

CORE CODEINE PRODUCT INFORMATION

Product description

This section should include:

- a description of the dosage form;
- a list of the active ingredients expressed quantitatively; and
- a list of the excipients expressed qualitatively

Pharmacology

Pharmacokinetics:

Codeine and its salts are well absorbed from the gastrointestinal tract: peak plasma-codeine concentrations occur at about one hour after ingestion of codeine phosphate.

Codeine is metabolised by *O*- and *N*-demethylation in the liver (via the cytochrome P450 system) to morphine (about ten per cent of a codeine dose is demethylated to morphine), norcodeine and other metabolites including normorphine and hydrocodone. Codeine and its metabolites are excreted almost entirely by the kidney, mainly as conjugates with glucuronic acid. Approximately 3% to 16% of a dose is eliminated unchanged in the urine.

Patients who metabolise drugs poorly via CYP2D6 are likely to obtain reduced benefit from codeine due to reduced formation of the active metabolite.

The plasma half-life of codeine has been reported to be between 3 and 4 hours after oral administration.

Pharmacodynamics/Mechanism of action:

Codeine acts centrally. It has an analgesic effect, which is thought to be due mainly to its partial metabolic conversion to morphine. Codeine has about one-sixth the analgesic activity of morphine.

Indications

This section must contain the indications of the product as specified in the ARTG. If the indications are not specified in the ARTG (e.g. for a non-validated grandfathered product), the indications must be as specified on the product label.

Contraindications

Codeine is contraindicated for use in patients:

- with known hypersensitivity or idiosyncratic reaction to codeine (or any of the other ingredients in the product)
- with acute respiratory depression
- with chronic constipation

- during labour when delivery of a premature infant is anticipated as it may produce codeine withdrawal symptoms in the neonate
- with active alcoholism
- with diarrhoea caused by pseudomembranous colitis or poisoning (until the causative organism or toxin has been eliminated from the gastrointestinal tract, since codeine may slow down the elimination, thereby prolonging the diarrhoea).

Refer to 'Interactions with other medicines' for additional information

Precautions

Codeine should be used with caution in patients:

- with decreased respiratory reserve e.g. asthma or COPD
- with pre-existing respiratory depression
- who have a history of drug abuse
- who are taking other respiratory depressants or sedatives, including alcohol
- who have had recent gastrointestinal tract surgery
- with raised intracranial pressure or head injury
- with prostatic hypertrophy
- with hepatic or renal impairment
- with hypotension
- with hypothyroidism

Codeine may obscure the diagnosis or the course of gastrointestinal diseases.

Prolonged use of codeine may produce physical and psychological dependence.

Codeine may cause drowsiness. Those affected should not drive or operate machinery.

Refer to 'Interactions with other medicines' for additional information

Use in pregnancy

Category A: Codeine has been taken by a large number of pregnant women and women of child bearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Opioid analgesics may cause respiratory depression in the newborn infant. Prolonged high-dose use of codeine prior to delivery may produce codeine withdrawal symptoms in the neonate.

Lactation

Trace amounts of codeine are excreted into breast milk. Therefore it is not recommended for breastfeeding mothers unless the potential benefits to the patient are weighed against the possible risk to the infant.

Use in the elderly

The elderly are more likely to have age related renal impairment and may be more susceptible to the respiratory depressant effects of codeine.

Interaction with other medicines

The following interactions with codeine have been noted:

- CNS depressants – concomitant use with central nervous system depressants (e.g. barbiturates, chloral hydrate, sedatives, alcohol and centrally acting muscle relaxants) can cause additive CNS depression
- Anticholinergics – concurrent use of codeine with anticholinergic agents may increase the risk of severe constipation and/or urinary retention
- Antihypertensives – hypotensive effects may be potentiated when used concurrently with codeine and lead to orthostatic hypotension
- Antiperistaltic antidiarrhoeals (e.g. kaolin, pectin and loperamide) – concurrent use with codeine may increase the risk of severe constipation
- Metoclopramide – codeine may antagonise the effects of metoclopramide on gastrointestinal activity
- Monoamine oxidase inhibitors (MAOIs) – concurrent administration or use within 14 days of ceasing MAOIs may enhance the potential respiratory depressant effects of codeine
- Opioid analgesics – concurrent use of codeine and other opioid receptor antagonists is usually inappropriate as additive CNS depression, respiratory depression and hypotensive effects may occur
- Substances that inhibit CYP2D6 such as quinidine, phenothiazines and antipsychotic agents can interfere with the metabolism of codeine to morphine, reducing the analgesic effect of codeine
- Tranquillisers, sedatives and hypnotics – codeine may potentiate the effects of these preparations

Adverse reactions

The most common adverse effects associated with codeine are nausea, vomiting, drowsiness, dizziness and constipation.

Other side effects are rare, especially at OTC dosage levels. These include: cough suppression, respiratory depression, euphoria, dysphoria, skin rashes, histamine release (hypotension, flushing of the face, tachycardia, breathlessness) and other allergic reactions.

Dosage

This section must contain the current dosage instructions of the registered product, as specified on the product label.

Overdosage

In case of overdose, immediately contact the Poisons Information Centre (in Australia, call 13 11 26; in New Zealand call 0800 764 766) for advice.

Presentation

Information should be included on:

- *the presentation, including dosage form and pack sizes;*
- *identifying details (eg. colour, shape, identifying markings);*
- *poisons schedule details; and*
- *name and address of the sponsor*

Include the date of approval as the date on which the notification application is lodged