

# PANADOL RAPID CAPLETS

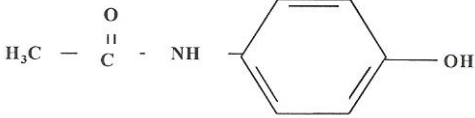
## PANADOL RAPID SOLUBLE TABLETS

### PRODUCT INFORMATION

#### NAME OF THE MEDICINE

Active ingredient: Paracetamol

Chemical structure:

Active ingredients	Chemical structure	CAS Registry Number
Paracetamol	 <chem>CC(=O)Nc1ccc(O)cc1</chem>	103-90-2

#### DESCRIPTION

##### PANADOL Rapid Caplets

Active ingredient: Paracetamol 500 mg/caplet (capsule-shaped tablet)

Excipients: Sodium bicarbonate, Cellulose – microcrystalline, Starch – pregelatinised maize, Starch – maize, Water – purified, Hypromellose, Magnesium stearate, Titanium dioxide, Polydextrose, Povidone, Calcium phosphate, Glycerol triacetate, Potassium sorbate, Macrogol 8000, Carnauba wax

##### PANADOL Rapid Soluble Tablets

Active ingredient: Paracetamol 500 mg/tablet

Excipients: Sodium bicarbonate, Citric acid – anhydrous, Sodium carbonate anhydrous, Sorbitol, Drydex Nature Identical Lemon Flavour 16-8320, Imitation Lemon Flavour 610406E, Imitation candied sugar flavour 650122U, Aspartame, Dimethicone 200, Povidone, Saccharin sodium, Permaseal Lemon Powder Flavour 84260-51, Sodium lauryl sulphate

## PHARMACOLOGY

### Pharmacodynamics

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.

### Pharmacokinetics

#### 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  $AUC_{(0-inf)}$  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)
<b>Fasting</b>		
$AUC_{(0-inf)}$ ( $\mu\text{g}\cdot\text{min}/\text{mL}$ )	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)
<b>Fed</b>		
AUC <sub>(0-inf)</sub> ( $\mu\text{g}\cdot\text{min}/\text{mL}$ )	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<sub>(0-inf)</sub> 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 overdose (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.

## INDICATIONS

For fast relief of acute pain. Reduces fever.

## CONTRAINDICATIONS

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

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.

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.

The maximum recommended daily dose of 8 PANADOL Rapid caplets contains 1.4 g (60 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.

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 aspartame, which is a source of **PHENYLALANINE** and so should not be used in patients with **PHENYLKETONURIA**.

### **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**

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

## **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. 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, 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.

## **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 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 ( $\geq 1/10$ ), 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.

<b>Body System</b>	<b>Undesirable Effect</b>	<b>Frequency</b>
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 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)

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).

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
- If symptoms persist, medical advice must be sought.
- Do not exceed the stated dose.
- Keep out of sight and reach of children.

### **Renal and Hepatic Impairment**

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

## **OVERDOSAGE**

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.

### **Management of Paracetamol Overdose**

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.

### **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.

## **PRESENTATION AND STORAGE CONDITIONS**

### **PANADOL Rapid caplets**

White, film-coated capsule-shaped tablets with flat edges. One face of the tablet is debossed with the letter "P".

Packs of 20 and 40 caplets. 'Handipak' of 10 caplets.

Not all pack sizes may be marketed.

Store below 30°C.

**PANADOL Rapid Soluble tablets**

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

Packs of 4 and 20 tablets.

Not all pack sizes may be marketed.

Store below 30°C.

**NAME AND ADDRESS OF THE SPONSOR**

GlaxoSmithKline Consumer Healthcare  
82 Hughes Avenue  
Ermington  
NSW 2115

**POISON SCHEDULE OF THE MEDICINE**

Packs of 24 caplets or tablets or less – Unscheduled

Packs of more than 24 caplets or tablets - S2, Pharmacy medicine

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

PANADOL Rapid caplets	AUST R 78692	24 May 2001
PANADOL Rapid Soluble tablets	AUST R 15509	10 September 1991

**DATE OF THE MOST RECENT AMENDMENT**

11 NOV 2015

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