
# **Codeine:** all formulations prescription-only

All combination codeine products will be reclassified as prescription-only medicines on 5 November, 2020. This change has been made to improve patient safety. This may result in more patients attending general practices to request treatment for pain because they can no longer purchase codeine products over-the-counter (OTC).

## KEY PRACTICE POINTS:

- The decision to reclassify all codeine-containing medicines as prescription-only was made because the risks to the community associated with OTC codeine were assessed as outweighing the benefits
- Prescribers in primary care may encounter more requests for codeine or other analgesics once codeine products are no longer available OTC; this is an opportunity to assess patients who may not have previously presented to general practice for their pain-related issue
- Pharmacists will need to recommend alternative pharmacological or non-pharmacological treatment methods or suggest that patients consult with their general practitioner if an underlying condition requires management
- It is important to distinguish patients who have been taking combination codeine products occasionally for intermittent pain from those who have an increased risk of adverse outcomes due to frequent use
- Patients who have been regularly using codeine products may have chronic pain; assess these patients to determine if there is an underlying cause that can be managed and if analgesic treatment could be improved, including recommending non-pharmacological interventions
- The possibility of codeine misuse should be considered in patients who specifically request codeine and are unwilling to engage in other treatment strategies
- If a patient is prescribed codeine, ensure they understand the treatment regimen and how to manage adverse effects if they occur, e.g. constipation

**For information on managing people in a pharmacy setting, see: "Codeine reclassified as a prescription medicine: a community pharmacy perspective", https://bpac.org.nz/2020/codeine-rx.aspx**

## The reclassification of codeine-containing products

From 5 November, 2020, all codeine-containing medicines will become prescription-only (Table 1).[1] This means that people wishing to use codeine combined with paracetamol or ibuprofen will need to consult with a registered prescriber. This change will not affect codeine 15 mg, 30 mg and 60 mg tablets as these are already prescription-only medicines.

The selection of OTC products available in pharmacies for "cold and flu" has also been affected by the reclassification (Table 1). However, products that did contain codeine have already been reformulated and the codeine-free preparations can continue to be purchased.

### People will be encouraged to seek treatment

The reclassification of OTC codeine products as prescription medicines reduces the options for self-managing acute pain. More people are therefore likely to seek assistance in purchasing OTC analgesics at community pharmacies or to present to general practices requesting treatment. In both situations, a clinical assessment may help improve how the patient's pain is managed, e.g. recommending the most appropriate analgesic regimen depending on the type and severity of pain, along with non-pharmacological interventions. In some cases, management of an underlying condition will mean that analgesic treatment is no longer required.

## The reasoning behind the reclassification

There is global concern about the availability of codeine OTC, and its association with adverse events, misuse and overdose.[4] Codeine is classified as a prescription-only medicine in at least 19 other countries, including Australia, China, France, Germany, Spain and Sweden. Codeine-related harms are more prevalent in countries where codeine is available without a prescription.[2, 4]

**Table 1:** Combination codeine medicines* that will be prescription-only medicines in New Zealand from 5 November, 2020[2, 3]

| Brand name | Amount of codeine | Additional active ingredients | Current status (prior to 5/11/20) |
|---|---|---|---|
| **Paracetamol analgesics** | | | |
| **Panadeine** | 8 mg | Paracetamol 500 mg | Pharmacist Only |
| **Relieve**† | 8 mg | Paracetamol 500 mg | Prescription Only |
| **Panadeine Extra** | 15 mg | Paracetamol 500 mg | Pharmacist Only |
| **Mersyndol** | 9.75 mg | Paracetamol 450 mg, doxylamine succinate 5 mg | Pharmacist Only |
| **Ibuprofen analgesics** | | | |
| **Ibucode Plus, Nurofen Plus, Panafen Plus** | 12.8 mg | Ibuprofen 200 mg | Pharmacist Only |
| **Codeine-containing cold and flu products**‡ | | | |
| **Codral Multi Action** | 9.5 mg | Paracetamol 500 mg, phenylephrine 5 mg, chlorphenamine 2 mg | Pharmacy Only |
| **Codral Cold & Flu** | 9.5 mg | Paracetamol 500 mg, phenylephrine 5 mg | Pharmacy Only |
| **Codral Day & Night Cold and Flu**** | 9.5 mg (day tablet) | Paracetamol 500 mg, phenylephrine 5 mg (day tablet) | Pharmacy Only |

* As at September, 2020

† Funded on prescription

‡ Codral products have all now been reformulated as codeine-free and the new formulations can continue to be sold OTC. These products were included in the table as some pharmacies may have remaining stock of codeine-containing formulations.

