

Managing Codeine Dependence

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Overview

- The issues:
 1. Pain
 2. Dependence
 3. Psychological factors
 4. Risk management
- Talking to patients about codeine
- How to assess and manage dependence
- When to refer

Terminology (AAPM 2001)

Table 10.7 Definitions of relevant terms

Tolerance (pharmacological)	<p>A predictable physiological decrease in the effect of a drug over time so that a progressive increase in the amount of that drug is required to achieve the same effect</p> <p>Tolerance develops to desired (eg analgesia) and undesired (eg euphoria, opioid-related sedation, nausea or constipation) effects at different rates</p>
Physical dependence	<p>A physiological adaptation to a drug whereby abrupt discontinuation or reversal of that drug, or a sudden reduction in its dose, leads to a withdrawal (abstinence) syndrome</p> <p>Withdrawal can be terminated by administration of the same or similar drug</p>
Addiction	<p>A disease that is characterised by aberrant drug-seeking and maladaptive drug-taking behaviours that may include cravings, compulsive drug use and loss of control over drug use, despite the risk of physical, social and psychological harm</p> <p>While psychoactive drugs have an addiction liability, psychological, social, environmental and genetic factors play an important role in the development of addiction</p> <p>Unlike tolerance and physical dependence, addiction is not a predictable effect of a drug</p>
Substance use disorder	<p>The essential feature of a substance use disorder is a cluster of cognitive, behavioural and psychological symptoms indicating that the individual continues using the substance despite significant substance-related problems (American Psychiatric Association 2013)</p>
Pseudoaddiction	<p>Behaviours that may seem inappropriately drug-seeking but are a result of undertreatment of pain and resolve when pain relief is adequate (Weissman 1989)</p>
Diversion	<p>Sharing, selling or trading prescribed drugs to someone for whom they are not prescribed (Arria 2011)</p> <p>Sourcing activities or paths which redirect psychoactive prescription drugs from legitimate production or medical-use environments into the hands of nonmedical consumers (Fischer 2010)</p>
Aberrant drug-related behaviours	<p>"Behaviours that may be suggestive of the development of abuse, addiction or misuse" (Moore 2009)</p>
Chemical coping	<p>"A state observed in certain patients on chronic opioid therapy who have a mixed response to opioid therapy and in whom aberrant drug-related behaviours are sometimes (but not consistently) exhibited. Chemical coping has been described as a 'middle ground' between compliance and addiction" (Pergolizzi 2012)</p>

Opioid use disorder

TABLE 1

Summarized DSM-5 diagnostic categories and criteria for opioid use disorder

Category	Criteria
Impaired control	<ul style="list-style-type: none">• Opioids used in larger amounts or for longer than intended• Unsuccessful efforts or desire to cut back or control opioid use• Excessive amount of time spent obtaining, using, or recovering from opioids• Craving to use opioids
Social impairment	<ul style="list-style-type: none">• Failure to fulfill major role obligations at work, school, or home as a result of recurrent opioid use• Persistent or recurrent social or interpersonal problems that are exacerbated by opioids or continued use of opioids despite these problems• Reduced or given up important social, occupational, or recreational activities because of opioid use
Risky use	<ul style="list-style-type: none">• Opioid use in physically hazardous situations• Continued opioid use despite knowledge of persistent physical or psychological problem that is likely caused by opioid use
Pharmacological properties	<ul style="list-style-type: none">• Tolerance as demonstrated by increased amounts of opioids needed to achieve desired effect; diminished effect with continued use of the same amount• Withdrawal as demonstrated by symptoms of opioid withdrawal syndrome; opioids taken to relieve or avoid withdrawal

- In order to be diagnosed with opioid use disorder the patient must meet **at least 2** of the 11 criteria (within a 12 month period)
- A patient meeting 2-3 indicates **mild** opioid use disorder, meeting 4-5 criteria indicates **moderate**, and 6-7 indicates **severe** opioid use disorder
- Persons who are prescribed opioids may exhibit **pharmacological dependence**, but would not necessarily be considered to have a substance use disorder

What is dependence (addiction)?

