Unintentional misuse of prescription medicines

There is a significant issue in the community with people taking hypnotics, opioids and other pain medicines long-term with no plan in place for stopping. It can be very challenging to withdraw medicines that have been used for many months or years if medicine use becomes problematic. Following a set of guiding principles for prescribing medicines that have a higher potential for misuse and regularly assessing goals of treatment can help to prevent this problem from occurring in the first place.

KEY PRACTICE POINTS:

- Formulate a practice strategy for prescribing medicines with a high potential for misuse, such as opioids, sedatives, hypnotics and gabapentinoids
- Follow a set of prescribing principles to reduce the risk of medicine misuse
- Limit the initial supply of medicine such as an opioid (e.g. < 5 days), to reduce the risk of long-term use
- Set individualised and functional goals for treatment, regularly assess progress, and review continuation of treatment when improvements are no longer taking place or treatment is not effective
- Pharmacists have a role in working with primary care clinicians to help identify and prevent prescription medicine misuse and in guiding a patient's decisions when purchasing over-the-counter medicines with potential for misuse

Losing control of medicines

In most cases, people do not set out to misuse medicines that are prescribed to them. It may begin with taking an occasional extra dose, taking two tablets instead of one or taking an "as needed" medicine regularly regardless of symptoms, but then over time neurological changes occur, and control is lost over these decisions. The choice to take a medicine is then perceived by the person as a necessary means to function day to day and they become trapped in a cycle of medicine misuse.

The reasons why people misuse medicines that are prescribed to them are multi-factorial and complex, including psychological and biological factors, coping mechanisms for pain and other symptoms, lack of family and social support, adverse living circumstances and challenging or traumatic life events. Prescribers can also significantly influence medicine misuse, in both positive and negative ways, e.g. setting an expectation that a medicine such as a benzodiazepine will be required lifelong or continuing a medicine without assessing its ongoing benefit.

When any medicine is prescribed, especially those that have the potential for misuse, the responsibility lies with the prescriber to set the boundaries for use, by ensuring that the patient understands why, how and when to use it and for how long; the dispensing pharmacist should reiterate this information.

Defining medicine misuse

Medicine misuse is generally described as: "using a medicine in a manner or dose other than prescribed".[1] This definition encompasses people who obtain medicines for the sole purpose of gaining a "high" (i.e. without a legitimate indication for the medicine) or for diversion (i.e. selling to others). However, the more common scenario in a primary care setting is a person who is using a medicine for the purpose it was prescribed, but at a higher dose, increased frequency or for a longer duration than indicated, e.g. a hypnotic medicine.[2] When medicine misuse becomes problematic, it may be classified as a substance use disorder, which is measured on a continuum from mild to severe (see: "Substance use disorder").[3]

Medicines with a higher potential for misuse include opioids (e.g. oxycodone, morphine, tramadol and codeine), sedatives and hypnotics (e.g. benzodiazepines and zopiclone), gabapentinoids (i.e. gabapentin and pregabalin) and stimulants (e.g. methylphenidate).[1] However, almost all prescription medicines have the potential for misuse. Medicines can also be misused for a variety of supposed reasons, for example, laxatives used for weight loss and bronchodilators used for increasing physical performance, although these scenarios are related to intentional misuse.

There is limited published evidence on the magnitude and extent of prescription medicine misuse in New Zealand, and much of it is unlikely to be reported. Issues related to opioid and benzodiazepine misuse are the most well documented. A recent pharmaceutical dispensing report by bpac^{nz} found that 20% of people prescribed zopiclone in New Zealand between July, 2017 and June, 2018 received more than 180 tablets; many of these people were receiving enough supply for use every second night.[4] Concern has also been expressed recently about the misuse of pregabalin and gabapentin in New Zealand.[5] Tramadol misuse is also an emerging issue.

