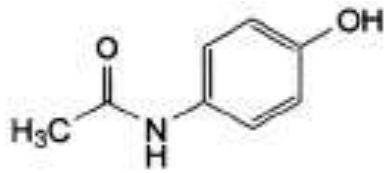
PRODUCT INFORMATION

CODAPANE XTRA Paracetamol 500 mg and Codeine Phosphate 15 mg Tablets

NAME OF THE MEDICINE

Active Ingredients: Paracetamol and Codeine Phosphate

Paracetamol:

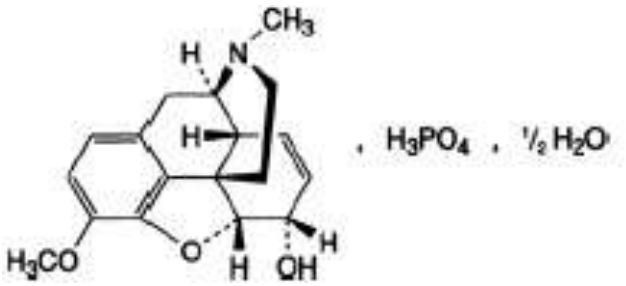


Molecular Formula: $C_8H_9NO_2$.

Molecular weight: 151.2

CAS: 103-90-2.

Codeine Phosphate:



Molecular Formula: $C_{18}H_{21}NO_3$, H_3PO_4, ½ H_2O.

Molecular weight: 406.4

CAS: 1444-62-6

DESCRIPTION

Codeine phosphate is a white or almost white, crystalline powder or small, colourless crystals. It is freely soluble in water, slightly soluble or very slightly soluble in ethanol (96%). Codeine phosphate is a cough suppressant and an analgesic.

Paracetamol is a white or almost white crystalline powder. It is sparingly soluble in water, freely soluble in alcohol, very slightly soluble in methylene chloride. Paracetamol is an analgesic and antipyretic

Actives: Each tablet contains Paracetamol 500mg and Codeine Phosphate 15mg

Excipients: Starch – Potato, Lactose, Povidone, Docusate Sodium, Silica - colloidal anhydrous, Magnesium Stearate.

PHARMACOLOGY

Pharmacodynamics

Paracetamol's analgesic mechanism of action has not been fully elucidated, but may involve blocking impulse generation at the bradykinin sensitive chemoreceptors that evoke pain.

The antipyretic effect of paracetamol rises from its ability to block the action of prostaglandin synthetase and so prevent the synthesis of prostaglandins in response to the pyrogen stimulus in the region of the anterior hypothalamus.

Codeine acts centrally. It produces analgesia by dulling the response to painful stimuli at several loci in the central nervous system. This causes an alteration in the sensation and affective response of pain.

There is evidence to suggest that a combination of paracetamol with codeine is superior in analgesic action to either drug administered alone.

Pharmacokinetics

Paracetamol: After oral administration, paracetamol is absorbed rapidly and completely from the small intestine; peak plasma levels occur 30 to 120 minutes after administration. Paracetamol is uniformly distributed throughout most body fluids; the apparent volume of distribution is 1 to 1.2 L/kg.

Paracetamol can cross the placenta and is excreted in milk. Plasma protein binding is negligible at usual therapeutic concentrations, but increases with increasing concentrations.

Paracetamol is metabolised by the hepatic microsomal enzyme system. In adults, at therapeutic doses, paracetamol is mainly conjugated with glucuronide (45 to 55%) or sulfate (20 to 30%). A minor proportion (less than 20%) is metabolised to catechol derivatives and mercapturic acid compounds via oxidation. Paracetamol is metabolised differently by infants and children compared to adults, the sulfate conjugate being predominant.

Paracetamol is excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol, with 85 to 90% of the administered dose eliminated in the urine within 24 hours of ingestion. The elimination half-life varies from one to four hours. Food intake delays paracetamol absorption.

Codeine: Codeine has about one-sixth of morphine's analgesic activity. It is well absorbed from the gastrointestinal tract and does not interfere with paracetamol absorption.

It is metabolised in the liver to morphine and norcodeine which, with codeine, are excreted in the urine, partly as conjugates with glucuronic acid. Excretion is almost complete within 24 hours.

Patients who metabolise drugs poorly via CYP2D6 are likely to obtain reduced benefit from codeine due to reduced formation of the active metabolite. This may be the case in about 8% of patients.

