



NSW Therapeutic Advisory Group Inc.
Promoting the quality use of medicines in public hospitals

Preventing and managing problems with opioid prescribing for chronic non-cancer pain



July 2015



An initiative of NSW clinical pharmacologists and pharmacists funded by the NSW Ministry of Health

Abbreviations

CNCP	chronic non cancer pain
COPD	chronic obstructive pulmonary disease
g	gram(s)
GP	general practitioner
IM	intramuscular
IV	intravenous
LSD	lysergic acid diethylamide
MAOI	monoamine oxidase inhibitor
mg	milligram(s)
NSW	New South Wales
OMEDD	oral morphine equivalent daily dose
PEG	Pain-Enjoyment-General Activity scale of pain intensity and interference
PSU	NSW Ministry of Health Pharmaceutical Services Unit
SC	subcutaneous
SNRI	serotonin noradrenaline reuptake inhibitor
SSRI	selective serotonin reuptake inhibitor
TCA	tricyclic antidepressant

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Recommended citation: NSW Therapeutic Advisory Group Inc.
Preventing and managing problems with opioid prescribing
for chronic non-cancer pain.

NSW TAG: Sydney, 2015

ISBN: 978-0-9586069-0-5



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Key messages

- ▶ A multidisciplinary approach with a focus on active self-management is recommended for patients with CNCP.
- ▶ Evidence does not support the routine use of opioids in the management of CNCP.
- ▶ However, if opioids are selected as part of a management plan for CNCP, the following principles are recommended:
 - Negotiate a trial of opioid therapy that explicitly identifies goals and duration of therapy
 - Keep oral morphine equivalent daily dose (OMEDD) \leq 60mg
 - Seek specialist advice if uncertain about advisability or conduct of the trial
- ▶ Opioids should be withdrawn if:
 - Acute pain episodes have resolved, or
 - There is no improvement in function during the trial, or
 - Adverse effects or other risks of therapy outweigh any benefit, or
 - Aberrant behaviours develop.
- ▶ After a successful trial of opioid therapy, as indicated by improved function and quality of life, ongoing treatment should be renegotiated on a regular basis, to include goals, duration and lowering of dose.

Risk mitigation strategies

- ▶ Check whether other prescribers have been involved in the patient's pain management.
- ▶ Avoid prescribing multiple opioids.
- ▶ Beware of prescribing opioids with other central nervous system depressants.
- ▶ Check for aberrant drug-related behaviours.

Purpose of guidance

The use of opioids for the long term management of chronic non-cancer pain (CNCP) is controversial. A multidisciplinary approach that emphasises non-pharmacological over pharmacological treatment and promotes self-management is generally preferred. However, it is also recognised that medicines including opioids can play a role in selected cases.

This practical guidance on the rational use of opioids is intended to assist clinicians to manage the complex medical, ethical and regulatory issues that arise when using opioids for chronic pain in adults in primary care. It is based on the best available evidence or expert consensus where research evidence is lacking.

This guidance does not extend to children and adolescents with CNCP. In this situation specialist advice should be sought.

Background

One in five people report chronic pain, defined as pain experienced every day for three or more months.^[1] For many, a biomedical 'cure' may not be realistic. However, it is generally possible to reduce pain and achieve and maintain an acceptable level of function in personal, social and occupational life by adopting an active self-management approach.

Patients with CNCP may present for management of:

- ▶ ongoing pain, or
- ▶ an exacerbation of CNCP, or
- ▶ acute pain from an unrelated injury or illness, or
- ▶ side effects from treatment.

The importance of a multidisciplinary and multidimensional approach that does not rely on drug therapy alone cannot be overemphasised.

The following resources are available for patients, carers and family members:

- ▶ [A short video about the causes and management of CNCP](#)
- ▶ [A fact sheet about the nature and science of pain](#)
- ▶ [A video about the use of medications, particularly opioids, for CNCP](#)

Comprehensive assessment

Assess each patient for physical, psychological and sociological contributors to pain and for potential problems if opioids are used.