** This product contains two different formulations of tablet for day and night; only the day formulation tablet contains codeine

Pharmacy Only = Can only be sold from a licensed pharmacy but can be self-selected from shelves

Pharmacist Only = Can only be sold by a pharmacist (not available for self-selection)

The main concerns associated with codeine being available OTC include:[4]

- Codeine may be used in place of a more appropriate treatment, e.g. using codeine first-line for migraine instead of a NSAID
- Codeine may be taken at higher doses or for longer periods than recommended, e.g. managing chronic pain with OTC codeine
- Other medicines present in combination codeine products may cause serious harm if the product is taken at higher doses or for longer periods, e.g. paracetamol or ibuprofen
- Codeine may be used inappropriately when the risks outweigh the benefits, e.g. when breastfeeding
- Codeine may be inadvertently or intentionally misused, e.g. dependence or diversion for recreational or illegal purposes

In November 2017, The Medicines Classification Committee (MCC) in New Zealand proposed to reclassify codeine as a prescription-only medicine.[1] After a consultation period and consideration of stakeholder feedback, the MCC decided on balance that the harms associated with OTC codeine products outweighed the potential benefits.[1] In October, 2019, the MCC recommended that all codeine-containing medicines should be reclassified as prescription medicines.[1] Evidence from Australia, where the change has already been made, suggests that reclassifying all OTC products that contain codeine as prescription-only medicines will reduce codeine-related harms (see: "The outcomes of the Australian experience").

## Codeine-related harms in New Zealand

Codeine poisoning was the third most common pharmaceutical cause of death recorded in the coronial database in New Zealand from 2008 to 2013, behind methadone and morphine.[5] Hospital records indicate that codeine or morphine accounted for half of all deaths by unintentional overdose in New Zealand from 1999 to 2008.[6] The concurrent use of benzodiazepines and/or alcohol is also frequently associated with codeine-related deaths.[7,8]

There is little published information about the extent of codeine misuse in New Zealand, although anecdotal reports suggest the problem is widespread. The misuse of OTC codeine products can be deliberate, but more frequently it occurs when the lines between chronic pain, self-medication and dependence become blurred. For example, a person may start taking a codeine product at the recommended dose for a legitimate reason, and it improves their pain, and makes them feel more relaxed, so they keep using it, and continue it even after the issue that caused the pain has resolved, and then they start exceeding the recommended daily dose, and eventually they find themselves unable to function without it. Often the person will rationalise that they are still treating their underlying condition, when in reality they are "treating" dependence and withdrawal symptoms.[4] Continuous use of opioids causes neuroadaptations that result in dependence, tolerance, decreased analgesic efficacy and hyperalgesia.[9]

Codeine is known to be a drug of intentional misuse in New Zealand. It is frequently taken by people who are misusing other substances and combination codeine products can be converted into "homebake" morphine/heroin.[10] In 2015, 34% of frequent injecting drug users and 12% of frequent methamphetamine users had taken codeine in the previous six months.[11]

Further information on the misuse of medicines is available from: "Unintentional misuse of prescription medicines", **https://bpac.org.nz/2018/misuse.aspx**

## Medicines co-formulated with codeine can cause significant harm in overdose

Many of the harms associated with OTC codeine are related to the medicines that are co-formulated with it, e.g. paracetamol and ibuprofen. In Australia from 2000 to 2013, 84% of codeine-related deaths were caused by multiple drug toxicity.[8] Paracetamol, ibuprofen or doxylamine (an antihistamine present with codeine and paracetamol in Mersyndol – Table 1) were found in 55% of cases of codeine-related deaths.[8]

**Paracetamol poisoning** can occur through a single acute ingestion of a very high dose (e.g. > 10 g) or cumulative exposure over time to supratherapeutic doses (e.g. >4 g per day for three or more consecutive days, with abdominal pain, nausea or vomiting).[12] Both scenarios can result in potentially fatal hepatotoxicity which may take several days to become apparent. Symptoms of hepatotoxicity include malaise, nausea and abdominal pains; an elevated ALT on a liver function test may be an incidental finding in a person who is subsequently revealed to have a history of prolonged use of paracetamol.

