiction treatment ‘withdrawal’ is used to describe the process and the acute symptoms, physical and psychological, that can accompany the cessation or reduction of use of any substance that has been used regularly over a prolonged period of time.

The purpose of ‘withdrawal management’ is to ensure the safety of the person, and others, as they stop or reduce substance use, and where possible to address withdrawal symptoms to alleviate acute distress. Appropriate withdrawal management planning depends on an accurate assessment of the person’s:

• patterns of substance use; what, how much, how often and last use
• withdrawal risks, risks to self and others, history of withdrawal
• co-existing problems; mental and physical health
• support systems; family, whānau and friends
• motivation; goals and resilience
• setting safety
• external sources of stress

It may be necessary to provide withdrawal management in a wide range of settings, from the person’s own home to general practice, general hospitals, police cells and prisons. Many people will stop or reduce substance use by choice while others will have this imposed on them through admission to hospital or prison. In the latter two situations people may not disclose substance use or may not be aware of the risk of withdrawal themselves. This can also be true when people present in a general practice or a general hospital setting. To provide appropriate care clinicians across a range of disciplines will need to be able to recognise the features of withdrawal from a range of substances and tailor responses accordingly.

Assessment

When a person presents to an addiction service requesting help with stopping using a substance or substances the first step is to identify the substances used and assess immediate risk, i.e. does the person have withdrawal symptoms and what risks are associated with this. If the person is not at immediate risk and is not intoxicated a comprehensive assessment should be carried out. This will provide the information needed to develop a treatment plan that suits the needs and situation of that person, including a plan for withdrawal management if needed. A comprehensive assessment generally includes:

• presenting issues
• detailed substance use history and patterns of substance use over time
• current substance use including; frequency, amounts, how used and last use
• impact of substance use and risk taking behaviour
• evidence of withdrawal, historical and current
• what the person identifies as problematic, if anything, about their substance use and their goals for treatment
• gambling history
• developmental history, family and whānau background and relationships, parenting responsibilities
• current living circumstances
• family and whānau substance use history and physical and mental health history
• cultural assessment and formulation, social connectedness and needs
• education and employment history
• history of trauma; physical, emotional and psychological
• physical health history and current issues and medication, noting any traumatic brain injuries (TBI), blood borne virus history and risks, and results of cognitive screening
• mental health history with current mental health status and medication
• forensic history and current or pending justice involvement
• risk assessment; self harm and harm to others including safety of children
• diagnoses
• formulation of issues
• treatment goals
• a negotiated treatment or management plan

Risk assessment and management

Risk assessment is an integral part of assessment and ongoing treatment. Depending on the substance or substances the person has been using there are specific risks to the person and or others that are associated with withdrawal. Risks include:

• exacerbation of co-existing mental health problems
• exacerbation of co-existing physical health problems
• low mood and suicidality
• anxiety and panic attacks
• irritability and anger
• aggression
• disturbed sleep and insomnia
• confusion
• dehydration due to vomiting and or diarrhoea
• elevated blood pressure
• arrhythmias
• delusions and psychosis
• hallucinations
• brain damage
• seizures
• death

In the context of withdrawal management it is important to assess the risk to the person and or others of supporting the person through the withdrawal process in their own home, in a social detoxification and withdrawal management facility or in a hospital setting. The great majority of people going through withdrawal can be supported through the process, with or without medication, in the community or in their own home. The decision to admit the person into a social detoxification and withdrawal management facility or a hospital depends very much on the outcome of the risk assessment and the degree of support the person would have available to them in the community.

Where withdrawal management is carried out in the community the issue of safety to operate a motor vehicle must be addressed with the person. People need to be advised that the physical and or psychological effects of substance withdrawal may make it unsafe for them to drive. Where people are prescribed medication as part of withdrawal management they should be strongly encouraged to not drive a vehicle at all while on medication. The continuation of withdrawal management and or medication should be reviewed if people fail to follow this advice. In situations where it is apparent that people are continuing to drive a motor vehicle while impaired or potentially impaired, either by withdrawal effects or medication, it may be necessary to inform the Police or New Zealand Transport Agency of the risks to the community of the person driving. The person planning on undertaking a managed withdrawal should be informed of these possible outcomes prior to embarking on the process.

For a more detailed description of a model of assessment refer to Screening, Assessment and Evaluation (alcohol and other drug, smoking and gambling), Matua Rakí 2011, and Te Ariari o te Oranga: the Assessment and Management of People with Co-existing Mental Health and Substance use Problems, Todd 2010.

Where the person is in acute withdrawal, and it is inappropriate to carry out a full comprehensive assessment, effort should be made to identify:
• recent substances used and how used
• last use
• current withdrawal symptoms
• current co-existing problems
• current risks and safety
Specialist addiction services may also carry out a range of physical examinations that could include:

- breathalysing the person for alcohol
- saliva testing to screen for recent substance use
- urine drug screening
- blood tests screening for physical impact and or confirmation of substance use
  - GGT
  - LFT
  - AST
  - MCV
  - FBC
  - CDT
  - Folates
  - Vit B12
  - Glucose
  - Electrolytes and Urea
  - Magnesium and Potassium
- blood testing for blood borne viruses
  - HBV
  - HCV
  - HIV
- taking blood pressure
- taking pulse
- checking for injection sites
- physical examination
- neuropsychological assessment/screening

**Co-existing problems**

The presence of co-existing problems can make the withdrawal process more distressing and risky for people who stop or reduce substance use. Practitioners will need to be aware of potential problems and adapt treatment to manage significant risks and possible consequences beforehand. Where people are prescribed medication for co-existing problems particular care needs to be taken when also prescribing medication for withdrawal management as some
medications may inhibit or enhance each other’s effects. This also includes some foodstuffs and complementary or natural therapies. Refer to Appendix 7 (from Todd, 2010) for a guide to some known and potential drug-drug and drug-medication interactions. Also see resources section for links to online sites to complement the information in Appendix 7. Where no interactions are indicated, it is wise to check multiple sources as no one source can be exhaustive or completely up to date.

Practitioners and clinicians will also need to be mindful of the existence of chronic pain problems through the withdrawal process. These may be pre-existing and could have contributed to the development of substance dependence or could emerge during withdrawal. In planned withdrawal management documented chronic pain problems need to be treated in consultation with pain specialists to reduce the chances of causing distress or undermining the withdrawal management process.

Ongoing monitoring of co-existing problems is necessary to further reduce risk and enhance likelihood of a successful withdrawal process. It is possible that ongoing substance use has masked a co-existing disorder that can emerge in withdrawal and require appropriate treatment.

Co-existing problems of particular concern during the withdrawal process include:

- depression
- bi-polar affective disorder
- anxiety
- psychosis
- borderline personality disorder
- conduct disorder
- anti social personality disorder
- neurological disorders
- brain injuries
- chronic pain
- malnutrition
- gastrointestinal disorders
- infection
- liver disorders
- cardiac disorders
- epilepsy
- respiratory disorders
Special populations

Older people
It is important to take into account that older people metabolise medication less effectively and drug accumulation can be common with regular use, especially with the longer acting benzodiazepines. Because of this older people can potentially experience benzodiazepine toxicity during withdrawal using diazepam. When supporting withdrawal in older people this risk requires close monitoring and possible adjustment of benzodiazepine doses and or choice of benzodiazepine. Diazepam can be replaced with clonazepam or oxazepam, neither of which have active metabolites and are therefore less likely to accumulate to toxic levels.

Young people
Most young people going through substance withdrawal can be safely managed in the community unless there are significant concerns relating to their mental health or other safety issues. Young people are developmentally more likely to be impulsive and reactive and the psychological impact of withdrawal may trigger depression and or suicidality.

Where available, referral to a specialist service for young people is recommended to help with withdrawal management for those young people presenting with severe dependence. Admission to an inpatient or residential setting may be necessary to assist the young person to manage withdrawal symptoms safely, especially if there are concerns around self harm and suicidality. Medication should be avoided unless necessary to safely manage increasing low mood, agitation, anxiety and aggression. Consultation with an addiction medicine specialist, physician or psychiatrist is recommended.

Pregnant women
Pregnant women may precipitate withdrawal when they realise they are pregnant and abruptly stop using substances. Abrupt cessation of substance use, especially CNS depressants, during pregnancy can carry significant risks for the foetus. This is particularly true in the first and third trimesters of pregnancy. Risks include infant mortality, miscarriages and low birth weight.

Secure facilities and prison inmates
Admission into a secure facility or incarceration with no access or very limited access to substances can precipitate involuntary withdrawal. The combination of loss of freedom and substance withdrawal can compound mood disorders and the risk of self harm and suicidality. Medical and nursing practitioners in secure facilities and prisons need to be aware of the possibility of people presenting in acute withdrawal and manage the symptoms safely. At times it can be difficult to distinguish between withdrawal and some mental health disorders and careful assessment and monitoring is needed to decide on an appropriate treatment plan.
Withdrawal management settings

Community home based withdrawal management

Many addiction services offer a community based home detoxification and withdrawal management service. This involves specialist addiction practitioners visiting people in their own home during the acute withdrawal period to provide supervision, encouragement, support and medication as needed. Along with an assessment of specific withdrawal risks addiction practitioners also assess the appropriateness of the person’s supports, their physical environment and general safety. When people have responsibility as a carer, either for children or dependent adults, negotiating alternative care arrangements for the duration of the managed withdrawal may be necessary. When withdrawal management is carried out in the community addiction practitioners visit people in their own homes as often as needed during acute withdrawal. When medication is used as part of withdrawal management this is supervised by specialist detoxification nurses. Addiction medicine specialists, physicians or psychiatrists are available for consultation as needed.

Social or respite service based withdrawal management

Social or respite detoxification and withdrawal management services are located in the main centres and provide a safer, supervised environment away from community and peer influences. Staff members are available for support and encouragement twenty four hours a day. Specialist nursing and medical staff members are available on call for consultation.

Social withdrawal management beds

The Government’s tackling methamphetamine initiative has made available thirty beds in residential treatment services nationally to assist those with methamphetamine dependence to have time out as a one-off opportunity or a lead-in to residential treatment.

Hospital based withdrawal management

Hospital based detoxification and withdrawal management is appropriate for people with severe problematic dependent substance use and or complicating factors. This includes:

- co-existing mental health problems
- other substance use
- a history or high risk of withdrawal related seizures
- a history or apparent withdrawal related complications such as dehydration
- co-existing physical health problems
- risks to the individual or community
Alternative and complementary therapies

There is no reliable evidence to support the use of natural alternatives or complementary therapies for use in managing substance withdrawal. However as an adjunct to withdrawal management some addiction services support the use of:

- acupuncture
- massage
- aromatherapy
- yoga
- vitamin, mineral and herbal supplements
- homeopathic remedies

Useful dietary supplements include:

- B Group Vitamins, especially high dose B1, B3 and B6
- vitamin C
- zinc
- magnesium

Products helpful for stress reduction, relaxation and sleep assistance include:

- DL-Phenylalanine
- valerian
- kava
- Rescue Remedy (homeopathic remedy)
- natural melatonin (tart cherry)

Products potentially helpful for nausea and vomiting include:

- ginger, Nux Vomica or Vomiplex (homeopathic remedies)
- peppermint

Products possibly helpful for joint pain include:

- calcium
- fish oils
- flax seed oil
- magnesium

Complementary therapies should not be used as an alternative to a planned and managed withdrawal process as the risks of doing so include:

- progression to severe withdrawal
- risk of injury to self and others due to altered mental state
- risk of dehydration or electrolyte imbalance
- seizures
- the person having a co-existing illness that is masked or mimicked by withdrawal
- accidents due to side effects such as hypotension

**Rongoā Māori**

Rongoā Māori has been described as a holistic range of approaches to health and well being that traditionally included “ritenga and karakia (incantations and rituals involved with healing), rongoā (physical remedies derived from trees, leaves, berries, fruits, bark and moss), mirimiri (similar to massage/physiotherapy), wai (use of water to heal), and surgical interventions.” (Ahuriri-Driscoll et al., 2008).

At times Kaupapa Māori health services and some tangata whaiorea undergoing withdrawal might want to utilise mirimiri, Rongoā and karakia to improve general health and well being, and to relieve distress and withdrawal symptoms. Being supportive of these techniques may help engagement and complement the process of withdrawal management. Supporting the use of traditional therapies may also help with engaging whānau or family who may wish to support tangata whaiorea through acute and protracted substance withdrawal.

For a description of Rongoā Māori and more detail of Rongoā rākau, or plant remedies, that may have potential applications in withdrawal management:
Alcohol
Alcohol

These guidelines have been developed to assist nursing and medical practitioners to identify alcohol withdrawal symptoms and to provide safe withdrawal management strategies for people who are dependent.

The active ingredient in alcohol is ethanol, also called ethyl alcohol. Ethanol has depressant effects on the central nervous system.

Alcohol enhances the action of 5-HT and acetylcholine at 5-HT3 and nicotinic acetylcholine receptors, increasing excitatory neurotransmission at these receptors. Acute alcohol exposure can also inhibit the action of NMDA and kainite at glutamate receptors, inhibit voltage-sensitive Ca2+ channels and enhance the action of GABA at inhibitory GABA A receptors.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific alcohol use history also includes:

- type and strength (% alcohol per volume) currently using
- time of last drink
- average number of standard drinks (STD’s) a day over time
- any drinking soon after waking
- needing to control shakes by using alcohol
- past history of seizures
- past history of hallucinations
- co-existing physical health problems
- current goals relating to use

Alcohol withdrawal

In mild withdrawal the only evidence of physiological withdrawal symptoms may be one to two days of sleep problems and mild irritability.

In people who are more severely alcohol dependent symptoms of withdrawal may be felt before their blood alcohol level reaches zero. This can follow abrupt cessation or a marked reduction in consumption levels. Withdrawal symptoms can occur within a few hours of their last use of alcohol as blood plasma levels fall, triggering the consumption of alcohol to relieve symptoms.
Early morning drinking occurs in some cases as the person is woken in the night by withdrawal symptoms.

Alcohol withdrawal can be associated with significant health risks and early identification of symptoms using the CIWA-Ar tool (Appendix 1) along with prompt tailored treatment reduces complications and the duration of withdrawal.

Withdrawal from commercially available methylated spirits, which has not contained methanol since 2007, should be dealt with as with alcohol. If the person has been using high concentration industrial methanol for a period of time it will be necessary for them to be stabilised on alcohol for two or three days prior to initiating a planned withdrawal.

