Parapane

Paracetamol

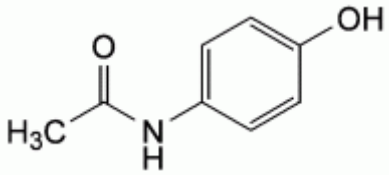
PRODUCT INFORMATION

NAME OF THE MEDICINE

Active ingredient: Paracetamol

Chemical name: N-(4-hydroxyphenyl)

Structural formula:



Molecular formula: 151.20

Molecular weight: $C_8H_9NO_2$

CAS Registry no.: 103-90-2

Description

Parapane is an analgesic and antipyretic agent. The active ingredient in Parapane capsule shaped tablets is 500 mg paracetamol. Parapane capsule shaped tablets also contain the following inactive ingredients: sodium metabisulfite, magnesium stearate and starch – pregelatinised maize. Parapane capsule shaped tablets do not contain any sugar, lactose or gluten.

Paracetamol is a white, odourless, crystalline powder. It is sparingly soluble in water; freely soluble in ethanol (96 %); very slightly soluble in chloroform and in ether.

Pharmacology

Paracetamol is a para-aminophenol derivative that exhibits analgesic and antipyretic activity. Its analgesic effect is thought to be due to inhibition of prostaglandin synthesis in the central nervous system and in the periphery and to a lesser extent, by blocking pain impulse generation in the periphery. The antipyretic effect is due to a central action on the hypothalamic heat regulating center to produce peripheral vasodilatation and subsequent heat loss.

Paracetamol does not possess anti-inflammatory activity. It is given by mouth for mild to moderate pain and fever.

Pharmacokinetics

After oral administration, paracetamol is absorbed rapidly and completely from the small intestine. This absorption process occurs by passive transport. Peak plasma levels occur within 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. An intermediate metabolite which may accumulate in overdosage is hepatotoxic and possibly nephrotoxic. 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. 85 to 90% of the administered dose is eliminated in the urine within 24 hours of ingestion. The elimination half-life varies from about one to three hours and may be prolonged in hepatic disease, the elderly and the neonate. Food intake delays paracetamol absorption

Indications

For the temporary relief of pain (and discomfort) associated with: headache, migraine headache, toothache, , muscular aches and pains, neuralgia, arthritis, rheumatics, menstruation/period pain, sore throat, osteoarthritis and symptoms of cold and flu. Reduces fever and/or the discomfort associated with fever.

Contraindications

Paracetamol is contraindicated in patients with active alcoholism or known hypersensitivity to the drug.

Precautions

Paracetamol should be administered with caution to patients with impaired renal or hepatic function, viral hepatitis, or taking other drugs that affect the liver (see **Interactions with other medicines***).*

In view of the increased risk of hepatotoxicity, the benefit should be weighed against the risk when administering paracetamol to patients with viral hepatitis or pre-existing hepatic disease. In such patients, hepatic function determinations may be required at periodic intervals during high dose or long-term therapy.

Paracetamol should also be administered with caution in patients with Gilbert's syndrome, as it has been reported that paracetamol is eliminated at a reduced rate in these patients.

Use in pregnancy (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 can cross the placenta, however no teratogenic effects have been observed in rats or mice after doses of up to 250 mg/kg.

A woman in the third trimester of pregnancy ingested paracetamol 22.5 g; early treatment with oral acetylcysteine resulted in a good outcome for both mother and foetus.

Use in lactation

Paracetamol is excreted in breast milk. The amount available for ingestion by the infant has been reported variously as less than 0.1% of a single 500 mg dose, and as 0.04 to 0.23% of a single 650 mg dose. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infant.

Use in the elderly

The elderly are more likely to have age related renal impairment; dose reduction may be required.

Interactions with other medicines

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.

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

Isoniazid may potentiate the hepatic toxicity of paracetamol.

Repeated high doses of paracetamol increase the anticoagulant response to coumarins. Anticoagulant dosage may require reduction if treatment with paracetamol is prolonged.

Paracetamol also may increase chloramphenicol concentrations.

Prolonged concurrent use of paracetamol and salicylates or NSAIDs may increase the risk of adverse renal effects.

Diflunisal may increase the plasma concentrations of paracetamol by 50%.

Adverse Events

Adverse effects of paracetamol are usually mild, although rare haematological reactions (agranulocytosis, anaemia, leucopenia, neutropenia, pancytopenia and thrombocytopenia) have been reported. Skin rashes and other allergic reactions occur occasionally. Renal failure and uraemia may occur with prolonged use of high doses in patients with severe renal failure.

Dosage and Administration

Take Parapane capsule shaped tablets with water or other fluid.

Adults and children 12 years and over. 500 mg to 1 g (1 to 2 capsule shaped tablets) every four to six hours as necessary. Maximum 8 capsule shaped tablets in 24hours.

Children 7 to 12 years. 250 to 500 mg (1 /2 to 1 capsule shaped tablet) every four to six hours. Maximum 4 capsule shaped tablets in 24 hours.

Overdosage

Acute overdosage with Paracetamol, whether accidental or deliberate, is relatively common and can be extremely serious because of the narrow margin between therapeutic and toxic doses.

Overdose can result in severe hepatic damage and sometimes acute renal tubular necrosis.

Symptoms

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

In adults, hepatotoxicity may occur after ingestion of a single dose of paracetamol of 10 to 15 g (20-30 capsule shaped tablets); a dose of 25 g (50 capsule shaped 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 hepatic 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.

If an overdose is taken or suspected, the Poisons Information Centre should be contacted immediately for advice (call 131 126), or the patient should go to a hospital straight away, even if they feel well, because of the risk of delayed, serious liver damage.

In cases of overdosage, methods of reducing the absorption of ingested drug are important. Administration of activated charcoal 50 g in 150 mL of water and 150 mL sorbitol 50% solution by mouth may reduce absorption of the medicine if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected. It is recommended that intravenous fluids (e.g. 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 eight 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 eight hours have elapsed since the overdosage was taken, the antidote may be less effective.

Presentation and Storage Conditions

Parapane White, capsule shaped tablet with break line on one side.
Available in pack sizes of 8's*, 10's*, 12's*, 16's*, 20's*, 24's*, 30's*, 32's*, 48's*, 50's*, 96's* and 100's.

* Currently not marketed in Australia.

Store below 30^0C.

Name and Address of the Sponsor

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Poison Schedule of the Medicine

Unscheduled	8's, 10's, 12's, 16's, 20's, 24's
S2 (Pharmacy Medicine)	30's, 32's, 48's, 50's, 96's, 100's

Date of First Inclusion on the Australian Register of Therapeutic Goods (the ARTG)

29/09/2008

Date of Most Recent Amendment

06/06/2013