

PANADOL Osteo Tablets

PRODUCT INFORMATION

DESCRIPTION

Active Ingredient: Paracetamol 665 mg

Excipients: Hypromellose
Starch – Pregelatinised Maize
Povidone
Magnesium Stearate
Croscarmellose Sodium
Stearic Acid
Glycerol Triacetate
Carnauba Wax

Contains no sugar, lactose or gluten.

PHARMACOLOGY

Pharmacodynamics

Paracetamol is a para-aminophenol derivative that exhibits analgesic and anti-pyretic activity. The mechanism of action is dependent on the inhibition of prostaglandin synthesis. It does not possess anti-inflammatory activity. It provides relief from mild to moderate pain and fever.

Chronic Pain

In patients with pain associated with osteoarthritis of the knee, PANADOL Osteo (2 tablets taken three times daily) and standard immediate release paracetamol (2 tablets taken 4 times daily) were clinically equivalent at a total daily dose of 4 g based on patient global assessment after treatment for 7 days.

PANADOL Osteo and standard immediate release paracetamol were not significantly different for a range of secondary efficacy parameters including pain during the day, pain on walking, pain relief, number of times woken during the night due to pain and duration or morning stiffness.

Since PANADOL Osteo (three times daily) was clinically equivalent to standard immediate release paracetamol (four times daily), it was concluded that PANADOL Osteo provides pain relief for up to 8 hours after dosing.

Acute Pain

In patients with post-surgical dental pain, a single dose of PANADOL Osteo (2 tablets) was therapeutically equivalent to standard immediate release paracetamol (2 tablets) based on patient global assessment 4 hours after treatment.

There was no significant difference between PANADOL Osteo and standard immediate release paracetamol in either development of analgesia or peak analgesic effect. Trends in favour of PANADOL Osteo were observed at the later time points. Furthermore, PANADOL Osteo was significantly more effective than standard immediate release paracetamol for the summed pain intensity difference at 6 hours ($p = 0.0344$) and 8 hours ($p = 0.0500$), as measured on a visual analogue scale.

From these results, it was concluded that PANADOL Osteo provides more prolonged analgesia than standard immediate release paracetamol. For the patient, this translates to longer lasting pain relief and the improved convenience of fewer doses. This is as expected for a formulation containing sustained release paracetamol and consistent with results from the pharmacokinetic studies.

Pharmacokinetics

PANADOL Osteo is a unique bi-layer tablet incorporating an immediate release and a sustained release dose of paracetamol.

The sustained release layer is formulated in such a manner that it rapidly hydrates to form a gel layer at the matrix periphery; the drug is then released from the matrix by a combination of diffusion and erosion of the gel layer.

PANADOL Osteo releases drug at a rate which ensures that therapeutically active plasma paracetamol concentrations are rapidly attained and maintained until up to 8 hours after administration.

Paracetamol is metabolised by the liver and excreted in the urine mainly as glucuronide and sulphate conjugates; less than 5% is excreted as unmodified paracetamol. Binding to the plasma proteins is minimal at therapeutic concentrations.

PANADOL Osteo and standard immediate release paracetamol were bioequivalent in volunteers with respect to dose-corrected $AUC_{(0-t)}$ and $AUC_{(0-inf)}$ in both fed and fasted states following administration of a single dose. This indicates that the extent of paracetamol absorption from PANADOL Osteo was equivalent to that of standard immediate release paracetamol. Food had little effect on the extent of paracetamol absorption from PANADOL Osteo demonstrating that PANADOL Osteo is suitable to be taken with or without meals. Paracetamol was rapidly absorbed after administration of PANADOL Osteo and was generally measurable in plasma within 15 minutes in fasted subjects. Mean plasma paracetamol concentrations above the minimum level required for analgesia ($>4\text{mcg/mL}$) were maintained until up to 6 to 7 hours after administration in fasted subjects and 7 to 8 hours in fed subjects.

At steady state, PANADOL Osteo was bioequivalent with standard immediate release paracetamol based on the comparison of AUCs during the final 24 hour dosing period of the study. Furthermore, comparison of the pharmacokinetic parameters indicated that PANADOL Osteo has the characteristics of a formulation containing sustained release paracetamol. Fluctuations in the peak and trough values for plasma paracetamol concentrations were significantly smaller for PANADOL Osteo than for standard immediate release paracetamol (mean fluctuation index = 0.957 and 1.388, respectively, $p < 0.001$). Consequently, PANADOL Osteo provided more consistent levels of paracetamol. Furthermore, the AUCs at steady state were equivalent indicating that there was no additional accumulation of paracetamol from PANADOL Osteo compared to standard immediate release paracetamol.