“a pattern of thinking and behaviour in which drug use and drug seeking becomes an end in itself, dominating and displacing other activities or behaviours, and ultimately causing harm to the individual”.

Drug use becomes the **pervasive and defining behaviour** in the life of the individual .

A chronic & relapsing condition characterised by:

- A **compulsion** to seek and use a drug
- A **loss of control** in limiting intake of substance
- **Craving** during periods of abstinence
- Developing a **negative emotional state** when access to the drug is prevented

Rescheduling of codeine

The impact and the opportunities

- GPs may see more patients requesting codeine to manage pain or reporting previously undisclosed dependent use of codeine.
- Be prepared to talk to patients about their codeine use and to address their concerns
- Discuss risks associated with codeine-containing analgesics (CCAs)
- Consider alternative pain management options
- Develop practice policies for prescribing medicines for pain
- Identify and manage dependence
- Know when to refer (allied health/pain specialist/AOD services)

Potential benefits

- Prevention of CCA related death
- Reduced incidence of CCA dependence
- Prevention of morbidity associated with excessive use of ibuprofen / paracetamol
- Opportunity to discuss alternative & effective pain management strategies

“Why can’t I get codeine painkillers anymore?”

- Explain reasons for scheduling changes:
 - Opioid analgesic overuse & dependence is a **growing problem** in Australia and OTC low-dose codeine products contribute to this
 - A growing number of people are overusing CCAs and suffering **serious health problems** related to ibuprofen & paracetamol
 - Under current arrangements (Schedule 3) the widespread availability of codeine analgesics is **insufficiently restricted and monitored**
 - For most people there is **little evidence** that low-dose codeine medicines are more effective than alternative medicines without codeine
 - Low-dose CCAs **not intended to treat long term conditions**. However the majority of consumers use them for this purpose.

How will patients present?

Many patients may not volunteer their use of codeine (stigma, shame, implications). Upcoming rescheduling may result in patients disclosing their use. This may be associated with significant anxiety and uncertainty.

Presentation may relate to mental health issues (anxiety, depression) or physical complaints (weakness, myalgia, abdominal pain)

– *unless you ask specifically, you won't find out*

- Worried about not being able to access codeine. May be starting to stockpile tablets
- Asking for codeine prescriptions to replace OTC codeine
- Asking for other (S8) opioid medications such as oxycodone or morphine
- Symptoms of opioid withdrawal if codeine has been reduced or stopped
- Asking about other pain management options
- Complications related to paracetamol/ibuprofen overuse

Case study: MW 49 y. o. female

- Referred to Next Step by GP
- Recently reported to GP that she was using 20 Panadeine Extra Strength tablets (Paracetamol 500mg/Codeine 12.8mg) per day for several weeks. *Further history: 30-40 tablets per day for 3-4 months.*
- Chronic lower back pain, recent death of disabled daughter, depression.
- Was carer for daughter, estranged from family
- Overdose attempt (quetiapine) after death of daughter
- History of Mersyndol overuse/dependence 10 years ago
- Benzodiazepine dependence and alcohol use disorder. No history of illicit drug use, IDU or prescription opioid misuse.
- No previous liver disease. LFTs normal apart from raised GGT.
- Seeking abstinence from codeine, concerned that OTC codeine would soon be unavailable. Ashamed about “being deceitful”.
- Attempts to reduce use of tablets unsuccessful and associated with intolerable discomfort and anxiety.

Assessment

- Reason for presentation
- Assessment of chronic pain
- Treatment history
- Opioid use
 - Features and severity of dependence
- Substance use history
- Medical and psychiatric history
- Screening for medical complications (paracetamol/ibuprofen)
- Social circumstances
- Motivation and goals
- Physical and mental state examination
- Investigations

Pain management

An opportunity for GPs to provide a comprehensive review of the pain, the patient, and to help patients understand and accept more effective and safe ways they may manage their pain.

