1 NAME OF THE MEDICINAL PRODUCT

Paracetamol 120 mg/5 ml Oral Suspension
Junior Parapaed 120mg/5ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml spoonful contains Paracetamol 120 mg.
For excipients, see 6.1

3 PHARMACEUTICAL FORM

Oral Suspension.
Cream to brown oral suspension with cherry odour and taste.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of mild to moderate pain and as an anti-pyretic. Used for the relief of pain and feverishness associated with teething, toothache, headache, colds, flu and post-immunisation pyrexia.

4.2 Posology and method of administration

For the relief of fever after vaccinations at 2, 3 and 4 months
2.5ml. This dose may be given up to 4 times a day starting at the time of vaccination. Do not give more than 4 doses in any 24 hour period. Leave at least 4 hours between doses. If your baby still needs this medicine two days after receiving the vaccine talk to your doctor or pharmacist.

Age: 2-3 months	**Dose**

Pain and other causes of fever – if your baby weighs over 4 kg and was born after 37 weeks	2.5 ml If necessary, after 4-6 hours, give a second 2.5 ml dose

- Do not give to babies less than 2 months of age
- Leave at least 4 hours between doses
- Do not give more than 2 doses. This is to ensure that fever that may be due to a serious infection is quickly diagnosed. If your child is still feverish after two doses, talk to your doctor or pharmacist.

Children aged 3 months – 6 years:

Child's Age	How Much	How often (in 24 hours)
3 – 6 months	2.5 ml	4 times
6 – 24 months	5 ml	4 times
2 – 4 years	7.5ml (5ml + 2.5ml)	4 times
4 – 6 years	10ml (5ml + 5ml)	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

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.

4.4 Special warnings and precautions for use

Care is advised in the administration of paracetamol to patients with severe renal impairment or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

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 to babies less than 2 months of age.
- For infants 2-3 months do not give more than 2 doses This is to ensure that fever that may be due to a serious infection is quickly diagnosed. If your child is still feverish after two doses, talk to your doctor or pharmacist.
- 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.
- If your baby still needs this medicine two days after receiving the vaccine talk to your doctor or pharmacist (leaflet).
- 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 sight and reach of children
- Talk to a doctor at once if your child takes too much of this medicine, even if they seem well (label).
- Talk to a doctor at once if your child takes too much of this medicine, even if they seem well. This is because too much paracetamol can cause delayed, serious liver damage (leaflet).

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

4.5 Interaction with other medicinal products and other forms of interaction

Drugs which induce hepatic microsomal enzymes such as alcohol. Concomitant barbiturates and tricyclic antidepressants may increase the hepatoxicity of Paracetamol particularly after overdose. Anti-convulsant or oral steroid contraceptives have the ability to reduce serum levels of Paracetamol by liver enzyme induction.
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.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.

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.

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 large doses of paracetamol, the plasma half-life of which can be prolonged.

The use of drugs that induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptives, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations 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 do 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 anaphylatic 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.

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

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 their disease improved after paracetamol withdrawal.

Nephrotoxicity following therapeutic doses of paracetamol is uncommon, but papillary necrosis has been reported after prolonged administration.

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 10 g or more of paracetamol. Ingestion of 5 g or more of Paracetamol may lead to liver damage if the patient has 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, 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 one 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 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 24 h from ingestion should be discussed with the NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol is an antipyretic analgesic. ATC code: 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 Calpol Sugar Free Infant Suspension Sachets.

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 Calpol Sugar Free Infant Suspension Sachets.

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 Calpol Sugar Free Infant Suspension Sachets. 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 Calpol Sugar Free Infant Suspension Sachets 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)
Magnesium Aluminium Silicate
Liquid Maltitol Syrup (E965)
Saccharin Sodium (E954)
Xanthan Gum
Cherry Flavour
Sodium Benzoate (E211)
Citric Acid (monohydrate)
Polysorbate 80 (E433)
Purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

Amber glass bottles – 5 years

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Pharmaceutical grade III amber glass bottles with child resistant, tamper evident caps.
Pack sizes: 70 ml and 100 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 04917/0083

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27/11/2009 / 29/10/2024

10 DATE OF REVISION OF THE TEXT

10/01/2026