Guidance for provision of a Pharmacist Only medicine
Combination analgesics containing codeine

Approved indication: temporary relief of moderate to severe pain

Consider professional obligations
A. Professional standards
B. Privacy
C. Documentation

Assess patient's needs
Consider:
D. Age
E. Symptoms
F. Duration of symptoms
G. Addiction susceptibility
H. Lifestyle and medical history
I. Prior treatment

Confirm recommendation is appropriate
Consider:
J. Efficacy of combination analgesics containing codeine and alternative actions
K. Contraindications and precautions
L. Use in pregnancy and lactation
M. Drug interactions

Provide counselling (supported by written information)
Consider:
N. Dosage
O. Treatment expectations
P. Adverse effects
Q. Follow up advice

Where timely referral is possible, refer when:
- Aged <18 years
- Aged >50 years with recent onset symptoms and underlying cause is unclear
- Pain associated with warning signs and symptoms
- Persistent pain
- History of drug or alcohol addiction
- Patient exhibits suspected addictive behaviour
- Symptoms have not resolved after 3–5 days using adequate doses of a combination analgesic containing codeine
- Suspected medication-overuse headache

Explanatory notes

A. Professional standards
The Professional Practice Standards (PPS) outline the appropriate actions to be taken by pharmacists and trained pharmacy staff in response to a direct product- or symptom-based request.
The Code of ethics for pharmacists provides guidance on the ethical framework through which effective health services should be delivered.

B. Privacy
Pharmacists must meet their obligations in relation to respecting the patient’s privacy and confidentiality in the provision of Pharmacist Only medicines and associated patient counselling.

C. Documentation
Pharmacists are encouraged to document the service provided according to the PPS (See Standard 1: Fundamental pharmacy practice). Documentation of referral is advised.

D. Age
Refer patients aged <18 years, or >50 years with recent onset symptoms and when underlying cause of pain is unclear.

E. Symptoms
Approved indications for combination analgesics containing codeine (CACC) include the temporary relief of moderate to severe pain associated with:
- headaches (including tension and migraine)
- dental surgery or toothache
- dysmenorrhoea
- musculoskeletal pain (e.g. backaches, sports injuries, arthritis, rheumatism)
- earache
- neuralgia
- cold and flu symptoms
- sore throat
- surgery, trauma or burns
- fever.

At doses found in over-the-counter (OTC) CACC, may not be effective for all indications (see Efficacy of CACC and alternative options).
Referral for further investigation is recommended when pain is associated with warning signs and symptoms suggestive of a serious underlying organic cause, for example:
- confusion
- drowsiness
- vomiting
- neurological signs persisting between headaches
- sudden, unexplained onset
- recent onset in a person aged >50 years or who is young and obese
- recent onset with cough, exertion or sexual activity
- head injury
- severe and debilitating pain.

F. Duration of symptoms
CACC have a limited role in chronic or persistent pain management. Excessive doses or long-term use of OTC CACC may lead to dependence. It is recommended that cautionary and advisory label (CAL) label 24 ‘For 3 days use only; can cause addiction’ be used for CACC.

Referral for further investigation is recommended when pain is persistent.

G. Addiction susceptibility
Physical dependence (e.g. signs such as sweating and agitation when medicine is withdrawn) can commonly occur in patients taking opioid therapy. Addiction to opioid analgesics (where patients seek medicine for a high) is uncommon in patients with persistent pain.

Addiction is more likely in patients with a history of drug or alcohol addiction. Factors that may be indicative of addictive behavior include:
- inappropriate use of drugs
- repeated reporting of CACC loss
- obtaining CACC from multiple sources
- multiple escalations of opioid dose without health professional advice
- resistant to changes to therapy when there is clear evidence of detrimental physical or psychological effects of opioid analgesic therapy.

Refer such patients to their doctor and/or experts in drug and alcohol management.

H. Lifestyle and medical history
A thorough lifestyle and medical history, including medicines, will help identify possible underlying causes of the pain, and assist in making recommendations for appropriate treatment. For example, headaches and migraines can be triggered by:
- food – chocolate, citrus fruit, caffeine intake or withdrawal, additives, tyramine-containing foods
- medicines – analgesic overdose or withdrawal, calcium channel blockers, dipyridamole, nitrates, NSAIDs, oestrogens, phosphodiesterase-5 inhibitors, proton pump inhibitors, alcohol
- physical factors – head trauma, stress or anxiety, hormone changes (e.g. menstruation, pregnancy), dehydration, hypoglycaemia (e.g. delayed or missed meals), strenuous physical activity, inadequate sleep, jaw tension and teeth grinding, poor posture, infection
- environment – sensory stimulation (e.g. glare, smells, noise), weather changes, smoke (e.g. cigarette).

I. Prior treatment
Prior treatment with a CACC does not necessarily indicate it is an appropriate analgesic choice. Refer for further investigation if current symptoms have not resolved with use of a CACC at an adequate dose and duration (3–5 days). Up to 10% of patients lack the enzyme (CYP2D6) that metabolises codeine to morphine. These patients obtain no detectable analgesic effect from codeine, but may unknowingly increase the risk of harm if they increase the dose or prolong use in an attempt to elicit a response. If treatment has been no more successful with a CACC than with a single ingredient preparation, consider alternative strategies rather than escalating the dose. Conversely some patients may be ultrarapid metabolisers and achieve higher levels of morphine causing adverse effects.

Refer for further investigation if medication-overuse headache is suspected; signs and symptoms may include:
- headache experienced on >15 days per month
- simple analgesics used on >15 days per month for more than 3 months
- acute migraine drugs (including CACC) used on >10 days a month for more than 3 months.