INDICATIONS

Temporary relief of moderate to severe acute pain associated with strong headaches, migraine headaches, dental surgery or toothache, menstrual pain and sports injuries (e.g. backaches and muscular pain).

CONTRAINDICATIONS

Hypersensitivity to paracetamol or codeine or other ingredients (see **DESCRIPTION**).

PRECAUTIONS

CODAPANE XTRA Paracetamol 500 mg and Codeine Phosphate 15 mg Tablets should be administered with caution to patients with hepatic or renal dysfunction. Codeine should be used with caution in patients with CNS depression or decreased respiratory reserve. Prolonged use of high doses of codeine may produce dependence.

Due to the preparation's sedative action, impairment of the mental and/or physical abilities required for the performance of potentially hazardous activities may occur. Hence, children engaging in bike riding and other hazardous activities should be supervised to avoid potential harm.

Adults should not drive, operate machinery or drink alcohol while taking this medication.

Use in pregnancy (Category A)

Category A: Both paracetamol and codeine have been taken by a large number of pregnant women and women of childbearing 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.

Use in lactation

Paracetamol and codeine both appear in breast milk in low concentrations. Maternal ingestion of paracetamol in recommended doses does not appear to present a risk to breastfed infants. However, codeine may cause respiratory depression in newborn infants.

CODAPANE XTRA Paracetamol 500 mg and Codeine Phosphate 15 mg Tablet is therefore not recommended for breastfeeding mothers unless the potential benefits to the patient outweigh the possible risk to the infant.

INTERACTIONS WITH OTHER MEDICINES

Anticoagulant dosage may require reduction if this medication is prolonged.

Paracetamol absorption is increased by drugs which increase gastric emptying, e.g. metoclopramide, and decreased by drugs which decrease gastric emptying, e.g. propantheline, antidepressants with anticholinergic properties and narcotic analgesics.

Paracetamol may increase chloramphenicol concentrations. The likelihood of paracetamol toxicity may be increased by the concomitant use of enzyme inducing agents, such as alcohol or antiepileptic drugs.

It is possible that interactions could occur between drugs that can inhibit CYP2D6 (such as quinidine, phenothiazines and antipsychotic agents) and codeine.

Concurrent administration of sedatives or tranquillizers may enhance the potential respiratory depressant effects of codeine.

ADVERSE EFFECTS

Paracetamol: Reports of adverse reactions are rare. Although the following reactions have been reported, a causal relationship to the administration of paracetamol has been neither confirmed nor refuted: dyspepsia, nausea, allergic and haematological reactions.

Codeine: Nausea and vomiting, constipation, dizziness and drowsiness have been reported at therapeutic doses of codeine. Very rarely, skin rashes may occur in patients hypersensitive to codeine. Prolonged use of large doses of codeine may result in physiological dependence.

DOSAGE AND ADMINISTRATION

Adults and children over 12 years: 2 Tablets four times a day if required (maximum 8 tablets in 24 hours).

Not recommended for children under 12 years of age.

OVERDOSAGE

Symptoms: Toxic symptoms include vomiting, abdominal pain, hypotension, sweating, central stimulation with exhilaration and convulsions in children, drowsiness, respiratory depression, cyanosis and coma. The most serious adverse effect of acute overdosage of paracetamol is a dose dependent, potentially fatal hepatic necrosis.

In adults, hepatotoxicity may occur after ingestion of a single dose of paracetamol 10 to 15 g (30 tablets); a dose of 25 g (50 tablets) or more is potentially fatal.

Symptoms during the first two days of acute poisoning by paracetamol do not reflect the potential seriousness of the intoxication. Major manifestations of liver failure, such as jaundice, hypoglycaemia and metabolic acidosis, may take at least three days to develop.

Treatment: In case of overdosage, contact the Poisons Information Centre (131 126).

PRESENTATION AND STORAGE CONDITIONS

CODAPANE XTRA Paracetamol 500 mg and Codeine Phosphate 15 mg Tablets are white to off white capsule shaped uncoated tablets, plain on one side and breakline on the other side. The products are presented in blister pack size of 10 tablets, 12 tablets, 20 tablets, 24 tablets, 30 tablets, and 40 tablets.

Store below 30^{o}C

NAME AND ADDRESS OF THE SPONSOR

Alphapharm Pty Ltd

Level 1, 30 The Bond

30-34 Hickson Road

Millers Point NSW 2000

POISON SCHEDULE OF THE MEDICINE

Schedule 3.

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (the ARTG)

01/08/2012