

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Vetopar 500mg/5ml Oral Solution
Paracetamol 500mg/5ml Oral Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol oral solution contains 500 mg paracetamol in each 5 ml
For excipients, see 6.1

3. PHARMACEUTICAL FORM

Oral solution.

A clear, pink, viscous solution with an odour of raspberry.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Paracetamol solution is indicated in the management of pain and fever associated with such conditions as the common cold, influenza and headache.

4.2 Posology and method of administration

For oral administration only.

Shake well before use.

Recommended Doses and Dosage Schedules

Adults and children 12 years and over:

The Optimal dosage range is 500 mg to 1 g paracetamol, i.e. 5 ml to 10 ml of Paracetamol oral solution (maximum 1g), which may be repeated every 4 to 6 hours to a maximum of 4 g paracetamol/ day (40 ml paracetamol oral solution).

Children aged 6 to 12 years:

The optimal dosage range is 250-500mg, i.e. 2.5 ml to 5 ml of paracetamol oral solution; these doses may be repeated every 4-6 hours when necessary up to a maximum of 4 doses per 24 hours.

Children under 6 years:

Not recommended.

The Elderly:

In the elderly, the rate and extent of paracetamol absorption is normal but plasma half-life is longer and paracetamol clearance is lower than in young adults.

4.3 Contraindications

Hypersensitivity to paracetamol or any of the other components of the preparation.

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.

Prolonged use except under medical supervision could be harmful.

If symptoms persist for more than 3 days or worsen at any time, consult your doctor.

Do not exceed the recommended dose.

Keep out of the reach and sight of children.

This product contains Glycerol and this is known to be harmful in high doses. It can cause headache, stomach upset and diarrhoea.

The label shall say: “Do not take with any other paracetamol-containing products” and “Immediate medical advice should be sought in the event of an overdose, even if you feel well.”

The leaflet shall say: “Immediate medical advice should be sought in the event of an overdose, even if the child seems well, because of the risk of delayed, serious liver damage.”

4.5 Interaction with other medicinal products and other forms of interaction

Patients who have taken barbiturates, tricyclic antidepressants and alcohol may show diminished ability to metabolize large doses of paracetamol, the plasma half-life of which can be prolonged.

Alcohol can increase the hepatotoxicity of paracetamol overdose.

Chronic ingestion of anticonvulsants or oral steroid contraceptives induces liver enzymes and may prevent attainment of therapeutic paracetamol levels by increasing first pass metabolism or clearance.

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

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 clinically significant amount. Available published data do not contraindicate breast feeding.

4.7 Effects on ability to drive and use machines

None known.

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.

Most reports of adverse reactions to paracetamol relate to overdose with the drug.

4.9 Overdose

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 the risk factors.

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 depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

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, coma and death. Acute renal failure with acute tubular necrosis, strongly suggested with 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. Any patient who had ingested around 7.5 g or more of paracetamol in the preceding 4 hours should undergo gastric lavage.

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 however 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 24h ingestion should be discussed with the NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Classification: N02B E01 other analgesics and antipyretics; Anilides

The site and mechanism of the analgesic effect of paracetamol is unclear. Paracetamol reduces fever by a direct action on the hypothalamic heat-regulating centers, which increases dissipation of body heat (via vasodilation and sweating). The action of endogenous pyrogen on heat-regulating centers is inhibited.

Paracetamol is almost as potent as aspirin in inhibiting prostaglandin synthetase in the CNS but its peripheral inhibition of prostaglandin synthesis is minimal, which may account for its lack of clinically significant anti-rheumatic or anti-inflammatory effects.

Paracetamol dose not inhibit platelet aggregation, affect prothrombin response or produce GI ulceration.

5.2 Pharmacokinetic properties

Absorption: Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations occur within 0.5 to 2 hours, with slightly faster absorption of liquid preparations.

Distribution : Usual analgesic doses produce total serum concentrations of 5 to 20 mcg/ ml; a good correlation between serum concentration and analgesic effect has not been found. Serum protein binding varies from 20 to 50% at toxic serum concentrations.

Metabolism: Paracetamol is extensively metabolized in the liver by glucuronisation and conjugation with sulphates. Approximately 4%

is metabolized via cytochrome P-450 to a toxic metabolite which is normally detoxified by preferential conjugation with hepatic glutathione and excreted in the urine as conjugates of cysteine and mercapturic acid. When paracetamol is used chronically or taken acutely in large doses, glutathione stores are depleted and hepatic necroses may occur.

Elimination: Paracetamol is excreted in the urine, mostly as metabolites; 2 to 4 % is excreted unchanged. The average elimination half-life is 1 to 4 hours; half-life is slightly prolonged in neonates (2.2 to 5 hours) and in cirrhotics.

5.3 Preclinical safety data

Data in the literature on toxic doses and serum levels of Paracetamol is limited, but Paracetamol is relatively non-toxic in therapeutic doses.

Paracetamol toxicity may result from a single toxic dose or from long term ingestion of the drug. It has been reported in the literature that children may be less susceptible to acute Paracetamol poisoning than adults. Hepatic necrosis is dose dependent and is the most serious acute toxic effect associated with over dosage. It is potentially fatal, and nausea, vomiting and abdominal pain usually occur within 2-3 hours after ingestion of toxic doses of the drug.

Acute toxic doses of Paracetamol in laboratory animals produce animals produce death from liver and renal damage.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate

Erythrosine (E127)

Glycerol

Macrogol 400

Propylene Glycol

Methyl parahydroxybenzoate

Propyl parahydroxbenzoate

Raspberry flavor No.1

Saccharin Sodium

Sodium citrate
Purified Water

6.2 Incompatibilities

Not relevant.

6.3 Shelf life

Unopened: 24 months

Opened: 3 months

6.4 Special precautions for storage

Do not store above 25 °C. Store in the original container.

6.5. Nature and content of container

Amber glass bottle with LD-polyethylene, tamper evident and child resistant cap. The bottle is packed in an outer carton.

A spoon with a 5 ml and 2.5 ml measure is supplied with this pack.

Pack size: 300ml and 200ml

6.6 Special precautions for disposal

No special instruction.

7 MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceuticals Limited

NLA Tower

12-16 Addiscombe Road

Croydon

Surrey

CRO OXT

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 12762/0173

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

13/02/2007

10 DATE OF REVISION OF THE TEXT

14/08/2009