For advice on managing paracetamol poisoning, contact the National Poisons Centre: **Ph. 0800 764 766**

**Non-steroidal anti-inflammatory drugs (NSAIDs)** are associated with a range of gastrointestinal adverse effects, e.g. dyspepsia, gastric ulcers and perforation, which are more likely to occur with high doses or prolonged use.[4] People may also develop anaemia from blood loss secondary to gastric ulcers. Renal dysfunction is a risk factor for acute kidney injury in people taking NSAIDs, especially frail elderly people. Prolonged use of NSAIDs can result in renal tubular acidosis and hypokalaemia.[4] Patients with hypokalaemia may present with muscle weakness and respiratory dysfunction.[4]

## Response to codeine is variable

When prescribed under clinical supervision, multi-modal analgesia, e.g. using paracetamol and/or a NSAID alongside an opioid, is recommended in the World Health Organisation (WHO) analgesic ladder to improve pain relief and to reduce the dose needed of the opioid.[13] There is substantial anecdotal evidence that many patients do benefit from the use of codeine with paracetamol or a NSAID. However, the benefit that people gain from the codeine component is variable.

### Combination products contain relatively low doses of codeine

The amount of codeine contained in currently available combination products is relatively low and may be sub-therapeutic for some people, i.e. 8–15 mg per tablet. The recommended dose of codeine for the treatment of mild to moderate pain is 30–60 mg.[3] Systematic reviews have reported that paracetamol or ibuprofen co-formulated with ≤ 15 mg codeine provide little additional analgesic benefit compared to either paracetamol or ibuprofen alone.[14–17]

### The efficacy of codeine depends on genetics

Codeine needs to be converted to morphine in the liver before it can provide an analgesic effect. The enzyme CYP2D6 converts 5–10% of codeine to morphine, which has a 200-fold higher affinity for μ-opioid receptors than codeine.[18] There are more than 100 known polymorphisms in the gene encoding the CYP2D6 enzyme, resulting in unpredictable and highly variable codeine metabolism between individuals.[19] Genetic testing for CYP2D6 variants is not widely available in New Zealand, but if carried out, people can be classified on a scale from poor to ultra-rapid metabolisers of codeine to morphine.[18] Those who are poor metabolisers gain little, if any, analgesic effect from codeine, whereas ultra-rapid metabolisers have significantly higher levels of morphine following the same dose of codeine and are more likely to experience adverse effects.[19, 20] Severe morphine toxicity, however, is unlikely in people taking OTC combination codeine products at recommended doses.

Eight to 10% of people of European descent are poor metabolisers of codeine and 3–5% are ultra-rapid metabolisers.[19] Up to 29% of Middle Eastern and North African populations are ultra-rapid metabolisers.[19] There are limited data available for the New Zealand population, but one source states that 5% of Māori and Pacific peoples have the poor metabolising phenotype; prevalence of the ultra-rapid phenotype is unknown.[21]

# Managing requests for pain treatment in general practice

The reclassification of codeine may encourage patients who have been self-managing pain to seek treatment in general practice. A clinical assessment will determine if codeine, another analgesic or an adjuvant treatment is appropriate and identify if the patient has any other relevant health issues, e.g. depression or anxiety. It is also important to distinguish patients who have been taking combination codeine products occasionally, e.g. for intermittent back pain, from those who have been taking codeine frequently over a long period and have an increased risk of adverse outcomes.

It is possible that some of the codeine-containing medicines that patients have been purchasing OTC will be withdrawn from the New Zealand market after the reclassification, due to low demand. The only combination codeine medicine that is currently funded on prescription is 8 mg codeine + 500 mg paracetamol tablets (Relieve). Patients who have been using other OTC medicines containing codeine, e.g. codeine + ibuprofen, will need to be prescribed individual medicine items or purchase a combination product at full cost once it has been prescribed, if it remains available.