- Comprehensive 'biopsychosocial' assessment
- Education
- Active self-management
- Reconsidering role for opioids

Reconsidering the role for opioids

- Discuss alternative non-medication strategies:
 - Realistic goals & activity pacing
 - Self-management (exercise, TENS, lifestyle changes, heat pack, liniment rubs)
 - Physiotherapy
 - Complementary approaches (massage, acupuncture, relaxation / meditation)
 - Referral to a clinical psychologist (CBT)

Medication options:

- paracetamol, NSAIDs or combination products?
- stronger opioids (S8)
- adjuvant medications (antidepressants, anticonvulsants)

Opioid prescribing

Opioid prescribing in general practice: a proposed approach

Milton L. Cohen MD, FRACP, FFPMANZCA Alex D. Wodak AM, MB BS, FRACP, FACHAM

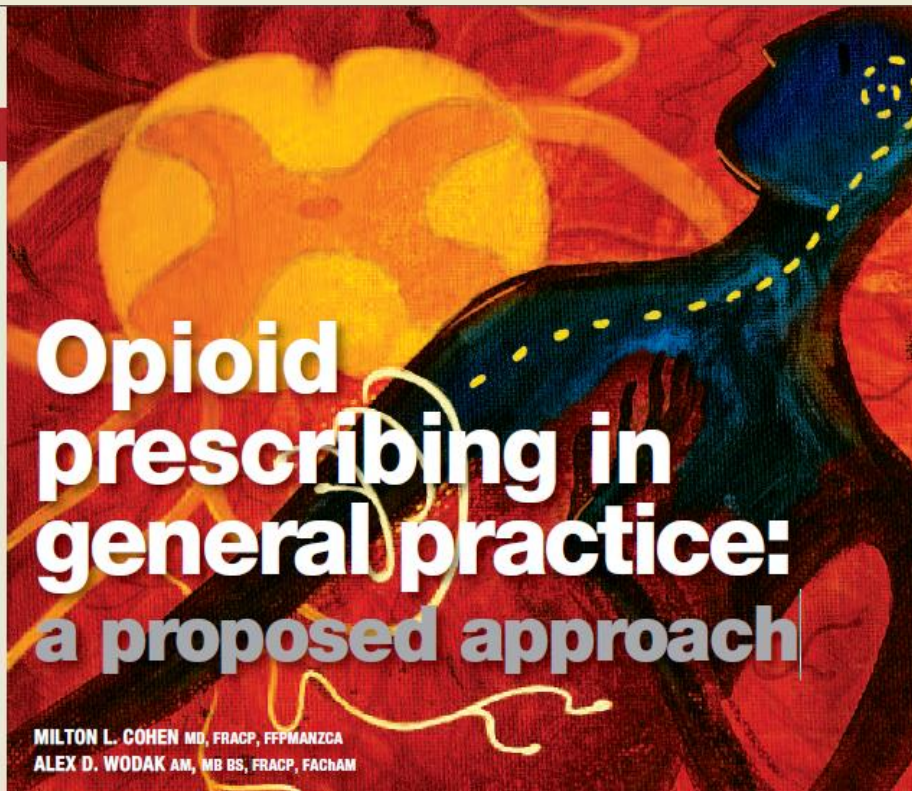
Medicine Today 2012; 13(1): 24-32

MedicineToday 2012; 13(1): 24-32

PEER REVIEWED FEATURE
POINTS: 2 CPD/2 PDP

Key points

- The experience of chronic pain has biological, psychological and social contributions, each of which you need to assess.
- Drug therapy for patients with chronic noncancer pain



GPs can facilitate opioid prescribing in their practices by following the five principles of opioid prescribing, utilising the five tools for assessment

FRAMEWORK FOR A PRACTICAL APPROACH TO OPIOID PRESCRIBING IN CHRONIC NONCANCER PAIN

5 principles

- Comprehensive assessment
- Poor response to other therapies
- Agreement regarding opioid trial
- Conduct of opioid trial
- Responses to difficulty achieving or maintaining goals in an opioid trial

