Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Calpol 120 mg/5 ml Infant Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Calpol Infant Oral Suspension contains -

Paracetamol 120 mg per 5 ml.

Excipients with known effect (per 5ml):
Sucrose 2202.48mg
Sorbitol Liquid (E420) 451.5mg
Propylene glycol (E1520) 13.63mg
Methyl parahydroxybenzoate (E218) 5.0mg
Propyl parahydroxybenzoate (E216) 1.0mg
Ethyl parahydroxybenzoate (E214) 2.0mg
Sodium 0.86mg
Carmoisine (E122) 0.075mg
Ethanol 0.008mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral suspension.
A viscous pink coloured suspension with a strawberry odour and taste.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Calpol Infant Suspension is indicated for the treatment of pain (including teething pain), and as an antipyretic.

4.2 Posology and method of administration

Infants aged 2-3 months:

Age : 2 – 3 months	**Dose**
1 . Post-vaccination fever	2.5 ml If necessary, after 4 - 6 hours, give a second 2.5 ml dose
2 . Other causes of Pain and Fever - if your baby weighs over 4 kg and was born after 37 weeks	

- Do not give to babies less than 2 months of age.
- Do not give more than 2 doses unless your doctor or nurse has advised otherwise.
- Leave at least 4 hours between doses.
- If further doses are needed, talk to your doctor or pharmacist.
- It is important to **shake the bottle** for at least 10 seconds before use.

Children aged 3 months – 6 years:

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

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.

Hepatic/renal dysfunction:
Caution should be excercised when administration the product to patient with severe hepatic or renal impairment.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Paracetamol should be administered with caution under the following circumstances (see section 4.2):

- Hepatic impairment
- Chronic alcoholism
- Renal impairment (GFR≤50ml/min)
- Gilbert's Syndrome (familial non-haemolytic jaundice)
- Concomitant treatment with medicinal products affecting hepatic function
- Glucose-6-phosphate dehydrogenase deficiency
- Haemolytic anaemia
- Glutathione deficiency
- Dehydration
- Chronic malnutrition
- Patients who are underweight (for adults, those under 50 kg)
- Elderly

In general, medicinal products containing paracetamol should be taken for only a few days without the advice of a physician or dentist and not at high doses.

If high fever or signs of secondary infection occur or if symptoms persist for longer than 3 days, a physician should be consulted.

Prolonged or frequent use is discouraged. Patients should be advised not to take other paracetamol containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver; in such cases medical assistance should be sought immediately.

Serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens - Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), have been reported very rarely in patients receiving paracetamol. 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.

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.

This product contains the following excipients which have recognised effects:

- Sucrose and sorbitol. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. Contains 2.2 g of sucrose per 5 ml. This should be taken into account in patients with diabetes mellitus.
- Sorbitol may cause gastrointestinal discomfort and have a mild laxative effect.
- Carmoisine (E122) which may cause allergic reactions.
- Methyl parahydroxybenzoate (E218), Propyl parahydroxybenzoate (E216), Ethyl parahydroxybenzoate (E214) which may cause allergic reactions (possibly delayed).
- This medicine contains less than 1 mmol sodium (23 mg) per 5ml, that is to say essentially 'sodium-free'.
- This medicine contains 13.63mg propylene glycol (E1520) in each 5ml dose, which is equivalent to 2.73mg/ml.
- This medicine contains 0.0007785mg of alcohol (ethanol) in each 5ml which is equivalent to 0.0001557 mg/ml. The amount in 5 ml is equivalent to less than 1ml beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

4.5 Interaction with other medicinal products and other forms of interactions

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.

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, especially in patients with risks factors (see section 4.4).

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 possible dose, for the shortest possible time at the lowest possible frequency.

When given to the mother in labelled doses, paracetamol crosses the placenta into the foetal circulation as early as 30 minutes after ingestion and is effectively metabolised by foetal sulphate conjugation.

Breastfeeding
Paracetamol is excreted in breast milk in low concentrations (0.1% to 1.85% of the ingested maternal dose). Maternal ingestion of paracetamol at the recommended dose is not considered to present a risk to the nursing infant.

4.7 Effects on ability to drive and use machines

Calpol has no or negligible influence on the ability to drive and use machines.

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 and < 1/10
Uncommon ≥1/1,000 and <1/100
Rare≥ 1/10,000 and <1/1,000
Very rare <1/10,000
Not known (cannot be estimated from the available data)

The ADRs identified 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 category	Adverse Drug Reaction Preferred Term
Blood and lymphatic system disorders	Not known	Agranulocytosis
	Not known	Haemolytic anaemia
	Not known	Thrombocytopenic purpura
Immune system disorders	Rare	Hypersensitivity
	Not known	Anaphylactic reaction
Hepatobiliary disorders	Not known	Hepatic function abnormal
	Not known	Hepatic necrosis
Skin and subcutaneous tissue disorders	Rare	Rash
	No known	Fixed eruption
	Not known	Rash pruritic
	Not known	Urticaria
Renal and urinary disorders	Uncommon	Nephropathy toxic
	Not known	Renal papillary necrosis (after prolonged administration)
Investigations	Not known	Transaminases increased

Liver damage has been reported after daily ingestion of excessive amounts of paracetamol. 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.

Low level transaminase elevations may occur in some patients taking labelled 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.

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, website: www.hpra.ie.

4.9 Overdose

Symptoms and signs

Hepatic necrosis is a dose-related complication of paracetamol overdose. In adults and adolescents (> 12 years of age), hepatic toxicity may occur following ingestion of greater than 7.5 to 10 grams over a period of 8 hours or less. Fatalities are infrequent

(less than 3-4% of untreated cases) and have rarely been reported with overdoses of less than 15 grams. In children (<12 years of age), an acute overdosage of less than 150 mg/kg has not been associated with hepatic toxicity.
It is considered that excess quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue.