For further information, see:

"Prescribing hypnotic medicines: a focus on zopiclone", **www.bpac.org.nz/report/snippet/zopiclone.aspx**

"Tramadol – not the safer opioid", Goodfellow Unit MedTalk with Dr Alistair Dunn, available from: **www.goodfellowunit.org/tramadol-not-safer-opioid**

Substance use disorder

The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) sets criteria for the diagnosis of substance use disorder (addiction). Individual substances are defined, e.g. alcohol use disorder, opioid use disorder, but the diagnostic characteristics of almost all of these disorders are the same.[3]

Substance use disorder is measured on a continuum from mild (two to three criteria) to severe (six or more criteria), based on the following criteria:[3]

- Taking the substance in larger amounts and for longer than intended
- Wanting to cut down or quit but not being able to
- Spending a lot of time obtaining the substance
- Craving or a strong desire to use the substance
- Repeatedly unable to carry out major obligations at work, school or home due to substance use
- Continued use despite persistent or recurring social or interpersonal problems caused or made worse by substance misuse, i.e. a "vicious cycle"
- Stopping or reducing important social, occupational or recreational activities due to substance use
- Recurrent use of the substance in physically hazardous situations
- Consistent use of the substance despite acknowledgement of persistent or recurrent physical or psychological difficulties from using it

Strategies to mitigate risk of prescription medicine misuse

The primary gateway to loss of control of medicine use is when a medicine is prescribed for an acute problem, without a plan and expectation in place for what symptoms it should be used to treat, how long and how frequently it should be taken, and how to stop it.

Most of the published literature on strategies to minimise medicine misuse is in relation to prescribing opioids. The general principles of this advice, however, can be applied to most medicines with the potential for misuse.

Prepare a practice strategy in advance

Primary care practices should agree on a policy for prescribing for and reviewing patients taking medicines with a high potential for misuse. The Medical Council of New Zealand recommends considering the following points when prescribing a high-risk medicine:[6]

- Do not prescribe more than one to three days' supply of medicine to a new or unfamiliar patient to the practice without having the opportunity to comprehensively assess the rationale and protocol for treatment
- Establish contact with the dispensing pharmacist and share information about the treatment protocol and any early requests for repeats (usually only necessary if there is a suspicion or high risk of medicine misuse)
- Be aware of pressure to prescribe or prescribing in isolation from practice colleagues
- Be satisfied that ongoing prescription of a medicine with potential for misuse is clinically indicated and evidence-based

Treatment plans should be documented in the patient's notes so other clinicians in the practice can follow the protocol.

Agree on a policy for repeat prescription requests, e.g. no early repeats and patients must be reviewed in person by a general practitioner at least three-monthly. Consider how to manage electronic prescription requests via patient portals.

Prepare a practice strategy/dialogue for responding to inappropriate requests for medicines with the potential for misuse and familiarise yourself with local referral protocols to specialist alcohol and drug services.[7]

Further information:

Examples of practice policies and dialogues are available from: **www.racgp.org.au/your-practice/guidelines/drugs-of-dependence-a**

Principles of safer prescribing of medicines with the potential for misuse

First consider: can I recommend something else? If a medicine is being prescribed for symptomatic relief, consider non-pharmacological management strategies that could be trialled first, and continued alongside any pharmacological treatment. For example, there are various behavioural techniques and environmental interventions that should be trialled in most people before considering a hypnotic medicine for insomnia. Also consider the appropriateness of the medicine for the clinical scenario, e.g. using paracetamol or NSAIDs instead of an opioid for mild to moderate pain.