**Figures:** Progress of alcohol withdrawal from time of last drink

Figure 2: Symptoms of alcohol withdrawal:

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<th>Moderate</th>
<th>Severe</th>
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<tr>
<td>restlessness</td>
<td>poor concentration</td>
<td>hallucinations</td>
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<tr>
<td>irritability</td>
<td>impaired memory and judgment</td>
<td>delusions</td>
</tr>
<tr>
<td>anxiety</td>
<td>increased sensitivity to sound, light, and tactile sensations</td>
<td>grand mal seizures</td>
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<tr>
<td>agitation</td>
<td>tremor (shakiness)</td>
<td>hyperthermia (high fever)</td>
</tr>
<tr>
<td>sleep problems</td>
<td>elevated heart rate</td>
<td>delirium with disorientation</td>
</tr>
<tr>
<td>intense dreaming, nightmares</td>
<td>increased blood pressure</td>
<td>fluctuation in level of consciousness</td>
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<td></td>
<td>anorexia</td>
<td>problems with eye movements</td>
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<td></td>
<td>nausea, vomiting</td>
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Daily consumption less than 8 standard drinks a day

Daily consumption between 8 and 15 standard drinks a day

Daily consumption more than 15 standard drinks a day

Features of complicated withdrawal

Hallucinations
- occur in 25% of people with severe alcohol dependence
- are generally more common in the first 48 hours but can occur up to day five
- are usually visual and tactile and are occasionally auditory
- can occur while the person is still orientated without delirium

Seizures
- occur in 15% of people with severe alcohol dependence
- risk increases to 70% if person has had a previous withdrawal seizure
- generally occur within the first 48 hrs
- are the 'grand mal' type of seizure
- are usually one or few in number

Note: Other potential causes of seizure should always be considered. These include:
- associated idiopathic epilepsy
- hypoglycaemia
- hypocalcaemia
- hypomagnesaemia
- subdural haematoma
**Delirium tremens (DTs)**

Delirium tremens is the most severe form of alcohol withdrawal syndrome and is a medical emergency. In people who are severely dependent delirium tremens typically occurs after two to five days of untreated severe withdrawal syndrome, though mild or moderate withdrawal symptoms may not precede delirium tremens.

Features include:

- fluctuations in blood pressure or pulse
- disturbance in fluid balance/electrolytes/hyperthermia
- gross tremor
- paranoid ideation
- confusion and disorientation
- extreme agitation or restlessness

**Risks associated with alcohol withdrawal**

Complications of prolonged heavy alcohol use that can lead to high mortality include:

- dehydration leading to cardiac arrhythmias
- hypotension
- renal failure
- pneumonia
- infection

Mortality rates should be less than 1% with adequate early management which includes:

- effective sedation
- intravenous fluids
- treatment of co-existing conditions

Amongst regular, daily or near daily, users of alcohol poor diet and nutrition exacerbated by impaired absorption, due to gastritis, liver damage, vomiting and diarrhoea and an increase in metabolic demand, can cause vitamin deficiencies. These include vitamins B1 (thiamine), B6 (pyridoxine) and C (ascorbic acid).

**Wernicke’s encephalopathy**

Wernicke’s encephalopathy is a brain injury resulting from a deficiency in vitamin B1. If not treated rapidly it can lead to permanent brain damage and memory loss.


*Symptoms of Wernicke’s encephalopathy include:*

- confusion
- nystagmus, with or without ophthalmoplegia (blurred vision)
- ataxia
- peripheral neuropathy (can be present in up to 80% of people with Wernicke’s encephalopathy)

*Note:* Wernicke’s encephalopathy can be difficult to diagnose in an intoxicated person as ataxia, confusion and nystagmus may also be attributed to intoxication.

**Prevention and Treatment**

Thiamine should be prescribed and offered as an oral medication to people at high risk of developing Wernicke’s encephalopathy:

- the malnourished or at risk of malnourishment
- those with decompensated liver disease
- in acute alcohol withdrawal
- before and during planned alcohol withdrawal

In acute need intravenous or intramuscular thiamine may be given undiluted by direct slow injection over ten minutes.

**Recommended intra muscular (IM) thiamine dosage**

Thiamine 100mg three to four times a day for at least three days until improvement is observed at which time it is replaced by oral thiamine, 50mg four times a day (qid) or 100mg two times a day (bd). Oral thiamine should be continued for at least one month.

*Note:* To reduce the risk of precipitating or worsening Wernicke’s encephalopathy IM thiamine must be given prior to administration of carbohydrates (e.g. glucose) to people in alcohol withdrawal (McClintock, A.D. et al. 1999). In an emergency situation where IV glucose is necessary and there may be a time delay before admission to hospital, administration of glucose prior to thiamine may be a safer treatment option.


For more information on precautions and other information prior to administration of thiamine: http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=23494#nlm34071-1

**Nutrition and hydration**

Food and fluid intake needs to be monitored during withdrawal from alcohol. Dehydration from vomiting, sweating and diarrhoea is a risk that could induce further complications. Fluids should be encouraged and electrolytes monitored, including magnesium and potassium, as part of medical management of alcohol withdrawal.

People presenting in withdrawal often have loss of appetite and education about healthy
eating should be part of withdrawal management and post withdrawal treatment. People with compromised physical health due to: liver damage, gastric inflammation, dental problems, low albumin or general poor health, should be referred for specialist dietary advice.

Management of alcohol withdrawal

The following are general principles for treatment planning for use in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement.

The revised CIWA-Ar (Appendix 1) provides a structured format to record the severity of withdrawal symptoms. Alongside its usefulness in initial assessment of withdrawal symptoms the CIWA-Ar can be used to monitor changing withdrawal symptoms and the efficacy of withdrawal management over time.

Withdrawal management setting

Community withdrawal management

Where community based home detoxification and withdrawal management services are available the majority of people withdrawing from alcohol, particularly those with low to moderate CIWA-Ar scores, can safely be managed and cared for in their own homes or in supported accommodation.

In-patient withdrawal management

The availability of 24 hour specialist nursing and medical supervision allows for the safer management of risk associated with alcohol withdrawal than in a community setting. This is particularly true for people with a known history of severe withdrawal, seizures and CIWA-Ar scores over 15.
Figure 3: Alcohol withdrawal severity and management settings

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Features</th>
<th>Withdrawal management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild withdrawal</strong></td>
<td>mild rise in temperature</td>
<td>Community or home withdrawal management</td>
</tr>
<tr>
<td>Mild to moderate dependence on assessment</td>
<td>mild hypertension</td>
<td>Requires monitoring by community detoxification nurse in consultation with G.P and or addiction service clinician/practitioner</td>
</tr>
<tr>
<td>Person has no significant physical or mental health problems</td>
<td>mild anxiety</td>
<td>Stable accommodation and commitment/support from appropriate family or whānau member or friend.</td>
</tr>
<tr>
<td>No apparent significant risks of complicated withdrawal</td>
<td>slight tremor</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mild sweating</td>
<td></td>
</tr>
<tr>
<td></td>
<td>nausea, vomiting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mild dehydration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>headaches</td>
<td></td>
</tr>
<tr>
<td></td>
<td>tachycardia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>dyspepsia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>sleep problems</td>
<td></td>
</tr>
<tr>
<td><strong>Moderate withdrawal</strong></td>
<td>mild rise in temperature e.g. 37°C</td>
<td>Community 24 hr supervised residential setting</td>
</tr>
<tr>
<td>Repeated unsuccessful attempts to withdraw at home</td>
<td>mild –moderate hypertension (diastolic reading of 100-110Hg)</td>
<td>Requires 24 hr supervision by support workers with training in substance withdrawal and or use of CIWA-Ar scale.</td>
</tr>
<tr>
<td>Person may have mild to moderate co-existing physical and or mental health problems</td>
<td>mild tremor</td>
<td>Up to date CPR training</td>
</tr>
<tr>
<td>Geographic isolation from community detoxification nurse</td>
<td>weakness</td>
<td>24 hr access to medical practitioner</td>
</tr>
<tr>
<td>Unstable home or living environment</td>
<td>dehydration</td>
<td>Access to community detoxification nurse and addiction medicine specialist, physician or psychiatrist for consultation</td>
</tr>
<tr>
<td>No past history of complicated withdrawal</td>
<td>headache</td>
<td>Medications blister packed and managed by residential support workers with support from community detoxification nurse during day.</td>
</tr>
<tr>
<td></td>
<td>moderate sweating</td>
<td></td>
</tr>
<tr>
<td></td>
<td>dyspepsia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>nausea, vomiting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>diarrhoea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>anorexia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>moderate anxiety (will respond to reassurance)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hyperventilation and panic attacks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>restlessness, agitation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>insomnia, nightmares</td>
<td></td>
</tr>
<tr>
<td>Indicators</td>
<td>Features</td>
<td>Withdrawal management setting</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Severe</td>
<td>Daily alcohol consumption of 15 or more standard drinks daily. (Blood alcohol level of 150mg/100mls)</td>
<td>Inpatient medical and withdrawal management</td>
</tr>
<tr>
<td></td>
<td>Past history of complicated withdrawal symptoms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serious co-existing physical and or mental health problems</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypertension (danger sign is diastolic pressure ≥ 120mmHg) or hypotension</td>
<td></td>
</tr>
<tr>
<td></td>
<td>raised temp ≥ 37°C</td>
<td></td>
</tr>
<tr>
<td></td>
<td>marked tremor</td>
<td></td>
</tr>
<tr>
<td></td>
<td>withdrawal seizures or history of seizures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>dehydration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>excessive sweating</td>
<td></td>
</tr>
<tr>
<td></td>
<td>nausea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>vomiting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>diarrhoea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>nausea, vomiting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>acute anxiety (may or may not respond to reassurance)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>restlessness and or aggression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hypersensitivity to stimulation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hallucination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>severe depressive disorder or severely depressed mood</td>
<td></td>
</tr>
<tr>
<td></td>
<td>psychosis related to substance use</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 hr care from experienced nursing and medical staff</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment for dehydration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment for altered electrolyte states</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessment of nutritional deficits</td>
<td></td>
</tr>
</tbody>
</table>
### Figure 4: Alcohol withdrawal management medication regime

<table>
<thead>
<tr>
<th>CIWA-Ar Score</th>
<th>Less than 8</th>
<th>8 to 15</th>
<th>15 and over</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>Provide oral thiamine, 100mg 3-4 times a day</td>
<td>Provide oral or IM thiamine, 100mg 3-4 times a day</td>
<td>Provide oral or IM thiamine, 100mg 3-4 times a day</td>
</tr>
<tr>
<td>1</td>
<td>Reassure support repeat CIWA-Ar four hourly if CIWA-Ar exceeds 8</td>
<td>10-20mg diazepam 4 hourly till settled maximum dose 60mg repeat CIWA-Ar four hourly if CIWA-Ar exceeds 15</td>
<td>20mg oral or IV diazepam 2 hourly till sedated or withdrawal symptoms reduce maximum dose 80mg repeat CIWA-Ar two hourly</td>
</tr>
<tr>
<td>2</td>
<td>As above</td>
<td>10-20mg diazepam 4 hourly till settled maximum dose 60mg repeat CIWA-Ar four hourly if CIWA-Ar is less than 10 over three consecutive screens reduce screening to six hourly</td>
<td>Same dose of diazepam that reduced withdrawal symptoms on Day 1 dispensed in four doses (qid) maximum dose 80mg repeat CIWA-Ar four hourly once symptoms reduce</td>
</tr>
<tr>
<td>3</td>
<td>As above</td>
<td>Half previous day’s dose of diazepam dispense in four doses (qid)</td>
<td>Half previous day’s dose of diazepam dispense in four doses (qid)</td>
</tr>
<tr>
<td>4</td>
<td>As above</td>
<td>Half previous day’s dose of diazepam dispense in four doses (qid)</td>
<td>Half previous day’s dose of diazepam dispense in four doses (qid)</td>
</tr>
<tr>
<td>5</td>
<td>As above</td>
<td>Half previous day’s dose of diazepam dispense in two doses (bd)</td>
<td>Half previous day’s dose of diazepam dispense in two doses (bd)</td>
</tr>
<tr>
<td>6</td>
<td>As above</td>
<td>Half previous day’s dose of diazepam dispense in one dose</td>
<td>Half previous day’s dose of diazepam dispense in one dose</td>
</tr>
</tbody>
</table>

Throughout the withdrawal process, make and document routine observations of: blood pressure, pulse, respiratory rate and pupil size.

Note:
- do not exceed stated maximum diazepam doses in a twenty four hour period without consulting a medical practitioner, addiction medicine specialist, physician or psychiatrist
- if the person is older and or has severe liver dysfunction consider replacing diazepam with clonazepam or oxazepam which have no active metabolites and are less likely to accumulate to toxic levels
  - follow similar reduction rates as above
- if the person in withdrawal is having distressing hallucinations use haloperidol for a brief period in consultation with an addiction medicine specialist, physician or psychiatrist
- where the person is known to have had a history of withdrawal seizures, or the risk of seizure is high, prophylactic sodium valproate may be helpful
  - commence on 600mg of sodium valproate initially, followed by 400mg eight hourly (tds) or 600mg twice daily (bd), for five to seven days
Figure 5: Alcohol withdrawal management pathways

Person seeks assistance and is screened by:
- General Practitioner
- NGO/DHB addiction service
- Community/iwi service

Person may be in involuntary/unplanned withdrawal due to incarceration or admission to hospital.

Does the person have severe: anxiety, mood, psychotic or confusional symptoms not explained by acute withdrawal?

Yes
- Specialist mental health assessment

No
- Does the person have mild (CIWA-Ar <8) withdrawal symptoms:
  - anxiety
  - agitation
  - irritability
  - insomnia
- Does the person have good supports?
- Is the person confident in their ability to manage?

Yes to both
- Self and GP managed withdrawal
  - support
  - reassurance
  - monitor
  - oral thiamine

No
- Does the person have mild-moderate (CIWA-Ar 8-15) withdrawal symptoms:
  - tremor
  - increased heart rate
  - increased blood pressure
  - nausea vomiting
- Does the person have some level of support at home?

Yes to both
- Community-based withdrawal management with nursing support
  - oral thiamine
  - stabilise on diazepam
  - taper dose over six days
  - support

No
- Is the person having moderate withdrawal symptoms?
- Does the person need respite from their environment?

Yes to both
- Social withdrawal management service admission

No
- Is there concern for safety of self or others?
- Is the person experiencing, or have they had in the past, severe (CIWA-Ar >15) withdrawal symptoms:
  - seizures
  - hallucinations
  - delusions
  - fluctuating consciousness
  - fever
- Does the person use other substances?
- Does the person have co-existing mental or physical health problems?

Yes
- Hospital /Inpatient admission for medically assisted withdrawal management
  - IV/IM thiamine
  - stabilise on diazepam
  - taper dose gradually over six days
  - if hallucinations present consider haloperidol
  - if history of seizures consider sodium valproate

No
- Follow-up treatment as needed
Amphetamine-Type Stimulants (ATS)
Amphetamine-Type Stimulants (ATS)

These guidelines have been developed to assist nursing and medical practitioners to identify amphetamine-type stimulant withdrawal symptoms and to provide safe withdrawal management strategies for people who are dependent.

Amphetamine-type stimulants (ATS) are a group of substances consisting of synthetic or man made stimulants including: amphetamine, dexamphetamine, methamphetamine, methcathinone, methylphenidate (ritalin), methylenedioxymethamphetamine (MDMA or ecstasy-type substances), methylenedioxyamphetamine (MDA), piperazines (BZP, TFMPP etc), methylmethcathinone (mephedrone) and many other substances chemically related to amphetamine.

