1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 250 mg/5 ml Oral Suspension

Six Plus Parapaed 250mg/5ml Oral Suspension

Galpharm Six Plus Pain Relief 250 mg/5 ml Oral Suspension

Tesco Paracetamol 250mg/5ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml spoonful contains Paracetamol 250mg,
Hydrogenated Glucose Syrup 3470mg,
Glycerol 63.10 mg and Ethanol 96% 148.93 mg.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral Suspension.

Cream/white to brown oral suspension with strawberry odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of mild to moderate pain and as an anti-pyretic.
It can be used in many conditions including headache, toothache, earache, sore throat, colds and influenza, aches and pains and post-immunisation fever.

4.2 Posology and method of administration

Child's Age	How Much	How often (in 24 hours)
6 – 8 years	One 5 ml spoonful (large end)	4 times
8 – 10 years	One 5.0 ml spoonful (large end) and one 2.5 ml spoonful (small end)	4 times
10 – 12 years	Two 5 ml spoonfuls (large end)	4 times
• Do not give more than 4 doses in any 24 hour period • Leave at least 4 hours between doses • Do not give this medicine to your child for more than 3 days without speaking to your doctor or pharmacist • Do not give to children under the age of 6 years		

Children aged 12 - 16 years: Two – three 5 ml spoonfuls (large end) up to 4 times a day.

Adults and children over 16 years: Two – four 5 ml spoonfuls (large end) up to 4 times a day.

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

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

4.3 Contraindications

Hypersensitivity to Paracetamol or any of the other constituents.

Patients with rare hereditary problem of fructose intolerance should not take this medicine.

4.4 Special warnings and precautions for use

Paracetamol Oral Suspension 250mg/5ml should be used with caution in severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease

Hydrogenated glucose syrup may have a laxative effect. Each 5 ml spoonful of this product contains 3.93g of hydrogenated glucose syrup. Calorific value 2.3 kcal/g of hydrogenated glucose syrup.

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 and sepsis, or in patients with malnutrition and other sources of glutathione 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.

The label should contain the following statements:

- Contains paracetamol.
- Do not give this medicine with any other paracetamol-containing product.
- For oral use only.
- Never give more medicine than shown in the table.
- Do not overfill the spoon.
- Always use the spoon supplied with the pack.
- Do not give more than 4 doses in any 24 hour period.
- Leave at least 4 hours between doses.
- Do not give this medicine to your child for more than 3 days without speaking to your doctor or pharmacist.
- As with all medicines, if your child is currently taking any medicine consult your doctor or pharmacist before taking this product.
- Do not store above 25°C. Store in the original package.

- Keep all medicines out of the reach and sight of children.
- Immediate medical advice should be sought in the event of an overdose, even if the child seems well (label).
- 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 (leaflet).

4.5 Interaction with other medicinal products and other forms of interaction

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

The anti-coagulant 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.

Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual's ability to metabolise larger doses of paracetamol, the plasma half-life of which can be prolonged.

The use of drugs which induce hepatic microsomal enzymes such as anti-convulsants or oral contraceptives may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentration of the drug and a faster elimination rate.

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 risks factors (see section 4.4)

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. 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.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data does not contraindicate breast-feeding.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

Adverse effects of Paracetamol are rare. Very rare cases of serious skin reactions have been reported. Very rarely hypersensitivity and anaphylactic reactions 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.

Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of the disease improved after paracetamol withdrawal.

SOC Metabolism and nutrition disorders

"High anion gap metabolic acidosis'' with frequency ''Not known'' (cannot be estimated from the available data)

Description of selected adverse reactions
High anion gap metabolic acidosis
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.

4.9 Overdose

Liver damage is possible in adults who have taken 10g or more 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 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 serve poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death. Acute renal failure with acute tubular necrosis, strongly suggest by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatits have been reports.

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.

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 concentration 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 suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24 hours form ingestion should be discussed with the NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol is an antipyretic analgesic, N02B E01. The mechanism of action is probably similar to that of aspirin and dependent on the inhibition of prostaglandin synthesis. This inhibition appears, however to be on a selective basis.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastro-intestinal tract. The concentration in plasma reaches a peak in 30 to 60 minutes and the half life in plasma is 1 to 4 hours after therapeutic doses. Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of the drug to plasma proteins is variable; 20 to 50% may be bound at the concentrations encountered during acute intoxication. Following therapeutic doses 90 to 100% of the drug may be recovered in the urine within the first day. However, practically no Paracetamol is excreted unchanged, and the bulk is excreted after hepatic conjugation.

5.3 Preclinical safety data

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

Mutagenicity

There are no studies relating to the mutagenic potential of Paracetamol Oral Suspension 250mg/5ml.

In vivo mutagenicity tests of paracetamol in mammals are limited and show conflicting results. Therefore, there is insufficient information to determine whether paracetamol poses a mutagenic risk to man.

Paracetamol has been found to be non-mutagenic in bacterial mutagenicity assays, although a clear clastogenic effect has been observed in mammalian cells in vitro following exposure to paracetamol (3 and 10 mM for 2h).

Carcinogenicity

There are no studies to the carcinogenic potential of Paracetamol Oral Suspension 250mg/5ml.

There is inadequate evidence to determine the carcinogenic potential of paracetamol in humans. A positive association between the use of paracetamol and cancer of the ureter (but not of other sites in the urinary tract) was observed in a case-control study in which approximate lifetime consumption of paracetamol (whether acute or chronic) was estimated. However, other similar studies have failed to demonstrate a statistically significant association between paracetamol and cancer of the urinary tract, or paracetamol and renal cell carcinoma.

There is limited evidence for the carcinogenicity of paracetamol in experimental animals. Liver cell tumours can be detected in rats following chronic feeding of 500 mg/kg/day paracetamol.

Teratogenicity

There is no information relating to the teratogenic potential of Paracetamol Oral Suspension 250mg/5ml.

In humans, paracetamol crosses the placenta and attains concentrations in the foetal circulation similar to those in the maternal circulation. Intermittent maternal ingestion of therapeutic doses of paracetamol are not associated with teratogenic effects in humans.

Paracetamol has been found to be foetotoxic to cultured rat embryo.

Fertility

There is no information relating to the effects of Paracetamol Oral Suspension 250mg/5ml on fertility. A significant decrease in testicular weight was observed when male Sprague-Dawley rats were given daily high doses of paracetamol (500 mg/kg/body weight/day) orally for 70 days.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol (96%)
Sorbitan Monooleate
Glycerol (E422)
Microcrystalline Cellulose and Carmellose Sodium
Hydrogenated Glucose Syrup (E965)
Saccharin Sodium (E954)
Xanthan Gum
Strawberry Flavour
Sodium Benzoate (E211)
Citric Acid (monohydrate)
Polysorbate 80
Purified Water.

6.2 Incompatibilities

None known.

6.3 Shelf life

Amber glass bottles – 2 years

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original container.

6.5 Nature and contents of container

Pharmaceutical grade III amber glass bottles with child resistant tamper evident caps.
Pack sizes: 70 ml and 80 ml.
A spoon with a 5 ml and 2.5 ml measure is supplied.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Limited
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 04917/0081

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/12/2024

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13/04/2026