1 NAME OF THE MEDICINE
Paracetamol

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Paracetamol 500 mg/tablet

Excipients:

PANADOL RAPID CAPLETS
The maximum recommended daily dose of 8 caplets contains 1.4 g (60 mmol) of sodium, which should be taken into account by those on a low sodium diet.

PANADOL RAPID SOLUBLE TABLETS
Each PANADOL Rapid Soluble tablet contains:

- 425.5 mg (18.5 mmol) of sodium, which should be taken into account by those on a low sodium diet.
- 50 mg of sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
- aspartame, which is a source of PHENYLALANINE and so should not be used in patients with PHENYLKETONURIA.

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

3 PHARMACEUTICAL FORM

PANADOL RAPID CAPLETS
White, film-coated capsule-shaped tablets with flat edges. One face of the tablet is debossed with the letter “P”.

PANADOL RAPID SOLUBLE TABLETS
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. 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.

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.

- 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.
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 and PANADOL Rapid Soluble tablets 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.

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

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

<table>
<thead>
<tr>
<th>Body System</th>
<th>Undesirable Effect</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Thrombocytopenia</td>
<td>Very rare</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Anaphylaxis&lt;br&gt;Cutaneous hypersensitivity reactions including, among others, skin rashes, angioedema, Stevens Johnson syndrome and Toxic Epidermal Necrolysis.</td>
<td>Very rare</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Bronchospasm, especially in patients sensitive to aspirin and other NSAIDS</td>
<td>Very rare</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>Hepatic dysfunction</td>
<td>Very rare</td>
</tr>
</tbody>
</table>

### 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 and PANADOL Rapid Soluble formulation.

Each PANADOL Rapid caplet contains about 7.5 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, 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$_{0-ce}$ 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.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Panadol n=27 arithmetic mean (SD)</th>
<th>Panadol Rapid n=27 arithmetic mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC(_{(0-\infty)}) (μg.min/mL)</td>
<td>3287 (782)</td>
<td>3348 (681)</td>
</tr>
<tr>
<td>Terminal T(_{1/2}) (min)</td>
<td>160 (17)</td>
<td>151 (17)</td>
</tr>
<tr>
<td>C(_{max}) (μg/mL)</td>
<td>18 (10)</td>
<td>24 (8)</td>
</tr>
<tr>
<td>T(_{max}) (min)</td>
<td>53 (28)</td>
<td>33 (18)</td>
</tr>
<tr>
<td>C(<em>{max})/T(</em>{max})</td>
<td>0.61 (0.78)</td>
<td>0.93 (0.56)</td>
</tr>
<tr>
<td><strong>Fed</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC(_{(0-\infty)}) (μg.min/mL)</td>
<td>3115 (692)</td>
<td>3284 (800)</td>
</tr>
<tr>
<td>Terminal T(_{1/2}) (min)</td>
<td>169 (22)</td>
<td>175 (22)</td>
</tr>
<tr>
<td>C(_{max}) (μg/mL)</td>
<td>11 (3)</td>
<td>13 (4)</td>
</tr>
<tr>
<td>T(_{max}) (min)</td>
<td>126 (47)</td>
<td>59 (35)</td>
</tr>
<tr>
<td>C(<em>{max})/T(</em>{max})</td>
<td>0.11 (0.08)</td>
<td>0.34 (0.33)</td>
</tr>
</tbody>
</table>

A bioequivalence study (Study A1030110), conducted in healthy volunteers, demonstrated that PANADOL Rapid is bioequivalent to PANADOL Rapid Soluble tablets for AUC\(_{(0-\infty)}\) 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.

**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 CAPLETS**


**PANADOL RAPID SOLUBLE tablets**


### 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

**PANADOL RAPID CAPLETS**

**PANADOL RAPID SOLUBLE TABLETS**

Store below 30°C.
6.5 **NATURE AND CONTENTS OF CONTAINER**

PANADOL RAPID CAPLETS
Packs of 20 and 40 caplets. ‘Handipak’ of 10 caplets.

PANADOL RAPID SOLUBLE TABLETS
Packs of 4 and 20 tablets.

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

\[
\text{Chemical structure}
\]

**CAS number**
103-90-2

7 **MEDICINE SCHEDULE (POISONS STANDARD)**

Unscheduled in packs of 20 caplets/ tablets or less.

Schedule 2 (Pharmacy Medicine) in packs of more than 20 caplets/tablets.

8 **SPONSOR**

GlaxoSmithKline Consumer Healthcare Australia
82 Hughes Avenue
Ermington
NSW 2115

Telephone: 02 9684 0888
Website: [www.gsk.com.au](http://www.gsk.com.au)

9 **DATE OF FIRST APPROVAL**

PANADOL RAPID CAPLETS
(AUST R 78692) 24 May 2001

PANADOL RAPID SOLUBLE TABLETS
(AUST R 15509) 10 September 1991
## 10 DATE OF REVISION

9 April 2018

### SUMMARY TABLE OF CHANGES

<table>
<thead>
<tr>
<th>Section Changed</th>
<th>Summary of new information</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Reformatted Product Information to new form.</td>
</tr>
<tr>
<td>4.2</td>
<td>Addition of minimum dosing interval and use for shortest duration of treatment.</td>
</tr>
<tr>
<td>4.6</td>
<td>The following statements have been added: 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.</td>
</tr>
</tbody>
</table>

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