Key questions when assessing pain are:

- How severe is the pain and what does it feel like?
- Where does the pain occur, how often is it occurring, and is it radiating?
- When did the pain start?
- What alleviates the pain?
- What makes the pain worse?
- Have any analgesics been used? If so, at what dose, frequency and duration, how effective were they, and did they cause any adverse effects?

For further information, see: "The principles of managing acute pain in primary care", **https://bpac.org.nz/2018/acute-pain.aspx**

## Always consider non-pharmacological interventions

Non-pharmacological interventions for pain are frequently beneficial and an important strategy for preventing acute pain from progressing to chronic pain,[19] although some interventions may not be accessible or affordable for patients, such as physiotherapy or cognitive behavioural therapy. Staying physically active and maintaining social contacts, where possible, may help patients to recover more quickly and improve their attitude towards their pain and recovery.

## Frequent OTC codeine use may be driven by chronic pain

Patients who report regularly using codeine-containing products or other OTC analgesia may have an underlying condition that is causing them chronic pain. In some cases, treatment of the underlying condition may remove the need for analgesia, e.g. initiation of urate-lowering treatment can prevent flares of gout if the patient is adherent to treatment.

Opioids have a limited role in the treatment of chronic pain. Non-pharmacological interventions should be the mainstay of treatment where possible, e.g. cognitive behavioural therapy may reduce anxiety, depression or insomnia related to the pain, acupuncture or massage may relieve musculoskeletal pain. Distraction techniques can prevent people from focusing on their pain, including listening to music, reading, meditation, mindfulness or any activity that is enjoyable but does not exacerbate the pain.

If an analgesic is required, non-opioid analgesics are preferred. If an opioid is needed, it should be prescribed at the lowest dose for the shortest possible time to minimise the risk of adverse effects and dependence.

Referral to a pain specialist or multidisciplinary pain service may be appropriate for patients with severe or complex symptoms.

Contact details for local pain clinics are available from local DHBs or via HealthPathways

Further information on managing chronic pain is available from: "Helping patients cope with chronic non-malignant pain: it's not about opioids", **https://bpac.org.nz/BPJ/2014/September/chronicpain.aspx**

## Consider the possibility of misuse before prescribing

The possibility of misuse should be considered if warning signs are present, such as patients requesting an analgesic without a clear indication or insistently requesting codeine, higher doses or a stronger opioid, asking for early repeats or reporting losing medicines or prescriptions.

Inappropriate codeine use may be overlooked if health professionals have stereotypes about the characteristics of people who misuse codeine. People who are misusing codeine are often well-educated, employed and perceive themselves as being different to others misusing stronger opioids.[7, 23] Females are equally likely as males to misuse codeine and compared to people taking strong opioids, those misusing codeine tend to be older.[7] People who are misusing codeine often take inappropriately high doses and have chronic pain, concurrent mental health issues, including psychological distress, or a family history of substance misuse.[7] They may also be taking other substances, e.g. alcohol or benzodiazepines.[25]

Further information is available from: "Identifying and managing addiction to opioids", **https://bpac.org.nz/BPJ/2014/October/opioid-addiction.aspx**

## The outcomes of the Australian experience

In Australia all medicines containing codeine have required a prescription since February, 2018. Many health organisations, health professionals and consumers in Australia supported the change, but potential concerns included:[22, 23]

- Limiting access to codeine for people who benefited from appropriate use, particularly those who did not have easy access to a general practitioner
- People stockpiling codeine-containing medicines prior to the reclassification
- An increase in workload for general practitioners as more patients presented requesting analgesics
- An increase in prescribing of other opioids, e.g. tramadol, or stronger opioids, e.g. oxycodone, as alternatives to codeine

**Reclassifying codeine improved safety**

An evaluation of evidence 12 months after the change to prescription-only supply of codeine concluded that codeine reclassification successfully reduced harm from codeine, and the amount of codeine used, in Australia.[24]

In the 12 months following the change, the New South Wales Poisons Information Centre (NSWPIC)* recorded a 51% average monthly decrease in calls involving codeine overdose and a 79% decrease in calls involving overdoses of formulations containing ≤ 15 mg of codeine.[24] There was no change in the number of calls relating to overdoses from other analgesics, medicines containing > 15 mg codeine or other opioids over this time period.[24]