ATS are central nervous system stimulants that appear to be similar to the neurotransmitters dopamine, noradrenaline and serotonin and act by promoting their release from nerve terminals and blocking their re-uptake.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific ATS use history includes:

- names and types of ATS used
- route of use and documentation of injecting sites
- average frequency and quantity of use, in milligrams, over time
- time of last use
- context of use
- periods of abstinence
- current or recent psychosis symptoms
- initial reasons for starting to use ATS
- current goals relating to use

ATS withdrawal

The severity of ATS withdrawal symptoms generally depends on how much, how long and how a person has been using ATS. Smoking and intravenous use of methamphetamine in particular is associated with greater symptom severity. Personality differences and pre-existing conditions can also impact on the severity of withdrawal.
Risks associated with ATS withdrawal

- ATS withdrawal is not physically dangerous and most people will complete withdrawal with mild to moderate symptoms.
- A past history of violence and aggression may indicate a risk of aggressive behaviour which could place other people at risk.
- Underlying mental health issues may emerge during withdrawal.
- Medication is likely to be appropriate with those people with severe withdrawal symptoms and or co-existing problems.
- Serotonin toxicity may occur due to elevated serotonin levels, especially if the person is also prescribed an SSRI.

Onset and duration of withdrawal

After stopping use many people who use ATS, ‘crash’, sleeping long hours and feeling fatigued and restless when awake. The ‘crash’ can last for up to three days. Following the ‘crash’ withdrawal begins. Most symptoms peak between days two and ten but some symptoms can persist for several months, especially sleep and mood problems.

Figure 6: Symptoms of ATS withdrawal

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>restlessness</td>
<td>poor concentration and memory</td>
<td>depression</td>
</tr>
<tr>
<td>lethargy</td>
<td>mood swings</td>
<td>hallucinations</td>
</tr>
<tr>
<td>low energy</td>
<td>anxiety</td>
<td>paranoia</td>
</tr>
<tr>
<td>irritability</td>
<td>anger</td>
<td>psychosis</td>
</tr>
<tr>
<td>agitation</td>
<td>diarrhoea</td>
<td></td>
</tr>
<tr>
<td>sleep problems</td>
<td>aches and pains</td>
<td></td>
</tr>
<tr>
<td>low mood</td>
<td>hunger</td>
<td></td>
</tr>
<tr>
<td></td>
<td>insomnia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>cravings</td>
<td></td>
</tr>
</tbody>
</table>

Management of ATS withdrawal

The following are general principles for treatment planning for use in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement.

Outpatient withdrawal management

Generally ATS withdrawal is not life threatening or physically risky and the function of withdrawal management is to provide support and reassurance through the withdrawal. Engagement
in ongoing treatment and relapse prevention is the main goal. To increase the likelihood of engagement:

- assume the person has cognitive problems and repeat information as often as needed
- address health issues that could be causing pain
- monitor mood states and suicidal ideation closely
- provide dietary advice about the need for sustained healthy eating and multivitamin use following likely poor nutrition while using ATS
- involve mental health services if anxiety, depression or psychosis emerge as problems post detoxification

**Inpatient withdrawal management**

Inpatient ATS withdrawal management is rarely required unless people are unable to cease use in the community because of lack of supports or they have severe withdrawal symptoms such as extreme anger and or psychotic symptoms. When people meet these criteria the specific needs of people in ATS withdrawal include:

- enough space for people to move around freely
- access to a range of activities to help with distraction and relaxation
- not panicking or reacting in a challenging manner
- limiting noise and environmental stressors
- ready access to beds for rest and sleep
- ready access to a variety of nutritious food

**Social withdrawal management beds**

The Government’s tackling methamphetamine initiative has made available 30 beds nationally to assist those with methamphetamine dependence to have time out as a one-off opportunity or a lead-in to residential treatment.

**Medication for ATS withdrawal**

To date no specific pharmacotherapy has been identified as being effective for treatment of ATS withdrawal.

Benzodiazepines (e.g. diazepam) can help to manage severe anxiety, agitation and irritability and sleep disturbances in the week or two after the initial ‘crash’ that follows stopping ATS use. This however needs to be managed under supervision from a specialist addiction service or a General Practitioner.
• On an outpatient basis:
  » ‘Close Control’ supervised diazepam, 5 to 10mg, three to four times daily for four to seven days
  » dose and duration is dependent on each individual presentation
  » discuss and review with an addiction medicine specialist, physician or psychiatrist

• On an inpatient basis:
  » 5 to 20mg, diazepam three to four times daily for seven to ten days
  » monitor closely and adjust as appropriate

*Benzodiazepines should not be used for ATS withdrawal management for longer than two weeks and use should be monitored daily.*

**Adjunctive medication**

Some ATS withdrawal symptoms may need to be treated with specific medications. What medication is appropriate to use should be discussed with an addiction medicine specialist, physician or psychiatrist.

**Antidepressants**

- can be helpful in combating the depressive symptoms frequently seen in methamphetamine withdrawal
- most antidepressants are not fully effective for some weeks so are not useful to treat acute low mood
- care also needs to be taken in case people have elevated serotonin levels as they will have increased risk of serotonin syndrome

**Antipsychotics**

- may help with sleep disturbances, agitation and anxiety at low doses
- can be prescribed by a GP in consultation with a specialist service as there may be contraindications with some antipsychotic medication
- are useful to manage psychoses that occur in ATS intoxication and withdrawal
- olanzepine has been shown to be better tolerated than haloperidol but both medications have been shown to be helpful in managing psychotic symptoms

**Melatonin**

- a synthetic supplement that mimics natural melatonin and helps with sleep disturbances
- evidence is limited for the effectiveness of melatonin when used in withdrawal management
- melatonin can be prescribed by a GP but is not funded by PHARMAC
Complementary therapies

There is no reliable evidence to support the use of natural alternatives or complementary therapies for use in managing ATS withdrawal. However natural alternatives can help with:

- anxiety
- sleep difficulties
- muscles aches
- relaxation
- irritability

Note: St John’s Wort also needs to be used with caution in people with possibly elevated serotonin levels because of the risk of developing serotonin syndrome. See Appendix 7.
Figure 7: Amphetamine-type stimulant withdrawal pathways

Person seeks assistance and is screened by:
- General Practitioner
- Alcohol Drug Helpline
- NGO/DHB addiction service
- Community/iwi service

Person may be in involuntary/unplanned withdrawal due to incarceration or admission to hospital.

Does the person have severe: anxiety, mood, psychotic or confusional symptoms not explained by acute withdrawal?
- Yes
  - Specialist mental health assessment

- No
  - Does the person have mild or no withdrawal symptoms:
    - lethargy
    - agitation
    - low mood
  - Does the person have good supports?
  - Is the person confident in their ability to manage?
  - Yes
    - Self and GP managed withdrawal
      - support
      - complementary therapies
  - No
    - Does the person have some level of support at home?
    - Yes
      - Community-based withdrawal management with nursing support
      - support
      - possibly medication
    - No
      - Does the person need respite from their environment?
      - Yes
        - Social withdrawal management service admission
      - No
    - Is there concern for safety of self or others?
    - Is the person experiencing severe withdrawal symptoms:
      - psychosis
      - hallucinations
      - depression
    - Does the person have co-existing mental or physical health problems?
    - Does the person use other substances?
    - Yes
      - Hospital /Inpatient admission for medically assisted withdrawal management
      - antipsychotic
      - antidepressant
      - benzodiazepine
    - No
      - Follow-up treatment as needed

Yes to both

Yes to all
Benzodiazepines
**Benzodiazepines**

These guidelines have been developed to assist nursing and medical practitioners to identify benzodiazepine withdrawal symptoms and to provide safe withdrawal management strategies for people who are dependent.

Benzodiazepines (BNZ) belong to the sedative-hypnotic group of substances which have depressant effects on the central nervous system.

Benzodiazepines enhance the effect of the neurotransmitter gamma-amino butyric acid (GABA), which results in sedative, hypnotic (sleep-inducing), anxiolytic (anti-anxiety), anticonvulsant, muscle relaxant and amnesic action.

**Assessment**

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific benzodiazepine use history includes:

- name of the benzodiazepine(s) used
- average quantity of use, dose (in milligrams), over time
- time of last use
- is the BNZ prescribed or non-prescribed
- initial reasons for starting taking BNZ’s
- past history of seizures
- current goals relating to use

There are two main types of benzodiazepine dependence observed in people who present for treatment. The most common in general practice is low dose dependency that has developed over many years. This is seen most often in women and older people. High dose dependence also occurs and is often seen in association with polysubstance use or a history of polysubstance use.

**Benzodiazepine withdrawal**

The primary aim of managed withdrawal is safety, with the person stopping use without major complications such as: delirium, seizures or serious mental health consequences such as suicidality.

Withdrawal is enhanced by having a clear management plan, effective communication and stabilisation and progressive withdrawal using a long acting benzodiazepine. Supervised daily
dispensing may also be considered necessary for safety reasons.

Developing a good therapeutic relationship, along with reassurance and a gradual dose reduction, appears to improve outcomes for people undergoing benzodiazepine withdrawal.

**Figure 8:** Onset and duration of benzodiazepine withdrawal:


**Onset and duration of benzodiazepine withdrawal**

- the onset of withdrawal from short-acting BNZ’s generally occurs within one to two days after stopping use
- the onset of withdrawal from long-acting BNZ’s generally starts two to seven days after stopping use
- withdrawal from short-acting BNZ’s typically produces a quicker and more intense onset of symptoms than longer acting BNZ’s
- the use of “therapeutic doses” of BNZ’s for as short a period as six weeks can result in neuro-adaptation and a withdrawal syndrome that may last from one to six weeks on stopping use
- not all individuals stopping BNZ’s will experience withdrawal symptoms and for those who do the symptoms are not always disabling
- BNZ withdrawal syndrome may last from six months to a year for those people who have been using BNZ’s on a long term basis
- using high doses of BNZ’s over a prolonged period of time is more likely to result in severe withdrawal symptoms
- withdrawal symptoms may also be more severe for those that are using more than one BNZ at a time

**Figure 9**: Symptoms of benzodiazepine withdrawal

<table>
<thead>
<tr>
<th>Common</th>
<th>Less common</th>
<th>Uncommon severe symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>anxiety</td>
<td>headache</td>
<td>delusions</td>
</tr>
<tr>
<td>insomnia, disturbed sleep</td>
<td>nightmares</td>
<td>paranoia</td>
</tr>
<tr>
<td>restlessness</td>
<td>tremor</td>
<td>hallucinations</td>
</tr>
<tr>
<td>agitation</td>
<td>fatigue</td>
<td>confusion</td>
</tr>
<tr>
<td>irritability</td>
<td>weakness</td>
<td>persistent tinnitus</td>
</tr>
<tr>
<td>depression</td>
<td>appetite/weight change</td>
<td>seizures</td>
</tr>
<tr>
<td>poor memory</td>
<td>tingling</td>
<td></td>
</tr>
<tr>
<td>poor concentration</td>
<td>dizziness, poor balance</td>
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<tr>
<td>muscle tension</td>
<td>blurred/double vision</td>
<td></td>
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<tr>
<td>aches and twitching</td>
<td>feelings of unreality</td>
<td></td>
</tr>
<tr>
<td>sweating</td>
<td>dry mouth</td>
<td></td>
</tr>
<tr>
<td></td>
<td>increased sensory perception</td>
<td></td>
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<tr>
<td></td>
<td>- metallic taste</td>
<td></td>
</tr>
<tr>
<td></td>
<td>flushing/sweating</td>
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<tr>
<td></td>
<td>palpitations</td>
<td></td>
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<tr>
<td></td>
<td>gastrointestinal upset</td>
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<td></td>
<td>urinary difficulties</td>
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</tr>
<tr>
<td></td>
<td>menstrual changes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>skin rashes, itching</td>
<td></td>
</tr>
</tbody>
</table>

**Management of benzodiazepine withdrawal**

The following are general principles for treatment planning for use in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement. Benzodiazepine withdrawal scales have not proven to be reliable and useful in treatment planning.

**Outpatient withdrawal management**

- diazepam is used for withdrawal management as it has a long half life, reducing the need for multiple daily doses to prevent the emergence of withdrawal symptoms
- if the person is older and or has severe liver dysfunction consider replacing diazepam with clonazepam or oxazepam which have no active metabolites and are less likely to accumulate to toxic levels
- convert the average daily dose into an ‘equivalent’ dose of diazepam using conversion chart (see Appendix 2)
- prescribe ‘equivalent’ dose in three or four divided doses per day
- stabilise person on ‘equivalent’ dose
• a typical guideline for reduction of dose is between 10-20% at weekly or fortnightly intervals
• if the person is on doses above 40mg of diazepam reduce by 5mg-10mg a week until the dose reaches 40mg and then reduce by 2.5mg-5mg a week
• regularly review and titrate the dose of diazepam to the severity of apparent and self reported withdrawal symptoms
• in general a reducing regime will take six to eight weeks
• depending on the person and their circumstances some reducing regimes may need to take between three months to a year
• if there is significant or distressing withdrawal symptoms that emerge at any time during the reduction the dose may be held for one to two weeks
• the effectiveness of the withdrawal management process may be improved by slowing down the rate of reduction when the person is on a lower dose, such as below 15mg diazepam

Low dose iatrogenic dependence can be safely managed by a General Practitioner with support and follow up from a specialist addiction service. In many areas community detoxification nurses may be available to support the withdrawal process and or monitor symptom severity as needed.

For people that present needing assistance for withdrawal from zopiclone it is recommended to follow the same general principles as for benzodiazepine withdrawal. Use the conversion chart to convert the dose of zopiclone over to an equivalent dose of diazepam (see Appendix 2) and commence a withdrawal regime as above.

Inpatient withdrawal management

The availability of 24 hour specialist nursing and medical supervision allows for a more rapid and safe reduction of benzodiazepine doses than in a community setting for those people assessed as having severe withdrawal risks and or severe co-existing problems. This can include people who have co-existing substance use problems and or are engaged in Opioid Substitution Treatment.

• convert the average daily BNZ dose into equivalent dose of diazepam using conversion chart (Appendix 2)
• divide the equivalent dose into three-four divided doses/day
• initiate a rapid reduction if the initial dose of diazepam is higher than 40mg a day, reducing by 10mg a day to 40mg a day
• from 40mg a day, reduce by 5mg every one to three days
• it may be necessary, depending on withdrawal severity, to hold the reduction and stabilise the person on a low dose and consider the withdrawal process being continued at a slower pace
• once on a lower dose the person can be transferred and managed by a specialist service in an outpatient setting if appropriate

Caution:
While diazepam is recommended for BNZ withdrawal management it needs to be used with extreme caution and may be contraindicated in certain conditions such as respiratory failure and or liver disease. If there are medical conditions that are negatively affected by long acting benzodiazepines then use of a short acting benzodiazepine should be considered.
Adjunctive medication

There is insufficient evidence based research to recommend specific alternative pharmacological treatment(s) for management of benzodiazepine withdrawal. However some medications that could be helpful can be considered on an individual basis following discussion with an addiction medicine specialist, physician or psychiatrist.