Further information:

"Understanding the role of opioids in chronic non-malignant pain", **www.bpac.org.nz/2018/opioids-chronic.aspx**

"I dream of sleep: managing insomnia in adults", **www.bpac.org.nz/2017/insomnia-1.aspx**

Prescribing principles

The following principles relate to prescribing opioids for chronic pain, but can be applied to any medicine with the potential for misuse:[2, 8]

1. Aim to diagnose and treat the underlying cause of the symptoms
2. Assess psychological wellbeing and risk of addiction, including past or present substance misuse (including alcohol), family history of substance misuse, relevant co-morbidities (e.g. mental illness), the patient's expectations about treatment, mood, family and social support
3. Discuss all available treatment options, including non-pharmacological treatments and coping strategies
4. Select medicines based on evidence of effectiveness, and discuss the anticipated benefits and possible risks of treatment with the patient, including neuroadaptation (tolerance) and substance use disorder (dependence/addiction)
5. Establish personalised goals of treatment, e.g. agree on functional achievements identified by the patient rather than assessing pain with a numerical pain scale; explain that treatment will be stopped if goals are not met or adverse effects occur
6. Initiate a medicine for a trial period before assessing its effect and deciding whether to continue treatment
7. When assessing the overall benefit of a medicine, consider the effect on symptoms, improvements in activity/functional goals, adverse effects, aberrant behaviours (e.g. escalating doses, early requests for repeats) and any change in mood or psychological wellbeing

8. Periodically review the underlying diagnosis and influence of the patient's co-morbidities on treatment success
9. Provide a written treatment plan to the patient that outlines how the medicine should be taken (dose, frequency, duration), what the goals of treatment are, how often they will be assessed, how and when the medicine will be discontinued and what to do if symptoms are not controlled or goals are not met
10. Document the treatment plan in the patient's electronic record, also record a measure or description of pre-treatment symptoms and function and reassessment of these measures

Further information:
Good prescribing practice, Medical Council of New Zealand, available from: **www.mcnz.org.nz/assets/News-and-Publications/Statements/Good-prescribing-practice.pdf**

Factors that increase the risk of medicine misuse include a personal or family history of substance misuse, including alcohol, and a history of serious mental illness, e.g., bipolar disorder, schizophrenia, major depression or anxiety, post-traumatic stress disorder, personality disorder, obsessive compulsive disorder, attention deficit disorder.[2, 9–11]

Psychosocial factors can also increase the likelihood of medicine misuse, such as a personal or family history of addictive behaviours or legal issues related to alcohol or drugs, and recent life changes, e.g. bereavement, social isolation, stress, financial pressures. Systematic reviews have found inconsistent evidence of any correlation between opioid misuse and demographic factors such as gender, employment status, ethnicity, marital status or level of education.[10]

The dose prescribed, and the number of days supply of a first prescription influences the likelihood of ongoing use and therefore medicine misuse. For example, an analysis of almost 1.3 million patient records in the United States found that among patients with non-malignant pain prescribed an opioid for the first time* the key factors that increased the probability of long-term use were when a first prescription supply exceeded 5, 10 or 30 days, after a second or third prescription and when the total cumulative dose reached ≥ 700 mg morphine equivalent.[12] Among patients prescribed one or more days of opioid treatment, 6% were still taking opioids one year later. However, 14% of people whose first prescription was for ≥ 8 days and 30% of those whose first prescription was ≥ 31 days were using opioids one year later. Approximately 14% of patients who received a repeat or second prescription for an opioid were still taking opioids after one year. Patients taking tramadol had the highest probability of long-term opioid use, however, this may reflect choice of medicine for long-term pain.[12]

* Patients were included if they had ≥ six months without an opioid prescription prior to this prescription

Prescribing to patients with risk factors

Depending on the individual scenario, a patient's risk factors may mean that a certain medicine is not appropriate, or it may mean that a medicine can be used, but with additional precautions and monitoring put in place. For example, restricting initial supply to two or three days only before review.[9, 10]

If a patient is currently dependent on a substance such as alcohol, a prescription medicine or an illicit drug, medicines with a high potential for misuse, such as opioids and hypnotics, are usually contraindicated; discuss treatment options with a pain or addiction specialist.[9]

Further information:
A Restriction Notice can be applied for if a patient has been obtaining a prescription medicine over a prolonged period and there is concern that they are likely to seek further supplies. For further information, see: **www.health.govt.nz/system/files/documents/pages/medicines-control-restriction-notices-v1.pdf**

Review the rationale for continued prescribing

Review medicines that may no longer be beneficial or appropriate. For example, patients discharged from hospital on multiple pain medicines can have a tapering protocol put in place and strong opioids stepped down to weaker analgesic options as their pain resolves.