Comprehensive assessment of CNCP addresses:

- ▶ Clinical features that might indicate underlying conditions such as inflammation, infection, neural pathology and neoplasm that require further evaluation and specific treatment ('red flags').^[2]
- ▶ Patient beliefs and understanding about diagnosis, prognosis, physical activity, work, recreation, nutrition, sleep, depression, anxiety, and self-esteem, sometimes referred to as 'yellow flags'.
- ▶ [A thorough medication history including use of over-the-counter and complementary medicines.](#)
- ▶ A standardised mental health assessment and a drug and alcohol history.

A comprehensive assessment is likely to require a longer follow-up appointment.

To inform assessment of CNCP in primary care, the brief three-item validated pain scoring system, PEG (Pain-Enjoyment-General Activity scale), can be used (Box 1). Scores (out of 30) give a reference point for the patient's overall wellbeing and can be used to compare the same patient seen at different times or by different practitioners.

[See Scenarios [4](#) and [6](#)]

[Abbey](#) and [Faces](#) pain scales are alternative tools to help assess patients with cognitive impairment, dementia or those from non-English speaking backgrounds.^[4]

Box 1: Pain-Enjoyment-General Activity scale

1. What number best describes your **pain on average** in the past week?

0	1	2	3	4	5	6	7	8	9	10
No pain										Worst possible pain

2. What number best describes how pain has interfered with your **enjoyment of life** in the past week?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

3. What number best describes how pain has interfered with your **general activity** in the past week?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

Adapted from Krebs et al [3]

Management of chronic non-cancer pain

Non-pharmacological strategies

[Non-pharmacological strategies](#) that support active self-management of CNCP, whether opioids are used or not, include:

- ▶ planned daily walks or exercise(s)
- ▶ physiotherapy/hydrotherapy
- ▶ counselling (may be available online or via telephone)
- ▶ relaxation therapy/mindfulness/yoga
- ▶ cessation of smoking
- ▶ nutritional change with support from a dietitian
- ▶ attending a group pain management program
- ▶ social connection

[See Scenarios [1](#), [5](#) and [6](#)]

If there is difficulty in establishing these strategies due to the patient's access, ability or willingness to participate, then *telephone advice* can be sought from [specialist pain medicine physicians](#), [pain centres](#) or other health professionals prior to a consultation (or in lieu of a consultation where it is impractical e.g. rural areas, long waiting times).

Pharmacological strategies

[Pharmacological strategies](#) may include use of paracetamol, non-steroidal anti-inflammatory drugs (either non-selective or COX-2 inhibitors), and [adjuvant drugs](#), such as some antidepressants or antineuropathic agents, for symptom control or in some cases to influence mechanism of pain production.

Use of opioids

There is good evidence for the use of opioids in acute pain, pain associated with cancer, palliation at the end of life and the management of opioid dependence.^[5-8] Evidence does not support the long-term effectiveness of opioids in CNCP. Opioids may have a short-term role while non-pharmacological strategies are being introduced. Once these are established the standard approach is gradual opioid withdrawal towards cessation.

A prescriber may choose NOT to use opioids OR to undertake a brief trial of opioids possibly followed, if successful, by a time-limited continuance phase.

The aim of an opioid trial is:

- ▶ to determine if a patient's condition is opioid responsive, and
- ▶ to establish the lowest dose to achieve a pre-determined improvement in function (such as using the PEG) and quality of life (such as return to work or social engagement). This dose may be ZERO.

Conduct of an opioid trial

An opioid trial entails:

- ▶ comprehensive assessment
- ▶ concurrent use of non-pharmacological strategies
- ▶ negotiation with the patient regarding agreed goals in terms of functional outcomes and duration of treatment
- ▶ risk assessment to determine duration of prescription and frequency of dispensing
- ▶ regular review of opioid use according to the [5As](#)^[9]:
 - **A**ctivity
 - **A**dverse effects
 - **A** aberrant behaviour (behaviour suggestive of opioid misuse – see Figure A)
 - **A**ffect (overall presentation of the patient)
 - **A**nalgesia
- ▶ review *at least* every 1-2 weeks during the 4-8 week trial phase, then regularly if there is a time-limited continuance phase

Information on individual agents is [available](#). If opioids are trialled for management of CNCP, long-acting (modified-release) preparations taken on a regular basis are preferred. Lower doses of these can be used to supplement on a “when required” basis rather than using immediate-release preparations. An oral morphine equivalent daily dose (OMEDD) of 60mg should not be exceeded without specialist advice.