Antidepressants

- can be helpful for people with persistent features of depression and or anxiety with a pre-existing DSMIV diagnosis
- if not already available assessment by a GP or psychiatrist should be considered
- SSRI’s (selective serotonin reuptake inhibitors) are the most commonly used antidepressants
- low dose tricyclic antidepressants have also been used as an aid for sleep difficulties (Ashton, 2002)

Antipsychotics

- may help with sleep disturbances, agitation and anxiety at low doses
- can be prescribed by a GP in consultation with a specialist service as there may be contraindications with some antipsychotic medication

Beta blockers

- can be used in the rare cases of withdrawal where severe palpitations, muscle tremors or motor jerks are causing significant problems
- can be prescribed regularly in low doses for a short period of time or taken on an as needed (prn) basis (Ashton, 2002)
- should be prescribed in consultation with an addiction medicine specialist, physician or psychiatrist

Melatonin

- a synthetic supplement that mimics natural melatonin and helps with sleep disturbances
- evidence is limited for the effectiveness of melatonin when used in withdrawal management
- melatonin can be prescribed by a GP but is not funded by PHARMAC
Zopiclone

- a non benzodiazepine hypnotic medication used in the treatment of insomnia
- carries the risk of developing dependency if used medium to long term
- best used for no longer than two weeks
- not recommended for use in withdrawal management

Complementary therapies

There is no reliable evidence to support the use of natural alternatives or complementary therapies for use in managing benzodiazepine withdrawal. However natural alternatives can help with:

- anxiety
- sleep difficulties
- muscles aches
- relaxation

Special populations

Older people

For older people the benefits of withdrawal can include:

- improved cognition
- alertness
- mobility
- reduced risk of incontinence
- a reduced risk of falls and fractures

The effectiveness for older people of a managed withdrawal, i.e. gradually tapering doses of benzodiazepines, is similar to the outcomes with younger people. (Ashton, 2002)

People with chronic physical illness

Similar to older people those with physical illnesses are generally unable to metabolise benzodiazepines efficiently and accumulation can occur. It is recommended that withdrawal is monitored closely and doses adjusted to the needs of the individual or a different long acting benzodiazepine is used for a reducing dose. If there are serious concerns an inpatient setting is recommended for managed withdrawal.
Pregnant women
Abrupt cessation of benzodiazepines is not recommended for pregnant women who are dependent on benzodiazepines. A gradual reduction regime under medical supervision is essential for safety.

Neonates
Babies born with benzodiazepine intoxication and or withdrawal can present with symptoms which can last for weeks after birth. These include:
- respiratory depression
- poor sucking
- hypotonia
- poor temperature regulation

Abrupt benzodiazepine withdrawal at birth has been shown to result in:
- neonatal irritability
- hypertonia
- seizures
- diarrhoea

Neonatal abstinence syndrome (NAS)
Onset may occur one to ten days after delivery and can last from seven days to one month.
- babies born to women who are benzodiazepine dependent should be observed in hospital for one week before discharge
- following this they should have weekly outpatient reviews for at least one month
- the Finnegan scale (Appendix 4) may be used to identify neonatal abstinence syndrome associated with benzodiazepines

Breastfeeding
- breastfeeding is not recommended for women who are using higher than therapeutic doses of BNZ's
- breastfeeding should be avoided for one to two hours after taking any BNZ (i.e. during peak BNZ plasma levels)
- breastfeeding should be discontinued if a baby appears sedated

Figure 10: Benzodiazepine withdrawal management pathways

Person seeks assistance and is screened by:
- General Practitioner
- NGO/DHB addiction service
- Community/iwi service

Person may be in involuntary/unplanned withdrawal due to incarceration or admission to hospital.

Does the person have severe: anxiety, mood, psychotic or confusional symptoms not explained by acute withdrawal?
- Yes
  - Specialist mental health assessment

No
- Does the person have mild withdrawal symptoms:
  - anxiety
  - agitation
  - low mood
- Has the person been on a low dose BNZ?
- Does the person have good supports?
- Is the person confident in their ability to manage?
  - Yes to both
    - Self and GP managed withdrawal
      - stabilise on low dose diazepam
      - taper dose gradually over time
      - support

No
- Does the person have mild-moderate withdrawal symptoms:
  - anxiety
  - agitation
  - depression
  - panic attacks
- Does the person have some level of support at home?
  - Yes to both
    - Community-based withdrawal management
      - with nursing support
      - stabilise on diazepam
      - taper dose gradually over time
      - support

No
- Is the person having moderate withdrawal symptoms?
- Does the person need respite from their home environment?
  - Yes to both
    - Social withdrawal management service admission

No
- Is there concern for safety of self or others?
- Is the person experiencing, or have they had in the past, severe withdrawal symptoms:
  - seizures
  - hallucinations
  - tinnitus
  - palpitations
  - delirium
- Does the person use other substances?
- Does the person have co-existing mental health or physical health problems?
  - Yes
    - Hospital /Inpatient admission for medically assisted withdrawal management

No
- Follow-up treatment as needed

Yes

Substance Withdrawal Management Guidelines
Cannabis
Cannabis

These guidelines aim to assist nursing and medical practitioners with the assessment and identification of cannabis withdrawal symptoms in order to be able to provide safer withdrawal management.

The main active ingredient of cannabis is Delta-9 tetra-hydrocannabinol (THC). Cannabidiol (CBD) is emerging as another significant active ingredient of cannabis. THC is thought to exert its effect by binding to cannabinoid CB1 receptors on pre-synaptic nerve terminals in the brain, activating G-proteins that activate/inhibit a number of signal transduction pathways.

The major effects of cannabis are on the central nervous, gastrointestinal and cardiovascular systems.

A range of ‘herbal highs’, e.g. Kronic, Puff, Dream, Marley, have been available in New Zealand for several years. Recently it has emerged that the main active ingredient in many of these products is a synthetic cannabinoid with a similar action to THC.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific cannabis use history includes:
- quantity of use, amount consumed, type of cannabis and potency
- duration, pattern and frequency of use
- mode of administration (smoked or eaten, mixed with tobacco)
- time and amount of last use
- past history of aggression and violence
- goals relating to use

Cannabis withdrawal

People wanting to withdraw from cannabis should be provided with a menu of intervention options. This may include the choice of sudden cessation, with or without symptomatic medication or a supported gradual reduction using psycho-social interventions.
Risks associated with cannabis withdrawal

- cannabis withdrawal is not physically dangerous
- most people will complete withdrawal with relatively mild symptoms
- a past history of violence and aggression may indicate a risk of aggressive behaviour which could place other people at risk
- underlying mental health issues may be unmasked during withdrawal
- suicidality and self injury may be a risk factor for people with a co-existing mood or psychotic disorder
- people with severe withdrawal symptoms and or co-existing problems may require appropriate medication

Onset and duration of withdrawal

Onset of cannabis withdrawal usually occurs one to two days after last use. Most symptoms peak between days two and six. It is important to note that withdrawal severity and duration will be dependent on the individual and the following variables:

- the amount, frequency and strength of cannabis used
- duration of current patterns of use
- stopping suddenly or reducing levels of use over time
- other substance use
- co-existing mental health problems
- co-existing physical health problems including chronic pain
- history of aggression or violence
- outpatient or inpatient setting

Note: The emergence of problems with aggression and anger may be delayed and can be evident for up to two to three weeks after stopping use. The duration and intensity of withdrawal symptoms tends to be correlated with the potency and amounts of cannabis used over time.
Figure 11: Cannabis withdrawal symptoms over time

Severity of signs and symptoms

Days

0 7 14 40

Insomnia, shakiness, decreased appetite
Irritability, restlessness, anxiety
Anger, aggression

Symptoms and duration of cannabis withdrawal. Reproduced with permission from NSW Department of Health (2008).

Figure 12: Symptoms of cannabis withdrawal

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>restlessness</td>
<td>poor concentration</td>
<td>aggression</td>
</tr>
<tr>
<td>irritability</td>
<td>mild depressive symptoms</td>
<td>exacerbation of existing mood disorder</td>
</tr>
<tr>
<td>nervousness</td>
<td>nausea</td>
<td>suicidality</td>
</tr>
<tr>
<td>anxiety</td>
<td>loss of appetite</td>
<td>headaches</td>
</tr>
<tr>
<td>agitation</td>
<td>increased appetite</td>
<td>insomnia</td>
</tr>
<tr>
<td>sleep problems</td>
<td>anger</td>
<td>vomiting</td>
</tr>
<tr>
<td></td>
<td>intense dreaming</td>
<td>heavy sweating</td>
</tr>
<tr>
<td></td>
<td>nightmares</td>
<td></td>
</tr>
</tbody>
</table>

Management of cannabis withdrawal

Comprehensive assessment, treatment planning and supportive counselling are the main strategies for managing cannabis withdrawal for the majority of people and can be safely provided in the community. Medication and or admission into a social withdrawal management service are rarely required apart from those people with co-existing problems, including other substance use, a history of aggression and or inappropriate home environments.

There is currently no validated assessment tool for monitoring the severity of cannabis withdrawal however the Cannabis Withdrawal Assessment Scale (De Crespigny et al., 2003) may be useful in clinical practice (Appendix 5).
**Medication for management of cannabis withdrawal**

To date no specific pharmacotherapy has been proven to significantly help with managing cannabis withdrawal.

Atypical antipsychotic medication, (e.g. quetiapine), has been used to help manage agitation, anxiety and sleep problems in cannabis withdrawal. There is no evidence to date to support this practice apart from anecdotal reports of efficacy. Use of antipsychotic medication for this purpose should be only considered in consultation with an addiction medicine specialist, physician or psychiatrist.

Benzodiazepines (e.g. diazepam) may help with managing very severe withdrawal symptoms such as extreme anxiety, agitation, irritability and aggression and prolonged sleep difficulties. This however needs to be managed under supervision from a specialist addiction service.

- **On an outpatient basis:**
  - ‘Close Control’- supervised daily dispensing – diazepam 5 to 10mg, three to four times daily for four to seven days
  - dose and duration is dependent on each individual presentation
  - discuss and review with an addiction medicine specialist, physician or psychiatrist

- **On an inpatient basis:**
  - 5 to 20mg, diazepam three to four times daily for seven to ten days
  - monitor closely and adjust as appropriate

Benzodiazepines should not be considered a treatment of choice for cannabis withdrawal management and if used should not be prescribed for longer than two weeks and use should be monitored on a daily basis.

Adjunctive medications that may be helpful managing some withdrawal symptoms include:

- paracetemol – headaches, muscular aches, sweating, chills and pain
- NSAID’s – headaches, muscular aches and pain
- magnesium – headaches and muscular aches
- antihistamines – nausea, nasal congestion
- metoclopromide – nausea
- prochlorperazine – nausea, nasal congestion

(Winstock and Lea, 2009)

**Complementary therapies**

In the absence of evidence based medication to assist with the management of cannabis withdrawal symptoms many addiction services use or recommend the use of alternative therapies for sleep disturbances and agitation.
These include:

- massage
- acupuncture
- herbal and mineral supplements
- kava
- valerian
- natural melatonin

Where the person has known liver problems some of these supplements may be contraindicated. Generally people will need to seek advice from trained practitioners in the community. **Note:** Ongoing monitoring of the persons wellbeing and mental health status post withdrawal is recommended as mental health symptoms may have been masked by ongoing cannabis use.

### Special populations

#### Pregnant women

There is limited research into the effects of cannabis on foetal development; however what does exist indicates a raised risk of low birth weight and possible developmental delays. Pregnant women should be advised to stop cannabis use and supported to do so, without the use of medication if possible. Reducing levels of use over time may be a helpful strategy.

#### Neonates

There is some evidence that neonates may experience mild withdrawal from cannabis following birth. The most common features that have been observed are:

- restlessness
- agitation and crying
- not settling
- poor sucking

Often withdrawal symptoms will not become apparent until at least the second week postnatal. Supportive settling techniques are the only recommended treatment.
Figure 13: Cannabis withdrawal management pathway

Person seeks assistance and is screened by:
- General Practitioner
- NGO/DHB addiction service
- Community/iwi service
Person may be in involuntary/unplanned withdrawal due to incarceration or admission to hospital.

Does the person have severe: anxiety, mood, psychotic or confusional symptoms not explained by acute withdrawal?

- Does the person have mild withdrawal symptoms:
  - anxiety
  - agitation
  - irritability
  - low mood
  - mild sleep problems
- Does the person have good supports?
- Is the person confident in their ability to manage?

Yes

Specialist mental health assessment

Supported managed withdrawal
- complementary therapies
- support

Yes to all

No

Community-based withdrawal management with nursing support
- complementary therapies
- pharmacotherapy
- support

Yes to both

Social withdrawal management service admission

Yes

No

Follow-up treatment as needed

No

Hospital /Inpatient admission for medically assisted withdrawal management
- ?benzodiazepine
- ?antipsychotic
- ?antidepressant

Yes

Yes to both

No

Yes

No

Yes
Gamma-Hydroxybutyrate (GHB)
Gamma-Hydroxybutyrate (GHB)

These guidelines have been developed to assist nursing and medical practitioners to identify gamma-hydroxybutyrate acid withdrawal symptoms and to provide safe withdrawal management strategies for people who are dependent.

Gamma-hydroxybutyrate acid (GHB) and its analogues, 1, 4-butanediol (1, 4-BD) and gamma-butyrolactone (GBL), are endogenous inhibitory neurotransmitters and anaesthetics, with a similar action to benzodiazepines. GHB is believed to possess partial agonist activity at the GABA-B receptor, and further activity may be related to conversion of GHB to GABA. GHB also has effects on dopamine, acetylcholine, serotonin, glutamate and opiate neurotransmission (Wojtowicz et al., 2008). The action of GHB on the central nervous system is known to be highly dose dependent. In high doses, profound sedation and seizures can occur (Cape et al., 2002).

Multiple substance use along with GHB is common. Attention should be focused on other central nervous system depressants such as alcohol, benzodiazepines and opioids as the person may require close monitoring to assess and identify the risks of central nervous system depression.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific GHB use history includes:

- average quantity (usually in “mls” as consumed as a liquid) and frequency of use over time
- time of last use
- other central nervous system depressants used concurrently
- history of seizures
- cognitive deficits and history of trauma
- peer affiliations
- initial reasons for starting to use GHB
- current goals relating to use

GHB withdrawal syndrome is not well documented and there is little in the way of international evidence or guidelines documenting withdrawal management strategies. Predicting the course of GHB withdrawal is difficult. Studies reviewing available literature report that severe dependence, as reflected in frequent use of GHB, can be associated with a severe, potentially life threatening withdrawal state that requires vigorous clinical management (McDonough et al., 2004).

As withdrawal from GHB following high dose dependent use could be life threatening management in a medical inpatient unit may be required.
GHB withdrawal

Withdrawal severity appears to be dependent on frequency of use and amounts used. Mild withdrawal may occur after occasional use but is more likely to occur after several weeks of daily use. Severe withdrawal tends to be associated with using GHB several times a day over an extended period of time. Withdrawal symptoms do not always progress from mild to severe in a predictable way.

