

*For the use only of Registered Medical Practitioners or a Hospital or a Laboratory*

**CALPOL**  
**TABLETS / SUSPENSION / PAEDIATRIC DROPS**  
**Paracetamol Tablets IP / Paracetamol Paediatric Oral Suspension IP**

**WARNING: Taking more than daily dose may cause serious liver damage or allergic reactions (e.g. swelling of the face, mouth and throat, difficulty in breathing, itching or rash)**

**QUALITATIVE AND QUANTITATIVE COMPOSITION**

***Tablets:***

*CALPOL TABLETS 500 mg (Paracetamol Tablets IP 500 mg)*

Each uncoated tablet contains Paracetamol IP 500 mg.

*CALPOL TABLETS 650 mg (Paracetamol Tablets IP 650 mg)*

Each uncoated tablet contains Paracetamol IP 650 mg.

***Suspension:***

*CALPOL SUSPENSION 120 mg/5 ml (Paracetamol Paediatric Oral Suspension IP 120mg)*

Each 5 ml contains:

Paracetamol IP 120 mg in a flavoured syrup base.  
Colour : Carmoisine

*CALPOL SUSPENSION 250 mg/5 ml (Paracetamol Paediatric Oral Suspension IP 250mg)*

Each 5 ml contains:

Paracetamol IP 250 mg in a flavoured syrup base.  
Colour : Carmoisine.

***Paediatric Drops:***

*CALPOL PAEDIATRIC DROPS 100 mg/ml (Paracetamol Paediatric Oral Suspension IP 100 mg)*

Each ml (approx. 20 drops) contains:

Paracetamol IP 100 mg.  
Colour: Sunset Yellow FCF.

## PHARMACEUTICAL FORM

Tablets

Suspension

## CLINICAL PARTICULARS

### Therapeutic Indications

Paracetamol is an analgesic and an antipyretic.

- Treatment of mild-to-moderate pain and treatment of fever including: Headache, Migraine, Muscle ache, Dysmenorrhoea, Sore throat, Musculoskeletal pain, Fever and pain associated with vaccination/immunisation, Pain after dental procedures / tooth extraction, Toothache, Earache / otalgia, Respiratory tract infections including cold and flu, Osteoarthritis pain.

### Posology and Method of Administration

Do not exceed the stated dose. The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.

#### Tablets

Oral administration only.

Minimum dosing interval: 4 hours.

Maximum daily dose: 4000 mg.

Adults (including the elderly) and children aged 12 years and over:

*CALPOL TABLETS 500 mg:* 1 to 2 tablets taken every 4 to 6 hours as required.

*CALPOL TABLETS 650 mg:* 1 tablet taken every 4 to 6 hours as required.

Children, 6 to 11 years:

No more than four doses in any 24-hour period.

Maximum duration of continued use without medical advice: 3 days.

Maximum daily dose: 60mg/kg presented in divided doses of 10 - 15 mg/kg throughout the 24-hour period.

Children, 6 to 8 years:

250mg (½ tablet)

Children, 9 to 11 years:

500mg paracetamol (1 tablet)

Children under 6 years:

Not recommended for children under the age of 6 years.

**Suspension**

Do not exceed the stated dose. The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.

Oral administration only.

Minimum dosing interval: 4 hours.

No more than four doses in any 24-hour period.

Maximum duration of continued use without medical advice: 3 days.

Maximum daily dosage: 60mg/kg presented in divided doses of 10 - 15 mg/kg throughout the 24-hour period.

Children aged 1 month and above:

Fever

*Treatment of fever in children 1 month - 3 months:*

If fever persists for >24 hours (4 doses) seek medical advice to exclude a serious infectious cause.

Post Vaccination guidance

*Post-vaccination fever in children 1 month - 3 months:*

A single dose of 10 - 15 mg/kg for symptomatic relief of fever following vaccination. If a second dose is required, leave at least 4 hours between doses. Medical advice should be sought if fever persists after a second dose.

### **Special populations**

- *Children*

See *Posology and Method of Administration* section for product specific information.

- *Renal Impairment*

Patients who have been diagnosed with renal impairment must seek medical advice before taking this medication. The restrictions related to the use of paracetamol products in patients with renal impairment are primarily a consequence of the paracetamol content of the drug (see *Special Warnings and Special Precautions for Use*).

- *Hepatic Impairment*

Patients who have been diagnosed with liver impairment must seek medical advice before taking this medication. The restrictions related to the use of paracetamol products in patients with hepatic impairment are primarily a consequence of the paracetamol content of the drug (see *Special Warnings and Special Precautions for Use*).