5 tools

- Brief Pain Inventory
- Opioid risk tool (or other instrument)
- Contact numbers for advice regarding prescribing regulations in the different Australian jurisdictions
- Opioid contract
- Chart of opioid 'equianalgesic' doses

5 criteria

- Analgesia
- Activity
- Adverse effects
- Affect
- Aberrant behaviours

Paracetamol poisoning

- Approach to managing patients with chronic supratherapeutic ingestion

Guidelines

Clinical focus

Summary statement: new guidelines for the management of paracetamol poisoning in Australia and New Zealand

A large proportion of accidental paediatric exposures and deliberate self-poisoning incidents involve paracetamol; it is the leading pharmaceutical agent responsible for calls to Poisons Information Centres in Australia and New Zealand. Management of paracetamol poisoning has altered since the previous guidelines were published in 2008, so that they do not reflect current practice by clinical toxicologists. The key changes from the previous guidelines concern the indications for administration of activated charcoal; the management of patients taking large or massive overdoses; modified-release and supratherapeutic ingestions; and paediatric liquid paracetamol ingestion.



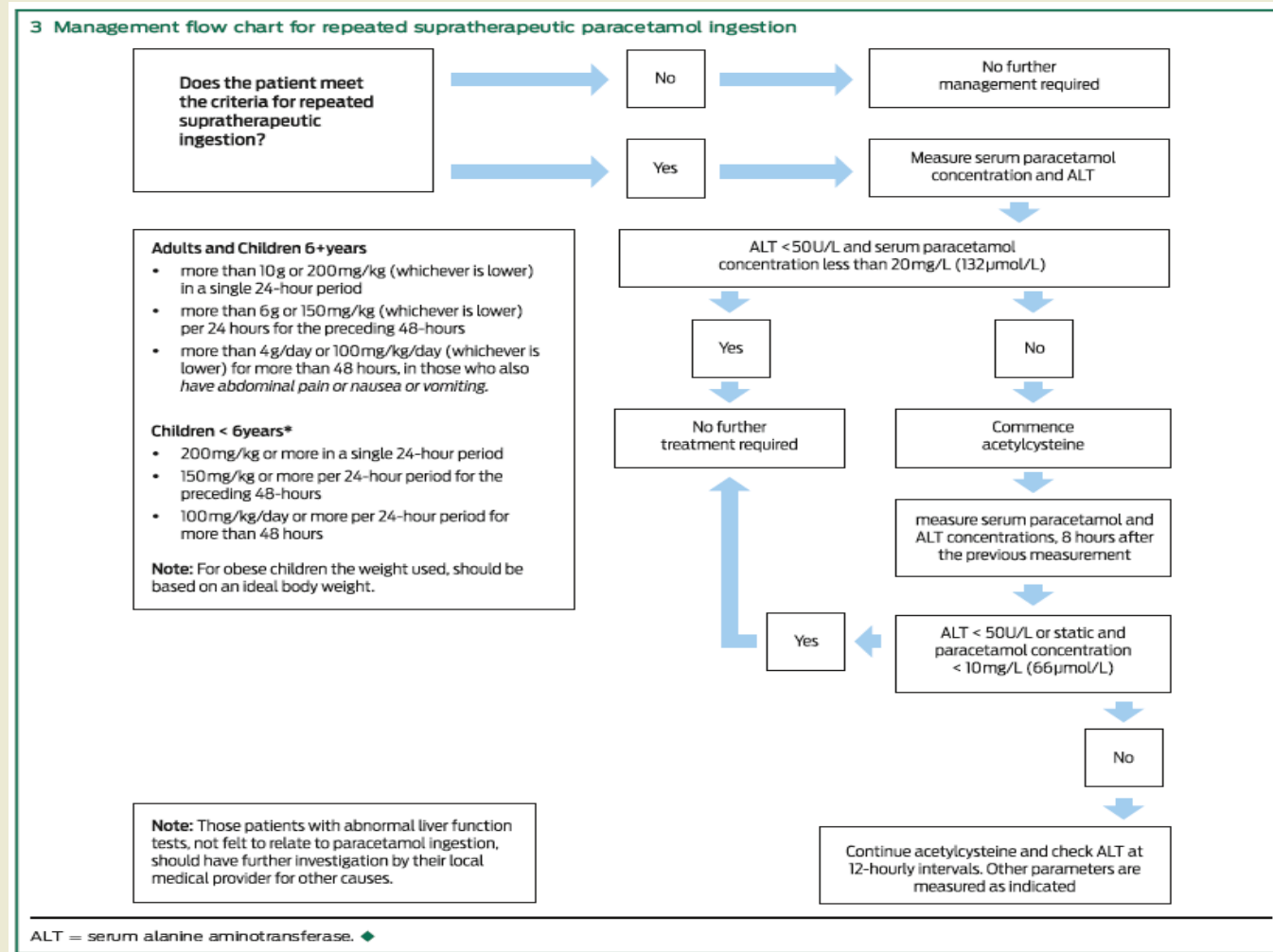
[Med J Aust.](#) 2015 Sep 7;203(5):215-8. [Chiew AL](#), [Fountain JS](#), [Graudins A](#), [Isbister GK](#), [Reith D](#), [Buckley NA](#).