A more complex scenario is taking over the care of a patient who is already established on a long-term treatment, e.g. a benzodiazepine or gabapentinoid. It is never too late to apply the principles of safer prescribing and establish goals for treatment and a strategy to slowly and cautiously reduce and discontinue medicines if use is not beneficial.

Further information:
Discontinuing benzodiazepines: "Overuse of benzodiazepines: still an issue?", **www.bpac.org.nz/BPJ/2015/February/benzodiazepines.aspx**

Discontinuing opioids: "Identifying and managing addiction to opioids", **www.bpac.org.nz/BPJ/2014/October/opioid-addiction.aspx**

Misuse of over-the-counter medicines: role of community pharmacists

Many medicines are available for purchase in pharmacies that have a similar potential for misuse as prescription medicines, e.g., codeine-containing analgesics, sedating antihistamines, laxatives, loperamide, decongestants, cough and cold preparations, paracetamol* and NSAIDs*.[13] Pharmacists have an opportunity to educate patients about strategies to avoid losing control of their use of a medicine. The patient-pharmacist interaction can strongly influence decision-making in terms of what medicines are purchased and how they are used.[14]

* Inappropriate use can result in medicine overuse headache, as well as liver and renal toxicity.

In a patient encounter involving the purchase of an over-the-counter (OTC) medicine with potential for misuse, the pharmacist should consider:[14]

- Inaccurate self-diagnosis
- Inappropriate dosage
- Prolonged use
- Adverse reactions and interactions with other medicines; especially in older people who may be taking multiple medicines
- Misconceptions or lack of information about risk
- Direct to consumer advertising of products, resulting in inappropriate product selection

There is no particular profile of a person who is likely to misuse medicines, therefore relying on the appearance of a patient to "screen" for misuse is not beneficial.[13]

The following strategies can be followed to reduce misuse of OTC medicines:[13, 14]

- Train staff to recognise possible OTC medicine misuse and follow set procedures; include locum pharmacists, weekend/casual staff and staff not usually involved in the sale of medicines
- Access information on local drug misuse; liaise with other pharmacies and general practices in the area
- Refer all requests for certain medicines to the supervising/senior pharmacist
- Restrict maximum quantity of medicine sold to an individual customer
- Do not display certain medicines openly
- Decline repeated sales of a certain medicine to an individual customer, e.g. restricted medicine sales that are noted, or known customers
- Educate patients about the misuse potential of certain medicines
- Provide oral or written medicine information
- Refer the patient to a general practitioner if there are any concerns
- Be aware of and use the Restricted persons list: **www.health.govt.nz/system/files/documents/pages/medicines-control-restriction-notices-v1.pdf**
- Become familiar with local alcohol and drug services that patients can be referred to

Further information:
The Pharmacy Practice Guidelines can be accessed from the Pharmaceutical Society of New Zealand website. Section 6: Substances of Misuse covers the context of misuse of medicines, recommendations on storage and supply and practice advice (e.g. dealing with the patient), available from: **www.psnz.org.nz**

Identifying medicine misuse

Despite following principles for prescribing to avoid medicine misuse, some patients will inevitably still misuse their medicine. Behaviours or clinical features that may indicate medicine misuse include:[9]

- Requesting a specific medicine and being unwilling to accept an alternative
- Self-directed dose escalations*
- Requesting repeat prescriptions earlier than expected
- Claims of lost prescriptions or medicine supply
- Symptoms and signs of withdrawal

* Escalating dose requirements are a normal physiological response to some medicines, e.g. opioids and benzodiazepines, due to dependence/neuroadaptation, however, patients should not be advised to initiate dose increases themselves.