### **Contraindications**

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

### **Special Warnings and Special Precautions for Use**

#### **All formulations:**

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.

Underlying liver disease increases the risk of paracetamol related liver damage. 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 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.

*In addition the following apply to specific presentations:*

*Suspension 120mg/5 ml and 250mg/5ml:*

Contains Sorbitol solution – Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Contains Methyl-, propyl- hydroxybenzoates may cause allergic reactions (possibly delayed).

*Paediatric Drops 100 mg/ml:*

Contains Methyl-, propyl- hydroxybenzoates may cause allergic reactions (possibly delayed).

### **Interaction with Other Medicaments and Other Forms of Interaction**

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.

### **Pregnancy and Lactation**

#### ***Pregnancy***

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.

#### ***Lactation***

Paracetamol is excreted in breast milk but not in a clinically significant amount at recommended dosages. Available published data do not contraindicate breast feeding.

### **Effects on Ability to Drive and Use Machines**

Unlikely to cause an effect on ability to drive and use machines.

### **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 ( $\geq 1/10,000$ ,  $< 1/1000$ ), 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.

***Post marketing data***

<b>Body System</b>	<b>Undesirable effect</b>	<b>Frequency</b>
Blood and lymphatic system disorders	Thrombocytopaenia	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 in patients sensitive to aspirin and other NSAIDs	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare

**Overdose**

***Signs and Symptoms***

PARACETAMOL OVERDOSE MAY BE INJURIOUS TO LIVER.

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.

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.

***Treatment***

Immediate medical management is required in the event of overdose, even if symptoms of overdose are not present.

Administration of N acetylcysteine or methionine may be required.

**PHARMACOLOGICAL PROPERTIES**

**Pharmacodynamic Properties**

Pharmacotherapeutic group: Anilides, ATC code: N02B E01.

### ***Mechanism of Action***

Paracetamol is an analgesic and antipyretic. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system.

### ***Pharmacodynamic Effects***

The lack of peripheral prostaglandin inhibition confers important pharmacological properties such as the maintenance of the protective prostaglandins within the gastrointestinal tract. Paracetamol is, therefore, particularly suitable for: patients with a history of disease or patients taking concomitant medication, where peripheral prostaglandin inhibition would be undesirable (such as, for example, those with a history of gastrointestinal bleeding or the elderly).

### **Pharmacokinetic Properties**

#### *All formulations:*

#### ***Absorption***

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract.

#### ***Distribution***

Binding to the plasma proteins is minimal at therapeutic concentrations.

#### ***Metabolism***

Paracetamol is metabolised in the liver and excreted in the urine mainly as glucuronide and sulphate conjugates.

#### ***Elimination***

Less than 5% is excreted as unmodified paracetamol.

#### *In addition the following apply to specific formulations:*

#### *Tablets:*

Paracetamol is rapidly absorbed from the gastrointestinal tract and is distributed into most body tissues. Binding to plasma proteins is minimal at therapeutic concentrations. Paracetamol is metabolised in the liver and excreted in the urine mainly as glucuronide and sulphate conjugates; less than 5% is excreted as unmodified paracetamol. The mean plasma half life is about 2.3 hours.

## **Clinical Studies**

### ***Sore throat***

A double blind, single-dose parallel study in 120 patients with upper respiratory tract infection with acute sore throat and objective evidence of tonsillopharyngitis demonstrated statistically and clinically significant efficacy of a single 1000 mg dose of paracetamol tablet in reducing pain intensity and providing pain relief in sore throat over at hourly intervals 6 hour period, compared with placebo. This study used validated measures and differences were clinically relevant.

### ***Headache***

Three large, randomised, double-blind studies assessing the efficacy of paracetamol in tension headache have been reported, comparing several doses of paracetamol with other analgesics and placebo. Two studies demonstrated statistically significant superior cumulative pain relief values and cumulative sums of pain intensity differences over 6 hours for paracetamol 1000 mg compared with placebo. Significant differences compared with placebo were observed from one hour after dosing, although separation of benefit commenced as early as 30 minutes after dosing. The third study demonstrated that paracetamol 1000 mg gave statistically significant superior pain relief compared to placebo.

### ***Muscle Ache***

A randomised, double-blind, placebo-controlled study investigated the effect of treatments including paracetamol (1000 mg) in combination with pseudoephedrine in patients with the common cold. General muscular ache was assessed during the study and a significant superiority over placebo ( $p < 0.05$ ) was demonstrated for the paracetamol combination.