1 Paracetamol dosing that may be associated with hepatic injury

	Adults and children > 6 years of age	Children (aged 0–6 years)*
Acute single ingestion	> 200 mg/kg or 10 g (whichever is lower) over a period of <8 hours	> 200 mg/kg over a period of < 8 hours
Repeated supratherapeutic ingestion	> 200 mg/kg or 10 g (whichever is lower) over a single 24-hour period > 150 mg/kg or 6 g (whichever is lower) per 24-hour period for the preceding 48 hours > 100 mg/kg or 4 g (whichever is lower) per 24-hour period, for more than 48 hours in those who also have symptoms indicating possible liver injury (eg, abdominal pain, nausea or vomiting)	> 200 mg/kg over a single 24-hour period > 150 mg/kg per 24-hour period for the preceding 48 hours > 100 mg/kg per 24-hour period for more than 48 hours

* For obese children, the body weight used for calculations should be an ideal body weight. ♦

Repeated supratherapeutic paracetamol ingestion



[Med J Aust.](#) 2015 Sep 7;203(5):215-8. [Chiew AL](#), [Fountain JS](#), [Graudins A](#), [Isbister GK](#), [Reith D](#), [Buckley NA](#).

Chronic supratherapeutic paracetamol ingestion

- Limited evidence to guide risk assessment
- Elevations in transaminases (up to > 8x upper limit of normal) can occur even after ingestion of therapeutic amounts (4g/day) for a prolonged period by healthy individuals (Watkins, 2006)
- Reports of individuals who have chronically ingested large amounts of paracetamol without any serious consequences
 - adaptive mechanisms that result in inactive metabolites rather than toxic metabolites (NAPQI)
 - **increases the efficiency of glucuronidation** (Tiller, 1992).
 - **increased sulphation products** and less glutathione-derived metabolites (Tredger, 1995)

Chronic supratherapeutic paracetamol ingestion

- Clinical anecdote:
 - 40 y.o. woman using 40 paracetamol/codeine tablets per day for 2 years, with no known complications
 - ceased abruptly and developed severe opioid withdrawal symptoms
 - returned to her former usage 3 days later
 - developed severe transaminitis and encephalopathy requiring ICU care for 1 week
- Protective adaptive metabolic effects can disappear rapidly.