Figure 14: Symptoms of GHB withdrawal

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>anxiety</td>
<td>tachycardia</td>
<td>tachycardia (may present as transient spikes)</td>
</tr>
<tr>
<td>sweating</td>
<td>nausea</td>
<td>hallucinations (visual, auditory, tactile)</td>
</tr>
<tr>
<td>restlessness</td>
<td>vomiting</td>
<td>delusions or paranoia</td>
</tr>
<tr>
<td>insomnia</td>
<td>abdominal cramps</td>
<td>psychosis in clear consciousness</td>
</tr>
<tr>
<td>mild hypertension</td>
<td>diarrhoea</td>
<td>delirium</td>
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<td></td>
<td></td>
<td>hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>rhabdomyolysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>seizures</td>
</tr>
</tbody>
</table>

Management of GHB withdrawal

The following are general principles for treatment planning in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement.

As the use of GHB is a fairly new phenomenon and withdrawal is apparently rare, withdrawal scales have not as yet been developed for use in treatment planning.

The onset of withdrawal symptoms can be rapid (one to six hours after the last dose) and symptoms prolonged (five to fifteen days). There is a possibility that chronic dependent use of GHB can contribute to the development of Wernicke’s encephalopathy and accordingly people should be provided prophylactic thiamine as in alcohol withdrawal (Friedman et al., 1996).

Outpatient withdrawal management

Community or supported outpatient withdrawal management is most suitable for people using less than three times or less than 30gm of GHB a day.

- provide thiamine as outlined in alcohol withdrawal guide
- on the first day dispense up to 40mg of diazepam orally till settled
- monitor physical state on daily basis
- if symptoms are not alleviated or worsen admit for inpatient withdrawal management
- on the second day of managed withdrawal maintain on the same dose of diazepam, split into four doses (qid), as was adequate to manage symptoms on day one
reduce to zero over seven days

Note: converting the person’s reported levels of use from “mls” into grams can only be approximate as more than 1gm of sodium GHB can be dissolved in 1ml of water.

Inpatient withdrawal management

The availability of specialist nursing and medical supervision allows for the safer management of risk than in a community setting. This is particularly true for people with a known history of severe withdrawal, seizures and very high levels of GHB use, i.e. over 30gm a day.

- provide thiamine as outlined in alcohol withdrawal guide
- in the absence of delirium provide up to 50mg of diazepam until settled
- in the presence of delirium provide up to 150mg of diazepam orally or intravenously
- do not exceed 150mg unless in consultation with addiction medicine specialist, physician or psychiatrist
- if the person is older and or has severe liver dysfunction consider using oxazepam or clonazepam as they have no active metabolites and are less likely to accumulate to toxic levels
- reduce diazepam, clonazepam or oxazepam doses over seven days or as symptoms persist
- if the person in withdrawal is having distressing hallucinations consider the use of haloperidol (2.5 to 5 mg) in consultation with an addiction medicine specialist, physician or psychiatrist
- in the presence of ongoing agitation phenobarbitone (30 to 60mg) may help symptoms to settle
- where more severe symptoms emerge admission into intensive care may be necessary
Figure 15: GHB withdrawal management pathway

Person seeks assistance and is screened by:
- General Practitioner
- NGO/DHB addiction service
- Community/iwi service
Person may be in involuntary/unplanned withdrawal due to incarceration or admission to hospital.

Does the person have severe: anxiety, mood, psychotic or confusional symptoms not explained by acute withdrawal?

Yes
- Specialist mental health assessment

No
- Does the person have mild withdrawal symptoms:
  - anxiety
  - agitation
  - insomnia
  - Does the person have good supports?
  - Is the person confident in their ability to manage?

Yes to all
- Supported managed withdrawal
  - support
  - reassurance
  - monitor
  - oral thiamine

No
- Does the person have some level of support at home?

Yes to both
- Community-based withdrawal management with nursing support
  - oral thiamine
  - stabilise on diazepam
  - taper dose over seven days
  - support

No
- Does the person have moderate withdrawal symptoms:
  - tremor
  - tachycardia
  - increased blood pressure
  - nausea, vomiting
  - Does the person have some level of support at home?

Yes to both
- Social withdrawal management service admission

No
- Is there concern for safety of self or others?
  - Does the person experiencing, or have they had in the past, severe withdrawal symptoms:
    - seizures
    - hallucinations
    - delusions
    - delirium
    - tachycardia
  - Does the person use other substances?
  - Does the person have co-existing mental or physical health problems?

Yes
- Hospital /Inpatient admission for medically assisted withdrawal management
  - oral thiamine
  - stabilise on diazepam
  - taper dose gradually over seven days
  - if hallucinations present consider haloperidol

No
- Follow-up treatment as needed
Inhalants
Inhalants

These guidelines have been developed to assist nursing and medical practitioners to identify inhalant withdrawal symptoms and to provide safe withdrawal management strategies for people who use inhalants regularly and may be dependent.

The term inhalant is used to describe the wide range of volatile substances whose chemical fumes can have psychoactive effects when inhaled.

Commonly used products include:

- liquids: glue, petrol, contact cement (rubber cement), thinners, lacquers, nail-polish remover, dry-cleaning fluids, amyl nitrite
- aerosols: spray paints, lighter fluid, cooking sprays, cosmetics, hairspray, toiletries, deodorants
- gases: butane, LPG, nitrous oxide

Chemicals found in inhalants include the following:

- propane
- butane
- n-hexane
- trichloroethylene
- freon
- benzene
- toluene
- xylene
- acetone
- methyl isobutyl ketone
- chlorinated hydrocarbons

The majority of inhalants used as intoxicants are central nervous system depressants with effects similar to alcohol. Effects include slurred speech, lack of coordination, euphoria, and dizziness. Inhalant use may also lead to light-headedness, hallucinations, and delusions. As the effects are short lived many people try to prolong them by repeated use over a short period of time and this can result in disinhibited behaviour. The chemicals in different types of inhalants may also produce side effects such as palpitations, burns, confusion, nausea, or vomiting.
Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific inhalant use history includes:

- type or types of inhalant used
- average quantity and frequency of use over time
- duration of regular inhalant use
- time of last use
- other central nervous system depressants used concurrently
- history of seizures
- cognitive deficits and history of trauma
- physical health issues
- peer affiliations
- initial reasons for starting to use inhalants
- current goals relating to use

Inhalant withdrawal

Inhalant withdrawal syndrome is not well recognised or documented in the international literature and there is limited evidence or guidelines for managing withdrawal symptoms. It is apparent however that long term inhalant use may result in withdrawal symptoms when use is stopped.

Withdrawal severity appears to be dependent on frequency and intensity of use and symptoms can occur within hours of stopping use. Withdrawal symptoms appear to peak two to five days after stopping use of inhalants.

Figure 16: Symptoms of inhalant withdrawal

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>tremor</td>
<td>tingling sensations</td>
<td>tachycardia</td>
</tr>
<tr>
<td>disturbed sleep</td>
<td>restlessness</td>
<td>hallucinations</td>
</tr>
<tr>
<td>tiredness</td>
<td>chills</td>
<td>delirium</td>
</tr>
<tr>
<td>nausea</td>
<td>cramps</td>
<td>seizures</td>
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<td>anxiety</td>
<td>agitation</td>
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<tr>
<td>irritability</td>
<td>headache</td>
<td></td>
</tr>
<tr>
<td>low mood</td>
<td>abdominal pain</td>
<td></td>
</tr>
<tr>
<td>sweating</td>
<td>intense craving</td>
<td></td>
</tr>
</tbody>
</table>
Management of inhalant withdrawal

The following are general principles for treatment planning in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement. As the use of inhalants is usually time and age limited and rarely proceeds to dependent use withdrawal is relatively rare. Inhalant withdrawal scales have not as yet been developed for use in treatment planning.

Medication for management of inhalant withdrawal

While an evidence base for treating inhalant withdrawal does not exist the following medications have been used to help manage inhalant withdrawal:

- phenobarbitone (15-40 mg/L) can be helpful for agitation, use for five to ten days at the most
- diazepam can help with agitation but doses should be conservative and increased slowly before being reduced over ten days at the most
- phenytoin (10-20 mg/L) may help reduce the risk of seizures
- lorazepam can help with agitation but doses should only be increased slowly with regular blood pressure monitoring
- electrolyte, potassium and phosphorus, replacement may help improve muscle strength (hypocalcaemia is frequently encountered during fluid and electrolyte replacement)


Inpatient withdrawal management

The availability of specialist nursing and medical supervision allows for the safer management of risk than in a community setting. This is particularly true for people with

- health complications due to inhalant use including cardiac problems, peripheral neuropathy and liver or kidney damage
- cognitive deficits due to inhalant use including memory loss, delusions and irritability
- a known history of severe withdrawal
- a history of seizures
Figure 17: Inhalant withdrawal management pathway

Person seeks assistance and is screened by:
• General Practitioner
• NGO/DHB addiction service
• Community/iwi service
Person may be in involuntary/unplanned withdrawal due to incarceration or admission to hospital.

Does the person have severe: anxiety, mood, psychotic or confusional symptoms not explained by acute withdrawal?

Yes

Specialist mental health assessment

No

• Does the person have mild withdrawal symptoms:
  – tremor
  – irritability
  – disturbed sleep
• Does the person have good supports?
• Is the person confident in their ability to manage?

Yes to all

Self and GP managed withdrawal
  – support
  – reassurance
  – monitor
  – oral thiamine

No

• Does the person have mild-moderate withdrawal symptoms:
  – nausea
  – agitation
  – anxiety
  – headache
• Does the person have some level of support at home?

Yes to both

Community-based withdrawal management with nursing support
  – ?medication
  – support

No

• Is the person having moderate withdrawal symptoms?
• Does the person need respite from their home environment?

Yes to both

Social withdrawal management service admission

No

• Is there concern for safety of self or others?
• Is the person experiencing, or have they had in the past, severe withdrawal symptoms:
  – seizures
  – hallucinations
  – delusions
  – tachycardia
• Does the person use other substances?
• Does the person have co-existing mental or physical health problems?

Yes

Hospital /Inpatient admission for medically assisted withdrawal management
  – electrolyte replacement
  – ? diazepam
  – ? phenobarbitone
  – ? phenytoin

No

Follow-up treatment as needed

Yes

Self and GP managed withdrawal – support
– reassurance
– monitor
– oral thiamine
Opioids
Opioids

These guidelines have been developed to assist nursing and medical practitioners to identify opioid withdrawal symptoms and to provide safe withdrawal management strategies for people who are dependent.

An opioid is any agonist substance with morphine-like activity that acts as a central nervous system depressant. Opioids produce their pharmacological actions, including analgesia, by acting on receptors located on neuronal cell membranes. The presynaptic action of opioids to inhibit neurotransmitter release is considered to be their major effect in the nervous system. There are three types of opioid receptor, mu, delta and kappa, which are coupled to intracellular mechanisms via G-proteins.

An opiate is a naturally occurring opioid, i.e. a substance derived from the juice of poppies. Other opioids are semi-synthetic chemical derivatives of morphine (e.g. heroin) and some are fully synthetic (e.g. pethedine, tramadol and methadone).

With the scarcity of imported heroin in New Zealand people use a variety of opioids, including over the counter (e.g. panadeine and neurofen plus) medications, depending on their personal preference and what is readily available to them.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific opioid use history includes:

- names of the opioids used
- prescribed or non prescribed use
- route of use and documentation of injecting sites
- average quantity of use, MST dose equivalence (in milligrams), over time
- time of last use
- peer affiliations
- periods of abstinence
- initial reasons for starting to use opioids
- current goals relating to use

Managed opioid withdrawal has significant risks and there is a high rate of relapse post treatment. Opioid substitution is evidence based treatment that has been shown to reduce many of the short and long term risks of dependent opiate use. Opioid substitution treatment (OST) is the preferred treatment for most people with opioid dependence. For this reason managed withdrawal should not routinely be offered to opioid dependent people unless appropriate.
Indications that managed withdrawal is appropriate include:

- limited duration of use
- iatrogenic dependence
- amounts, mode and frequency of use have been relatively controlled and consistent over time
- positive supports
- engagement in appropriate post withdrawal treatment
- evidence of capacity to manage withdrawal symptoms
- no other substance use issues
- no, or well managed, co-existing physical and or mental health problems

**Opioid withdrawal**

The primary aim of a managed opioid withdrawal is reducing the acute physical and psychological discomforts that are the major symptoms of stopping opioid use. When withdrawal symptoms are not managed the rate of relapse is extremely high.

Withdrawal is best managed with a clear management plan, effective communication and stabilisation and progressive withdrawal using a long acting oral opioid. Supervised daily dispensing is recommended to reduce the risk of diversion.

**Figure 18:** Opioid withdrawal symptoms over time

Symptoms and duration of opioid withdrawal.
Reproduced and used with permission of NSW Department of Health (2008).
Onset and duration of opioid withdrawal

- Opioid withdrawal is influenced by the type of opioid that the person has been using, how long they have been using and tolerance.
- The onset of withdrawal from short acting opioids, such as codeine, morphine and oxycodone, typically occurs between eight to twelve hours after last use.
- Withdrawal symptoms from short acting opioids will usually abate within five to ten days.
- The onset of withdrawal from long acting opioids, such as methadone, tends to occur between twenty four to forty eight hours after last use.
- Long acting opioids will have a more protracted withdrawal of ten to twenty days, due to their long half-life.
- The severity of withdrawal is also influenced by other substances that people may be using, including benzodiazepines.

**Figure 19: Symptoms of opioid withdrawal**

<table>
<thead>
<tr>
<th>Common</th>
<th>Less common</th>
</tr>
</thead>
<tbody>
<tr>
<td>disturbed sleep</td>
<td>fear</td>
</tr>
<tr>
<td>yawning</td>
<td>irritability</td>
</tr>
<tr>
<td>muscle aches</td>
<td>anorexia/ weight loss</td>
</tr>
<tr>
<td>abdominal and back pains</td>
<td>elevated blood pressure</td>
</tr>
<tr>
<td>sweating</td>
<td>headaches</td>
</tr>
<tr>
<td>cramps</td>
<td>urinary frequency</td>
</tr>
<tr>
<td>pilo-erection/goose bumps</td>
<td>dysphoria</td>
</tr>
<tr>
<td>fatigue</td>
<td>hot and cold flushes</td>
</tr>
<tr>
<td>dilated pupils</td>
<td>lacrimation</td>
</tr>
<tr>
<td>diarrhoea</td>
<td>twitching</td>
</tr>
<tr>
<td>runny nose</td>
<td>light sensitivity</td>
</tr>
<tr>
<td>craving</td>
<td></td>
</tr>
<tr>
<td>nausea</td>
<td></td>
</tr>
<tr>
<td>vomiting</td>
<td></td>
</tr>
<tr>
<td>restlessness</td>
<td></td>
</tr>
<tr>
<td>agitation</td>
<td></td>
</tr>
<tr>
<td>anxiety</td>
<td></td>
</tr>
</tbody>
</table>

Management of opioid withdrawal

The following are general principles for treatment planning in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement. Opioid withdrawal severity can be measured with the Clinical Opiate Withdrawal Scale (COWS, Appendix 6).
Outpatient withdrawal management

Buprenorphine

Buprenorphine has been shown to be as effective in opioid withdrawal as methadone and may shorten the duration of withdrawal. Buprenorphine is a partial agonist with a high affinity for receptors but lower activity compared to most opioids. Buprenorphine is not funded by PHARMAC for use in addiction treatment and people who choose to use it for withdrawal management will need to fund it themselves.

