

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol capsules 500mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol BP 500.00mg

3 PHARMACEUTICAL FORM

Hard gelatin capsule

Red/White size 0 gelatin capsule with P500 printed on cap and body.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Paracetamol is indicated for use for relief from the symptoms of headache, toothache, period pains, rheumatic pains, colds and influenza, and for pyrexia.

4.2 Posology and method of administration

Oral administration

Adults: 1 - 2 capsules every 4 - 6 hours to a maximum of 8 capsules daily.
Children: 6 - 12 years: 1 capsule, repeating the dose every 4 - 6 hours when necessary. Not more than 4 capsules a day.

Not suitable for children under 6 years.

4.3 Contraindications

Hypersensitivity to Paracetamol and/or other constituents.

4.4 Special warnings and precautions for use

Care is advised in the administration of Paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Do not exceed the recommended dose.

Patients should be advised not to take other paracetamol-containing products concurrently.

Warnings for the Label:

Immediate medical advice should be sought in the event of an overdose, even if you feel well. Do not take with any other paracetamol-containing products.

Warnings for the Leaflet:

Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol:

Drugs which induce hepatic microsomal enzymes such as alcohol, barbiturates and tricyclic anti-depressants may increase the hepatic toxicity of paracetamol after overdosage.

The speed of absorption of Paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine.

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of Paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Pregnancy and lactation

Paracetamol:

Epidemiological studies in human pregnancy have shown no ill effects due to Paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use.

Paracetamol is excreted in breast milk but not in a clinically significant amount.

Available published data do not contraindicate breast feeding.

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to Paracetamol.

With prolonged use or overdosage, hepatic necrosis, acute pancreatitis and nephrotoxicity have been reported.

4.9 Overdose

Paracetamol

Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk Factors

If the patient

(a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St. John's Wort or other drugs that induce liver enzymes.

Or

(b) Regularly consumes ethanol in excess of recommended amounts.

Or

(c) Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of Paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule.

If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24 hours from ingestion should be discussed with the NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol has analgesic and antipyretic effects but has only weak anti-inflammatory effects. These actions are considered to be due to inhibition of the biosynthesis of prostaglandins.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastro intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from 1-4 hours.

Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations. A minor hydroxylated metabolite which is usually produced in very small amounts by mixed function oxidises in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage.

Practically no paracetamol is excreted unchanged, and the bulk is excreted after hepatic conjugation with glucuronic acid (about 60%) sulphuric acid (about 35%) or cysteine (about 3%).

Children have less capacity for glucuronidation of the drugs than do adults. When high doses are ingested paracetamol undergoes N-hydroxylation to form N-acetyl-benzo quinoneimine, a highly reactive intermediate. This metabolite reacts with sulphhydryl groups in proteins and glutathione. When hepatic necrosis is the result.

A review of the absorption and fate and bioequivalence of Paracetamol was carried out by Hunt et Al.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch BP
Lactose BP
Polyvinylpyrrolidone (Kollidon K30) BP
Sodium Starch Glycollate BP
Magnesium Stearate BP
Water BP
Starch BP

Capsule Shell components:

Body:

Titanium Dioxide
Gelatin

Cap:

Erythrosin
Indigotin
Titanium Dioxide
Gelatin

Composition of Ink

Shellac
Propylene Glycol
Strong Ammonia Solution
Potassium Hydroxide
Black Iron Oxide
Dehydrated Alcohol
Isopropyl Alcohol
Butyl Alcohol

6.2 Incompatibilities

None stated.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Paracetamol should be stored in a cool dry place. Keep container tightly closed.

6.5 Nature and contents of container

Blister pack (consists of aluminium foil and white PVC or blister pack composed of PVC film and aluminium foil, (foil: DIN 55 559 compliant) 48 and 96 capsules.

Polyethylene/Polypropylene containers with tamper evident closures, with the exception of OTC packs which will have child resistant closures with 50, 100, 250, 500, 1000 capsules.

6.6 Special precautions for disposal

None stated.

7 MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceuticals Limited
NLA Tower, 12-16 Addiscombe Road
Croydon, Surrey, CR0 0XT
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 12762/0427

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07/01/2009

10 DATE OF REVISION OF THE TEXT

07/01/2009

11 DOSIMETRY (IF APPLICABLE)

**12 INSTRUCTIONS FOR PREPARATION OF
RADIOPHARMACEUTICALS (IF APPLICABLE)**