An approach to managing chronic supratherapeutic paracetamol ingestion

- **Recent break in using:** manage as per acute single ingestion
- **Ongoing chronic use:**
 - Symptomatic (nausea, vomiting, RUQ pain) – refer to ED
 - Asymptomatic (clinically well) - biochemical analysis (ALT, paracetamol levels) for those who satisfy criteria for repeated supratherapeutic ingestion (as per guidelines). If paracetamol level $\geq 20\text{mg/L}$ and/or ALT raised ($\geq 50\text{ U/L}$), refer to ED for management of paracetamol poisoning

- **Seek advice**



Ibuprofen/Codeine: Screening for complications

- History and examination
 - Tiredness, lethargy, muscle weakness, myalgia, muscle cramps, haemetemesis/meleena, abdominal pain.
 - Pallor, CVS, abdo exam, muscle power and tendon reflexes
- Investigations
 - FBC, Iron studies
 - Urea and electrolytes (including Cl and HCO₃), Ca, PO₄
 - ??Urine pH and anion gap
 - ECG

Features suggestive of codeine dependence

- Consuming **large quantities** of OTC CCAs
- Attending **multiple pharmacies** each day
- Seeing **multiple GPs** for pain medication scripts
- Taking opioids for **psychological effect** rather than pain e.g. self medicating anxiety, depression
- **Altering** the medication in order to concentrate available codeine
- Self-identify a **loss in control** over use or presenting in opiate withdrawal
- Has a past or current history of **substance use disorder**

Types of codeine use patterns

Therapeutic dependence – long term OTC use

- taking daily recommended dose for prolonged periods (years)
- dose escalation – intent to manage pain, commonly headaches
- lifting mood, reducing anxiety, or numbing emotions

Non-medical / recreational use

- using purely for euphoric effect, often have good knowledge of ingredients and harms
- use of harm reduction (e.g. cold water extraction)
- possibly originating with pain control needs and transitioning

High dose dependence

- very high daily doses (over 100 tablets in some cases)
- opioid withdrawal, continued use despite harms, multiple pharmacies each day

What does opioid withdrawal look like?

Table 2: Common symptoms and time frame of opioid withdrawal⁽¹⁾

Stage of withdrawal	Common symptoms
Early	<ul style="list-style-type: none">• Runny eyes and nose, sneezing, yawning• Sweating, hot and cold flushes• Loss of appetite• Goosebumps
Peak	<ul style="list-style-type: none">• Strong cravings• Stomach cramps and diarrhoea• Nausea and vomiting• Body aches• Restlessness, agitation, irritability and insomnia• Lethargy and poor concentration• Hot and cold flushes with increased sweating
Late	<ul style="list-style-type: none">• Physical symptoms begin to subside• Psychological symptoms such as lethargy, irritability, cravings and insomnia may persist but in lower severity

Managing codeine withdrawal

Low Level Use (< 12 tabs per day)

- +/- mild withdrawal symptoms not requiring medical intervention
- reassure, provide information and normalise: short term and manageable
- alternative analgesia

Moderate Level Use (12 - 16 tabs per day)

- opiate withdrawal symptoms - a specific challenge. May amplify existing pain
- trial of non-medicated dose reduction
- cautious attempt at clonidine assisted opiate withdrawal
- consider referral to the Drug and Alcohol Withdrawal Network (DAWN) for withdrawal support in the patient's own home

High Level Use (> 16 tabs per day)

- likely more significant withdrawal - may warrant a higher level of medical intervention
- if above management strategies are unsuccessful, consider referral to local Community Alcohol and Drug Service (CADS)

Significant Codeine Dependence

- Suboxone (buprenorphine/naloxone) assisted codeine withdrawal or opioid substitution treatment (OST) may be appropriate

Managing codeine withdrawal

Reassure, normalise experience

Self-management strategies

Symptomatic medications:

- **Clonidine (α -adrenergic antagonist)**
 - effective in reducing many of the symptoms of withdrawal
 - requires close monitoring due to its adverse effects (including hypotension, bradycardia and drowsiness)
 - baseline BP/HR
 - avoid if hypotensive or bradycardic
 - test dose of 50mcg of clonidine
 - doses are usually in the range 50–150mcg every 6 hours
 - usually tapered and ceased by day 5