J. Efficacy of CACC and alternative options
CACC are rarely first-line therapies. Non-drug therapies for all pain types should be explored, for example:
- headaches/migraines – avoidance of triggers, stress reduction and relaxation interventions
- musculoskeletal pain – rest, ice compression, elevation (RICE) for acute injury; physiotherapy for osteoarthritis
- postherpetic neuralgia – ice massage, TENs.

When drug therapy is warranted, single ingredient preparations should be trialled first. First-line therapies are dependent on the cause and duration of symptoms, and generally involve the following options (some may require a doctor’s prescription):
- headaches (including tension and migraine) or sore throat – paracetamol, aspirin or NSAIDs
- dental surgery or toothache – NSAIDs, or antibiotics if infection present
- dysmenorrhoea – combined oral contraceptives or NSAIDs
- musculoskeletal pain (e.g. backaches, sports injuries, arthritis, rheumatism) – paracetamol, weak opioids or NSAIDs
- earache – paracetamol or NSAIDs
- neuralgia: postherpetic – aspirin or paracetamol; trigeminal – carbamazepine
- cold and flu symptoms – paracetamol or NSAIDs with intranasal saline, corticosteroids or decongestants
- surgery, trauma or burns – regular paracetamol or NSAIDs with moderate to strong opioids
- fever – paracetamol.

The lowest effective dose of codeine has not been established but it is generally accepted that doses below 30 mg are unlikely to be effective. Note that CACC available as Pharmacist Only medicines contain less codeine than that recommended for effective pain relief. Single ingredient preparations may therefore be as effective as CACC with less risk of adverse effects.

K. Contraindications and precautions
Contraindications to the use of codeine include hypersensitivity to codeine, morphine or oxycodone; acute respiratory depression; active alcoholism; chronic constipation; and diarrhoea due to toxins or pseudomembranous colitis.

Also consider profiles of other ingredients in combination products.

L. Use in pregnancy and lactation
Pregnancy – for products containing two or more active ingredients, the categorisation is based on the most restrictive component:
- codeine – category A (but high doses in pregnancy may cause withdrawal or respiratory depression in newborn)
- paracetamol – category A
- ibuprofen – category C
- aspirin – category C
- doxylamine – category A

Lactation – consider safety of all ingredients in CACC:
- codeine – although only trace amounts excreted in breast milk, use not recommended as risk of adverse effects in infants if mother is an ultrarapid metaboliser
- paracetamol – safe to use
- ibuprofen – may be used in recommended doses. Ibuprofen and diclofenac are the NSAIDs of choice in breastfeeding mothers.
- aspirin – 75–150 mg may be used cautiously if necessary.
- doxylamine – small amounts excreted. May cause paradoxical excitement or irritability in infant. Anticholinergic effects may inhibit lactation.

M. Drug interactions
The concurrent use of other analgesics (for the current problem or coexisting conditions) should also be considered to avoid duplication of therapy.

Drug interactions with codeine include:
- other CNS depressants (e.g. tranquillisers, sedatives, hypnotics, alcohol, sedating antihistamines) – potentiation of effects, increasing the risk of respiratory depression, profound sedation or coma
- antihistamines with anticholinergic effects – increased risk of severe constipation and/or urinary retention
- cimetidine – reduced metabolism of codeine, increasing the risk of toxicity
- rifampicin – increased metabolism of codeine resulting in inadequate analgesia.

Also consider interactions with other ingredients in the combination product.

N. Dosage
Dosing (including maximum daily doses) will be limited by the other included ingredients. For adults:
- paracetamol: 500–1,000 mg 3–4 hourly (maximum 4 g daily)
- aspirin: 300–900 mg 3–4 hourly (maximum 4 g daily)
- ibuprofen: 200–400 mg 6–8 hourly (maximum 2,400 mg daily)
- doxylamine: 5–10 mg 4–6 hourly.
O. Treatment expectations

The onset of action of codeine is within 15–30 minutes, with analgesia maintained for 4–6 hours.1 Referral to a medical practitioner is recommended if symptoms are not adequately relieved with recommended doses, or if the patient experiences severe and debilitating symptoms.

P. Adverse effects

Regular use of codeine is commonly associated with drowsiness and constipation.

Advice on adverse effects associated with other ingredients in CACC should also be provided.

References

5. eMIMS cloud. Sydney: MIMS Australia Pty Ltd; 2014.
10. Contacts for Drug and Alcohol Services (24-hour help lines for patients): ACT: 02 6207 9977 NSW: 02 9361 8000 or 1800 422 599 NT: 08 8922 8399 (Darwin) or 08 8951 7580 (Alice Springs) or 1800 131 350 QLD: 07 3216 2414 or 1800 177 833 SA: 08 8363 8618 or 1300 131 340 TAS: 03 9416 1818 or 1800 811 944 VIC: 1800 888 236 WA: 08 9442 5000 or 1800 198 0249
15. Pharmacy Department, the Royal Women’s Hospital. Pregnancy and breastfeeding medicine guide. Melbourne: Royal Women’s Hospital; 2010.

Q. Follow up advice

A pain management plan is recommended for any person taking analgesics for persistent or recurring pain. It helps patients take an active role in managing their pain and empowers them to deal with exacerbations. A pain management plan also promotes collaboration between patient and healthcare providers.

Provision of a consumer medicine information (CMI) leaflet and Opioids for pain relief Self Care Fact Card or other printed information for consumers is appropriate.