SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

CALPOL Infant Sugar Free Colour Free 120 mg/5 ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

CALPOL Infant Sugar Free Colour Free 120 mg/5 ml Oral Suspension contains 120 mg Paracetamol in each 5 ml.

Excipients: maltitol liquid ((E965) contains 2.72 g maltitol liquid in each 5ml), sorbitol liquid ((E420) contains 0.97 g of sorbitol liquid per 5ml), sodium (contains 0.86mg per 5ml), benzyl alcohol, propylene glycol (E1520), methyl parahydroxybenzoate (E218), ethyl parahydroxybenzoate (E214) and propyl parahydroxybenzoate (E216). See section 4.4 for further information.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral Suspension.

An off-white strawberry flavoured suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

CALPOL Infant Sugar Free Colour Free 120 mg/5 ml Oral Suspension is indicated for the treatment of mild to moderate pain and as an antipyretic. It can be used in many conditions including headache, toothache, earache, teething, sore throat, colds and influenza, aches and pains and post-immunisation fever.

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	7.5 ml (5 ml + 2.5 ml)	4 times
4 – 6 years	10 ml (5 ml + 5 ml)	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.

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.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Do not exceed the recommended dose. Taking more than the recommended dose (overdose) may cause liver damage. In case of overdose, get medical help straight away. Quick medical attention is critical for adults as well as children even if signs or symptoms are not noticed.

Taking this product with other paracetamol-containing medicines could lead to overdose and should therefore be avoided.

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. Chronic alcohol users should consult a doctor before use.

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 or 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.

Sorbitol and maltitol may cause gastrointestinal discomfort and have a mild laxative effect. Each 5 ml spoonful of this product contains 0.97 g sorbitol liquid and 2.72 g of maltitol liquid. Calorific values: 2.6 kcal/g sorbitol and 2.3 kcal/g maltitol.

Due to the presence of maltitol liquid (E965) and sorbitol liquid (E420), patients with rare hereditary problems of fructose intolerance should not take this medicine.

Ethyl (E214), Propyl (E216) and Methyl (E218) parahydroxybenzoate may cause allergic reactions (possibly delayed).
This medicine contains less than 1 mmol sodium (23 mg) per 5 ml, that is to say essentially ‘sodium-free’.

This medicine contains 14.32 mg propylene glycol (E1520) in each 5 ml dose, which is equivalent to 2.86 mg/ml. Caution in babies less than 4 weeks old. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates.

This medicine contains 0.16 mg benzyl alcohol in each 5 ml which is equivalent to 0.03 mg/ml. Benzyl alcohol may cause allergic reactions. Benzyl alcohol has been linked with the risk of severe side effects including breathing problems ("gasping syndrome") in young children. Caution in newborn babies (up to 4 weeks old). Caution in children under 3 years old; do not use for more than 1 week due to increased risk due to accumulation.

Ask your doctor or pharmacist for advice if you are pregnant or breastfeeding, or if you have a liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis")

Patients should be informed about the signs of serious skin reactions and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

<u>The label contains the following statements:</u>
Contains paracetamol.
Do not give anything else containing paracetamol while giving this medicine.
Do not give more medicine than the label tells you to. If your child does not get better, talk to your doctor.
For oral use only.
Always use the syringe supplied with the pack. Do not give to babies less than 2 months of age.
For infants 2-3 months no more than 2 doses should be given. 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 other medicine consult your doctor or pharmacist before using this product.
Keep out of the sight and reach of children.
Do not store above 25°C. Keep bottle in the outer carton.
It is important to shake the bottle for at least 10 seconds before use.
Talk to a doctor at once if your child takes too much of this medicine, even if they seem well.

<u>The leaflet contains the following statements:</u>
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.

Very rare cases of serious skin reactions have been reported. Symptoms may include:
- Skin reddening

- Blisters
- Rash

If skin reactions occur or existing skin symptoms worsen, stop use and seek medical help right away.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs which induce hepatic microsomal enzymes
Metabolism of paracetamol possibly accelerated by carbamazepine, fosphenytoin, phenytoin, phenobarbital, primidone (also isolated reports of hepatotoxicity).

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.

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).

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.

4.6 Fertility, pregnancy and lactation

Pregnancy
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.

When given to the mother in therapeutic doses (1 g single dose), paracetamol crosses the placenta into foetal circulation as early as 30 minutes after ingestion and is metabolised in the foetus by conjugation with sulfate and increasingly with glutathione.

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

Fertility
There is no information relating to the effects of this medicine on fertility.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Adverse drug reactions (ADRs) identified during clinical trials and post marketing experience with paracetamol are listed below by System Organ Class (SOC).

The frequencies are defined according to the following convention:

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).

