

New Zealand Data Sheet

Product Description

Pharmacist's Own™ Pain Relief capsule-shaped tablets (caplets)

Paracetamol 500 mg per tablet & Codeine Phosphate 10 mg per tablet

Blister packs of 36 white, capsule-shaped tablets

Composition

Actives

Paracetamol 500 mg

Codeine Phosphate 10 mg

Excipients

Cellulose - microcrystalline

Croscarmellose sodium

Magnesium Stearate

Povidone

Stearic acid

Pregelatinised maize starch

Crospovidone

Contains no lactose, sugar, gluten, yeast, artificial colouring, preservatives and alcohol.

Pharmacology & Pharmacokinetics

Paracetamol

Paracetamol is an analgesic with antipyretic activity.

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 (44 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 1 to 4 hours. Food intake delays paracetamol absorption.

Codeine phosphate

Codeine has about one-sixth of the analgesic activity of morphine. 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.

Indications

Pharmacist's Own™ Pain Relief provides pain relief from

- headache,
- period pain,
- back pain, and
- toothache.

Contraindications

Pharmacist's Own™ Pain Relief should not be administered to patients with the following conditions:

- Known hypersensitivity to paracetamol, codeine or other opioids, or to any other ingredient in the product (refer to Description).

Codeine phosphate

- Acute respiratory depression
- Obstructive airways disease
- Acute alcoholism
- Head injuries or conditions in which intracranial pressure is raised
- Patients at risk of paralytic ileus
- Hepatic failure
- Acute asthma

Warnings & Precautions

Pharmacist's Own™ Pain Relief should be administered with caution to patients with the following conditions:

Paracetamol

- Hepatic or renal dysfunction

Codeine phosphate

- Hypothyroidism
- Adrenocortical insufficiency e.g. Addison's Disease
- Impaired kidney or liver function.
- Prostatic hypertrophy
- Shock/hypotension
- Myasthenia gravis
- Convulsions / convulsive disorders
- Gall bladder disease or gall stones
- Recent gastro-intestinal surgery
- Urinary tract surgery
- Reduced respiratory function or history of asthma
- Obstructive and inflammatory bowel disease – codeine reduces peristalsis, increases tone and segmentation in the bowel and can raise colonic pressure.
- Patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment.

Hypersensitivity

Codeine phosphate

Maculopapular rash, fever, splenomegaly and lymphadenopathy have been seen as part of a codeine hypersensitivity reaction.

Dependence

Codeine phosphate

Taking codeine regularly for a long time can lead to addiction. Stopping treatment can result in withdrawal symptoms. Codeine is not a satisfactory substitute for patients dependent on morphine. Regular use of analgesics for headache can result in an overuse syndrome.

Withdrawal

Codeine phosphate

Abrupt withdrawal of codeine precipitates a withdrawal syndrome. Symptoms may include tremor, insomnia, restlessness, irritability, anxiety, depression, anorexia, nausea, vomiting, diarrhoea, sweating, lacrimation, rhinorrhoea, sneezing, yawning, piloerection, mydriasis, weakness, pyrexia, muscle cramps, dehydration and increase in heart rate, respiratory rate and blood pressure. These effects can also occur in neonates exposed to codeine *in utero* (see use in pregnancy).

Tolerance diminishes rapidly after withdrawal so a previously tolerated dose may prove fatal.

Genetic polymorphism

Codeine phosphate

Codeine is metabolised to morphine by cytochrome P450 2D6. Some patients are ultra-rapid metabolisers and are at higher risk of toxic opioid effects. Some patients are slow metabolisers and these patients may not experience adequate analgesic effect with codeine.

Use in pregnancy

The drugs found in Pharmacist's Own™ Pain Relief have 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. The balance of benefits and risks should be considered carefully.

Codeine phosphate

Opioid analgesics cross the placenta. Regular use during pregnancy may cause physical dependence in the foetus, leading to withdrawal symptoms (convulsion, irritability, excessive crying, tremors, hyperactive reflexes, fever, vomiting, diarrhoea, sneezing and yawning) in the neonate. Prolonged high-dose use of Codeine prior to delivery may produce Codeine withdrawal symptoms in the neonate.

Use during lactation

Not recommended for use by breastfeeding mothers.

Codeine phosphate

Codeine is excreted into breast milk. However with usual analgesic doses, concentrations are generally low.

However, infants of nursing mothers taking codeine may have an increased risk of morphine overdose if the mother is an ultra-rapid metaboliser of codeine.

Nursing mothers taking codeine, who are ultra-rapid metabolisers, may have higher morphine levels in their breast milk, which may lead to life-threatening or fatal side effects in nursing babies.

When prescribing codeine for a nursing mother, the lowest dose for the shortest amount of time to relieve pain or cough should be prescribed. Nursing patients should be told how to recognize signs of high morphine levels in themselves and their babies.

Signs of high morphine levels in a mother are extreme sleepiness and trouble caring for the baby.

Breastfed babies usually nurse every two to three hours and should not sleep more than four hours at a time. If the baby shows signs of increased sleepiness (more than usual), difficulty breastfeeding, breathing difficulties, or limpness, the mother should immediately seek medical advice.

Use in children

Not recommended for children under 12 years of age.

Codeine phosphate

Children up to 2 years of age may be more susceptible to the effects, especially the respiratory depressant effects of opioid analgesics. Paradoxical excitation is especially likely to occur in paediatric patients receiving these medicines.

Use in elderly

Codeine phosphate

Geriatric patients may be more susceptible to the effects, especially the respiratory depressant effects, of medications containing codeine. Also, geriatric patients are more likely to have prostatic hypertrophy or obstruction and age-related renal function impairment, and are therefore, more likely to be adversely affected by opioid-induced urinary retention. The risk of constipation and faecal impaction is also greater in the elderly.