Nationwide, sales of products containing ≤ 15 mg of codeine from suppliers to community pharmacies and hospitals dropped approximately ten-fold, with no significant change in sales of higher strength codeine.[24] Sales of combination codeine products did, however, briefly increase prior to the rescheduling, suggesting some people may have stockpiled codeine products.[24]

The Royal Australian College of General Practitioners has reported that concerns that general practitioners would be overwhelmed by additional requests for codeine seem unfounded.[24]

* The NSWPIC receives approximately 50% of Australia's poisons centre calls

## Decide which analgesic or adjuvant is indicated

Codeine is a treatment option at Step 2 of the WHO analgesic pain ladder (with or without non-opioid analgesics) for patients with mild to moderate pain*; other options at this step are tramadol and dihydrocodeine.[13] There is no evidence that any one of the weak opioids provides superior pain relief to another, although individual clinical circumstances may mean that one is preferred, e.g. codeine may be preferable to tramadol in people taking other serotonergic medicines.

* N.B. Codeine is also indicated for diarrhoea and non-productive cough and may occasionally be prescribed for these reasons in adults.[3]

Further information on tramadol is available from: "Prescribing tramadol appropriately", **https://bpac.org.nz/2018/tramadol.aspx**

**Consider whether an opioid is the best choice**

Codeine, or another opioid, may **not** be the most appropriate medicine for a range of conditions, e.g:

- For migraine the first-line medicines are a NSAID or paracetamol with a triptan trialled if simple analgesics have been ineffective, see: "Diagnosing and managing headache in adults in primary care", **https://bpac.org.nz/2017/headache.aspx**
- Dysmenorrhoea is better managed with use of a NSAID, e.g. naproxen, or initiating a hormonal contraceptive, see: "Contraception: which option for which patient", **https://bpac.org.nz/2019/contraception/options.aspx**
- Neuropathic pain may be treated with a tricyclic antidepressant, see: "Managing patients with neuropathic pain", **https://bpac.org.nz/BPJ/2016/May/pain.aspx**

**Paracetamol used concurrently with a NSAID is a highly effective analgesic regimen for acute pain.** A meta-analysis found that paracetamol (500 mg) + ibuprofen (200 mg) provided patients with superior relief of acute pain compared with 21 other analgesic regimens, with lower rates of adverse effects than placebo.[15] Patients may receive benefit in some situations from the short-term addition of as-needed codeine to paracetamol and NSAIDs.

## Managing requests for analgesics in pharmacies

Community pharmacists will have a reduced range of products they can sell OTC after the reclassification of codeine. Other treatments for managing pain will need to be recommended. Consultation with a general practitioner should be advised if an opioid may be appropriate or if it is suspected that the person has an untreated underlying condition.

Further information specific to pharmacists is available from: "Codeine reclassified as prescription medicine: a community pharmacy perspective", **https://bpac.org.nz/2020/codeine-rx.aspx**

## If codeine is required, how to prescribe it safely

The recommended dose of codeine for the treatment of mild to moderate pain is 30 – 60 mg, taken every four hours, if necessary, to a maximum of 240 mg per day.[3] A reasonable approach for patients who have never, or very rarely, taken codeine is to initiate them on 15 mg tablets, with instructions to take one or two tablets for the first dose. Patients can then adjust the dose as required depending on adverse effects and their level of pain (with clear instructions on what their maximum dose can be). Codeine should only be prescribed for the expected duration of mild to moderate pain, depending on the cause, e.g. two to three days. Paracetamol or a NSAID can be prescribed concurrently, and then continued when codeine is withdrawn, as pain decreases to a mild level.