The following should NOT be used in an opioid trial for CNCP:

- ▶ immediate-release opioids
- ▶ injectable opioids, e.g. pethidine, morphine
- ▶ methadone (without specialised advice, including advice on dose conversion) due its complicated pharmacokinetics
- ▶ hydromorphone (without specialist advice) due to the high oral morphine equivalent dose of the lowest available dose formulations
- ▶ fentanyl (without specialist advice) due to the high oral morphine equivalent dose of the lowest available dose formulations

Older adults are more sensitive to opioids. If opioids are used, the starting dose should be 25 - 50% of the usual adult dose, adjusted carefully depending on response and monitored frequently for analgesic and adverse effects.^[4]

Any beneficial response to an opioid in a trial should be evident at an OMEDD ≤ 60mg. Wean and cease the opioid or seek consultation if OMEDD is approaching 60mg without obvious improvement in function and quality of life.

Figure A. Spectrum of aberrant drug-related behaviours ^[10]



Table 1 can be used to calculate an *approximate* OMEDD of an opioid. [See Scenarios 3-7]

Table 1. Guide to Opioid Equivalence

This table has been developed by Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists for the purpose of comparing opioid regimens. The intention is to illustrate the relative potency of different opioids by converting to an approximate oral morphine equivalent daily dose (OMEDD).[¥]

The conversion factors listed are the consensus view of an expert panel derived from the best evidence available. However, they are derived from group studies and may not be appropriate for any given individual. Various factors influence the metabolism and excretion of opioids, particularly hepatic and renal status, and increasing age.

Hence caution is recommended if these conversion factors are used to guide opioid switching in clinical practice.

If opioid rationalising is undertaken a conservative approach involves converting to a new opioid at 50-60% of the equianalgesic dose as determined from the table. Consultation with an experienced colleague or a pain medicine or addiction medicine specialist may be helpful.

Route of administration	Opioid	Unit	Conversion factor
Oral (swallowed)	codeine	mg/day	0.13
	dextropropoxyphene	mg/day	0.1
	hydromorphone	mg/day	5
	morphine	mg/day	1
	oxycodone	mg/day	1.5
	tapentadol	mg/day	0.4
	tramadol	mg/day	0.2
Sublingual	buprenorphine	mg/day	40
Transdermal	buprenorphine	micrograms/hr	2
	fentanyl	micrograms/hr	3
Injectable	morphine (sc, iv)	mg/day	3
	oxycodone (sc, iv)	mg/day	3
	pethidine (iv, im)	mg/day	0.4
Rectal	oxycodone	mg/day	1.5

Example

Codeine phosphate 30mg (as Panadeine Forte®), 8 per day represents codeine 240mg per day which is approximately equianalgesic with oral morphine 30mg (240 x 0.13) per day (OMEDD). If considering changing to modified-release oxycodone, the starting dose would be 5mg twice daily which is equivalent to 15mg OMEDD (ie 50% of 30mg).

[¥] This table is an abridged [version](#) omitting proprietary names and injectable preparations less commonly used in primary care.

A number of available opioid products are perceived to carry less risk of overdose, dependence or diversion (“tamper resistant”). However, these problems can occur with ANY opioid product.

Reducing the dose of opioids

Dose reduction, with the goal of cessation of opioids, is indicated:

- where there is a lack of effectiveness (unsuccessful trial)
- at the end of the agreed continuance phase
- where adverse effects are limiting
- where opioids are misused

If cessation is not achieved, the aim is to determine the lowest dose of opioid associated with improved function and quality of life.

If more than one opioid is currently being used, the regimen should be rationalised to a single oral modified-release opioid. [See Table 1] When stabilised, the dose of opioid should be reduced gradually over a time period as negotiated with the patient, supported by active self-management. Although there is no evidence regarding the ideal rate for dose reduction, the following consensus approaches have been used successfully:

(a) **fast** reduction by 10 – 25 % of the daily dose per *week*, [See Scenarios 2 and 4], or

(b) **slow** reduction by a 10 – 25 % of the daily dose per *month* if a patient has been using opioids for some years. [See Scenarios 3, 6 and 7]

A prescriber is under no obligation to *continue* opioids against their better judgement. The prescriber can insist on dose reduction/cessation or consult a specialist for advice.

