PACKAGE INSERT TEMPLATE FOR PARACETAMOL TABLET

Brand or Product Name

[Product name] Tablet 500mg

Name and Strength of Active Substance(s)
Paracetamol 500mg

Product Description

[Visual description of the appearance of the product (colour, odour, superficial markings, ident, coated/uncoated, size of table, dimensions)]
eg White, circular flat beveled edge tablets marked '500' on one side
Round, white to off-white, film coated, 9.5 mm diameter biconvex tablets plain on both faces

Pharmacodynamics

Paracetamol is a centrally acting analgesic and antipyretic with minimal anti-inflammatory properties.

Analgesic
The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (specifically cyclooxygenase (COX)-2) and, to a lesser extent, through a peripheral action by blocking pain-impulse generation.
The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitize pain receptors to mechanical or chemical stimulation

Antipyretic
Paracetamol act centrally on the hypothalamic heat-regulating center to produce peripheral vasodilatation resulting in increase blood flow through the skin, sweating and heat loss.
Paracetamol reduces fever by inhibiting the formulation and release of prostaglandins in the CNS and by inhibiting endogenous pyrogens at the hypothalamic thermoregulator center

Pharmacokinetics

Following oral administration paracetamol is rapidly absorbed.
Paracetamol absorption takes place mainly in the small intestine and therefore the rate of absorption is depending on the rate of gastric emptying. It has been shown that drugs which delay gastric emptying also delay the absorption of paracetamol whereas metoclopramide (a drug

which increases the rate of gastric emptying) accelerates absorption of the analgesic through the total amount absorbed doses not increase.
The presence of food in the stomach has also been reported to reduce the rate of absorption of paracetamol. Alterations in gastric pH have no appreciable effect on paracetamol absorption.
During absorption, the amount of paracetamol which is inactivated is negligiable and it has been shown that paracetamol dose not affect gastric mucosal permeability and does not produce mucosal bleeding.

Peak plasma concentrations are reached 1 hour after absorption. The plasma half life is 1 to 3 hours.
Paracetamol penetrates the brain and is present in breast milk of human.
Paracetamol is metabolized by the microsomal enzyme system of the liver. This metabolism is mainly to the glucuronide and sulphate conjugates, accounting for approximately 49% and 26% of the ingested dose respectively. About 4% is excreted as free paracetamol. Other minor pathways include the production of catechol derivatives and cysteine conjugates (via glutathione). Paracetamol excretion is rapid and occurs via the urine.

Indication

For the relief of fever

For the relief from mild to moderate including: headache, migraine, backache, musculoskeletal pain, myalgia and neuralgia, dysmenorrhea, pain of osteoarthritis, toothache, pain after dental procedures/tooth extraction, pain after vaccination and the discomfort from colds, influenza and sore throats.

Recommended Dosage

Adults and children aged 12 years and over:

500mg to 1g paracetamol, taken every 4-6 hours as required up to a maximum of 4 g daily.

Children

6 to 11 years:

250mg -500mg every 4 to 6 hours as required.

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

Mode of Administration
Oral

Contraindications

Hypersensitivity to paracetamol or any of the other ingredients/components of the product.
Severe and active hepatic impairment

Warnings and Precautions
[Specific package insert requirement for paracetamol]

> This preparation contains PARACETAMOL.
> Do not take any other paracetamol
> containing medicines at the same time.

- Keep out of reach of children.
- Do not take if allergic to paracetamol.
- Patients should contact their health care provider if symptoms persist (if the pain lasts for more than 10 days, if there is redness or fever lasts more than 3 days).
- Paracetamol should be given with care to patients with impaired kidney or liver function.
- Large doses should be avoided in patients with hepatic impairment. Paracetamol overdose may harm the liver.
- Do not exceed recommended dose.
- It should be given with care to patients with alcohol dependence.
- Paracetamol provides symptomatic relief only, additional therapy to treat the cause of the pain or fever should be instituted when necessary.

Effects on Ability to Drive and Use Machines
It is unlikely to impair a patient's ability to drive or use machinery.

Interactions with Other Medicaments

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.

Statement on Usage During Pregnancy and Lactation

Use in pregnancy:
•Considered to be the analgesic of choice in pregnant patients.

•Although it crosses placenta, paracetamol is considered to be safe in normal therapeutic doses for short-term use as a minor analgesic/antipyretic in pregnancy.

Use in lactation:
•Excreted in breast milk.
•Maternal ingestion of paracetamol in normal therapeutic doses does not appear to present a risk to the nursing infant.

Adverse Effects / Undesirable Effects
Adverse effects of paracetamol are rare and usually mild, although haematological reactions have been reported. Skin rashes and other hypersensitivity reactions occur occasionally.

Overdose and Treatment
Symptoms:
Toxic symptoms include vomiting, abdominal pain, hypotension and sweating. The most serious adverse effect of acute overdose of paracetamol is a dose-dependent, potentially fatal hepatic necrosis. Clinical and laboratory evidence of hepatoxicity may be delayed for up to one week. Major manifestations of liver failure such as jaundice, hypoglycemia and metabolic acidosis may take at least 3 days to develop.

Treatment:
In cases of overdose, methods of reducing the absorption of ingested drug are important. Gastric lavage is essential even if several hours have elapsed. Prompt administration of 50g activated charcoal and 500ml iced mannitol 20% by mouth, may reduce absorption. If the history suggests that 15g Paracetamol or more has been ingested, administer one of the following antidotes:

Acetylcysteine 20% i.v.: Administer intravenously, 20% acetlcysteine immediately without waiting for positive urine test or plasma level results: initial dose of 150mg/kg over 15 minutes, followed by continuous infusion of 50mg/kg in 500ml 5% glucose/dextrose over 4 hours and 100mg/kg in 1L 5% glucose/dextrose over 16 hours; or

OR

Oral Methionine: 2.5g immediately followed by three further doses of 2.5g at four hourly intervals. For a 3 year old child, 1g methionine every four hours for four doses has been used;

OR

Oral Acetylcysteine 5%: 140mg/kg as a loading dose, then 70mg/kg every 4 hours for a total of 17 maintenance doses. If more than ten hours have elapsed since the overdosage was taken, the antidote may be in ineffective

Storage Conditions
[Store below…°C]

Dosage Forms and Packaging Available
[Packaging type & pack size eg Alu-alu blister of 10s X 10/box, HDPE bottle of 30s/box etc]

Name and Address of Manufacturer
[Name & full address of manufacturer]

Name and Address of Marketing Authorization Holder
[Name & full address of marketing authorization holder]

Date of Revision of Package Insert
[day/month/year]