### ***Migraine***

A large parallel group study assessed the efficacy of paracetamol 1000 mg compared with placebo in a single migraine attack. The paracetamol was significantly superior to placebo at 2 hours post-dose for headache response rate, pain-free rate and for other migraine headache symptoms such as photophobia, phonophobia and functional disability.

A large cross-over study assessed the efficacy of paracetamol 1000 mg compared with dihydroergotamine, paracetamol/dihydroergotamine combination and placebo in four consecutive migraine attacks. All active treatments were significantly superior to placebo in reducing intensity of pain at 1 and 2 hours, and brought a significantly faster abatement of pain. A second crossover study compared paracetamol 900 mg with ibuprofen 400 mg in the treatment of classical migraine. Both treatments significantly reduced severity of pain compared with baseline.



### ***Dysmenorrhoea***

Two placebo-controlled studies examined paracetamol efficacy in dysmenorrhoea. The first study was part of a pooled analysis which compared paracetamol 1000 mg with naproxen sodium 220 mg and placebo. The design was a randomised, double-blind, single dose, cross-over study in patients with primary dysmenorrhoea of moderate to severe intensity. For paracetamol, maximal pain relief was observed at 2 hours post-dose. Paracetamol showed significant pain relief at 2, 3 and 4 hours after administration versus placebo ( $p < 0.01$ ) and numerically superior pain relief at 5, 6 and 7 hours after administration. The second study demonstrated that paracetamol 650 mg was superior to placebo in reducing menstrual pain.

### ***Dental Pain***

Six studies in dental pain are reviewed. All were large studies, randomised, group comparative and double-blind in design. All except one were placebo controlled. The non-placebo controlled study compared two doses of paracetamol with codeine 60 mg. One study was performed in pre-operative pain, all others were post-operative assessments. In all studies paracetamol 1000 mg was shown to be statistically superior to placebo or to codeine 60 mg. In one study effervescent paracetamol was shown to have a faster onset of analgesia than standard immediate release paracetamol tablets.

### ***Osteoarthritis***

A meta-analysis has of the efficacy of paracetamol in the treatment of osteoarthritis showed that paracetamol was significantly more effective in relieving pain due to osteoarthritis than placebo.

### ***Musculoskeletal pain***

A study has been performed in acute and chronic moderately severe musculoskeletal pain (including ligament/bone pain, low back strain, osteoarthritis and 14 other conditions) in 90 patients. Pain was significantly reduced compared with baseline in the paracetamol group, but comparisons with placebo were not performed.

### ***Respiratory tract infections, including cold and flu symptoms***

A large, well-designed study in adults with upper respiratory tract infection assessed the efficacy of 500 mg and 1000 mg doses of paracetamol compared with aspirin (500 mg or 1000 mg) or placebo for 6 hours after treatment. Compared to placebo, significant reductions were seen in the mean intensity of headache, aching and feverish discomfort ( $p < 0.001$ ) at 2, 4 and 6 hours after paracetamol 1000 mg. Compared to placebo, significant reductions were seen in the mean intensity of headache ( $p < 0.001$ ) at 2, 4 and 6 hours after paracetamol 500 mg. Further, with the 500 mg paracetamol dose, feverish discomfort ( $p < 0.001$  at 2 and 4 hours and  $p < 0.025$  at 6 hours) and achiness ( $p < 0.01$  at 1 and 4 hours) were significantly reduced as compared to placebo.

Two open-label, randomised comparative studies in children with upper respiratory tract infections report significant ( $p<0.05$ ) reductions in fever after the first dose of paracetamol.

In patients with an acute sore throat and at least one current symptom of upper respiratory tract infection, 1000 mg paracetamol showed significantly greater total pain relief over 30 minutes, 1 hour, and 6 hours compared with matching placebo.

### ***Earache / otalgia***

In a small study (26 children, aged 18 month-13 years and 9 adults, aged 15-65 years) patients with acute otalgia were randomised to receive oral paracetamol or aural choline salicylate dosed every 3-4 hours until pain relief was achieved. All patients receiving paracetamol ( $n=17$ ) had reported pain relief within a time period of 10-90 minutes, 3 patients had mild pain, 9 patients had moderate pain and 5 had stronger pain.

A large, well-designed randomised controlled trial of 219 children (aged 1-6 years) with otitis media assessed the efficacy of 2 days' treatment with paracetamol (10 mg/kg three times daily, [ $n=73$ ]), ibuprofen (10 mg/kg three times daily) or placebo. Tympanic score was reduced in all three groups at day 2; however there was no significant difference between the three treatment groups.