Adverse effects of opioids

A range of [adverse effects](#) beyond constipation and sedation can occur. The risk and severity of adverse effects is increased when opioids are used:

- ▶ concurrently with medicines with sedating effects, particularly benzodiazepines, or alcohol
- ▶ in older patients
- ▶ in patients with co-morbid respiratory disease or hepatic or renal impairment
- ▶ in patients with acute illness that might impair hepatic or renal function (due to reduced opioid elimination)

Frequent review is needed in all circumstances.

Serotonin syndrome has been reported with tramadol, fentanyl and pethidine, particularly when used concurrently with other serotonergically-active agents including over-the-counter and complementary medicines.^[11] [See Table 2] Isolated reports have also occurred with tapentadol.

Table 2. Drugs that may contribute to serotonin toxicity ^[12]

Class	Drugs
antidepressants	MAOIs (including moclobemide), SNRIs, SSRIs, St John's wort, TCAs
opioids	dextromethorphan, fentanyl, pethidine, tramadol, tapentadol
stimulants	hallucinogenic amphetamines, phentermine
others	illicit drugs (e.g. 'ecstasy', LSD, cocaine), rasagiline, selegiline, linezolid, lithium, methylene blue, tryptophan

Combination analgesics such as codeine and ibuprofen or dextropropoxyphene and paracetamol carry additional significant risks (e.g. dependence, gastrointestinal ulceration, cardiotoxicity) with little additional efficacy.

Patients on opioids may need regular laxative prescription.

When to refer a patient to a specialist pain medicine physician?

[Specialist advice](#) is recommended for any patient:

- ▶ taking OMEDD > 60mg (or > 30mg in patients who are elderly or who have co-morbidities impairing renal or hepatic function),
- ▶ with moderate to high levels of psychological distress associated with pain,
- ▶ using an opioid for > 90 days,
- ▶ failing to respond to multidisciplinary management in primary care.

Role of urinary drug screens

When carried out before and irregularly during opioid prescribing, urinary drug screens can be helpful to:

- corroborate patient self-reports,
- identify aberrant behaviour (e.g. use of other or illicit substances), and
- monitor compliance with pain management plans.

Unexpected results from such screens should be interpreted within their limitations: fentanyl, buprenorphine, synthetic drugs, anabolic steroids, and usually oxycodone are not routinely detected and must be requested as additional tests (at extra cost to the patient). Drug misusers may adopt a variety of methods, such as switching urine samples, to influence results.

Regulatory requirements and prescription monitoring programs

There are jurisdictional differences between states with regard to authority requirements:

[\[ACT\]](#) [\[NSW\]](#) [\[NT\]](#) [\[QLD\]](#) [\[SA\]](#) [\[TAS\]](#) [\[VIC\]](#) [\[WA\]](#)

NSW Ministry of Health, Pharmaceutical Services Unit

An Authority from PSU is required for a medical practitioner to prescribe a Schedule 8 drug of addiction **if a patient is considered 'drug dependent'**. The Authority, issued under the *Poisons and Therapeutic Goods Act 1966*, not only ensures the prescribing is legal but provides a regulatory structure to manage the prescribing. It limits the prescribing to one practitioner and provides a maximum dose that cannot be exceeded. It can include mandatory conditions such as structured reduction regimens, urinary drug screens and staged supplies to avoid dose escalation or diversion, and referral to multidisciplinary specialist services.

If a patient is not considered drug dependent an Authority will be required to prescribe the following Schedule 8 opioids beyond 8 weeks:

- any injectable or inhaled formulation
- methadone, buprenorphine (excluding transdermal) and hydromorphone

This Authority has a maximum duration of 6 months. [See Scenarios [3-7](#)]

An explanation of [legal requirements](#) and [further information](#) (including the storage and disposal of opioids) is available or speak to a Senior Pharmaceutical Officer Ph: 02 9424 5923.

GPs can report concerns about patients misusing opioids to PSU (or the appropriate authority in the jurisdiction).