Geriatric patients may metabolize or eliminate opioid analgesics more slowly than younger adults. Lower doses or longer dosing intervals than those usually recommended for adults may be required, and are usually therapeutically effective for these patients.

Effects on the ability to drive and use machines

Codeine phosphate

Codeine may cause drowsiness or a decrease in alertness in some patients. Patients should be cautioned about operating vehicles or machinery, or engaging in activities which require them to be fully alert.

Interactions With Other Drugs

Anticoagulant dosage may require reduction if medication is prolonged.

Paracetamol

The rate of 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, 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 anticonvulsant drugs.

Codeine phosphate

Interactions have been noted with the following:

- Monoamine Oxidase Inhibitors – due to the possible risk of excitation or depression, avoid concomitant use and for 14 days after discontinuation of MAOI.
- Alcohol – enhanced sedative and hypotensive effect, increased risk of respiratory depression
- Hypnotics and anxiolytics – enhanced sedative effect, increased risk of respiratory depression
- Anticholinergics – risk of severe constipation which may lead to paralytic ileus and/or urinary retention
- Metoclopramide and domperidone – antagonistic effect on GI activity
- Anti-diarrhoeal drugs – increased risk of severe constipation

- Anaesthetics – enhanced sedative and hypotensive effect
- Tricyclic antidepressants – enhanced sedative effect
- Antipsychotics – enhanced sedative and hypotensive effect
- Opioid antagonists – may precipitate withdrawal symptoms
- Quinidine – reduce analgesic effect
- Antihypertensive drugs – enhanced hypotensive effect
- Ciprofloxacin – avoid premedication with opioids as they reduce ciprofloxacin concentration
- Ritonavir – may increase plasma levels of opioid analgesics
- Mexiletine – delayed absorption of mexiletine
- Cimetidine – inhibits the metabolism of opioid analgesics causing increased plasma codeine concentrations.

Adverse Reactions

Paracetamol

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

- dyspepsia,
- nausea,
- allergic reactions and
- haematological reactions.

Codeine phosphate

Immune system disorders: rash, urticaria, pruritus, difficulty breathing, increased sweating, redness of flushed face, angioedema.

Nervous system disorders: confusion, drowsiness, malaise, tiredness, vertigo, dizziness, changes in mood, hallucination, CNS excitation (restlessness/excitement), convulsions, mental depression, headache, nightmares, raised intracranial pressure, tolerance or dependence, dysphoria, hypothermia.

Eye disorders: miosis, blurred or double vision

Cardiac disorders: bradycardia, palpitations, hypotension, orthostatic, hypotension, tachycardia.

Respiratory, thoracic and mediastinal disorders: respiratory depression

Gastrointestinal disorders: constipation, biliary spasm, nausea, vomiting, dry mouth.

Musculoskeletal, connective tissue and bone disorders: muscle rigidity

Renal & urinary disorders: ureteral spasm, anti-diuretic effect, urinary retention.

Reproductive system and breast disorders: decrease in libido and potency.

Withdrawal effects: abrupt withdrawal precipitates a withdrawal syndrome. Symptoms may include tremor, insomnia, restlessness, irritability, anxiety, depression, anorexia, nausea, vomiting, diarrhoea, sweating, lacrimation, rhinorrhoea, sneezing, yawning, piloerection, mydriasis, weakness, pyrexia, muscle cramps, dehydration and increase in heart rate, respiratory rate and blood pressure.

Tolerance diminishes rapidly after withdrawal so a previously tolerated dose may prove fatal.

Regular prolonged use of codeine is known to lead to addiction and tolerance.

Prolonged use of a painkiller for headaches can make them worse.

Overdose

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 overdose 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 15g (30 tablets). A dose of 25g (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

Treatment consists primarily of management of paracetamol toxicity; naloxone is the treatment of choice for codeine intoxication. In cases of overdose, methods of reducing the absorption of ingested drug are important. Gastric lavage is essential even if several hours have elapsed. Prompt administration of activated charcoal 50mg and iced mannitol 20% 500mL by mouth may reduce absorption.

If the history suggests that paracetamol 15g or more has been ingested, administer one of the antidotes, which follow:

Intravenous acetylcysteine 20%.

Administer acetylcysteine immediately without waiting for positive urine test or plasma level results. Initial dose 150mg/kg over 15 minutes, followed by continuous infusion of 50mg/kg in glucose 5% 500mL over four hours and 100mg/kg in glucose 5% 1L over 16 hours.

Oral methionine

2.5g immediately followed by three further doses of 2.5g every four hours. For a 3 year old child, methionine 1g every four hours for 4 doses has been used.

If more than 10 hours have elapsed since the overdose was taken, the antidote may be ineffective. When treatment for paracetamol toxicity has been initiated, naloxone 400 microgram may be administered subcutaneously, intramuscularly or intravenously; intravenous doses may be repeated at intervals of 2 to 3 minutes if necessary. Assisted respiration may be required.

Dosage and Administration

Adults and children 12 years and over – Take 1 to 2 tablets with water every 4 to 6 hours as required. Do not exceed 8 tablets in 24 hours.

Not recommended for children under 12 years of age.

Do not take this medicine for longer than 48 hours (children 12 years and older) or a few days (adults) at a time, unless advised by a doctor.

Presentation

White capsule-shaped tablet.
In blister packs of 36 tablets.

Medicine Classification

Pharmacist Only Medicine

Name and Address of Sponsor

PSM Healthcare Ltd trading as API Consumer Brands
PO Box 76 401
Manukau City
Auckland 2241
New Zealand

Made in New Zealand

Prepared

14th March 2011