ADRs are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available or 2) when incidence is unavailable, frequency category is listed as Not known.

System Organ Class (SOC)	Frequency	Adverse Drug Reaction (Preferred Term)
Blood and lymphatic system disorders	Not known	Blood disorder (including thrombocytopenia and agranulocytosis) [1]
Immune System Disorders	Very rare Very rare	Anaphylactic reaction Hypersensitivity
Hepatobiliary disorders	Not known	Liver injury[2]
Skin and Subcutaneous Tissue disorders	Very rare Not known Not known Not known	Rash Fixed eruption Rash pruritic Urticaria
Renal and urinary disorders	Uncommon Not known	Nephropathy toxic Renal papillary necrosis[3]
Investigations	Not known	Transaminases increased[4]
Metabolism and nutrition disorders	Not known	High anion gap metabolic acidosis

[1] Reported following paracetamol use, but not necessarily causally related to the drug

[2] Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year

[3] Reported after prolonged administration

[4] Low level transaminase elevations may occur in some patients taking therapeutic doses of paracetamol; these elevations are not accompanied with liver failure and usually resolve with continued therapy or discontinuation of paracetamol.

Very rare cases of serious skin reactions have been reported.

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.

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 or search for MHRA Yellow Card in the Google Play or Apple App Store

4.9 Overdose

Liver damage is possible in adults and adolescents (≥12 years of age) who have taken 7.5gor more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue. 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, hyperhidrosis, malaise, vomiting, anorexia, and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. This may include hepatomegaly, liver tenderness, jaundice, acute hepatic failure and hepatic necrosis.

Abnormalities of glucose metabolism and metabolic acidosis may occur. Blood bilirubin, hepatic enzymes, INR, prothrombin time, blood phosphate and blood lactate may be increased.

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.

Haemolytic anaemia (in patients with glucose-6-phosphate dehydrogenase [G6PD] deficiency): Haemolysis has been reported in patients with G6PD deficiency, with use of paracetamol in overdose.

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 the 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 concentrations 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 patient who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Analgesics and Antipyretics (Anilides)
ATC Code: N02 BE01

Paracetamol has analgesic and antipyretic effects similar to those of aspirin and is useful in the treatment of mild to moderate pain. It has only weak anti-inflammatory effects.

5.2 Pharmacokinetic properties

Absorption
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations are reached 30-90 minutes post dose and the plasma half-life is in the range of 1 to 3 hours after therapeutic doses.

Distribution
Drug is widely distributed throughout most body fluids.

Biotransformation
Metabolism occurs almost entirely via hepatic conjugation with glucuronic acid (about 60%), sulphuric acid (about 35%) or cysteine (about 3%). Small amounts of hydroxylated and deacetylated metabolites have also been detected.

Children have less capacity for glucuronidation of the drug than do adults.

In overdosage there is increased N-hydroxylation followed by glutathione conjugation. When the latter is exhausted, reaction with hepatic proteins is increased leading to necrosis.

Elimination
Following therapeutic doses 90-100% of the drug is recovered in the urine within 24 hours.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity, genotoxicity, and carcinogenicity.

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

Maltitol liquid (E965)
Sorbitol liquid (non crystallising) (E420)
Glycerol
Microcrystalline cellulose and carmellose sodium
Xanthan gum
Ethyl parahydroxybenzoate (E214)
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Polysorbate 80
Strawberry Flavour 500286E (containing propylene glycol (E1520) and benzyl alcohol)
Purified water

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C. Keep bottle in the outer carton.

6.5 Nature and Contents of Container

Amber glass bottle with a two-piece white plastic child-resistant external cap, fitted with an inner plastic cap, including a tamper evident ring fitted with a polyethylene or polyvinylidene chloride (PVDC) polyethylene laminate faced wad.

Or

Amber glass bottle with a two-piece white plastic child-resistant external cap (in polypropylene), fitted with an inner plastic cap, including a tamper evident ring, in high density polyethylene (HDPE). The cap contains a plug made of Low Density Polyethylene (LDPE).

Or

Amber glass bottle with a two-piece white plastic child-resistant external cap (in polypropylene), fitted with an inner plastic cap, including a tamper evident ring, in high density polyethylene (HDPE). A HDPE disk platine and a Press-In-Bottle Adapter (PIBA, commonly named plug), made of Low-Density Polyethylene (LDPE).

Pack sizes
70 ml and 100 ml. A syringe with a 5 ml and 2.5 ml measure is supplied with this pack. Not all pack sizes may be marketed.

6.6 Special precautions for disposal <and other handling>

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited
50 – 100 Holmers Farm Way

High Wycombe
Buckinghamshire
HP12 4EG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 15513/0300

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15/10/2024

10 DATE OF REVISION OF THE TEXT

20/03/2025