Note: The Authority from the NSW Ministry of Health is the legal authority to prescribe the drug. It is independent of an authority from Medicare Australia to prescribe under the Pharmaceutical Benefits Scheme (PBS), which is solely for the purpose of **subsidising the medication** cost to the patient.

Medicare Australia

Medicare Australia administers a [Prescription Shopping Information Service](#):

Ph: 1800 631 181

Additionally a prescriber may consider obtaining the patient's permission to authorise Medicare Australia to release Medicare or Pharmaceutical Benefits Scheme claims information to a [third party](#).

SCENARIO 1

Adult patient with low back pain for six weeks

A 45-year-old man developed acute low back pain six weeks ago as he was unloading camping equipment whilst arguing with his wife on a family holiday. Despite early physiotherapy his pain has persisted and he has continued to use over-the-counter codeine/paracetamol 10/500mg tablets with marginal benefit. He visits his general practitioner (GP) after the holiday and requests stronger analgesics and spinal imaging. No clinical 'red flag' features are present, but he is fearful of structural damage.

Recommended approach:

His GP explains and reassures him that spinal imaging and surgical opinion are unnecessary because there are no clinical features to suggest a harmful underlying condition. He is advised to cease codeine since opioids are unlikely to be of benefit in this situation. A management plan is developed that includes giving patient information on the [neurobiology of pain](#), a staged return to functional activity, [education](#) about the linkage between mind and body and the potential contribution to nervous system sensitisation of unresolved emotions. The patient agrees to see his physiotherapist for mobility exercises and undertake relaxation therapy.

Key Message:

- ▶ Opioids are unlikely to be effective for episodes of non-"red flag" [low back pain](#) that persist beyond the usual natural history of recovery.

SCENARIO 2

Adult patient discharged from hospital after surgery

A 55-year-old man was discharged from hospital on modified-release oxycodone 20mg twice daily following admission for surgery. He visits his GP for follow-up medication seven days later.

Recommended approach:

Since the acute pain phase (related to the nociception of acute injury) has passed and he is healing satisfactorily, the modified-release oxycodone can be quickly decreased (for example by 10mg of the daily dose per week). Paracetamol can be used if required, with further review depending on clinical progress. Giving the patient a clear explanation of these steps is an important role for the GP.

Note: There is a risk of discharge medication being continued indefinitely if there has been poor communication between health practitioners or because of patient distress.

Key Message:

- ▶ Opioids initiated for acute pain should be reduced and ceased at the earliest opportunity.

SCENARIO 3

Poor control of CNCP despite increasing opioid dose

A 62 year old man has had chronic low back pain since a work-related injury ten years ago. This was initially managed with modified-release morphine but over the years with development of osteoarthritis, a motor vehicle accident and several falls, modified-release morphine was replaced by modified- and immediate-release oral oxycodone. Another specialist recommended patches, and after the latest hospital admission oral morphine solution was added for ease of swallowing. The patient states that he requires all these opioids to control his pain.

The patient is currently taking codeine/paracetamol 30/500mg x two tablets four times a day, modified-release oxycodone 60mg three times a day, immediate-release oxycodone 10mg x two tablets when required if the weather is cold, transdermal fentanyl 75 micrograms/hour every 3 days and oral morphine solution 20mg when required for exacerbation of pain. The OMEDD of this regimen is at least 500mg:

Medicine	Route	Daily dose	Conversion factor	OMEDD
Codeine	Oral	240mg	0.13	30mg
Oxycodone modified-release	Oral	180mg	1.5	270mg
Oxycodone when required	Oral	40mg	1.5	60mg
Morphine solution when required	Oral	20mg	1	20mg
Fentanyl patch	Topical	75 micrograms/hour	3	225mg
Total				605mg

Recommended approach:

His new GP discusses the lack of scientific evidence for long-term opioid therapy. He has telephone discussions with a local pain medicine specialist regarding an appropriate management plan and the NSW Ministry of Health Pharmaceutical Services Unit to obtain advice on the Authority application process and information on local specialist services. The GP and patient negotiate and agree a plan to convert to a single modified-release opioid at OMEDD 320mg, stabilise the dose, then slowly reduce and cease it over eight months while putting in place supported multidisciplinary self-management strategies. Adjuvant use of pregabalin or gabapentin could be considered.

