PRODUCT INFORMATION
Panadeine® EXTRA

COMPOSITION

Each caplet brand of capsule-shaped tablet contains:
- Paracetamol 500 mg
- Codeine phosphate 15 mg
- Maize Starch
- Purified Talc
- Pregelatinised Maize Starch
- Povidone
- Stearic Acid
- Potassium Sorbate
- Magnesium Stearate

MATERIAL OF ANIMAL ORIGIN
None

ACTIONS

Analgesic and antipyretic.
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 CNS. 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 (45-55%) or sulfate (20-30%). 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 sulphate conjugates. Less than 5% is excreted as unchanged paracetamol with 85-90% 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

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 (eg. backaches and muscular pain).
CONTRAINDICATIONS

Hypersensitivity to paracetamol or codeine or other ingredients (see composition).

PRECAUTIONS

Panadeine EXTRA 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 whilst taking this medication.

Use in Pregnancy
Category A

Use in Lactation
When Panadeine EXTRA is administered to a nursing mother, alternative arrangements should be made for feeding the infant.

Drug Interactions
Anticoagulant dosage may require reduction if Panadeine EXTRA medication is prolonged.

Paracetamol absorption is increased by drugs which increase gastric emptying, eg. metoclopramide, and decreased by drugs which decrease gastric emptying, eg. 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 anti-epileptic 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 effects of codeine.
ADVERSE REACTIONS

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. 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 caplets four times a day if required (maximum 8 caplets 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 10 to 15 g (30 tablets) of paracetamol; 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.

In case of overdosage, contact the Poisons Information Centre (13 11 26).

PRESENTATION

Panadeine EXTRA caplets
Capsule-shaped tablets (white, marked PAN 15): 12s and 24s (retail pack) and 6s (health professional sample pack).
POISON SCHEDULE

S3: Pharmacist Only Medicine

SPONSOR

GlaxoSmithKline Australia Pty Ltd
(t/a GlaxoSmithKline Consumer Healthcare)
82 Hughes Avenue
Ermington NSW 2115

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