### Contraindications and cautions for codeine

Codeine is contraindicated in children aged under 12 years and in people with conditions where respiratory depression or impaired gastric motility would be a concern (e.g. acute head injury, ulcerative colitis), and used with caution in people with impaired respiratory function (e.g. asthma, COPD, obstructive sleep apnoea) or acute abdominal pain (e.g. gallstones).[3] Metabolites of codeine accumulate in people with impaired renal function, therefore it is generally avoided in this situation.[3] Codeine is contraindicated in people who are known to be ultra-rapid metabolisers.[3]

Codeine is contraindicated in breastfeeding and should be avoided in pregnancy unless the benefit outweighs the risk.[3] Codeine and morphine are excreted in breast milk; if the mother is an ultra-rapid metaboliser (which is unlikely to be known), this can lead to sedation and respiratory depression in the breastfed infant due to opioid toxicity.[20] There are case reports of fatal respiratory arrest in infants after breastfeeding from mothers who took codeine.[19] There is also a risk that the adverse effects of codeine in the mother, e.g. drowsiness, may prevent her from noticing the symptoms of opioid toxicity in her infant or cause her to inadvertently harm the baby while sleeping.[20]

For a complete list of cautions and contraindications to codeine, refer to the New Zealand Formulary: **https://nzf.org.nz/nzf_2477**

## Managing the adverse effects of codeine

The common adverse effects of codeine are the same as for all opioids, and include sedation, pruritus, nausea, vomiting, slowing of gastric motility, urinary retention and respiratory depression.[3, 19]

Patients prescribed codeine can be advised to increase their dietary fibre intake, if possible, and to ensure they are well hydrated. A laxative should always be prescribed to patients who are taking codeine regularly, unless there are clinical reasons for not doing so.[3] Stimulant laxatives are often prescribed for the prevention of opioid-induced constipation, e.g. docusate with senna or bisacodyl.[26] Sennoside B tablets (partially funded) may be prescribed if a patient is unable to tolerate other stimulant laxatives. Bulk-forming laxatives should be avoided in patients taking opioids.

If a patient taking codeine experiences nausea or vomiting, it may be possible to reduce the dose, otherwise switch to an alternative analgesic. An anti-emetic could be considered if there were no suitable alternative analgesics and the patient needed to continue taking an opioid, e.g. prochlorperazine, cyclizine or metoclopramide. Patients should not drive or operate machinery if codeine causes sleepiness or confusion and this may mean that some people are only able to take it in the evening.

Further information on the treatment of opioid-induced constipation is available from: **https://bpac.org.nz/2019/constipation.aspx**

## Confirm the patient understands the treatment plan

Ensure patients understand their analgesic regimen, including:

- The dose, frequency and dosing interval for each medicine, including any extra doses for breakthrough pain
- Adverse effects and how these can be managed, e.g. preventing constipation, taking medicines at night if sedation is a problem or taking the medicines with food
- The likely timeframe for pain resolution and guidance on how to reduce the dose and stop the medicine(s) as pain improves
- The need for the treatment duration to be as short as possible to reduce the risk of opioid dependence

A template for creating a pain management plan is available from: **www.guild.org.au/__data/assets/pdf_file/0017/6209/patient-resource-my-pain-management-plan-nps-medicines-wise4e0a9a33c06d6d6b9691ff000026bd16.pdf**