Early symptoms following a potentially hepatotoxic overdose may include: anorexia, nausea, vomiting, diaphoresis, pallor and general malaise.

If a paracetamol extended release product is involved, it may be appropriate to obtain an additional plasma paracetamol level 4-6 hours following the initial paracetamol level.

Serious toxicity or fatalities have been extremely infrequent following an acute paracetamol overdose in young children, possibly because of differences in the way they metabolize paracetamol.

In paracetamol overdosage with liver cell damage, paracetamol half-lifeis often prolonged from around 2 hours in normal adults to 4 hours or longer. However liver cell damage has been found in patients with a paracetamol half life less than 4 hours. Diminution of $^{14}CO_2$ excretion after ^{14}C-aminopyrine has been reported to correlate better with liver cell damage in paracetamol overdosage than do either plasma paracetamol concentration or half-life, or conventional liver function test measurements.

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, phenobarbital, 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.

The following are clinical events associated with paracetamol overdose that if seen with overdose are considered expected, including fatal events due to fulminant hepatic failure or its sequelae.

Adverse Drug Reactions Identified with Overdose of Paracetamol

Metabolism and Nutrition Disorders:
Anorexia

Gastrointestinal Disorders:
Vomiting, Nausea, Abdominal discomfort

Hepatobiliary Disorders:
Hepatic necrosis, Acute hepatic failure, Jaundice, Hepatomegaly, Liver tenderness

General Disorders and Administration Site Conditions:
Pallor, Hyperhidrosis, Malaise

Investigations:
Blood bilirubin increased, Hepatic enzymes increased, International normalised ratio increased, Prothrombin time prolonged, Blood phosphate increased, Blood lactate increased

The following clinical events are sequelae to acute hepatic failure and may be fatal. If these events occur in the setting of acute hepatic failure associated with paracetamol overdose (adults and adolescents: ≥12 years of age: >7.5 g within 8 hours; children <12 years of age: >150 mg/kg within 8 hours), they are considered expected.

Expected Sequelae to Acute Hepatic Failure Associated with Paracetamol Overdose

Infections and Infestations:
Sepsis, Fungal infection, Bacterial infection

Blood and Lymphatic System Disorders:
Disseminated intravascular coagulation, Coagulopathy, Thrombocytopenia

Metabolism and Nutrition Disorders:
Abnormalities of glucose metabolism, Hypoglycaemia, Hypophosphatemia, Metabolic Acidosis, Lactic Acidosis

Nervous System Disorders:
Coma (with massive paracetamol overdose or multiple drug overdose), Encephalopathy, Brain oedema

Cardiac Disorders:
Cardiomyopathy, Cardiac arrhythmias

Vascular Disorders:
Hypotension

Respiratory, Thoracic and Mediastinal Disorders:
Respiratory failure

Gastrointestinal Disorders:
Pancreatitis, Gastrointestinal haemorrhage

Renal and Urinary Disorders:
Acute renal failure with acute tubular necrosis

General Disorders and Administration Site Conditions:
Multi-organ failure

Treatment
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 and any patient who had ingested around 7.5 g or more of paracetamol in the preceding 4 hours should undergo gastric lavage. Administration of oral methionine or intravenous N-acetylcysteine which may have beneficial effect up to at least 48 hours after overdose may be required. General supportive measures must be available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N02BE01 - Other analgesics and antipyretics
Paracetamol is a centrally acting, non-opiate, non-salicylate analgesic. Paracetamol is a clinically proven analgesic/antipyretic, and it is thought to produce analgesia by elevation of the pain threshold and antipyresis through action on the hypothalamic heat-regulating centre. Single-dose studies (12.5 mg/kg) of paracetamol in febrile children showed an onset of fever reduction within 15 to 30 minutes.

5.2 Pharmacokinetic properties

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. Drug is widely distributed throughout most body fluids. Following therapeutic doses 90-100% of the drug is recovered in the urine within 24 hours almost entirely following 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.

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

Sucrose
Sorbitol Liquid (non-crystallising) (E420)
Glycerol
Xanthan gum
Dispersible Cellulose
Polysorbate 80
Acesulfame Potassium
Strawberry flavour, 500018E (containing propylene glycol (E1520) and ethanol)
Methyl Parahydroxybenzoate (E218)
Propyl Parahydroxybenzoate (E216)
Ethyl Parahydroxybenzoate (E214)
Carmoisine (E122)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container

6.5 Nature and contents of container

A. 60ml, 70ml, 100ml and 140ml amber glass bottle with a two-piece plastic child resistant, tamper evident closure fitted with a polyethylene or polvinylidine chloride (PVDC) laminate faced wad. A spoon with a 5 ml and 2.5 ml measure is supplied with all packs of this product.

B. 60ml, 70ml, 100ml and 140ml amber glass bottle with a three-piece plastic child resistant, tamper evident closure fitted with a polyethylene or polvinylidine chloride (PVDC) laminate faced wad. A spoon with a 5 ml and 2.5 ml measure is supplied with all packs of this product.

C. 60ml, 70ml, 100ml and 140ml 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). A measuring syringe is provided in the secondary packaging. The syringe is made of polypropylene for the barrel and of violet-coloured high density polyethylene (HDPE) for the plunger.

D. 60ml, 70ml, 100ml and 140ml 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). A measuring syringe is provided in the secondary packaging. The syringe is made of polypropylene for the barrel and of violet-coloured high density polyethylene (HDPE) for the plunger.

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

Johnson & Johnson (Ireland) Limited
Airton Road
Tallaght
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0330/017/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1 April 1978

Date of last renewal: 1 April 2008

10 DATE OF REVISION OF THE TEXT

April 2022