Note: This case is an extreme example of what can happen over time with multiple prescribers, poor communication and the absence of a pain management plan.

Although there is no evidence of behaviour suggesting opioid misuse, the patient may be considered 'drug dependent' based on the extreme OMEDD of 605mg. Medical practitioners are advised to apply to PSU for an Authority to prescribe **ANY** Schedule 8 drug. [See [Regulatory requirements](#)]

Key Messages:

- ▶ Check whether other prescribers have been involved in the patient's pain management.
- ▶ Negotiate a pain management plan with all patients on opioids with the view to minimising dose.

SCENARIO 4

“Drug-seeking” in the context of dependency/addiction

A 48 year old man with a history of substance use and binge drinking in his twenties has presented with chronic ankle pain following a fall from a ladder. His GP prescribed transdermal fentanyl patches as an ‘abuse-proof’ formulation. There are concerns that he is diverting the patches. Frequently scripts have been presented early because the patient claims that the patches have fallen off. Each time he has a consultation with his GP he has the patch on and there are no obvious track marks.

Currently he is prescribed transdermal fentanyl 75 micrograms/hour every three days. He has not been identified by the Prescription Shopping Information Service and there have been no recent reports to PSU or the relevant state regulatory body. His urine drug screen, which specifically included fentanyl assay, showed only fentanyl. He complains that 75 micrograms/hour is not controlling the pain or enabling sleep and he requests stronger patches. He has not regained regular employment due to his problem as he can hardly cope with things at home. His partner also has health problems. His PEG scores remain between 24 and 27.

Recommended approach:

This ‘opioid trial’ has failed. Behaviours suggesting opioid misuse are present. Consider the following:

- Conversion: The patient’s dose should be reduced by using the ‘fast’ approach with either lower dose patches or by switching to an oral modified-release opioid. Transdermal fentanyl 75 micrograms/hour is approximately equivalent to OMEDD 225mg. An appropriate starting daily dose of modified-release oral morphine would be 120-150mg (i.e. half of the original OMEDD).
- Collaboration: It is recognised that these situations can be confronting and potentially threatening to the practitioner. Advice from other health professionals involved in patient care is recommended. (Contact with professional societies for guidance in managing difficult situations or patients is suggested).
- Containment: Opioid supply can be dispensed as a daily to weekly pick up from the patient’s pharmacy with frequent (weekly) review to address concerns about his medication control. **Note:** This staged medication supply differs from supervised supply where the patient is actually observed taking their medication by dispensing staff.

This is an example of a ‘drug dependent’ patient according to the *Poisons and Therapeutic Goods Act 1966* and therefore an Authority from the NSW Ministry of Health is required prior to prescribing.

SCENARIO 5

Older person with multiple sites of pain

An 85 year old woman has chronic pain associated with osteoarthritis. Despite regular paracetamol, her joint pain limits her ability to perform activities of daily living. Non-steroidal anti-inflammatory drugs are unsuitable considering her co-morbidities. Her regular medicines are paracetamol 1g three times a day, perindopril 4mg daily, indapamide 1.25mg daily, atorvastatin 40mg daily, citalopram 20mg daily, omeprazole 40mg daily, vitamin D 1000 units daily and temazepam 10mg at night when required.

Her GP commenced her on transdermal buprenorphine 5 micrograms/hour and observed good functional improvement. After six months pain was again limiting her independence, and her GP added modified-release oxycodone 5mg twice daily. Three months later she sustained a crush fracture of a lumbar vertebra in a fall. The pain was managed initially with **immediate-release** oxycodone, which was changed to **modified-release** oxycodone 10mg twice daily. A year later, she was still using transdermal buprenorphine 5 micrograms/hour (OMEDD 10mg) and **modified-release** oxycodone 10mg twice daily (OMEDD 30mg). She still had pain limiting her activities of daily living, was having recurrent falls, had developed mild cognitive impairment, and could no longer manage at home.

Recommended approach:

If opioids were to be used with the increase in chronic pain after six months this patient should have been treated with a single agent: either transdermal buprenorphine, or **modified-release** oral opioid. Prescribing multiple opioids increases the risk of adverse effects.