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## References


1. Medsafe. Reclassification of codeine. 2020. Available from: www.medsafe.govt.nz/profs/class/ReclassificationOfCodeine.asp (Accessed Aug, 2020).
2. Medsafe. Classification of codeine: Information paper for the Medicines Classification Committee. 2019. Available from: www.medsafe.govt.nz/profs/class/Agendas/Agen63/MCC63_53a_Reclassificationofcodeine.pdf (Accessed Aug, 2020).
3. New Zealand Formulary (NZF). NZF v100. Available from: www.nzf.org.nz (Accessed Oct, 2020).
4. Nielsen S, Van Hout MC. Over-the-Counter Codeine-from Therapeutic Use to Dependence, and the Grey Areas in Between. Curr Top Behav Neurosci 2017;34:59–75. doi:10.1007/7854_2015_422
5. Fountain JS, Reith DM, Tomlin AM, et al. Deaths by poisoning in New Zealand, 2008-2013. Clin Toxicol (Phila) 2019;57:1087–94. doi:10.1080/15563650.2019.1582777
6. Peiris-John R, Kool B, Ameratunga S. Fatalities and hospitalisations due to acute poisoning among New Zealand adults. Intern Med J 2014;44:273–81. doi:10.1111/imj.12364
7. Nielsen S, MacDonald T, Johnson JL. Identifying and treating codeine dependence: a systematic review. Med J Aust 2018;208:451–61.
8. Roxburgh A, Hall WD, Burns L, et al. Trends and characteristics of accidental and intentional codeine overdose deaths in Australia. Med J Aust 2015;203:299. doi:10.5694/mja15.00183
9. 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
10. Harris M. The 'do-it-yourself' New Zealand injecting scene: implications for harm reduction. Int J Drug Policy 2013;24:281–3. doi:10.1016/j.drugpo.2012.06.007
11. Wilkins C, Prasad J, Romeo J. Recent trends in illegal drug use in New Zealand, 2006-2016. 2017.
12. Starship Clinical Guidelines. Paracetamol poisoning. 2020. Available from: https://www.starship.org.nz/guidelines/paracetamol-poisoning/
13. Anekar AA, Cascella M. WHO Analgesic Ladder. In: StatPearls. Treasure Island (FL): StatPearls Publishing 2020. Available from: http://www.ncbi.nlm.nih.gov/books/NBK554435/ (Accessed Aug, 2020).
14. Toms L, Derry S, Moore RA, et al. Single dose oral paracetamol (acetaminophen) with codeine for postoperative pain in adults. Cochrane Database Syst Rev 2009;:CD001547. doi:10.1002/14651858.CD001547.pub2
15. Moore RA, Wiffen PJ, Derry S, et al. Non-prescription (OTC) oral analgesics for acute pain - an overview of Cochrane reviews. Cochrane Database Syst Rev 2015;:CD010794. doi:10.1002/14651858.CD010794.pub2
16. Derry S, Karlin SM, Moore RA. Single dose oral ibuprofen plus codeine for acute postoperative pain in adults. Cochrane Database Syst Rev 2015;:CD010107. doi:10.1002/14651858.CD010107.pub3
17. Shaheed C, Maher C, McLachlan A. Investigating the efficacy and safety of over-the-counter codeine containing combination analgesics for and codeine based antitussives. 2016. Available from: www.tga.gov.au/sites/default/files/review-efficacy-and-safety-over-counter-codeine-combination-medicines.pdf (Accessed Aug, 2020).
18. Chidambaran V, Sadhasivam S, Mahmoud M. Codeine and opioid metabolism: implications and alternatives for pediatric pain management. Curr Opin Anaesthesiol 2017;30:349–56. doi:10.1097/ACO.0000000000000455
19. Working Group of the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. Acute pain management: scientific evidence. 2015. Available from: http://fpm.anzca.edu.au/documents/apmse4_2015_final (Accessed Aug, 2020).
20. Medsafe. Spotlight on codeine. 2018;39:18–9.
21. Helsby NA. CYP2C19 and CYP2D6 genotypes in Pacific peoples. Br J Clin Pharmacol 2016;82:1303–7. doi:10.1111/bcp.13045
22. Therapeutic Goods Administration. Public submissions on scheduling matters referred to the ACMS#17 March 2016 (codeine). 2016. Available from: www.tga.gov.au/scheduling-submission/public-submissions-scheduling-matters-referred-acms17-march-2016-codeine (Accessed Aug, 2020).
23. Roberts R, Nielsen S. Changes for codeine. Aust Prescr 2018;41:2–3.
24. Cairns R, Schaffer AL, Brown JA, et al. Codeine use and harms in Australia: evaluating the effects of re-scheduling. Addiction 2020;115:451–9. doi:10.1111/add.14798
25. Drug and Alcohol Services Australia. Managing patients with regular OTC codeine use. 2018. Available from: www.sahealth.sa.gov.au/wps/wcm/connect/ce32e126-276e-42fb-a0a2-2358ff9a8e41/OTC+GP+management+factsheet+-+CEC+approved+05+04+18+FINAL+V1.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-ce32e126-276e-42fb-a0a2-2358ff9a8e41-n5jo2nN (Accessed Aug, 2020).
26. Nelson AD, Camilleri M. Opioid-induced constipation: advances and clinical guidance. Ther Adv Chronic Dis 2016;7:121–34. doi:10.1177/2040622315627801


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