

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

PANADOL[®] Rapid Caplets, Paracetamol 500mg, film coated tablet
PANADOL[®] Rapid Soluble Tablets, Paracetamol 500 mg, soluble tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Paracetamol (BP) 500 mg/caplet or tablet

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Panadol Rapid caplets

Film-coated tablet.

White to off-white capsule shaped film coated tablets with flat edges. One face of the tablet is debossed with the letter "P" and "--" on the other side.

Panadol Rapid Soluble tablets

Soluble tablet.

Large white round flat, 7/8" diameter, bevelled-edge tablet, plain on both faces.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For fast relief of acute pain.

Fast effective temporary relief of pain and discomfort associated with headache/tension headache, migraine headache, toothache, muscular aches, cold and flu symptoms, sore throat and period pain. Helps reduce fever.

4.2 Dose and method of administration

PANADOL Rapid caplets

Adults and children aged 12 years and over: 2 caplets, orally, every four to six hours with water as required (maximum of 8 caplets in 24 hours). Maximum daily dose: 4000 mg.

Children under 12 years: Not recommended for children under the age of 12 years.

PANADOL Rapid Soluble tablets

Adults and children aged 12 years and over: 2 tablets dissolved in a glass of water at room temperature every four to six hours as required (maximum of 8 tablets in 24 hours). Maximum daily dose: 4000 mg.

Children under 12 years: Not recommended for children under the age of 12 years.

General Dosage Instructions:

Adults: Do not use for more than a few days at a time without medical advice.

Children 12-17 years: Do not use for more than 48 hours except on medical advice.

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- Should not be used with other paracetamol-containing products.
- Minimum dosing interval: 4 hours.
- The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.
- If symptoms persist, medical advice must be sought.
- Do not exceed the stated dose.
- Keep out of sight and reach of children.

4.3 Contraindications

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

The maximum recommended daily dose of 8 PANADOL Rapid caplets contains 1.4 g (61 mmol) sodium which should be taken into account by those on a low sodium diet.

Each PANADOL Rapid Soluble tablet contains 425.5 mg (18.5 mmol) sodium which should be taken into account by those on a low sodium diet.

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Each PANADOL Rapid Soluble tablet contains 50 mg sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

PANADOL Rapid Soluble tablets contain **PHENYLALANINE** and should not to be used by **PHENYLKETONURICS**. Phenylalanine is present in the ingredient aspartame.

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. Anticoagulant dosage may require reduction if PANADOL medication is prolonged.

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

Paracetamol absorption is decreased by substances that decrease gastric emptying, eg 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 drugs.

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

Colestyramine reduces the absorption of paracetamol if given within one 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 small amounts (<0.2%) in breast milk but not in a clinically significant amount at recommended dosages. Available published data do not contraindicate breast-feeding. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infants.

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4.7 Effects on ability to drive and use machines

PANADOL Rapid caplets and PANADOL Rapid Soluble tablets are unlikely to cause an effect on the ability to drive or use machinery.

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 skin rashes, among others, angioedema and Stevens Johnson syndrome and Toxic Epidermal Necrolysis	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm 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.

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

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 may require liver transplant or lead to death. Acute pancreatitis has been observed with hepatic dysfunction.

Administration of N-acetylcysteine may be required.

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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.

Symptoms and Management of Excessive Sodium bicarbonate

In the event of overdose, clinicians should be aware of the sodium and bicarbonate content in the PANADOL Rapid and PANADOL Rapid Soluble formulation.

Each PANADOL Rapid caplet contains about 7.65 mmol of sodium and 7.5 mmol of bicarbonate.

Each PANADOL Rapid Soluble effervescent tablet contains about 18.5 mmol of sodium and 16 mmol of bicarbonate.

High doses of sodium bicarbonate may result in gastrointestinal symptoms including stomach cramps, belching, flatulence, abdominal pain, nausea, bloating and abdominal distension.

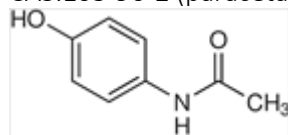
In addition, excessive sodium may cause hypernatraemia; electrolytes should be monitored and patients managed accordingly.

Excessive bicarbonate may lead to hypokalaemia and metabolic alkalosis, especially in patients with impaired renal function. Treatment consists mainly of appropriate correction of fluid and electrolyte balance.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

CAS:103-90-2 (paracetamol)



Paracetamol MW 151.17

ATC code Paracetamol, N02BE01'

Paracetamol is a para-aminophenol derivative that exhibits analgesic and anti-pyretic activity. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system. It is given by mouth for mild to moderate pain and fever.

5.2 Pharmacokinetic properties

Absorption

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Food intake delays paracetamol absorption.

PANADOL Rapid is a tablet formulation which contains sodium bicarbonate and is intended to increase the rate of gastric emptying (by forming an isosmotic solution of sodium bicarbonate in the stomach) thereby allowing more rapid absorption of paracetamol. Paracetamol is rapidly absorbed from the post-gastric mucosa but not from the stomach.

