

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

PANADOL® Tablets with Optizorb® Formulation, Paracetamol 500mg, tablet
PANADOL® Caplets with Optizorb® Formulation, Paracetamol 500mg, tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:

Paracetamol 500 mg/tablet (round or capsule-shaped)

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

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.

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 break line on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic 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.

4.2 Dose and method of administration

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

Adults and children over 12 years:

1 to 2 tablets / caplets every four to six hours with water.

Maximum of 8 tablets / caplets in 24 hours. Maximum daily dose: 4000 mg.

Children 7 to 12 years:

½ to 1 tablet / caplet every four to six hours with water.

Maximum of 4 tablets / caplets 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 for the shortest duration of treatment.

NEW ZEALAND DATA SHEET

Should not be used with other paracetamol-containing products.

Minimum dosing interval: 4 hours.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

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 may require liver transplant or lead to death.

Paracetamol should be used with caution in 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. The restrictions related to the use of paracetamol in patients with liver or kidney impairment are primarily a consequence of the paracetamol content of the drug.

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, are chronic heavy users of alcohol or have sepsis.

In patients with glutathione depleted states 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 children - Not recommended for children below age 7, except on medical advice.

4.5 Interactions with other medicines and other forms of interaction

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.

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.

NEW ZEALAND DATA SHEET

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.

4.6 Fertility, pregnancy and lactation

Use in pregnancy

As with the use of any medicine during pregnancy, pregnant women should seek medical advice before taking paracetamol.

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 breast milk but not in a clinically significant amount at recommended dosages. Available published data do not contraindicate breast-feeding.

4.7 Effects on ability to drive and use machines

Panadol Tablets / Caplets (with Optizorb formulation) have no significant effect on the ability to drive or use machines.

4.8 Undesirable 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 ($\geq 1/10$), common ($\geq 1/100$, $< 1/10$), uncommon ($\geq 1/1,000$, $< 1/100$), rare ($\geq 1/10,000$, $< 1/1,000$), 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, among others, skin rashes, angioedema, Stevens Johnson syndrome and Toxic Epidermal Necrolysis.	Very rare

NEW ZEALAND DATA SHEET

Respiratory, thoracic and mediastinal disorders	Bronchospasm, especially in patients sensitive to aspirin and other NSAIDs	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Experience following overdose with paracetamol indicates that the clinical signs of liver injury occur usually after 24 to 48 hours and have peaked after 4 to 6 days.

Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity.

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

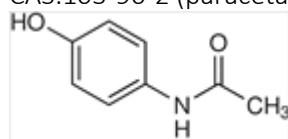
Administration of N-acetylcysteine may be required.

If an overdose is taken or suspected, the National Poisons Centre should be contacted immediately for advice (0800 764 766), or the patient should go to the hospital straight away, even if they feel well, because of the risk of delayed, serious liver damage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

CAS:103-90-2 (paracetamol)



Paracetamol MW 151.17

ATC code Paracetamol, N02BE01'

Paracetamol is an antipyretic and analgesic. 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).

NEW ZEALAND DATA SHEET

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral administration. Paracetamol is distributed into most body tissues. Plasma protein binding is negligible at usual therapeutic doses but increases with increasing doses. The elimination half-life varies from about 1 to 3 hours.

Paracetamol is metabolised extensively in the liver and excreted in the urine mainly as inactive glucuronide and sulphate conjugates. Less than 5% is excreted unchanged. The mean plasma half-life is about 2.3 hours. 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 over dosage (more than 150mg/kg or 10g total paracetamol ingested) and if left untreated can cause irreversible liver damage.

Paracetamol is metabolised differently by premature infants, newborns, infants and young children compared to adults, the sulphate conjugate being predominant.

PANADOL TABLETS / CAPLETS (with the OPTIZORB™ formulation) contain a disintegrant system which optimises tablet dissolution compared to standard immediate release PANADOL tablets.

Human scintigraphy data demonstrate that paracetamol tablets with OPTIZORB generally start to disintegrate by 5 minutes post dose. Human pharmacokinetic data demonstrate that paracetamol can generally be detected in plasma by 10 minutes. In a human scintigraphy study, the mean time to onset of disintegration for PANADOL CAPLETS (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® (with the OPTIZORB™ formulation) compared to standard immediate release 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 (with the OPTIZORB formulation) compared to standard immediate release PANADOL tablets.

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

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch - pregelatinised maize, calcium carbonate, alginic acid, croscopovidone, 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.

It contains no sugar, lactose or gluten.

6.2 Incompatibilities

No known incompatibilities

NEW ZEALAND DATA SHEET

6.3 Shelf life

Shelf life of the product is 3 years from the date of manufacture.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

PANADOL TABLETS (with the OPTIZORB formulation) - Blister packs of 12, 20, 50, 100 tablets

PANADOL CAPLETS (with the OPTIZORB formulation) - Blister packs of 12, 20, 48, 96 caplets.

6.6 Special precautions for disposal and other handling

No special requirements

7. MEDICINE CLASSIFICATION

General Sale Medicine in packs of 12, 20 tablets / caplets.

Pharmacy Only medicine: packs of 48, 96 caplets; 50 or 100 tablets

8. SPONSOR

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9. DATE OF FIRST APPROVAL

PANADOL TABLETS (with the OPTIZORB formulation) 12/01/12

PANADOL CAPLETS (with the OPTIZORB formulation) 29/04/10

10. DATE OF REVISION OF THE TEXT

20 August 2017

Summary table of changes

<u>Section changes</u>	<u>Summary of new changes</u>
All	Transferred to new data sheet template
4.2	Addition of advice to: Use for shortest duration of treatment
4.4	Additional warnings and precautions added
4.6	Addition of advice to seek medical advice before using if pregnant.
4.9	Addition of the expected timing of clinical signs of liver injury and that acute pancreatitis has been observed.

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