INDICATIONS

PANADOL Osteo is effective for the relief of persistent pain associated with osteoarthritis and muscle aches and pains such as backache. PANADOL Osteo also provides effective, temporary relief of pain and discomfort associated with headache, tension headache, period pain, toothache and pain after dental procedures, and cold & flu. Reduces fever.

CONTRAINDICATIONS

Hypersensitivity to paracetamol or to any of the excipients.

PRECAUTIONS

Panadol should be administered with caution to patients with hepatic or renal dysfunction.

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 fetus having been observed.

Use in Lactation

Paracetamol is excreted in breast milk. The amount available for ingestion by the infant has been reported variously as less than 0.1% of a single dose of paracetamol 500 mg and 0.04 to 0.23% of a single 650 mg dose. These results are based on immediate release preparations of paracetamol. There is no data available on the excretion of sustained-release paracetamol preparations in breast milk. However, it is not expected that PANADOL Osteo would provide any increase in the excretion of paracetamol in breast milk as this product is designed to maintain rather than increase plasma paracetamol concentrations compared to immediate release preparations. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infant.

Use in Children

Not recommended for children under 12 years of age.

INTERACTIONS

Anticoagulant dosage may require reduction if Panadol medication is prolonged.

Paracetamol absorption from immediate release preparations is increased by drugs which increase gastric emptying, eg metoclopramide, and decreased by drugs which decrease gastric emptying, eg propantheline, antidepressants with anticholinergic properties, narcotic analgesics. However, concurrent administration of metoclopramide may reduce the absorption of paracetamol from this sustained release dosage form, as it accelerates gastric emptying and intestinal transit.

Paracetamol may increase chloramphenicol concentrations. The likelihood of paracetamol toxicity may be increased by the concomitant use of enzyme inducing agents such as alcohol or anticonvulsant drugs.

ADVERSE REACTIONS

Reports of adverse reactions are rare. Although the following adverse reactions have been reported, a causal relationship to the administration of paracetamol has been neither confirmed nor refuted: dyspepsia, nausea, allergic and haematological reactions.

DOSAGE AND ADMINISTRATION

PANADOL Osteo tablets are to be administered orally, with or without food.

Adults and children over 12 years. Two tablets, swallowed whole, every 6 to 8 hours (maximum of 6 tablets in any 24 hours). The tablets must not be crushed.

OVERDOSAGE

Paracetamol overdose may cause hepatic failure. Immediate medical management is required in the event of overdose, even if symptoms of overdose are not present.

Because PANADOL Osteo contains sustained release paracetamol, absorption will be prolonged in overdose. It is recommended that for the management of overdose, where PANADOL Osteo is suspected, that an additional plasma paracetamol level be obtained 4-6 hours after the initial measurement. If either level is above or close to the treatment line on the paracetamol overdose nomogram, administration of antidote would be indicated.

Treatment

Prompt treatment is essential even when there are no obvious symptoms.

In cases of over dosage, methods of reducing absorption of ingested drug are important. Prompt administration of activated charcoal 50 g in 150 mL of water and 150 mL sorbitol 50% solution by mouth may reduce absorption. It is recommended that intravenous fluids such as Normal Saline be given concurrently. Gastric lavage is indicated if the patient is unwilling or unable to drink an activated charcoal/sorbitol mixture.

If the history suggests that paracetamol 150mg/kg body weight or 15 g total or more has been ingested, administer the following antidote:

Intravenous acetylcysteine 20%: Administer acetylcysteine immediately without waiting for positive urine test or plasma level results if 8 hours or less since overdose ingestion. Initial dose 150 mg/kg over 15 minutes, followed by continuous infusion of 50 mg/kg in glucose 5% 500 mL over four hours and 100 mg/kg in glucose 5% 1 L over 16 hours.

POISONS SCHEDULE

Tablets (96s) - S2 Pharmacy Medicine

STORAGE

Store below 30 degrees Celsius.

PRESENTATION

Modified-release, bi-layer, capsule-shaped, white film-coated tablet marked with "8" logo.

SPONSOR

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a division of
GlaxoSmithKline Australia Pty Ltd
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TGA Approval: Approved 17 February 2005

<p>PBS Information: Restricted Benefit. Relief of persistent pain associated with osteoarthritis. Refer to PBS Schedule for further information.</p>
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