Buprenorphine can precipitate withdrawal in patients who are using high doses of opioids, especially methadone.

To reduce the risk of precipitated withdrawal buprenorphine should not be prescribed until people are showing objective signs of withdrawal (COWS ≥ 13).

In the event of precipitated withdrawal people should be treated symptomatically with adjunctive medication. They should not be prescribed any opioid until the next scheduled dose of buprenorphine.

Figure 20: Buprenorphine managed opioid withdrawal regime

<table>
<thead>
<tr>
<th>Day</th>
<th>Buprenorphine dose (morning)</th>
<th>Buprenorphine dose (evening)</th>
<th>Total daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2-4mg, (withdrawal present)</td>
<td>2-4mg prn (COWS ≥ 13)</td>
<td>4-8mg</td>
</tr>
<tr>
<td>2</td>
<td>4mg</td>
<td>2-4mg prn (COWS ≥ 13)</td>
<td>4-8mg</td>
</tr>
<tr>
<td>3</td>
<td>4mg</td>
<td>2mg prn (COWS ≥ 13)</td>
<td>4-6mg</td>
</tr>
<tr>
<td>4</td>
<td>2mg</td>
<td>2mg prn (COWS ≥ 13)</td>
<td>2-4mg</td>
</tr>
<tr>
<td>5</td>
<td>2mg prn (COWS ≥ 13)</td>
<td>No dose</td>
<td>2mg</td>
</tr>
<tr>
<td>6</td>
<td>No dose</td>
<td>No dose</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>No dose</td>
<td>No dose</td>
<td></td>
</tr>
</tbody>
</table>

This table indicates a proposed withdrawal regime. Depending on withdrawal severity some people may require a higher starting dose of buprenorphine and or a more protracted regime.

Methadone

Using methadone to manage opioid withdrawal symptoms is indicated when the person is using up to 40mg methadone or an equivalent amount of other opioids. The initial dose should be no more than 40mg. (Ministry of Health, 2008).

Caution: People prescribed methadone must be reviewed four hours after their first dose and again on the fourth day as methadone is known to accumulate in the liver and stable plasma levels on a set dose may not be achieved for up to five days.

It is useful for the person to stabilise on methadone for up to two weeks prior to commencing a reduction. The rate of reduction can be individually tailored and reviewed as needed. It is reasonable to support a slow reduction (1 to 2mg week) while withdrawal remains an appropriate and or desired form of treatment.
Other opioids

Withdrawal from opioids such as codeine based medications can be managed by stabilising and then reducing the dose of an alternative opioid agonist, such as Dihydrocodeine (DHO).

Adjunctive medication

Adjunctive medication can be indicated either as a standalone treatment, potentially useful in custodial settings, or to support withdrawal along with opioid agonists. The following medications can be prescribed for symptomatic relief of symptoms of withdrawal.

**Figure 21: Adjunctive medications**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonidine</td>
<td>75-150mcg qid for up to three days reduce by a quarter of the third day’s dose or patches, typically tts1/2 one patch weekly</td>
<td>relieves many symptoms of withdrawal, chart regular</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10mg three times daily, (po/pr), prn for up to three or four days</td>
<td>nausea and vomiting</td>
</tr>
<tr>
<td>Loperamide</td>
<td>4mg stat 2mg with each loose motion max 16 mg in 24 hours 2mg one to two times daily for up to five days</td>
<td>diarrhoea</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>25-50mg, tds, prn max 200mg daily</td>
<td>agitation and irritability</td>
</tr>
<tr>
<td>Zopiclone</td>
<td>7.5mg if no effect within 2 hours another 7.5mg max 15mg in 24 hours for up to two weeks</td>
<td>insomnia</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>1g, qid, (Q4 hours) max of 4000mg in 24 hours max 2000mg in 24 hours with impaired liver functions and or liver disease</td>
<td>headaches, myalgia, arthralgia</td>
</tr>
<tr>
<td>Buscopan</td>
<td>10-20mg, pm, qid for up to three or four days</td>
<td>abdominal cramps</td>
</tr>
</tbody>
</table>

There are a range of medications that can be used for those people who do not tolerate these medications or experience severe withdrawal despite their use. These medications include:

- diazepam
- baclofen
- gabapentin
These medications should not be prescribed without consultation with an addiction medicine specialist, physician or psychiatrist.

**Nutrition and hydration**
Fluid loss through sweating, vomiting and diarrhoea can lead to dehydration. People should be encouraged to drink 2 to 3 litres of fluids daily and to eat light and healthy meals as able.

**Inpatient opioid withdrawal management**
There is very little evidence to support the need for admission to an in-patient setting for uncomplicated opioid withdrawal management. Inpatient withdrawal management should be considered for people with co-existing problems including: moderate to severe co-existing physical health disorders, moderate to severe co-existing mental health disorders and pregnant women.

Opioid withdrawal management in an inpatient setting is similar to management in the community or at a social withdrawal management service.

**Complementary therapies**
There is no reliable evidence to support the use of natural alternatives or complementary therapies for use in managing opioid withdrawal. However natural alternatives can help alleviate some withdrawal symptoms such as, anxiety, sleep difficulties and muscles aches and can also promote relaxation. Complementary therapies should not be used as an alternative to a planned and managed withdrawal process.

**Special populations**

**Pregnant women**
Abrupt cessation of opioids is not recommended for pregnant women who are dependent on opioids. Opioid withdrawal during the first and third trimester of pregnancy is associated with a higher risk of spontaneous abortion and premature delivery. Stabilisation on methadone for the duration of the pregnancy is the recommended treatment. If the woman insists on undergoing withdrawal this should preferably be carried out in the second trimester under medical supervision with small dose reductions at any one time to reduce the stress on the foetus. (Ministry of Health, 2008)

**Neonates**
Babies born with opioid intoxication and or withdrawal can present with symptoms which can last for several days after birth. These include:
- respiratory depression
• poor sucking
• hypotonia
• poor temperature regulation

**Neonatal abstinence syndrome (NAS)**

Abrupt opioid withdrawal at birth has been shown to result in:

• high-pitched crying
• irritability
• tremor/jittering
• sleeping difficulties
• stuffy nose
• sneezing
• feeding difficulties due to sucking problems
• tense arms, legs and back
• poor weight gain
• vomiting/diarrhoea
• rapid breathing
• skin irritation

NAS (Neonatal abstinence syndrome) onset may occur one to ten days after delivery and can last from seven days to a month.

• babies born to women who are opioid dependent should be observed in hospital for one week before discharge
• following discharge babies should have weekly outpatient reviews for at least one month
• the Adapted Finnegan scale (Appendix 4) is used to identify neonatal abstinence syndrome associated with opioids

**Breastfeeding**

• breastfeeding is recommended for women who are on a stable dose of methadone except in the presence of maternal HIV
• breastfeeding should be discontinued if a baby appears overly sedated
Figure 22: Opioid withdrawal management pathway

Person seeks assistance and is screened by:
- General Practitioner
- NGO/DHB addiction service
- Community/iwi service

Person may be in involuntary/unplanned withdrawal due to incarceration or admission to hospital

---

**Does the person have mild (COWS<12) withdrawal symptoms:**
- anxiety/agitation/restlessness
- aches/pains
- insomnia/tiredness
- cramps/diarrhoea/vomiting

- Has the person been using low dose opioids short term?
- Does the person have good supports?
- Is the person confident in their ability to manage?

---

**Does the person have severe: anxiety, mood, psychotic or confusional symptoms not explained by acute withdrawal?**

- Specialist mental health assessment

---

**Does the person have mild (COWS=13-24) withdrawal symptoms:**
- anxiety/agitation/restlessness
- aches/pains
- insomnia/tiredness
- cramps/diarrhoea/vomiting

- Does the person have some level of support at home?

---

**Does the person have moderate (COWS=25-36) withdrawal symptoms?**
- Does the person need respite from their home environment?

---

**Does the person have severe (COWS >36) withdrawal symptoms:**
- anxiety/agitation/restlessness
- aches/pains
- insomnia/tiredness
- cramps/diarrhoea/vomiting

- Does the person use other substances?
- Does the person have co-existing mental or physical health problems

---

**Self and GP managed withdrawal**
- stabilise on DHC or buprenorphine
- taper dose over six days
- support

---

**Community-based withdrawal management with nursing support**
- stabilise on buprenorphine or methadone
- taper dose of buprenorphine over six days
- taper dose of methadone at negotiated rate (e.g. 1-2 mg/wk)
- support/adjunctive medication

---

**Social withdrawal management service admission**
Manage withdrawal as above

---

Follow-up treatment as needed

---

**Hospital/Inpatient admission**
for medically assisted withdrawal management.
Manage withdrawal as above.
Resources, References, Appendices
Resources

For a list of CYP450 substrates, enhancers and inducers which indicate the potential for interactions between medications and some other substances:
http://medicine.iupui.edu/clinpharm/ddis/ClinicalTable.aspx

For quick reference to complement the above resource and the drug-drug drug-medication interactions described in Appendix 7:

References


**Appendix 1: Clinical Institute Withdrawal Assessment of Alcohol Scale Revised (CIWA-Ar)**

<table>
<thead>
<tr>
<th>Clinical Institute Withdrawal Assessment of Alcohol Scale Revised</th>
<th>Patient label</th>
</tr>
</thead>
<tbody>
<tr>
<td>DATE: ______________</td>
<td>---------------</td>
</tr>
<tr>
<td>Time:</td>
<td>Score</td>
</tr>
<tr>
<td>Nausea and vomiting (Do you feel sick? Have you vomited?)</td>
<td></td>
</tr>
<tr>
<td>0 Nil nausea</td>
<td>4 Intermittent/dry retching</td>
</tr>
<tr>
<td>1 Mild nausea, no vomiting</td>
<td>7 Constant nausea, retching and vomiting</td>
</tr>
<tr>
<td>Tremor (arms extended, fingers spread)</td>
<td></td>
</tr>
<tr>
<td>0 No tremor</td>
<td>4 Moderate with arms extended</td>
</tr>
<tr>
<td>1 Not visible – can be felt fingertip to fingertip</td>
<td>7 Severe even with arms not extended</td>
</tr>
<tr>
<td>Paroxysmal Sweating (observation)</td>
<td></td>
</tr>
<tr>
<td>0 No sweat visible</td>
<td>4 Beads of sweat visible</td>
</tr>
<tr>
<td>1 Barely perceptible, palms moist</td>
<td>7 Drenching sweats</td>
</tr>
<tr>
<td>Anxiety (Do you feel nervous?) (observation)</td>
<td></td>
</tr>
<tr>
<td>0 No anxiety: at ease</td>
<td>4 Moderately anxious or guarded</td>
</tr>
<tr>
<td>1 Mildly anxious</td>
<td>7 Acute panic as seen in delirium or schizophrenic reactions.</td>
</tr>
<tr>
<td>Agitation (observation)</td>
<td></td>
</tr>
<tr>
<td>0 Normal activity</td>
<td>4 Moderately fidgety and restless</td>
</tr>
<tr>
<td>1 Somewhat more than normal</td>
<td>7 Pacing, or thrashing activity about constantly</td>
</tr>
<tr>
<td>Tactile disturbances (Any itching, pins and needles, burning or other sensations) (observation)</td>
<td></td>
</tr>
<tr>
<td>0 None</td>
<td>4 Moderately severe tactile hallucinations (for example bugs crawling)</td>
</tr>
<tr>
<td>1 Very mild itching or pins and needles or numbness</td>
<td>5 Severe tactile hallucinations</td>
</tr>
<tr>
<td>2 Mild itching, pins and needles or numbness</td>
<td>6 Extremely severe tactile hallucinations</td>
</tr>
<tr>
<td>3 Moderate itching, pins and needles or numbness</td>
<td>7 Continuous tactile hallucinations</td>
</tr>
</tbody>
</table>

*Substance Withdrawal Management Guidelines*
**Clinical Institute Withdrawal Assessment of Alcohol Scale Revised**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DATE:</strong></td>
<td>____________</td>
<td>Time:</td>
</tr>
<tr>
<td><strong>Score</strong></td>
<td>Time:</td>
<td></td>
</tr>
</tbody>
</table>

**Auditory disturbances (Increased awareness of sounds? Sensitivity to loud noises or hearing voices?) (observation)**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not present</td>
</tr>
<tr>
<td>1</td>
<td>Very mild sensitivity</td>
</tr>
<tr>
<td>2</td>
<td>Mild harshness or ability to frighten</td>
</tr>
<tr>
<td>3</td>
<td>Moderate harshness or ability to frighten</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe hallucinations</td>
</tr>
<tr>
<td>5</td>
<td>Severe hallucinations</td>
</tr>
<tr>
<td>6</td>
<td>Extremely severe hallucinations</td>
</tr>
<tr>
<td>7</td>
<td>Continuous hallucinations</td>
</tr>
</tbody>
</table>

**Visual disturbances (Does light hurt your eyes? Is colour different, are you seeing things that you know are not there?) (observation)**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not present</td>
</tr>
<tr>
<td>1</td>
<td>Very mild sensitivity</td>
</tr>
<tr>
<td>2</td>
<td>Mild sensitivity</td>
</tr>
<tr>
<td>3</td>
<td>Moderate sensitivity</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe hallucinations</td>
</tr>
<tr>
<td>5</td>
<td>Severe hallucinations</td>
</tr>
<tr>
<td>6</td>
<td>Extremely severe hallucinations</td>
</tr>
<tr>
<td>7</td>
<td>Continuous hallucinations</td>
</tr>
</tbody>
</table>

**Headache (Does your head feel different, is there a band around your head?) (do not rate for dizziness or light-headedness)**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not present</td>
</tr>
<tr>
<td>1</td>
<td>Very mild</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe</td>
</tr>
<tr>
<td>5</td>
<td>Severe</td>
</tr>
<tr>
<td>6</td>
<td>Very severe</td>
</tr>
<tr>
<td>7</td>
<td>Extremely severe</td>
</tr>
</tbody>
</table>

**Clouding of sensorium (What day is this? What is this place?)**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Oriented, can do serial addition</td>
</tr>
<tr>
<td>1</td>
<td>Cannot do serial addition, uncertain of date</td>
</tr>
<tr>
<td>2</td>
<td>Disorientated for date by no more than 2 calendar days</td>
</tr>
<tr>
<td>3</td>
<td>Disorientated for date by more than 2 calendar days (re-orientate if necessary)</td>
</tr>
<tr>
<td>4</td>
<td>Disorientated for place (re-orientate if necessary)</td>
</tr>
</tbody>
</table>

**Mild Withdrawal** 0-8

**Moderate Withdrawal** 8-15

**Severe Withdrawal** 15+

**Total**

**Time**

**Signature**

**TEMPERATURE, PULSE AND BLOOD PRESSURE RECORDINGS NEED TO BE DOCUMENTED ON OBSERVATION CHART IN CONJUNCTION WITH THE CIWA-Ar ASSESSMENT**

