AUSTRALIAN PRODUCT INFORMATION
PANADOL RAPID (PARACETAMOL) CAPLETS

1 NAME OF THE MEDICINE

Paracetamol

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Paracetamol 500 mg/tablet

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

For the full list of excipients, see section 6.1 List of Excipients.

3 PHARMACEUTICAL FORM

PANADOL RAPID CAPLETS
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.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For fast relief of acute pain. Reduces fever.

4.2 DOSE AND METHOD OF ADMINISTRATION

PANADOL Rapid caplets

Adults and children aged 12 years and over: 2 caplets 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.

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.

- Should not be used with other paracetamol-containing products.
- Minimum dosing interval: 4 hours.
- Do not exceed the stated dose.
- 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 to any of the excipients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Identified 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 may require liver transplant or lead to death.

If symptoms persist, medical advice must be sought.

Keep out of sight and reach of children.

High Anion Gap Metabolic Acidosis

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or patients with malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Use in hepatic impairment

Paracetamol should be used with caution in patients with impaired liver function: Underlying liver disease increases the risk of paracetamol-related liver damage.

Patients who have been diagnosed with liver 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, 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.

Use in renal impairment

Paracetamol should be used with caution in patients with 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 kidney impairment must seek medical advice before taking this medication.

Use in the elderly

No data available.

Paediatric use

PANADOL Rapid caplets are not recommended for children under 12 years of age.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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 anticoagulants 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.

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

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy – 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.

As with the use of any medicine during pregnancy, pregnant women should seek medical advice before taking paracetamol. The lowest effective dose and shortest duration of treatment should be considered.

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. Available published data do not contraindicate breastfeeding.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

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 doses 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.

Table 1: 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
Respiratory, thoracic and mediastinal disorders	Bronchospasm, especially in patients sensitive to aspirin and other NSAIDS	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare
Metabolism and nutrition disorders	High anion gap metabolic acidosis: Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.	Unknown (cannot be estimated from the available data)

4.9 OVERDOSE

If an overdose is taken or suspected, contact the Poisons Information Centre immediately for advice (131 126), 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.

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

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.

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.

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

High doses of sodium bicarbonate may result in gastrointestinal symptoms including stomach cramps, belching, flatulence, abdominal pain, 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

Mechanism of action

Paracetamol is a 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. It is given by mouth for mild to moderate pain and to reduce fever.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract with peak plasma concentration occurring about 10 to 60 minutes after oral administration. 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.

A pivotal bioequivalence study (Study A1030019), conducted in healthy volunteers, demonstrated that PANADOL Rapid was bioequivalent to standard PANADOL tablets for $AUC_{(0\text{-}inf)}$ 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 2.

Table 2. 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		
$AUC_{(0\text{-}inf)}$ (µg.min/mL)	3287 (782)	3348 (681)

Terminal $T_{½}$ (min)	160 (17)	151 (17)
C_{max} (µg/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		
$AUC_{(0\text{-}inf)}$ (µg.min/mL)	3115 (692)	3284 (800)
Terminal $T_{½}$ (min)	169 (22)	175 (22)
C_{max} (µg/mL)	11 (3)	13 (4)
T_{max} (min)	126 (47)	59 (35)
C_{max}/ T_{max}	0.11 (0.08)	0.34 (0.33)

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 extensively in the liver and excreted in the urine mainly as inactive 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 overdosage (more than 150 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 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.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

PANADOL RAPID TABLETS

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.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

PANADOL RAPID CAPLETS
Packs of 12, 16, 20, 32, 40, 48 and 80 caplets. 'Handipak' of 8 and 10 caplets.

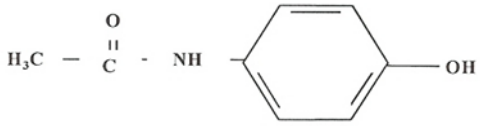
Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



CAS number

103-90-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled in packs of 16 caplets or less.

Schedule 2 (Pharmacy Medicine) in packs of more than 16 caplets, but less than 50 caplets.

Schedule 3 (Pharmacist Only Medicine) in packs of more than 50 caplets.

8 SPONSOR

Haleon Australia Pty Ltd
Level 48, 8 Parramatta Square,
10 Darcy Street, Parramatta NSW
2150

FREECALL Australia: 1800 028 533
Website: www.haleon.com

9 DATE OF FIRST APPROVAL

PANADOL RAPID TABLETS
(AUST R 332528) 26 March 2020

10 DATE OF REVISION

10 July 2025

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.4 4.5 4.8	Addition of information related to high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis