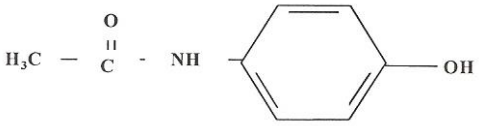
PANADOL® CAPLETS / TABLETS (OPTIZORB® formulation)

PRODUCT INFORMATION

NAME OF THE MEDICINE

Active ingredients	Chemical structure	CAS Registry Number
Paracetamol		103-90-2

DESCRIPTION

Paracetamol is a white, crystalline powder with a slightly bitter taste. It is sparingly soluble in water, freely soluble in alcohol and very slightly soluble in dichloromethane.

Active ingredient: Paracetamol 500mg

Excipients: Starch - pregelatinised maize, calcium carbonate, alginic acid, crospovidone, povidone, magnesium stearate, silica - colloidal anhydrous, parahydroxybenzoates (sodium methyl, sodium ethyl, sodium propyl), OPADRY complete film coating system YS-1-7003 WHITE, carnauba wax, water - purified.

Contains no sugar, lactose or gluten.

PHARMACOLOGY

Pharmacodynamics

Paracetamol is para-aminophenol derivative that exhibits analgesic and anti-pyretic activity.. It does not possess anti-inflammatory activity. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system. The lack of peripheral prostaglandin inhibition confers important pharmacological properties such as the maintenance of the protective prostaglandins within the gastrointestinal tract. Paracetamol is therefore particularly suitable for patients with a history of acid peptic disease, or on concomitant medication, where peripheral prostaglandin

inhibition would be undesirable (such as, for example, those with a history of gastrointestinal bleeding or in the elderly).

Pharmacokinetics

Absorption
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral administration. Food intake delays paracetamol absorption.

Distribution
Paracetamol is distributed into most body tissues. Plasma protein binding is negligible at usual therapeutic doses but increases with increasing doses.
Metabolism
Paracetamol is metabolised extensively in the liver and excreted in the urine mainly as inactive glucuronide and sulfate conjugates.. The metabolites of paracetamol include a minor hydroxylated intermediate which has hepatotoxic activity. This intermediate metabolite is detoxified by conjugation with glutathione., However, it can accumulate following paracetamol overdosage (more than 150mg/kg or 10g total paracetamol ingested) and, if left untreated, can cause irreversible liver damage.

Paracetamol is metabolised differently by, infants and children compared to adults, the sulfate conjugate being predominant.

Excretion
Paracetamol is excreted in the urine mainly as the inactive glucuronide and sulphate conjugates. Less than 5% is excreted unchanged. The elimination half-life varies from about one to three hours. Approximately 85% of a dose of paracetamol is excreted in urine as free and conjugated paracetamol within 24 hours after ingestion.

PANADOL CAPLETS and TABLETS (with the OPTIZORB formulation) contain a disintegrant system which optimises tablet dissolution compared to standard PANADOL tablets.
In a human scintigraphy study, the mean time to onset of disintegration for PANADOL CAPLETS and TABLETS (with the OPTIZORB formulation) was 6.4 minutes.

Human pharmacokinetic data demonstrate that early absorption of paracetamol (fraction of dose over the first 60 minutes) is 32% greater from PANADOL® CAPLETS® and TABLETS (with the OPTIZORB formulation) compared to standard PANADOL tablets ($p<0.0001$). There is also less between-subject and less within-subject variability ($p<0.0001$) in early absorption of paracetamol from PANADOL CAPLETS and TABLETS (with the OPTIZORB formulation) compared to standard PANADOL tablets.

Maximum plasma concentration of paracetamol is reached faster for PANADOL CAPLETS and TABLETS (with the OPTIZORB formulation) compared to standard PANADOL tablets in fasted and fed states ($p < 0.01$).

Total extent of absorption of paracetamol from PANADOL CAPLETS and TABLETS (with the OPTIZORB formulation) is equivalent to that from standard PANADOL tablets.

INDICATIONS

For the fast effective relief of pain and discomfort associated with headache, tension headache, muscular aches, toothache, migraine headache, cold & flu symptoms, arthritis/osteoarthritis, backache and period pain. Helps reduce fever.

CONTRAINDICATIONS

These products are contraindicated in patients with a previous history of hypersensitivity to paracetamol or to any of the excipients.

PRECAUTIONS

Contains paracetamol. Do not use with any other paracetamol- containing products. The concomitant use with other products containing paracetamol may lead to an overdose.

