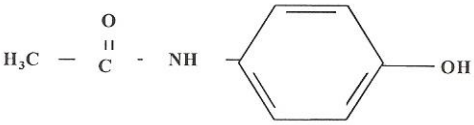
# PANADOL BACK & NECK PAIN RELIEF CAPLETS

# PRODUCT INFORMATION

## NAME OF THE MEDICINE

| Active ingredients | Chemical structure | CAS Registry Number |
|---|---|---|
| Paracetamol |  | 103-90-2 |

## DESCRIPTION

### PANADOL Back & Neck Pain Relief 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

## 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 Back & Neck Pain Relief 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 Back & Neck Pain Relief 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 Back & Neck Pain Relief was equivalent to that of standard PANADOL. $T_{max}$ was statistically significantly earlier with PANADOL Back & Neck Pain Relief 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 Back & Neck Pain Relief in both the fasting and fed states. This indicates that at a dose of 2x500 mg tablets, the rate of paracetamol absorption from PANADOL Back & Neck Pain Relief 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 Back & Neck Pain Relief, fasting and fed orally.**

| **Parameter** | **Panadol**<br>n=27<br>arithmetic mean (SD) | **Panadol Back & Neck Pain Relief**<br>n=27<br>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 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.

## INDICATIONS

For fast relief of acute pain.

## CONTRAINDICATIONS

This product is contraindicated in patients with a previous history of hypersensitivity to paracetamol or any of the exipients.

## 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.

If symptoms persist, medical advice must be sought.

Keep out of sight and reach of children.

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

### 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 Back & Neck Pain Relief caplets are not recommended for children under twelve 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, 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 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 (≥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.

| Body System | Undesirable Effect | Frequency |
|---|---|---|
| Blood and lymphatic system disorders | Thrombocytopenia | Very rare |
| Immune system disorders | Anaphylaxis<br>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 Back & Neck Pain Relief Caplets**
*Adults and children aged 12 years and over:* 2 caplets every four to six hours as required (maximum of 8 caplets 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.

- Take with water
- Should not be used with other paracetamol-containing products.
- Minimum dosing interval: 4 hours. .
- If symptoms persist, medical advice must be sought.
- Do not exceed the stated dose.
- The lowest dose necessary to achieve efficacy should be used.
- 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 Back & Neck Pain Relief Caplet formulation. Each caplet contains about 7.5 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.

## PRESENTATION AND STORAGE CONDITIONS

### PANADOL Back & Neck Pain Relief Caplets

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

Packs of 20 caplets. ‘Handipak’ of 10 caplets.

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 20 caplets or less – Unscheduled

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

| | | |
|---|---|---|
| PANADOL Back & Neck Pain Relief caplets | AUST R 141412 | 02 July 2007 |

## DATE OF THE MOST RECENT AMENDMENT

09 NOV 2015