Managing codeine withdrawal

Other medications for symptomatic relief

Symptoms	Suggested treatments
Nausea & vomiting	<ul style="list-style-type: none">- Metoclopramide PO/IM 10mg three times daily PRN. Maximum of 5 days treatment- Ondansetron PO 4-8mg BD PRN. 2nd line treatment if nausea is severe
Muscle aches & pain	<ul style="list-style-type: none">- Paracetamol PO 1000mg every 4-6 hours PRN. Maximum 4000mg in 24hrs- Ibuprofen PO 400mg every 6-8 hours PRN
Agitation and/or anxiety	<ul style="list-style-type: none">- Diazepam PO PRN. Adjust dose to clinical needs and risks
Insomnia	<ul style="list-style-type: none">- Temazepam PO 10-20mg PRN at night. Encourage to cease after day 5
Abdominal cramps	<ul style="list-style-type: none">- Hyoscine butylbromide PO 20mg every 6 hours PRN.- Paracetamol may also provide some pain relief
Diarrhoea	<ul style="list-style-type: none">- Loperamide PO PRN 2mg after loose bowel motion. Maximum of 16mg in 24hrs

- Cautious use of sedative –limit to 7 days, advise re overuse/dependence

Withdrawal setting

Home-based Withdrawal

- GPs can prescribe withdrawal medications
- responsible support person at home (preferably)
- If unsure / unfamiliar – speak with an addiction medicine doctor at your local Community Alcohol & Drug Service (CADS)
- Referral to the Drug and Alcohol Withdrawal Network (**DAWN**) – 9388 5000

Residential Withdrawal Services

1. Referral to local **CADS** for consideration of admission to the **Next Step Inpatient Withdrawal Unit**
2. Serenity Withdrawal Unit
<http://www.cyrenianhouse.com/services/serenity-withdrawal-unit/>

Maintaining abstinence after withdrawal

Sustained success contingent upon successfully addressing:

1. Pain issues
2. Mental health issues – anxiety, depression, trauma grief, abuse
3. Relationship issues – family discord, marital problems
4. Psychosocial issues – accommodation, employment, legal, friends/family who use, boredom
5. Post Acute Withdrawal Syndrome (PAWS)

Importance of psychological therapy and counselling

- Many patients who have codeine dependence have underlying mental health issues or chronic pain – initial use of codeine may have been to manage these problems
- Anecdotally, high co-occurrence of early age psychological trauma, history of abuse, personality disorders, other substance use disorders
- Use of codeine to numb emotional/mental/physical pain
- Abrupt cessation of codeine use occurring with detox or commencement of OST may result in significant escalation in anxiety or psychological distress
- Essential that patients are supported with strategies to manage these symptoms (e.g. CBT, relapse prevention, managing cravings, mindfulness, relaxation techniques etc.)
- Consider referral to a psychologist (MHCP) or AOD counselling service/CADS.

Opioid substitution treatment (OST) for OTC codeine dependence

- In 2016, the National Opioid Pharmacotherapy Statistics indicated that codeine was the opioid drug of dependence for 5% of clients receiving opioid substitution pharmacotherapy.
- Careful consideration of the implications
- Suitable where significant & sustained dependence has been established. Patient history likely to include:
 - **multiple pharmacy access of OTC codeine medications,**
 - **high intake (e.g. 30 or more tablets daily),**
 - **may have history of past substance use disorder**

Opioid substitution treatment (OST)



Principles of OST

- Replacement of opioid of concern with highly regulated, supervised oral once daily dose of long half life opioid.
- Provide suppression of breakthrough withdrawal symptoms with minimal euphoria.
- Allows exit from the chaos of swinging from intoxication to withdrawal.
- Buys time and space to change.

Role in codeine dependence:

- **Reduction and cessation in codeine use**
- **Reduced morbidity/mortality from complications**
- **Improve health, wellbeing and social functioning**

Methadone and Buprenorphine

- Three medications are registered for long term maintenance for opioid dependent people:
 - Methadone oral liquid (available since 1969)
 - Buprenorphine (Subutex) tablets (available since 2000)
 - Buprenorphine-naloxone (Suboxone) tablets (available since 2005) or film (available since 2011)
- Both effective at stopping withdrawal from heroin and other opioids

What does OST involve?