The increase in her opioid dose required three months later after the crush fracture should have been reviewed after 4-6 weeks when the acute pain component should have resolved. The cumulative dose at this time, OMEDD 40mg, was higher than most older patients can tolerate. She may have benefitted from a Home Medicines Review. Her exposure to centrally acting drugs, including opioids, citalopram and temazepam, should be minimised as these drugs all increase the risk of falls, cognitive impairment and functional dependence. Physiotherapy or hydrotherapy might also support her.

It is unlikely that this patient would be considered drug dependent according to the *Poisons and Therapeutic Goods Act*. Therefore an Authority from PSU would not be required to prescribe transdermal buprenorphine or oral oxycodone.

Key Messages:

- ▶ Avoid prescribing multiple opioids.
- ▶ Beware of prescribing opioids with other central nervous system depressants.

SCENARIO 6

Transfer of care: adult patient using injectable opioids

A 56 year old woman with recurring headaches is wheelchair-bound and has a long history of pain-associated dependent behaviour. Her long-term GP retired last year, having prescribed her morphine ampoules 30mg three times a day for self-injection for approximately twelve years. The last Authority from PSU for the injections expired ten years ago. Oral morphine solution 10mg/mL when required has recently been added. She has not visited a pain clinic for four years and is unwilling to attend again as the recommendation at the last visit was to transfer to a **long-acting** oral opioid formulation. The patient has never prescription-shopped or used illicit drugs. Her current PEG score is 28 but no pain measurements were done by the previous doctor. She has reported intolerance to other opioids. She has also trialed botulinum toxin injections, lignocaine infusions and other alternative migraine therapies but reports that only opioid injections give any real relief. She has taken diazepam 10-15mg a day for anxiety and occasional oxazepam at night for many years. A GP in the same practice has agreed to take over management of this patient but is not happy with the situation.

Recommended approach:

The patient's pain management plan requires revision. There is no justification for continuing injectable morphine in this patient. The oral morphine solution and benzodiazepines add to the risk of serious adverse events including death.

The complexity of this case is best managed by a specialist and the nearest pain clinic can be contacted initially for telephone advice. The OMEDD of her current injectable regimen is more than 270mg/day. The patient needs to be gradually switched to a single oral opioid, "capturing" the current opioid requirement, ultimately in a long-acting formulation such as oral modified-release morphine. After stabilisation, this can be titrated down slowly, for example by 10mg of the daily dose per month. Regular review and ongoing patient education is necessary. Smoking cessation may help manage her pain; she may also benefit from slow reduction and cessation of benzodiazepines.

The prescribing of injectable drugs of addiction for longer than two months requires an Authority from PSU. Applications are likely to be referred to the Ministry of Health Medical Committee for a recommendation. Medical practitioners who 'inherit' patients on established, entrenched regimens of injectable opioids are advised to seek advice from a Senior Pharmaceutical Officer at PSU as soon as possible.

Key Messages:

- ▶ There is no role for injectable opioids in CNCP.
- ▶ Seek early specialist advice from the nearest pain clinic and from PSU by telephone or email for any new patient using injectable opioids.

SCENARIO 7

Adult patient with stable pain post cancer treatment

A 32 year old man underwent curative treatment for osteosarcoma of the distal right femur with above-knee amputation and chemotherapy. He had leg pain pre-operatively and has had phantom limb pain in his right leg post-surgery. He is now taking **modified-release** morphine 200mg twice daily, **immediate-release** liquid morphine 20mg when required (up to 160mg daily) and pregabalin 75mg twice daily. He denies any other substance use, but reports high levels of anxiety about body image and using his prosthesis.

Recommended approach:

A comprehensive assessment is needed to distinguish between stump pain, phantom limb pain and cancer recurrence. In this case the management approach needs to be altered since he no longer has cancer pain.