A Cochrane review reports that at 48 hours, children in the paracetamol group had less pain than those allocated to placebo. This data is based on the Cochrane authors' analysis of the results in the above-cited trial.

### ***Fever***

A large, well designed study in 392 adults with fever (associated with upper respiratory tract infection) assessed the efficacy of 500 mg ( $n=79$ ) and 1000 mg ( $n=79$ ) doses of paracetamol compared with placebo ( $n=78$ ) for 6 hours after treatment. Both doses of paracetamol were effective compared to placebo ( $p<0.001$ ) over the 4 hour period and significant temperature reduction for paracetamol persisted for a minimum of 6 hours. Another large, placebo-controlled study in 154 adults assessed a single 650 mg dose of paracetamol in an endotoxin-induced model of fever. This study showed a statistically significant and clinically relevant change from baseline in temperature over 8 hours for paracetamol ( $n=30$ ) compared with placebo ( $n=30$ ). Other controlled studies have demonstrated the antipyretic efficacy of paracetamol in children.

### **Preclinical Safety Data**

Non-clinical safety data for paracetamol have not revealed findings that are of relevance to the recommended dosage and use of the product.

## PHARMACEUTICAL PARTICULARS

### List of Excipients

#### CALPOL TABLETS 500 mg and 650 mg

Starch Maize, Pregelatinised Starch, Methylparaben, Magnesium Stearate, Purified Water.

#### CALPOL SUSPENSION 120 mg/5ml

Sucrose, Sorbitol Solution, Agar, Microcrystalline Cellulose, Methyl Hydroxybenzoate, Propyl Hydroxybenzoate, Sodium Citrate, Citric Acid Monohydrate, Sodium Lauryl Sulphate, Strawberry Flavour, Carmoisine, Purified Water.

#### CALPOL SUSPENSION 250 mg/5ml

Sucrose, Sorbitol solution 70%, Agar, Microcrystalline Cellulose, Methyl Hydroxybenzoate, Propyl Hydroxybenzoate, Sodium Citrate, Citric Acid Monohydrate, Sodium Lauryl Sulphate, Colour Carmoisine, Strawberry Flavour, Purified Water.

#### CALPOL PAEDIATRIC DROPS 100 mg/ml

Sucrose, Liquid Glucose, Xanthan Gum, Glycerin, Monoammonium Glycyrrhizinate, Methyl Hydroxybenzoate, Propyl Hydroxybenzoate, Sodium Chloride, Sodium Citrate, Citric Acid Monohydrate, Sunset Yellow FCF, Peppermint, Purified Water.

### Incompatibilities

No data available.

### Shelf Life

#### CALPOL TABLETS 500 mg and 650 mg

#### CALPOL SUSPENSION 120 mg/5ml and 250 mg/5ml

#### CALPOL PAEDIATRIC DROPS 100 mg/ml

The expiry dates are indicated on the label and packaging.

### Special Precautions for Storage

#### CALPOL TABLETS 500 mg and 650 mg

Store at temperature not exceeding 30°C. Protect from light and moisture.

CALPOL SUSPENSION 120 mg/5ml

Store in a well closed container at temperatures not exceeding 30°C. Protect from direct sunlight. Do not freeze.

CALPOL SUSPENSION 250 mg/5ml

Store in a well closed container at temperatures not exceeding 30°C. Protect from direct sunlight. Do not freeze.

CALPOL PAEDIATRIC DROPS 100 mg/ml

Store in a well closed container at temperatures not exceeding 30°C. Protect from direct sunlight. Do not freeze.

Keep out of reach of children.

**Nature and Specification of Container**

CALPOL TABLETS 500 mg and 650 mg

Blister strips in a carton

or

High density polyethylene (HDPE) container with induction sealing

CALPOL SUSPENSION 120 mg/5ml

Bottle with a measuring cup.

CALPOL SUSPENSION 250 mg/5ml

Bottle with a measuring cup.

CALPOL PAEDIATRIC DROPS 100 mg/ml

Bottle with a dropper in a carton.

All pack presentations may not be marketed in the country.

**Instructions for Use / Handling**

CALPOL TABLETS 500 mg and 650 mg

No special requirements.

CALPOL SUSPENSION 120 mg/5ml and 250 mg/5ml

Shake well before use.

*CALPOL PAEDIATRIC DROPS 100 mg/ml*

Unscrew the cover on the dropper. Pull out the teat and screw the dropper on to the bottle after removing the metal cap.

Shake well before use.

**For further information please contact:**

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