Panadeine
Tablet, Caplets and Rapid Soluble tablets

PRODUCT INFORMATION

DESCRIPTION

Active Ingredients

Paracetamol 500 mg
Codeine Phosphate 8 mg

Excipients

Tablets - Starch - maize, talc - purified, stearic acid, titanium dioxide, povidone, starch pregelatinised maize, potassium sorbate.

Caplets – Starch - maize, talc - purified, stearic acid, titanium dioxide, povidone, starch pregelatinised maize, potassium sorbate, hypromellose, glycerol triacetate, carnauba wax, blue film-coat.

Rapid Soluble tablets - Sodium carbonate, citric acid - anhydrous, dimethicone 200/350, sodium bicarbonate, sorbitol, aspartame, saccharin sodium, povidone, sodium lauryl sulfate, lemon flavours.

Contains no sugar, lactose or wheat starch.

PHARMACOLOGY

Paracetamol is a para-aminophenol derivative that exhibits analgesic and anti-pyretic activity. It does not possess anti-inflammatory activity. It is given by mouth or rectally for mild to moderate pain and fever.

Codeine phosphate is an opioid analgesic which binds with stereospecific receptors at many sites within the central nervous system. It alters processes affecting both the perception of pain and the emotional response to pain. Codeine has about one-sixth of the analgesic activity of morphine.

Pharmacokinetics

After oral administration, paracetamol is absorbed rapidly and completely from the gastrointestinal tract; peak plasma levels occur 10 to 60 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 breast 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 1 to 3 hours. Food intake delays paracetamol absorption.

Codeine phosphate is absorbed from the gastrointestinal tract and peak plasma concentrations are reached one hour after oral administration.

Codeine is metabolised in the liver to morphine and norcodeine. Codeine and its metabolites are excreted almost entirely by the kidney within 24 hours. The metabolites are mainly conjugates with glucuronic acid.

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 varies between three and four hours after oral administration.

INDICATIONS

For the temporary relief of pain and discomfort associated with

▪ Headache	▪ Arthritis
▪ Migraine headache	▪ Toothache
▪ Tension headache	▪ Nneuralgia
▪ Period pain	▪ Cold & flu symptoms
▪ Back pain	▪ Dental procedures
▪ Muscle pain	▪ Sore throat
Reduces fever.	

CONTRAINDICATIONS

Known sensitivity to paracetamol, codeine or any of the other ingredients. Active alcoholism. Acute respiratory depression.

PRECAUTIONS

Panadeine 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.

Panadeine Clear should be used with caution if restricted salt intake is indicated.

Panadeine is for the relief of minor and temporary ailments and should be used strictly as directed. Prolonged use without medical supervision could be harmful.

Use in Pregnancy & Lactation
Category A - Drugs which 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.

Paracetamol is excreted in breast milk. Peak concentrations of 10 to 15 mcg/mL have been measured within 1 to 2 hours of a single 650 mg maternal dose. The half life of paracetamol in breast milk is 1.35 to 3.5 hours. Neither paracetamol or its metabolites were detected in the urine of breastfed infants following the maternal 650 mg dose.

Panadeine may be used during pregnancy on the advice of a doctor. However, it is recommended that non-drug therapies such as rest and massage are tried first.

Use in Children
Not recommended for children under 7 years of age.

INTERACTIONS
Anticoagulant dosage may require reduction if Panadeine 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, 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.

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 tranquillisers may enhance the potential respiratory depressant affects of codeine.

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

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.

DOSAGE AND ADMINISTRATION

Tablets - Adults and children over 12 years. 2 tablets (maximum 8 tablets / day). Children 7 to 12 years. ½ to 1 tablet (maximum 4 tablets / day). Take with water and repeat every three to four hours if necessary.

Caplets - Adults and children over 12 years. 2 Caplets (maximum 8 caplets /day). Children 7 to 12 years. ½ to 1 caplet (maximum 4 caplets / day). Take with water and repeat every three to four hours if necessary.

Rapid Soluble tablets - Adults and children over 12 years. 1 to 2 tablets (maximum 8 tablets /day). Children 7 to 12 years. ½ to 1 tablet (maximum 4 tablets / day). Panadeine Clear tablets should be dissolved in at least half a glass of water.

OVERDOSAGE

Accidental overdose is usually rare due to the high therapeutic index of the product.

Paracetamol overdose can result in severe liver damage and sometimes acute renal tubular necrosis.

Toxic symptoms of paracetamol overdose include vomiting, abdominal pain, hypotension, sweating, central stimulation with exhilaration and convulsions in children, drowsiness, respiratory depression, cyanosis and coma.

In adults, hepatoxicity may occur after ingestion of a single dose of paracetamol 10 to 15 g (20 to 30 tablets or 10 to 15 times the normal dose); 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

Prompt treatment is essential even when there are no obvious symptoms.

In cases of overdosage, methods of reducing absorption of ingested drug are important. Prompt administration of activated charcoal 50 g in 150 mL of water and 150 mL sorbitol 50% solution by mouth may reduce absorption. It is recommended that intravenous fluids such as Normal Saline be given concurrently. Gastric lavage is indicated if the patient is unwilling or unable to drink an activated charcoal/sorbitol mixture.

If the history suggests that paracetamol 15 g or more has been ingested, administer the following antidote:

Intravenous acetylcysteine 20%. Administer acetylcysteine immediately without waiting for positive urine test or plasma level results if 8 hours or less since overdose ingestion. Initial dose 150 mg/kg over 15 minutes, followed by continuous infusion of 50 mg/kg in glucose 5% 500 mL over four hours and 100 mg/kg in glucose 5% 1 L over 16 hours.

If more than 8 hours have elapsed since the overdosage was taken, the antidote may be less effective.

POISONS SCHEDULE
12's, 16's, 20's, 24's: S2 - PHARMACY ONLY
Other pack sizes: S3 - PHARMACIST ONLY MEDICINE except NSW: S2 - PHARMACY MEDICINE

STORAGE
Store below 30 degrees Celsius.

PRESENTATION
Tablets: Flat, round white 1.27cm tablet with bevelled edges. Front face marking "PANADEINE" with a break bar on the back face. Packs of 12, 24, 50 and 100.

Caplets: Blue film-coated capsule-shaped tablets, marked Panadeine with break-bar on the back face. Packs of 16, 24 and 48.

Rapid Soluble tablets (formerly CLEAR): Large white round flat 22 cm diameter, bevelled edge tablets, plain on both faces. Packs of 20.

SPONSOR
GlaxoSmithKline Consumer Healthcare
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GlaxoSmithKline Australia Pty Ltd
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TGA approved 29 July, 1997.
Modified 21 August, 1997.
Modified 20 May, 1998 to correct dosage as per approved packaging and descriptions.
Modified 1 October, 1998 to change tablet description.
Modified 30 June, 2000 to replace capsules with caplets and TGA approved 06/07/2000
Modified 4 October, 2001 to replace tablets with revised tablets and TGA approved 30/10/2001.
Modified 6 December, 2001 to include more restrictive wording to the *Pharmacokinetics* and *Interactions* sections.
Notification of change in sponsor name dated 13 November 2002.
Modified 14 January 2005 to include indications for 'Dental procedures' and 'Sore throat' and TGA approved 1 February 2005.