Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Six Plus Parapaed Paracetamol Oral Suspension 250 mg/5 ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains 250mg of Paracetamol.

Excipients:
Liquid Maltitol (E965) 3.93g/5ml (equivalent to 2.95g dry substance)
Ethanol 96% 150.00mg/5ml
Sunset Yellow (E110) 0.30mg/5ml

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral suspension,
Orange to orange/brown coloured suspension with an orange flavour and odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As an analgesic or anti-pyretic in the treatment of teething pain, toothache, headache, migraine, neuralgia, sore throat, feverishness, colds, flu and post-immunisation fever.

4.2 Posology and method of administration

Oral 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.

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

4.3 Contraindications

Hypersensitivity to paracetamol or any of its constituents.

4.4 Special warnings and precautions for use

- Do not give with any other paracetamol-containing products.
- 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.
- Keep all medicines out of the reach and sight of children.

Contains Paracetamol. Prolonged use except under medical supervision can be harmful. If symptoms persist, your doctor should be consulted.

Immediate medical advice should be sought in the event of an overdose, even if the patient feels well because of the risk of irreversible liver damage.

Caution is recommended in patients with hepatic and renal impairment or alcohol dependence. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Patients with rare hereditary problems of fructose intolerance should not take this medicine. This product contains Liquid Maltitol (E965), calorific value 2.3 kcal/g. Each 5 ml dose contains 3.93g {equivalent to 2.95g dry substance}.

Each 5ml dose contains 150mg of 96% ethanol (alcohol), equivalent to 3.6 ml beer or 1.5ml of wine. Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high risk groups such as patients with liver disease or epilepsy.

Sunset Yellow (E110) may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interactions

Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose. Barbiturates, tricyclic antidepressants and acute alcohol intake may decrease the ability to metabolise large doses of paracetamol, the plasma life of which can be prolonged.
Drugs that induce hepatic microsomal enzymes e.g. oral contraceptives and anti-convulsants may increase the metabolism of paracetamol, resulting in decreased plasma concentration and a faster elimination rate of the drug.
Anion-exchange resins: Cholestyramine reduces adsorption of paracetamol.
Domperidone and Metoclopramide: Metoclopramide accelerated absorption of paracetamol (enhanced effect)
Anticoagulants: Prolonged regular use of paracetamol possibly enhances warfarin with increased risk of bleeding.
Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4)

4.6 Fertility, pregnancy and lactation

Problems in humans have not been documented. However, controlled studies have not been carried out. Risk-Benefit must be considered since paracetamol crosses the placenta and is excreted in breast milk. 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.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Side effects at therapeutic doses are rare with most reports of adverse reactions to Paracetamol relating to overdosage of the drug.

Very rare cases of serious skin reactions have been reported.

Blood and lymphatic system disorders	
Very rare (< 1/10,000)	Blood disorders, thrombocytic purpura, haemolytic anaemia and agranulocytosis.
Gastrointestinal disorders	
Very rare (< 1/10,000)	Acute pancreatitis
Immune system disorders	
Very rare (< 1/10,000)	Hypersensitivity
Hepatobiliary disorders	
Very rare (< 1/10,000)	Hepatic necrosis
Skin and subcutaneous tissue disorders	
Rare (< 1/1,000)	Skin rash
Renal and urinary disorders	
Uncommon (> 1/1000, < 1/100)	Nephrotoxic effects
Very rare (< 1/10,000)	Papillary necrosis

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

As little as 10-15g may cause severe hepatocellular necrosis and, less frequently, renal tubular necrosis. Nausea and vomiting, the only early features of poisoning, usually settle within 24 hours. Persistence beyond this time, often associated with onset of right subcostal pain and tenderness usually indicates development of hepatic necrosis. Liver damage is maximal 3-4 days after ingestion and may lead to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death.

Therefore despite a lack of significant early symptoms, patients who have taken an overdose of paracetamol should be transferred to hospital urgently. Gastric emptying is carried out if the overdose was taken within 4 hours of hospital admission. Antidotes such as acetylcysteine and methionine protect the liver if given within 10-12 hours of ingestion; acetylcysteine may also be effective up to and beyond 15 hours but expert advice is essential.

Patients at risk of liver damage and therefore requiring treatment can be identified from a single measurement of the plasma-paracetamol concentration, related to the time from ingestion provided this time interval is not less than 4 hours; earlier samples may be misleading.

The concentration is compared against a reference line joining plots of 200 mg/litre (1.32 mmol/litre) at 4 hours and 30 mg/litre (0.2 mmol/litre) at 15 hours, on a semi-logarithmic graph. Those whose concentrations are above that line are treated either with acetylcysteine intravenously or with methionine by mouth.

Patients on enzyme-inducing drugs (e.g. Carbamazepine, phenobarbitone, phenytoin, rifampicin, and alcohol) may develop toxicity at lower plasma-paracetamol concentration; they should be treated with acetylcysteine if their plasma-paracetamol is 50% or more of the standard reference line. In remote areas, emesis should be induced if the patient presents symptoms within 4 hours of the overdose.

Methionine (2.5g) should be given by mouth once vomiting has occurred; it is seldom practical to give acetylcysteine outside hospital. Once the patient reaches hospital the need to continue treatment with the antidote will be assessed from the plasma-paracetamol concentration (related to the time from ingestion).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N02BE01
Pharmaceutical group: Other analgesics and antipyretics – Anilides

Paracetamol has analgesic and anti-pyretic properties but no anti-inflammatory properties except at very high doses. Paracetamol inhibits prostaglandin synthesis, more centrally than peripherally.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and completely absorbed from the gastrointestinal tract. Paracetamol is rapidly distributed throughout the body and is primarily metabolised in the liver. About 85% is conjugated with glucuronide and sulphate and about 10% is conjugated with glutathione.

Excretion of the biotransformation products is via the kidney. The elimination half life is approximately 2-3 hours.

In overdose, glucuronide pathways become saturated and excess paracetamol is metabolised via the glutathione hepatic pathway. Hepatic glutathione is rapidly depleted and an intermediate hydroxylamine metabolite accumulates and binds to liver proteins causing irreversible damage.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium magnesium Silicate
Xanthan gum
Glycerol (E422)
Liquid maltitol (E965)
Sodium benzoate (E211)
Citric acid monohydrate
Saccharin sodium (E954)
Polysorbate 80
Sorbitan oleate
Ethanol 96%
Orange Flavour
Sunset yellow (E110)
Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container to protect from moisture/light

6.5 Nature and contents of container

Amber glass bottles, with HDPE child resistant screw cap.
Pack sizes: 70 ml, 100 ml, 140 ml, 150 ml, 200 ml, 500 ml, 1 litre, 2 litre.
A spoon with a 2.5 ml and 5 ml measure is supplied with the 70 ml-200 ml pack sizes.

High density polyethylene bottle, with HDPE child resistant cap.
Pack sizes: 500 ml, 1 litre, 2 litre.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Ltd,
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0281/002/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 May 1994

Date of last renewal: 20 May 2009

10 DATE OF REVISION OF THE TEXT

May 2022