1. NAME OF THE MEDICINAL PRODUCT

MANTRA DROPS (Paracetamol Oral Solution 100 mg/ml)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Paracetamol BP…..100 mg

3. PHARMACEUTICAL FORM

Oral Solution
A pink coloured syrup with a pleasant taste.

4. CLINICAL PARTICULARS

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.

` **Posology and method of administration**

For oral administration only.

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

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.

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.

Contraindications:

Hypersensitivity to paracetamol or any of the other components of the preparation.
Patients with severe hepatic dysfunction.
Do not use this medicine in children and adolescents under 16 years.

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.
Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed serious or irreversible 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 may cause alcohol like symptoms.
Glycerol: this is known to be harmful in high doses. It can cause headache, stomach upset and diarrhoea.

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).

Fertility,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.

Effects on ability to drive and use machines

None known.

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 overdosage with the drug.

Cases of acute pancreatitis have been reported. Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdosage.

Allergic reactions occur occasionally.

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

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. 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.

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. PHARMACOLOGICAL PROPERTIES

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.

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.

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

List of excipients

Propylene Glycol

Glycerin

Alcohol (Ethanol 96%)

PVP- K30

Citric Acid

Methyl paraben

Propyl paraben

Sodium Saccharin

Sodium Metabisulphite

Incompatibilities

None

Shelf life

3 years

Special precautions for storage

Store in cool & dry place, below 30°C.

Nature and contents of container

20 ml Amber Glass Bottle

7. MARKETING AUTHORISATION HOLDERJAWA

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