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 500mg paracetamol in each 5ml

Excipients with known effect

Methyl parahydroxybenzoate (E 218),	2 mg/5ml
Propyl parahydroxybenzoate (E 216)	0.5 mg/5ml
Glycerol (E 422)	1500 mg/5ml
Propylene glycol (E 1520)	1500mg/5ml
Sodium Citrate	7.5mg/5ml
Saccharin Sodium	20mg/5ml

For the full list of excipients, see section 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.

For patients who are unable to tolerate solid dose formulations or lower strength preparations of paracetamol containing products.

4.2 Posology and method of administration

Posology:

Recommended Doses and Dosage Schedules

Adults and young persons 16 years and over:

The Optimal dosage range is 500mg (5ml) to 1000mg (10ml) up to three to four times a day, as required, to a maximum of 4 g paracetamol/ day (40 ml paracetamol oral solution).

The dose should not be repeated more frequently than every four hours, and not more than four doses should be taken in any 24 hour period.

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

Paediatric Population
Do not use this medicine in children and adolescents under 16 years.

Method of administration
For oral administration only.

It is important to shake the bottle for at least 10 seconds well before use.

4.3 Contraindications

Hypersensitivity to paracetamol or any of the excipients listed in section 6.1.

Patients with severe hepatic dysfunction.

Do not use this medicine in children and adolescents under 16 years.

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 take with any other paracetamol-containing products.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment andsepsis or in patients with malnutrition or other sources of gluthione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Talk to a doctor at once if you take too much of this medicine, even if you feel well. This is because too much paracetamol can cause delayed, serious liver damage.

Do not exceed the recommended dose.

Keep out of the sight and reach of children.

Excipient warnings:

This product contains the following excipients:

Parahydroxybenzoates: these may cause allergic reactions (possibly delayed).

Propylene glycol: this medicine contains 1530 mg propylene glycol in each 5ml. Therefore, this medicine should be used with caution in pregnancy, breastfeeding, liver or kidney disease.

Glycerol: may cause headache, stomach upset and diarrhoea.
This medicine contains 4.25mg/5ml (0.18 mmol) of sodium which is essentially 'sodium free'.

4.5 Interaction with other medicinal products and other forms of interaction

The hepatotoxicity of Paracetamol, particularly after overdosage, may be increased by drugs which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants and alcohol.

Alcohol can increase the hepatotoxicity of paracetamol 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.

Antivirals: Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risk factors. (See section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy:
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.
A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Breast-feeding:
Paracetamol is excreted in breast milk but not in clinically significant amount. Available published data do not contraindicate breast feeding.

Fertility:
There are no data on the effects of this medicine on human fertility.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

The information below lists reported adverse reactions, ranked using the following frequency classification:
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse Events
Blood and lymphatic system disorders	Not known	Blood dyscrasia including thrombocytopenia and agranulocytosis[1]
Immune system disorders	Not known	Anaphylactic shock, angioedema, anaphylactic reaction, urticaria, hypersensitivity, rash
Metabolism and nutrition disorders	Not known	High anion gap metabolic acidosis[4]
Gastrointestinal disorders	Not known	Acute Pancreatitis[2]
Skin and subcutaneous disorders	Very Rare	Serious skin reactions
Renal and urinary disorders	Uncommon	Nephropathy toxic[3]

[1]But these were not necessarily causally related to Paracetamol.

[2]Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdosage.

[3]Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses, except after prolonged administration.

[4] Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal

product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

Symptoms:
Symptoms of paracetamol overdosage 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. Hyperglycaemia has been reported. 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 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 represent with serious hepatic dysfunction beyond 24h ingestion should be discussed with the NPIS or a liver unit.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics; Anilides
ATC Code: N02B E01

Mechanism of action:
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 an 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 20mcg/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.

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6.1 List of excipients

Citric acid monohydrate
Erythrosine (E127)
Glycerol (E 422)
Macrogol 400
Propylene Glycol (E 1520)
Methyl parahydroxybenzoate (E 218)
Propyl parahydroxybenzoate (E 216)
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.

Do not refrigerate or freeze.

Store in the original container.

Do not use 3 months after you first open it. Take it back to the pharmacy.

6.5 Nature and contents of container

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

A polypropylene syringe with 10ml measure along with adaptor is supplied with this pack.

Pack size: 300ml and 200ml
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special instruction

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals Ltd,

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69 Old Broad Street,

London, EC2M 1QS,

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 12762/0173

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13/02/2007 / 13/10/2011

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07/02/2025