### Appendix 2: Absorption rates, half life and equivalent daily doses of common benzodiazepines

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Equivalent dose to 5mg diazepam</th>
<th>Time to peak concentration</th>
<th>Elimination half life</th>
<th>Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>Valium</td>
<td>5mg</td>
<td>30-90min</td>
<td>20-48 hours</td>
<td>Long</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Xanax</td>
<td>0.5-1.0mg</td>
<td>60 min</td>
<td>6-25 hours</td>
<td>Short</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Rivotril</td>
<td>0.5mg</td>
<td>2-3 hours</td>
<td>22-54 hours</td>
<td>Long</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Ativan</td>
<td>1mg</td>
<td>2 hours</td>
<td>12-16 hours</td>
<td>Short</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>Serepax</td>
<td>15-30mg</td>
<td>2-3 hours</td>
<td>4-15 hours</td>
<td>Short</td>
</tr>
<tr>
<td>Nitrazepam</td>
<td>Mogadon</td>
<td>2.5-5mg</td>
<td>2 hours</td>
<td>16-48 hours</td>
<td>Long</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Normison</td>
<td>10-20mg</td>
<td>30-60 min/tablets 2 hours</td>
<td>5-15 hours</td>
<td>Short</td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>Rohypnol</td>
<td>1-2mg</td>
<td>1-2 hours</td>
<td>20-30 hours</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Halcion</td>
<td>0.25</td>
<td>1-3 hours</td>
<td>2-5 hours</td>
<td>V. Short</td>
</tr>
<tr>
<td>Zopiclone</td>
<td>Imovane</td>
<td>7.5mg</td>
<td>5 hours</td>
<td></td>
<td>V. Short</td>
</tr>
</tbody>
</table>

**Note:**
- Elimination half life: Time for the plasma drug concentration to decrease by 50%
- Duration of action (approx.):
  - Very short <6 hours
  - Short <12 hours
  - Intermediate <24 hours
  - Long >24 hours

Adapted from: Drug and Alcohol Withdrawal Clinical Practice Guidelines (NSW Department of Health, 2008).
**Appendix 3: Example of a three times daily (tds) low dose diazepam reduction regime**

<table>
<thead>
<tr>
<th>Stage</th>
<th>0800hrs</th>
<th>1400hrs</th>
<th>2000hrs</th>
<th>Total diazepam equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 (5mg tablets)</td>
<td>5mg</td>
<td>5mg</td>
<td>5mg</td>
<td>15mg</td>
</tr>
<tr>
<td>Stage 2 (5mg tablets)</td>
<td>5mg</td>
<td>2.5mg</td>
<td>5mg</td>
<td>12.5mg</td>
</tr>
<tr>
<td>Stage 3 (5mg tablets)</td>
<td>5mg</td>
<td>2.5mg</td>
<td>2.5mg</td>
<td>10mg</td>
</tr>
<tr>
<td>Stage 4 (2mg tablets)</td>
<td>4mg</td>
<td>2mg</td>
<td>2mg</td>
<td>8mg</td>
</tr>
<tr>
<td>Stage 5 (2mg tablets)</td>
<td>3mg</td>
<td>2mg</td>
<td>2mg</td>
<td>7mg</td>
</tr>
<tr>
<td>Stage 6 (2mg tablets)</td>
<td>2mg</td>
<td>2mg</td>
<td>2mg</td>
<td>6mg</td>
</tr>
<tr>
<td>Stage 7 (2mg tablets)</td>
<td>2mg</td>
<td>1mg</td>
<td>2mg</td>
<td>5mg</td>
</tr>
<tr>
<td>Stage 8 (2mg tablets)</td>
<td>2mg</td>
<td>1mg</td>
<td>1mg</td>
<td>4mg</td>
</tr>
<tr>
<td>Stage 9 (2mg tablets)</td>
<td>1mg</td>
<td>1mg</td>
<td>1mg</td>
<td>3mg</td>
</tr>
<tr>
<td>Stage 10 (2mg tablets)</td>
<td>1mg</td>
<td>-</td>
<td>1mg</td>
<td>2mg</td>
</tr>
<tr>
<td>Stage 11 (2mg tablets)</td>
<td>1mg</td>
<td>-</td>
<td>-</td>
<td>1mg</td>
</tr>
<tr>
<td>Stage 12</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0 mg</td>
</tr>
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</table>
## Appendix 4: Adapted Finnegan scale

<table>
<thead>
<tr>
<th>Systems</th>
<th>Signs and Symptoms</th>
<th>Score</th>
<th>0200 hrs</th>
<th>0400 hrs</th>
<th>0600 hrs</th>
<th>0800 hrs</th>
<th>1000 hrs</th>
<th>1200 hrs</th>
<th>1400 hrs</th>
<th>1600 hrs</th>
<th>1800 hrs</th>
<th>2000 hrs</th>
<th>2200 hrs</th>
<th>2400 hrs</th>
<th>Daily Wt.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Nervous System Disturbances</td>
<td>High pitched cry</td>
<td>2</td>
<td></td>
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<tr>
<td></td>
<td>Continuous high pitched cry</td>
<td>3</td>
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<tr>
<td></td>
<td>Sleeps &lt; 1 hour after feeding</td>
<td>3</td>
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<td>Sleeps &lt; 2 hours after feeding</td>
<td>2</td>
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<td>Hyperactive moro reflex</td>
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<td></td>
<td>Markedly hyperactive moro reflex</td>
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<tr>
<td></td>
<td>Mild tremors disturbed</td>
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<tr>
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<td>Moderate severe tremors disturbed</td>
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<tr>
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<td>Mild tremors undisturbed</td>
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<td>Moderate severe tremors undisturbed</td>
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<td>Increased muscle tone</td>
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<tr>
<td></td>
<td>Myoclonic jerks</td>
<td>3</td>
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<td>Generalised convulsions</td>
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<tr>
<td>Metabolic/Vasomotor/Respiratory disturbances</td>
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<td>Fever &lt; 101°F (39.3°C)</td>
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<td>Fever &gt; 101°F (39.3°C)</td>
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<td>Frequent yawning (&gt; 3-4 times/interval)</td>
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<td>Nasal stuffiness</td>
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<tr>
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<td>Sneezing (&gt;3-4 times/interval)</td>
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<tr>
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<td>Respiratory rate &gt; 60/min</td>
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<td>Respiratory rate &gt; 60/min with retractions</td>
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<tr>
<td>Gastrointestinal disturbances</td>
<td>Excessive sucking</td>
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<td>Poor feeding</td>
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<td>Regurgitation</td>
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<td>Projectile vomiting</td>
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<tr>
<td></td>
<td>Loose stools</td>
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<td></td>
<td>Watery stools</td>
<td>3</td>
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</tr>
<tr>
<td>Summary</td>
<td>Total score</td>
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<tr>
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<td>Scorer's initials</td>
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<td>Status of therapy</td>
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</tr>
</tbody>
</table>

Appendix 5: Cannabis Withdrawal Assessment Scale (CWAS)

Drug & Alcohol Services Council, SA, 2002

Note: Total Score is indicative of increasing or decreasing severity of withdrawal. Scores are not directly linked to pharmacological management as occurs with alcohol scores based on the CIWA-Ar.

Surname: ___________________________  Given name: ___________________________
Date of birth: ___________________________

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Temperature</th>
<th>Pulse</th>
<th>Respiration rate</th>
<th>Blood pressure</th>
<th>Pupil size</th>
<th>Reaction</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Score range = 0-7

Restlessness/agitation
Racing thoughts
Mood changes
Feelings of unreality
Fear
Drowsiness
Hunger
Appetite
Total

Sleep (0800 obs only)
Other symptoms

Scoring: 0 = no symptoms, 4 = moderate symptoms, 7 = severe symptoms

Appendix 6: Clinical Opioid Withdrawal Scale (COWS)

<table>
<thead>
<tr>
<th>Reason for this assessment:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient's name:</td>
<td>Date and time _____ / _____ / _____ :______</td>
<td></td>
</tr>
<tr>
<td>Reason for this assessment:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resting Pulse rate:</th>
<th>Measure after patient is sitting for one minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 pulse rate 80 or below</td>
<td>0 no GI symptoms</td>
</tr>
<tr>
<td>1 pulse rate 81-100</td>
<td>1 stomach cramps</td>
</tr>
<tr>
<td>2 pulse rate 101-120</td>
<td>2 nausea or loose stool</td>
</tr>
<tr>
<td>4 pulse rate greater than 120</td>
<td>3 vomiting or diarrhoea</td>
</tr>
<tr>
<td></td>
<td>5 multiple episodes of diarrhoea or vomiting</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GI Upset</th>
<th>over last ½ hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no GI symptoms</td>
<td>0 no GI symptoms</td>
</tr>
<tr>
<td>1 stomach cramps</td>
<td>1 stomach cramps</td>
</tr>
<tr>
<td>2 nausea or loose stool</td>
<td>2 nausea or loose stool</td>
</tr>
<tr>
<td>3 vomiting or diarrhoea</td>
<td>3 vomiting or diarrhoea</td>
</tr>
<tr>
<td>5 multiple episodes of diarrhoea or vomiting</td>
<td>5 multiple episodes of diarrhoea or vomiting</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sweating</th>
<th>Over past ½ hour not accounted for by room temperature or patient activity.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no report of chills or flushing</td>
<td>0 no tremor</td>
</tr>
<tr>
<td>1 subjective report of chills or flushing</td>
<td>1 tremor can be felt, but not observed</td>
</tr>
<tr>
<td>2 flushed or observable moistness on fact</td>
<td>2 slight tremor observable</td>
</tr>
<tr>
<td>3 beads of sweat on brow or face</td>
<td>4 gross tremor or muscle twitching</td>
</tr>
<tr>
<td>4 sweat streaming off face</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tremor</th>
<th>Observation of outstretched hands</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no tremor</td>
<td>0 no tremor</td>
</tr>
<tr>
<td>1 tremor can be felt, but not observed</td>
<td>1 tremor can be felt, but not observed</td>
</tr>
<tr>
<td>2 slight tremor observable</td>
<td>2 slight tremor observable</td>
</tr>
<tr>
<td>4 gross tremor or muscle twitching</td>
<td>4 gross tremor or muscle twitching</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Restlessness</th>
<th>Observation during assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 able to sit still</td>
<td>0 no yawning</td>
</tr>
<tr>
<td>1 reports difficulty sitting still, but is able to do so</td>
<td>1 yawning once or twice during assessment</td>
</tr>
<tr>
<td>3 frequent shifting or extraneous movements of legs/arms</td>
<td>2 yawning three or more times during assessment</td>
</tr>
<tr>
<td>5 unable to sit still for more than a few seconds</td>
<td>4 yawning several times/minute</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Yawning</th>
<th>Observation during assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no yawning</td>
<td>0 no yawning</td>
</tr>
<tr>
<td>1 yawning once or twice during assessment</td>
<td>1 yawning once or twice during assessment</td>
</tr>
<tr>
<td>2 yawning three or more times during assessment</td>
<td>2 yawning three or more times during assessment</td>
</tr>
<tr>
<td>4 yawning several times/minute</td>
<td>4 yawning several times/minute</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pupil size</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0 pupils pinned or normal size for room light</td>
<td>0 none</td>
<td></td>
</tr>
<tr>
<td>1 pupils possibly larger than normal for room light</td>
<td>1 patient reports increasing irritability or anxiousness</td>
<td></td>
</tr>
<tr>
<td>2 pupils moderately dilated</td>
<td>2 patient obviously irritable or anxious</td>
<td></td>
</tr>
<tr>
<td>5 pupils so dilated that only the rim of the iris is visible</td>
<td>4 patient so irritable or anxious that participation in the assessment is difficult</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anxiety or Irritability</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0 none</td>
<td>0 none</td>
<td></td>
</tr>
<tr>
<td>1 patient reports increasing irritability or anxiousness</td>
<td>1 patient reports increasing irritability or anxiousness</td>
<td></td>
</tr>
<tr>
<td>2 patient obviously irritable or anxious</td>
<td>2 patient obviously irritable or anxious</td>
<td></td>
</tr>
<tr>
<td>4 patient so irritable or anxious that participation in the assessment is difficult</td>
<td>4 patient so irritable or anxious that participation in the assessment is difficult</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone or Joint aches</th>
<th>If patient was having pain previously, only the additional component attributed to opioid withdrawal is scored</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 not present</td>
<td>0 not present</td>
</tr>
<tr>
<td>1 mild diffuse discomfort</td>
<td>1 mild diffuse discomfort</td>
</tr>
<tr>
<td>2 patient reports severe diffuse aching of joints/muscles</td>
<td>2 patient reports severe diffuse aching of joints/muscles</td>
</tr>
<tr>
<td>4 patient is rubbing joints or muscles and is unable to sit still because of discomfort</td>
<td>4 patient is rubbing joints or muscles and is unable to sit still because of discomfort</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gooseflesh skin</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0 skin is smooth</td>
<td>0 skin is smooth</td>
<td></td>
</tr>
<tr>
<td>3 piloerrection of skin can be felt or hairs standing up on arms</td>
<td>3 piloerrection of skin can be felt or hairs standing up on arms</td>
<td></td>
</tr>
<tr>
<td>5 prominent piloerrection</td>
<td>5 prominent piloerrection</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Runny nose or tearing</th>
<th>Not accounted for by cold symptoms or allergies</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 not present</td>
<td>0 not present</td>
</tr>
<tr>
<td>1 nasal stuffiness or unusually moist eyes</td>
<td>1 nasal stuffiness or unusually moist eyes</td>
</tr>
<tr>
<td>2 nose running or tearing</td>
<td>2 nose running or tearing</td>
</tr>
<tr>
<td>4 nose constantly running or tears streaming down cheeks</td>
<td>4 nose constantly running or tears streaming down cheeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Score</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>The total score is the sum of all 11 items</td>
<td>The total score is the sum of all 11 items</td>
<td></td>
</tr>
<tr>
<td>Initials of person completing assessment:</td>
<td>Initials of person completing assessment:</td>
<td></td>
</tr>
</tbody>
</table>

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

Appendix 7: Drug–Drug and Drug–Medication Interactions

This appendix is copied from *Te Ariari o te Oranga: the Assessment and Management of People with Co-existing Mental Health and Substance Use Problems* (Todd, 2010) and accompanies the text in Section 4.6.4 (pp. 118-9).

This is intended to be a guide to drug-drug and drug-medication interactions. Interactions between psychoactive substances are potentially important, though much is unknown, especially for interactions between prescribed medications and illicitly taken substances. This section highlights some key interactions to be aware of, but it is not comprehensive. Note that the absence of an interaction described here does not mean it does not exist and therefore the combination is safe.

Interactions may arise through a number of mechanisms, including synergistic effects on neurotransmitter systems, augmentation of side-effects and alterations in the metabolism of a drug. Alterations in metabolism are potentially complex and often involve the cytochrome (CYP450) system in the liver. There is a wide range of cytochromes, and where drugs taken at the same time are metabolised by the same cytochrome, metabolism may be affected by either inhibition or induction of the enzymes. The main cytochromes of relevance for CEP are CYP2D6 and CYP3A4. A table of CYP450 interactions is available at: http://medicine.iupui.edu/clinpharm/DDIs/table.asp

As noted, there are likely to be important interactions that are not mentioned, and many of the interactions that are mentioned are theoretical or based on a small number of case reports. There is also considerable interpersonal variation in these interactions. This section should therefore be used as a guide to possible interactions, and in most cases drugs that interact should still be prescribed, but cautiously, and the effects monitored.