Paracetamol overdose may cause liver failure which can lead to liver transplant or death.

- Panadol should be administered with caution to patients with: Impaired liver function: Underlying liver disease increases the risk of paracetamol-related liver damage
- Impaired kidney function: Administration of paracetamol to patients with moderate to severe renal impairment may result in accumulation of paracetamol conjugates.

Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.

Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index or are chronic heavy users of alcohol.

In patients with glutathione depleted states such as sepsis, the use of paracetamol may increase the risk of metabolic acidosis.

If symptoms persist, medical advice must be sought.

Keep out of sight and reach of children.

Use in pregnancy

Category A
Paracetamol has 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.

Use in Lactation
Paracetamol is excreted in small amounts (<0.2%) in breast milk. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infants.

Use in children
Not recommended for children below age 7, except on medical advice.

Effects on ability to drive and use machinery
Panadol Caplets have no significant effect on the ability to drive or use machines.

INTERACTIONS WITH OTHER MEDICINES
The following interactions with paracetamol have been noted:

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding. Occasional doses have no significant effect. Anticoagulant dosage may require reduction if paracetamol and anticoaguants are taken for a prolonged period of time..

Paracetamol absorption is increased by substances that increase gastric emptying, e.g. metoclopramide.

Paracetamol absorption is decreased by substances that decrease gastric emptying, e.g. propantheline, antidepressants with anticholinergic properties, and narcotic analgesics.

Paracetamol may increase chloramphenicol concentrations.

The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes such as alcohol and anticonvulsant agents.

Paracetamol excretion may be affected and plasma concentrations altered when given with probenecid.

Colestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol.

ADVERSE EFFECTS

Adverse events from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by System Organ Class and frequency. The following convention has been utilised for the classification of undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from available data).

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

Body System	**Undesirable Effect**	**Frequency**
Blood and lymphatic system disorders	Thrombocytopenia	Very rare
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angioedema and Stevens Johnson syndrome	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm, especially in patients sensitive to aspirin and other NSAIDs	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare

DOSAGE AND ADMINISTRATION

PANADOL® CAPLETS® / TABLETS (with the OPTIZORB formulation) are to be administered orally, with or without food.

Adults and children over 12 years: 1 to 2 tablets every four to six hours with water.
Maximum of 8 tablets in 24 hours. Maximum daily dose: 4000 mg.

Children 7 to 12 years: ½ to 1 tablet every four to six hours with water.
Maximum of 4 tablets in 24 hours.

For Adults: Do not use for more than a few days at a time, except on medical advice.
For children ages 7-17: Do not use for more than 48 hours, except on medical advice.

Do not exceed the stated dose.

The lowest dose necessary to achieve efficacy should be used.

PANADOL CAPLETS / TABLETS (with the OPTIZORB formulation) should not be used with other paracetamol containing products.

OVERDOSAGE

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

Treatment
Immediate medical management is required in the event of an overdose, even if the symptoms of overdose are not present.

Paracetamol overdose may cause liver failure which can lead to liver transplant or death.

Administration of N-acetylcysteine may be required.

Activated charcoal may reduce absorption of paracetamol if given within one hour after oral 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.

PRESENTATION AND STORAGE CONDITIONS

PANADOL® CAPLETS (with the OPTIZORB formulation) are white to off-white, capsule shaped, film-coated tablets with “P” in a circle on one side and a breakline on the other.

Packs of 12, 20, 48 or 96 Caplets.

PANADOL® TABLETS (with the OPTIZORB formulation) are white to off-white, film-coated round tablets embossed with the circled “P” on one side and a breakline on the other.

Packs of 12, 20, 50 or 100 Tablets.

Store below 30ºC. Keep out of reach of children.

NAME AND ADDRESS OF THE SPONSOR

GlaxoSmithKline Consumer Healthcare
82 Hughes Avenue
Ermington NSW 2115

POISON SCHEDULE OF THE MEDICINE

Unscheduled in packs of 12, or 20 Caplets.

Schedule 2 (Pharmacy Medicine) in packs of 48 or 96 Caplets.
Schedule 2 (Pharmacy Medicine) in packs of 50 or 100 Tablets

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

PANADOL Caplets with OPTIZORB	AUST R 160821	3 April 2009
PANADOL Tablets with OPTIZORB	AUST R 186245	6 July 2011

DATE OF MOST RECENT AMENDMENT

09 NOV 2015

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