Frequent use of an **immediate-release** opioid formulation causes a withdrawal/intoxication cycle. All opioids should be rationalised to an appropriate dose of **modified-release** opioid, in this case morphine. The patient's current OMEDD is 560mg. However a daily dose which is less than the sum of the immediate- and modified-release doses, for example 340mg, should be tried with frequent review. Once the opioid dose has been stabilised, it would be maintained for some weeks/months while pregabalin is increased and assessed for effectiveness (or other treatments, including non-pharmacological interventions, added) before being slowly reduced and ceased.

Given the patient's high opioid use, telephone advice from a pain specialist should be sought ahead of a specialist appointment. A multidisciplinary review assessing the patient's anxiety and function with prosthesis is important.

Although there is no evidence of behaviour suggesting opioid misuse, the patient may be considered 'drug dependent' based on the extreme OMEDD of 560mg. Medical practitioners are advised to apply to PSU for an Authority to prescribe ANY Schedule 8 drug. [See [Regulatory requirements](#)]

Key Message:

- ▶ Neuropathic pain and anxiety are often poorly opioid responsive.

References

- [1] [Blyth FM, March LM, Brnabic AJ](#), et al. Chronic pain in Australia: a prevalence study. *Pain* 2001; 89: 127-134 [PMID: 11166468]
- [2] Cohen ML, Wodak AD. Opioid prescribing in general practice: a proposed approach. *Medicine Today* 2012; 13(1): 24-32
- [3] [Krebs EE, Lorenz KA, Bair MJ](#), et al. Development and Initial Validation of the PEG, a Three-item scale Assessing Pain Intensity and Interference. *J Gen Intern Med* 2009; 24(6): 733-8 [PMID: 19418100]
- [4] Analgesic Expert Group. Therapeutic Guidelines: Analgesic. Version 6. Melbourne: [Therapeutic Guidelines](#) Limited, 2012.
- [5] Macintyre PE, Schug SA, Scott DA, Visser EJ, Walker SM; APM:SE Working Group of the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine (2010), Acute Pain Management: Scientific Evidence (3rd edition), ANZCA & FPM, Melbourne. <http://www.fpm.anzca.edu.au/resources/books-and-publications/>
- [6] [Caraceni A, Hanks G, Kassa S](#) et al. Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. *Lancet Oncol* 2012; 13: e58-68 [PMID: 22300860]
- [7] NHS National Institute for Health and Care Excellence (NICE). Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults (CG140), May 2012 [Accessed at <http://publications.nice.org.uk/opioids-in-palliative-care-safe-and-effective-prescribing-of-strong-opioids-for-pain-in-palliative-care-cg140> on 27 March 2014]
- [8] [Amato L, Davoli M, Perucci C](#) et al. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. *Journal of Substance Abuse Treatment* 2005; 28(4): 321-329 [PMID: 15925266]
- [9] [Faculty of Pain Medicine](#), Australian and New Zealand College of Anaesthetists. Recommendations regarding the use of opioid analgesics in patients with chronic non-cancer pain. June 2015
- [10] Cohen ML, Wodak AD. The judicious use of opioids in managing chronic noncancer pain. *Medicine Today* 2010; 11(2): 10-18
- [11] Australian Medicines Handbook 2014 (online). Adelaide: Australian Medicines Handbook Pty Ltd, April 2014. [Accessed at <http://www.amh.net.au> on 27 March 2014]

Appendix 1: Process of guidance development

This guidance was prepared by a Project Team (MC, AD, AB), with the support and advice regarding content and scenario development from a multidisciplinary Subject Matter Expert Advisory Group (see Appendix 2), which was convened by the NSW Therapeutic Advisory Group (TAG) Editorial Committee, as per its published [guidance development processes](#). Guidance development included a) review of published research evidence; b) input from a multidisciplinary group of

health professionals from hospital and primary care settings with recognised expertise in pain medicine, addiction medicine, paediatric, adult and geriatric clinical pharmacology and therapeutics, regulatory management of drugs of addiction, health technology assessment and medicines evaluation and clinical pharmacy; and, c) external consultation via invitation with key national organisations.

Appendix 2: Acknowledgments

The contribution of the following members of the multidisciplinary Subject Matter Expert Advisory Group is gratefully acknowledged.

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External Consultation

NSW TAG acknowledges with thanks the assistance of individuals and organisations who provided comments and constructive suggestions during the external consultation process.

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Australian College of Rural and Remote Medicine

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