There are several potentially severe and fatal interactions. The combination of the following medications and drugs is best avoided:

- lorazepam and alcohol, which has been associated with significant respiratory and cardiac depression (this appears to be more likely with lorazepam than with other benzodiazepines)
- amyl nitrate and sildenafil (viagra) or tadalafil (cialis), which have been associated with potentially fatal hypotension
- ecstasy and ritonavir, which has been associated with fatalities reported
- ecstasy and monoamine oxidase inhibitors, including moclobemide, which have been associated with fatalities
- amphetamines and monoamine oxidase inhibitors, including moclobemide, which have been associated with a severe hypertensive crisis

**Nicotine**

The main effect of nicotine on other drugs is via the polycyclic aromatic hydrocarbons in tobacco smoke and their induction of certain CYP450 enzymes. This increases the metabolism and reduces serum levels of a range of drugs, though there are other mechanisms that may be involved. The dosage of such medications may need to be increased in smokers and reduced upon cessation of smoking to avoid the emergence of side-effects.
Reduced blood levels may occur with the combination of tobacco use and the following drugs:

- alprazolam and other benzodiazepines
- beta-blockers, especially propranolol
- caffeine
- chlorpromazine
- clozapine (reduction in blood levels may be marked)
- corticosteroids
- haloperidol
- heparin
- inhaled insulin (currently unavailable; causes a significant increase in insulin levels, contraindicated in current or recent tobacco users)
- mexiletine
- olanzapine (mild effects, so may not need dose adjustment)
- pentazocine
- theophylline
- tricyclic antidepressants (especially imipramine and nortriptyline)

In addition, it should be noted that through other mechanisms, there may be an increased risk of myocardial infarction when tobacco smokers take oral contraceptives.

**Figure 23: Interactions between alcohol and medications**

<table>
<thead>
<tr>
<th>Medication class</th>
<th>Medication</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaesthetic agents</td>
<td>Fluothane, propofol,</td>
<td>Risk of liver damage; higher dosages needed to induce anaesthesia</td>
</tr>
<tr>
<td>Analgesics – non-opioid</td>
<td>Aspirin and NSAIDs</td>
<td>Increased risk of gastric bleeding</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Metronidazole and tinidazole (antabuse-type reaction), griseofulvin, quinacrine</td>
<td>Reduced effectiveness, nausea/vomiting, headache, seizures</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>Warfarin</td>
<td>Increased clotting time with acute alcohol use; reduced clotting time with chronic use</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Tricyclic antidepressants</td>
<td>Increased sedation, impaired motor skills</td>
</tr>
<tr>
<td></td>
<td>Monoamine oxidase inhibitor</td>
<td>Tyramine-rich drinks (beer, red wine) may cause severe hypertension and, rarely, cardiac arrhythmias</td>
</tr>
<tr>
<td></td>
<td>Serotonin-specific re-uptake inhibitors (fluoxetine, citalopram, paroxetine)</td>
<td>May enhance the intoxicating effects of alcohol</td>
</tr>
<tr>
<td>Antidiabetic agents</td>
<td>Tolbutamide</td>
<td>Acute intoxication increases and chronic consumption reduces tolbutamide availability</td>
</tr>
<tr>
<td>Medication class</td>
<td>Medication</td>
<td>Effects</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Diphenhyramine (Benadryl)</td>
<td>Increased sedation and dizziness, especially in elderly</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td></td>
<td>Enhanced side-effects, especially sedation, hypotension, impaired judgment and motor incoordination; possible increase in akathisia and dystonic reactions (small case series)</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Phenytoin</td>
<td>Increased phenytoin levels with acute alcohol consumption</td>
</tr>
<tr>
<td>Antiulcer drugs</td>
<td>Ranitidine, cimetidine</td>
<td>May increase alcohol levels</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Nitroglycerin, reserpine,</td>
<td>Possible increased postural hypotension</td>
</tr>
<tr>
<td>meds</td>
<td>methyldopa, hydralazine,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>guanethidine</td>
<td></td>
</tr>
<tr>
<td>Mood stabilisers</td>
<td>Lithium</td>
<td>Increased motor incoordination; lithium may slightly reduce intoxicating effects of alcohol in some</td>
</tr>
<tr>
<td></td>
<td>Valproate</td>
<td>Increased sedation, especially in early phases of valproate treatment</td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
<td>Increased sedation, possible respiratory depression, risk of overdose</td>
</tr>
<tr>
<td>Sedatives</td>
<td>All benzodiazepines</td>
<td>Sedation, motor incoordination</td>
</tr>
<tr>
<td></td>
<td>Lorazepam</td>
<td>Respiratory and cardiac depression (avoid in acute intoxication)</td>
</tr>
</tbody>
</table>

**Sources:**
- NIAAA Alcohol Alert January 1995, no. 27 PH 355 publication
- Alcohol-drug Interactions, University Health Service (UHS) Health Promotion Office, Rochester University: http://www.rochester.edu/uhs/healthtopics/Alcohol/interactions.html

As noted, the interaction between lorazepam and alcohol may lead to possible cardiac and respiratory depression and should be avoided.

Where sedation and incoordination are noted, tangata whaiora should be advised not to drive and to avoid using machinery.

Advice about not combining alcohol with specific medications should be given carefully, especially where the risk or severity of complications is mild. Tangata whaiora are as likely to stop medication as alcohol, if advised not to combine them. This is especially the case in the treatment of mood problems, especially bipolar disorder, where mood stabilisers are likely to reduce alcohol consumption and the potential complications are usually mild.

**Cannabis**

Much of the information on cannabis interactions comes from research into the synthetic tetrahydrocannabinol (THC) analogue dronabinol. It should be noted that cannabis has a number of extra actions due to the large number of other compounds it also contains.
**Figure 24:** Interactions between cannabis and medications

<table>
<thead>
<tr>
<th>Other medication</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines, cocaine, other sympathomimetics</td>
<td>Hypertension, tachycardia, possibly cardiotoxicity</td>
</tr>
<tr>
<td>Atropine, scopolamine, antihistamines and other anticholinergics</td>
<td>Tachycardia, drowsiness</td>
</tr>
<tr>
<td>Amitriptyline, amoxapine, desipramine, other tricyclic antidepressants</td>
<td>Additive tachycardia, hypertension, drowsiness</td>
</tr>
<tr>
<td>Disulfiram (antabuse)</td>
<td>Possible hypomania (single case)</td>
</tr>
<tr>
<td>Benzodiazepines, alcohol, lithium, opioids, buspirone, antihistamines, other CNS depressants</td>
<td>Additive drowsiness and CNS depression</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Increased theophylline metabolism, similar to the effects of smoking tobacco.</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Possible hypomania (single case)</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Intoxication enhanced by naltrexone</td>
</tr>
</tbody>
</table>

**Note:** CNS = central nervous system

There is some evidence that THC intoxication is enhanced by naltrexone (Haney et al., 2003), though other studies contradict this (Wachtel and de Wit, 2000).

Prior recent exposure to nicotine may enhance some of the effects of cannabis, especially in males (Penetar et al., 2005), though it has been shown that THC ameliorates acute nicotine withdrawal and that the cognitive effects of nicotine withdrawal (memory) are greater in marijuana users (Viveros et al., 2006).

**Stimulants**

Stimulants are drugs that are both prescribed and used illicitly. Amphetamines are metabolized by CYP2D6 and inhibitors of this enzyme such as paroxetine and fluoxetine. The concomitant use of methylphenidate (ritalin) and monoamine oxidase inhibitors is contraindicated due to the risk of hypertensive crisis. Methylphenidate may decrease the effectiveness of medications used to treat high blood pressure and may increase levels of warfarin and tricyclic antidepressants.

Methamphetamine has many potential interactions. The following are the major interactions that can occur; in combination with:

- selegiline – hypertensive crisis (contraindicated)
- bupropion – increased risk of seizures
- tramadol – seizures
- SSRIs and venlafaxine – potential increase in amphetamine activity, potential serotonin syndrome with some (e.g. dexamphetamine)
- linezolid (a new antibiotic) – has monoamine oxidase inhibitor actions (contraindicated)
- sibutramine (reductil) – contraindicated due to adrenergic and serotoninergic reuptake inhibition
Other medications with stimulant actions, especially those affecting the adrenergic system, can lead to increased blood pressure and pulse rate (e.g. chlorpheniramine, phenylephrine, dextromethorphan and brompheniramine), which are often found in cough mixtures. Antacids can increase amphetamine absorption and therefore actions.

**MDMA (Ecstasy)**

MDMA is potentially hepatotoxic, and liver function should be monitored when prescribing other medications that are also hepatotoxic, such as naltrexone and sodium valproate. It also releases large amounts of serotonin and is mainly metabolised by CYP2D6. There is therefore a risk of serotonergic syndrome, especially in combination with drugs like fluoxetine, citalopram, paroxetine, venlafaxine buproprion and pethidine.

The most serious combinations include:
- ecstasy and MAOIs, including moclobemide (which has been associated with fatal interactions)
- ecstasy and ritonavir (fatalities have been reported)

Inhibition of metabolism via CYP2D6 inhibition can occur with:
- fluoxetine
- paroxetine
- bupropion
- methadone
- haloperidol
- quinidine
- ritonavir (antiviral agent)

Enhanced serotonergic effects can occur with:
- amphetamines
- St John’s wort
- tramadol
- venlafaxine
- lithium
- clomipramine

(Oesterheld et al., 2004)
**Benzodiazepines and other sedatives**

Benzodiazepines differ in terms of their metabolism. Most are metabolised by the CYP450 system in the liver and therefore are affected by other medications that increase or decrease the activity of that system. Medications that induce CYP450, such as St John’s wort, carbamazepine, phenytoin and rifampicin, therefore decrease the action of these benzodiazepines. Medications that reduce the activity of CYP450, and therefore increase the effects of benzodiazepines, include oral contraceptives, antibiotics, antidepressants and antifungal agents. Benzodiazepines that are not metabolised by the CYP450 system, and therefore are not affected by these interactions, include lorazepam, oxazepam and temazepam.

**Opioids**

**Pethidine**

Pethidine has the potential to induce a serotonin syndrome when used together with other drugs including:

- dextromethorphan
- pentazocine
- tramadol
- tricyclic antidepressants
- selective serotonin reuptake inhibitors (SSRIs)
- monoamine oxidase inhibitors (MAOIs), including moclobemide

Pethidine can increase risk of seizures in combination with the following drugs:

- theophylline
- tricyclic antidepressants
- fluoroquinolones (which can potentiate the seizure potential of pethidine)

**Methadone**

The tendency for methadone to prolong the QT interval may be enhanced by other drugs that do the same. A list of these can be found at: http://www.azcert.org/medical-pros/drug-lists/printable-drug-list.cfm

**Precipitation of opioid withdrawal**

This can result from:

- buprenorphine
- pentazocine
- naltrexone
- naloxone
- tramadol
Unpredictable interactions
These can result from combining opioids with:
- antiretroviral drugs
- benzodiazepines
- cannabis
- cyclizine
- interferon + ribavirin
- methylphenidate
- opioids
- promethazine
- tricyclic antidepressants.

Decreased methadone effects
This can result from combining methadone with:
- some antiretroviral drugs
- alcohol
- carbamazepine
- phenytoin
- rifampicin
- St John's wort
- tobacco
- urinary acidifiers

Increased effects of methadone
These can be induced by combining methadone with:
- cimetidine
- some antiviral drugs
- diazepam
- dihydroergotamine
- alcohol
- erythromycin
- fluconazole
- grapefruit
• moclobemide
• omeprazole
• serotonin-specific reuptake inhibitors
• verapamil
• cyclizine
(Leavitt, 2005)

Morphine
Morphine may interact with monoamine oxidase inhibitors to cause serotonin syndrome.

Solvents and volatile substances
Solvents may sensitize the heart to adrenaline, and this has been associated with sudden cardiac death when adrenaline is co-administered. This usually only occurs in emergency medicine situations.

Other commonly prescribed medications

Naltrexone
• opioid antagonist, precipitates opioid withdrawal in those with physiological dependence on opioids
• otherwise known significant drug interactions

Serotonin-specific reuptake inhibitors (SSRIs) (fluoxetine and citalopram)
The use of SSRIs with monoamine oxidase inhibitors is contraindicated. SSRIs may lower the seizure threshold and should be used cautiously with other drugs that do the same. Serotonin syndrome may occur when SSRIs are used with other drugs that enhance serotonin activity, or with drugs that inhibit SSRI metabolism.

Antipsychotics (risperidone, quetiapine, olanzapine, clozapine, chlorpromazine)
Antipsychotics may be associated with an increased risk of seizures and cardiac arrhythmias especially in those with QT prolongation. This risk may be enhanced with other drugs that have similar effects, particularly amphetamines.

Bupropion (Zyban)
The use of bupropion and monoamine oxidase inhibitors is contraindicated. The metabolism of bupropion may be inhibited by paroxetine, sertraline and antiretroviral agents, increasing its blood levels. Bupropion inhibits the CYP2D6 isoenzyme and may increase blood levels of drugs metabolised by this enzyme, including most antidepressants (e.g. nortriptyline, imipramine,
desipramine, paroxetine, fluoxetine, sertraline), antipsychotics (e.g. haloperidol, risperidone, thioridazine), beta-blockers (e.g. metoprolol) and antiarrhythmics, and antipsychotics. Bupropion can also lower the seizure threshold and should be used with other drugs that act similarly only with great caution. This is especially so in tangata whaiora with bulimia or anorexia nervosa due to possible increases in seizure risk in this population.

Varenicline

There are no known or predictive drug interactions of significance.

References


Source


This document is available in hard copy and is downloadable from: http://www.moh.govt.nz/moh.nsf/indexmh/assessment-mang-people-coexisting-mental-health
Appendix 8: Withdrawal Management Reference Group

Many thanks to the contributions and expertise of the members of the Reference Group:
Shelley Andrews, Clinician, Rongo Atea Youth Alcohol and Drug Treatment Service, Waikato
Steph Anderson, Detox Nurse, Nelson Addiction Service, Nelson Marlborough DHB
Michelle Fowler, Youth Specialty Services, Canterbury DHB
Susanna Galea Dr., CADS Service Clinical Director / Consultant Psychiatrist, Waitemata DHB
Moira Gilmour, Speciality Nurse Detox, CADS, Detox Unit, Capital Coast DHB
Truusje Hewson, Charge Nurse Manager, Kennedy Detox Unit, Canterbury DHB
Helen Liley Dr., Lead Clinician, Auckland Methadone Service, Waitemata DHB
Fraser Todd Dr., Senior Lecturer, NAC, University of Otago/Consultant Psychiatrist, Youth Specialty Services, Canterbury DHB

With contributions from;
Jenny Wolf, Project Manager Addictions, Addiction Treatment Services, Ministry of Health

and members of the Matua Raki Team:
Raine Berry Director
Vanessa Caldwell Project manager
Terry Huriwai Senior Advisor
Ashley Koning Project Leader
Patricia Rainey Project Coordinator
Rhonda Robertson Consumer Advisor