- Daily supervised dosing at a nominated pharmacy over 12 to 36 months (often for much longer periods)
- Cost \$4 -\$8 per day, no subsidies
- Regular medical review – very few days to 3-monthly
- Counselling/case management +/- referral to psychologist
- Manage underlying mental and physical health issues
- Provide strategies for ceasing opioid use, relapse prevention and coming off treatment
- Slow dose reduction over 6-18 months
- WA Record of Drug Dependent Persons

The Community Program for Opioid Pharmacotherapy (CPOP)

CPOP is a program managed by the Medicines and Poisons Regulatory Branch and Next Step Drug & Alcohol Services to enable the provision of methadone and buprenorphine for the treatment of opioid dependence across WA.

- Approx 3800 patients in WA
- 60% methadone and 40% buprenorphine.
- 50% of patients are treated by Community Prescribers, 40% by doctors from Next Step Drug and Alcohol Services, and 10% by medical practitioners in Corrective Services.
- around 140 doctors authorised to prescribe
- Over 250 pharmacies
- all WA prisons also participate in the program.

Who can provide OST?

- Doctors authorised by DOH – doctors at Next Step, community GP prescribers and prison doctors
- Training via Next Step, requires 1 day and enables prescribing of both methadone and buprenorphine
- Lack of prescribers in WA

‘Suboxone V’

- Online training - usually takes just under two hours.
- Following completion of the training program medical practitioners can obtain authority from the Department of Health allowing the prescription of Suboxone **for up to five patients.**
- To register for the CPOP Suboxone Prescriber Online Training or for further information on CPOP please contact the Coordinator of Provider Support
- **Phone: (08) 9219 1896**
- **Email: craig.carmichael@mhc.wa.gov.au**

Case study: MW 49 y. o. female

Management and early progress:

- Assessment and discussion of treatment options over three appointments: explored gradual reduction/withdrawal/OST
- Elected to start Suboxone – inducted with close monitoring and frequent review
- Reassurance and support to manage anxiety and emotional lability. Supportive partner
- Encouraged engagement with clinical psychologist and referral to a psychiatrist. Extremely reluctant but eventually agreed
- Compliant with daily Suboxone dosing
- Not used any codeine since commencement of treatment
- Continues to struggle with anxiety and cravings.
- Increase in alcohol use

Resources

Patient Resources

- www.tga.gov.au/codeine-information-hub-how-and-where-get-advice
- nps.org.au/medical-info/consumer-info/medicines-with-codeine-what-you-need-to-know
- painhealth.csse.uwa.edu.au
- The Alcohol and Drug Support Line (ADSL) 24 hrs (08) 9442 5000 or 1800 198 024 (country callers)

Clinicians

- Community Alcohol and Drug Services (CADS) www.mhc.wa.gov.au/getting-help/community-alcohol-and-drug-services
- Drug and Alcohol Withdrawal Network (DAWN) (08) 9382 6049
- Community Pharmacotherapy Program (08) 9219 1896
- Next Step Clinical Advisory Service (CAS) (08) 9442 5042
- www.scriptwise.org.au
- The Royal Australian College of General Practitioners. Prescribing drugs of dependence in general practice, Part C1: Opioids, Part C2: The role of opioids in pain management. East Melbourne, Vic: RACGP, Oct 2017

Clinical Advisory Service (CAS)

- The Clinical Advisory Services operates a 24/7 phone service for health professionals providing clinical advice on all issues relating to patient management involving alcohol and drug use.
- The CAS is staff by experienced medical practitioners from Next Step Drug & Alcohol Services

Phone: 9442 5042 Freecall: 1800 688 847



Other info on the internet

- <https://www.tga.gov.au/final-decision-re-scheduling-codeine-frequently-asked-questions>
- <https://www.tga.gov.au/codeine-info-hub>
- <https://www.nps.org.au/medical-info/clinical-topics/over-the-counter-codeine-changes-to-supply>

Questions?

Contact Details:

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(08) 9219 1919

Thank you