Strategies for confirming medicine misuse

There are several strategies that can be put in place to help detect medicine misuse. The challenge with this, however, is that although it promotes transparent communication between the clinician and the patient it can jeopardise trust. In addition, there is limited evidence about how effective these strategies actually are in reducing medicine misuse.[10]

Therefore the following strategies should be undertaken with caution and judgement of the individual clinical scenario:[10]

- Drug testing; gold standard but not often done in primary care in New Zealand and tests not available for every medicine; drug "screening" kits may be used in some settings, e.g. workplaces.
- Medicine counts; ask the patient to bring in their supply of medicine and check this against the expected number of tablets remaining.
- Clinical audit of notes; to track prescription history of patients to ensure they are not receiving the same medicine from multiple prescribers at the practice or over time
- Formal treatment contract (as opposed to the general treatment plan as agreed between the prescriber and patient); specifying that the patient agrees to receive prescriptions from only one prescriber and one pharmacy (necessary if prescribing a restricted medicine), not to divert the medicine and not to request early repeats

Further information:

"Substance use disorder", Goodfellow Unit Podcast with Dr Sam McBride, available from: **www.goodfellowunit.org/podcast/substance-use-disorder-sud**

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References

1. National Institute on Drug Abuse. Misuse of prescription drugs. 2018. Available from: www.drugabuse.gov/publications/research-reports/misuse-prescription-drugs/summary (Accessed Oct, 2018).
2. Ballantyne JC. Opioids for the Treatment of Chronic Pain: Mistakes Made, Lessons Learned, and Future Directions. Anesth Analg 2017;125:1769–78. doi:10.1213/ANE.0000000000002500
3. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fifth edition (DSM-5). Arlington, VA: American Psychiatric Association 2013. Available from: www.psychiatry.org/psychiatrists/practice/dsm (Accessed Oct, 2018).
4. bpacnz. Prescribing hypnotic medicines: a focus on zopiclone. bpacnz, 2018. Available from: www.bpac.org.nz/report/snippet/zopiclone.aspx (Accessed Oct, 2018).
5. Ponton R. Pregabalin misuse: preventing potential problems in New Zealand. N Z Med J 2018;131:50–4.
6. Medical Council of New Zealand. Good prescribing practice. 2016. Available from: www.mcnz.org.nz/assets/News-and-Publications/Statements/Good-prescribing-practice.pdf (Accessed Jul, 2016)
7. The Royal Australian College of General Practitioners. Prescribing drugs of dependence in a general practice, Part A. 2014. Available from: www.racgp.org.au/your-practice/guidelines/drugs-of-dependence-a/4-accountable-prescribing/41-being-an-accountable-prescriber-of-drugs-of-dependence (Accessed Oct, 2018).
8. Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. Pain Med 2005;6:107–12.
9. Kahan M, Srivastava A, Wilson L, et al. Misuse of and dependence on opioids: study of chronic pain patients. Can Fam Physician 2006;52:1081–7.
10. Voon P, Karamouzian M, Kerr T. Chronic pain and opioid misuse: a review of reviews. Substance Abuse Treatment, Prevention, and Policy 2017;12. doi:10.1186/s13011-017-0120-7
11. Webster LR, Webster RM. Predicting Aberrant Behaviors in Opioid-Treated Patients: Preliminary Validation of the Opioid Risk Tool. Pain Medicine 2005;6:432–42. doi:10.1111/j.1526-4637.2005.00072.x
12. Shah A, Hayes C, Martin B. Characteristics of initial prescription episodes and likelihood of long-term opioid use - United States, 2006-2015. Morb Mortal Wkly Rep 2017;66:265–9.
13. McBride AJ, Pates R, Ramadan R, et al. Delphi survey of experts' opinions on strategies used by community pharmacists to reduce over-the-counter drug misuse. Addiction 2003;98:487–97.
14. Sansgiry SS, Bhansali AH, Bapat SS, et al. Abuse of over-the-counter medicines: a pharmacist's perspective. Integr Pharm Res Pract 2017;6:1–6. doi:10.2147/IPRP.S103494

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