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A pivotal bioequivalence study (Study A1030019), conducted in healthy volunteers, demonstrated that PANADOL Rapid was bioequivalent to standard PANADOL tablets for $AUC_{(0-inf)}$ under both fasting and fed conditions following the administration of a dose of 1000 mg (2x500mg tablets). This indicates that at a dose of 2x500 mg tablets, the extent of paracetamol absorption from PANADOL Rapid was equivalent to that of standard PANADOL. T_{max} was statistically significantly earlier with PANADOL Rapid in both the fasting and fed states. The C_{max}/T_{max} ratio which is a measure of the rate of absorption was also statistically significantly higher for Panadol Rapid in both the fasting and fed states. This indicates that at a dose of 2x500 mg tablets, the rate of paracetamol absorption from PANADOL Rapid was faster than standard PANADOL. A summary of the pharmacokinetic parameters from the bioequivalence Study A1030019 is included in Table 1.

Table 1. Study A1030019: Pharmacokinetic parameters for 1000mg paracetamol after 2x500mg tablets PANADOL and 2x500mg tablets PANADOL Rapid fasting and fed orally.

Parameter	Panadol n=27 arithmetic mean (SD)	Panadol Rapid n=27 arithmetic mean (SD)
Fasting		
$AUC_{(0-inf)}$ ($\mu\text{g}\cdot\text{min}/\text{mL}$)	3287 (782)	3348 (681)
Terminal $T_{1/2}$ (min)	160 (17)	151 (17)
C_{max} ($\mu\text{g}/\text{mL}$)	18 (10)	24 (8)
T_{max} (min)	53 (28)	33 (18)
C_{max}/T_{max}	0.61 (0.78)	0.93 (0.56)
Fed		
$AUC_{(0-inf)}$ ($\mu\text{g}\cdot\text{min}/\text{mL}$)	3115 (692)	3284 (800)
Terminal $T_{1/2}$ (min)	169 (22)	175 (22)
C_{max} ($\mu\text{g}/\text{mL}$)	11 (3)	13 (4)
T_{max} (min)	126 (47)	59 (35)
C_{max}/T_{max}	0.11 (0.08)	0.34 (0.33)

A bioequivalence study (Study A1030110), conducted in healthy volunteers, demonstrated that PANADOL Rapid is bioequivalent to PANADOL Rapid Soluble tablets for $AUC_{(0-inf)}$ and C_{max} under both fasting and fed conditions following the administration of a dose of 1000 mg (2x500 mg tablets). This indicates that at a dose of 2x500 mg tablets, the rate and extent of paracetamol absorption from PANADOL Rapid was equivalent to that of PANADOL Rapid Soluble.

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Distribution

Paracetamol is distributed into most body tissues. Binding to the plasma proteins is minimal at therapeutic concentrations but increases with increasing doses.

Metabolism

Paracetamol is metabolised in the liver and excreted in the urine mainly as glucuronide and sulphate 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 overdose (more than 200 mg/kg or 10 g total paracetamol ingested) and, if left untreated, can cause irreversible liver damage.

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

Excretion

Paracetamol is excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unmodified paracetamol with 85% to 90% of the administered dose eliminated in the urine within 24 hours of ingestion. The elimination half-life varies from one to three hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Panadol Rapid

Sodium bicarbonate, Cellulose – microcrystalline, Starch – pregelatinised maize, Sodium Starch Glycolate, Starch – maize, Water – purified, Magnesium stearate, Hypromellose, Colloidal Anhydrous Silica, Povidone, Titanium dioxide, Polydextrose, Glycerol triacetate, Carnauba wax, Macrogol 8000.

Panadol Rapid Soluble

Sodium bicarbonate, Citric acid, Sodium carbonate, Sorbitol, Lemon flavour, aspartame, Dimeticone, Povidone, Saccharin sodium, Sugar flavour, Sodium lauryl sulfate

6.2 Incompatibilities

No known incompatibilities

6.3 Shelf life

Panadol Rapid

36 months from date of manufacture.

Panadol Rapid Soluble

36 months from date of manufacture.

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6.4 Special precautions for storage

Panadol Rapid

Store below 30°C.

Panadol Rapid Soluble

Store below 30°C.

6.5 Nature and contents of container

Panadol Rapid

Blister packs of 10, 20, 40 and 80 caplets

Panadol Rapid Soluble

Blister packs of 12 and 20 tablets

6.6 Special precautions for disposal and other handling

No special requirements.

7. MEDICINE SCHEDULE

Packs of 20 caplets or tablets or less - General sale

Packs of more than 20 caplets or tablets - Pharmacy only

8. SPONSOR

GlaxoSmithKline Consumer Healthcare New Zealand Ltd

Private Bag 106600

Downtown

Auckland 1143

Tel 09 367 2900

9. DATE OF FIRST APPROVAL

Panadol Rapid

15/08/2002

Panadol Rapid Soluble

25/02/1991

10. DATE OF REVISION OF TEXT

31 March 2020

Summary table of changes

<u>Section changes</u>	<u>Summary of new changes</u>
3.0	Update product description of Panadol Rapid caplets
4.4	Update quantity of sodium for 8 PANADOL Rapid caplets
4.9	Update quantity of sodium for PANADOL Rapid caplets

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6.1	Update list of excipients for PANADOL Rapid
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