SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Calpol 6 Plus Suspension.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol Ph. Eur 250mg in each 5ml.

Excipients with known effect:
Sorbitol 70% solution
Propylene glycol
Sunset yellow
Methyl parahydroxybenzoate
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

For the treatment of mild to moderate pain (including teething pain) and as an antipyretic.

4.2. Posology and Method of Administration

The lowest dose necessary to achieve efficacy should be used.
Do not exceed the stated dose.

6 to 12 years:

Child's Age	**How Much**	**How often (in 24 hours)***
Under 6 years	Not recommended	N/A
6 – 8 years	5 ml	4 times
8 – 10 years	7.5 ml (5 ml + 2.5 ml)	4 times
10 – 12 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

Children aged 12-16 years: 10 – 15ml (Two to three 5 ml doses) up to 4 times a day.
Adults and children over 16 years: 10 – 20 ml (Two to four 5 ml doses) up to 4 times a day.
It is important to **shake the bottle** for at least 10 seconds before use**.**

Use in the Elderly: In the elderly the dosage of paracetamol is as for adults (500 mg to 1 g every 4 to 6 hours up to a maximum of 4 g daily) as the rate and extent of paracetamol absorption is normal. The dosage may need to be adjusted in the elderly as the plasma half-life is longer and paracetamol clearance is lower than in young adults.

The dosage should not be continued for more than 3 days without consulting a doctor.

For oral administration

Hepatic Dysfunction

Caution should be exercised when administering Calpol 6 Plus Suspension to patients with severe hepatic impairment. Dose-related toxicity has been reported; avoid large doses.

Renal Dysfunction

Caution should be exercised when administering Calpol 6 Plus Suspension to patients with moderate to severe renal impairment.

4.3. Contra-indications

This product is contra-indicated in patients with known hypersensitivity to paracetamol or any of the other constituents.

4.4. Special Warnings and Precautions for Use

Contains paracetamol. Do not use with any other paracetamol- containing products. The concomitant use with other products containing paracetamol may lead to an overdose.

Paracetamol overdose may cause liver failure which can lead to liver transplant or death.

Paracetamol should be used with caution in patients with severe hepatic or renal dysfunction, and in patients taking other drugs that affect the liver. Liver function tests may be required at periodic intervals during high dose or long term therapy, especially in patients with pre-existing hepatic disease. Care should be taken in giving Calpol 6 Plus suspension to patients with alcohol dependence or glucose-6-phosphate dehydrogenase deficiency.

Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index or are chronic heavy users of alcohol.

In patients with glutathione depleted states such as sepsis, the use of paracetamol may increase the risk of metabolic acidosis.

Sorbitol: This medicine contains 1.03 mg sorbitol in each 5 mL oral solution which is equivalent to 0.205 mg/mL. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicine.

Sodium: This medicine contains less than 1 mmol sodium (23 mg) per 5 mL, that is to say essentially ‘sodium-free’.

Propylene glycol: This medicine contains less than 1 mg propylene glycol per 5 mL of oral solution which is equivalent to less than 1 mg/kg/day. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates.

This medicine contains sunset yellow which may cause allergic reaction.

This medicine contains methyl parahydroxybenzoate which may cause allergic reactions (possibly be delayed).

Calpol 6 Plus should not be diluted. Where a dilution of Calpol 6 Plus Suspension is prescribed, a suspension of paracetamol specially prepared for use in children should be dispensed instead.

The label contains the following statements:

Shake the bottle thoroughly
Keep out of reach of children
Do not exceed the stated dose
Do not take more than 4 doses in 24 hours
Do not repeat doses more frequently than 4 hourly
Do not give for more than 3 days without consulting a doctor

In case of overdose seek medical attention immediately
If you are currently taking any other medicine consult your doctor or pharmacist before taking this product. Patients should be advised not to take other paracetamol-containing products concurrently.
If symptoms persist consult your doctor
Do not store above 25^{o}C
Store in the original container
Do not refrigerate or freeze.
Protect from light
Contains paracetamol

4.5. Interactions with other Medicaments and other forms of Interaction

Patients who have taken barbiturates, tricyclic antidepressants, and alcohol may show diminished ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

Alcohol and hepatotoxic medications reduce the capacity of the liver to metabolise paracetamol and can increase the hepatotoxicity of paracetamol overdosage. This may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol.
Chronic use of paracetamol enhances the effects of anticoagulants.
Cholestyramine reduces absorption of paracetamol. Metoclopramide and domperidone accelerate absorption of paracetamol. Plasma levels of chloramphenicol may increase with concurrent administration of paracetamol.
Concurrent use of paracetamol with non-steroidal anti-inflammatory drugs (NSAID) may increase the risk of adverse renal effects. Prolonged concurrent use of paracetamol and aspirin or other salicylates may increase the risk of renal damage (such as analgesic nephropathy and renal papillary necrosis).

Chronic ingestion of anticonvulsants or oral steroid contraceptives induce liver enzymes and may prevent attainment of therapeutic paracetamol levels by increasing first pass metabolism or clearance.

Interactions with laboratory tests: Paracetamol may interfere with a number of test results; blood glucose, urate, bilirubin, lactate dehydrogenase and transaminase concentrations, urine 5-hydroxyindoleacetic acid determination, prothrombin time and pancreatic functioning using bentiromide.

4.6. Pregnancy and Lactation

Paracetamol crosses the placenta. There is no known hazard in normal dosage, but like all non-essential medications paracetamol should be avoided especially during the first trimester unless considered essential by the physician.

Paracetamol is excreted in breast milk but there is no evidence that this is clinically significant.

4.7. Effects on Ability to Drive and Use Machines

None known.

4.8. Undesirable Effects

Paracetamol has been widely used and when taken at the usual recommended dosage, side effects are mild and infrequent and reports of adverse reactions are rare.

Skin rashes and other allergic reactions occur rarely.

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

Isolated cases of thrombocytopenic purpura, methaemoglobinaemia, haemolytic anaemia and agranulocytosis have been reported. Rarely, renal colic, sterile pyuria, uraemia, azotaemia, acute pancreatitis and hepatitis have occurred.

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. Papillary necrosis has been reported after prolonged administration.

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 national reporting system:
ADR Reporting website: www.medicinesauthority.gov.mt/adrportal

4.9. Overdose

Paracetamol overdose may cause liver failure which can lead to liver transplant or death

Potentially fatal liver damage is likely in adults who have taken 15g or more of paracetamol. As little as 10g may lead to liver necrosis. Patients taking enzyme-

inducing drugs or with a history of alcoholism may have increased susceptibility. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are employed) become irreversibly bound to liver tissue.

Pallor, anorexia, nausea, diarrhea, abdominal pain, increased sweating and vomiting are frequent early symptoms of paracetamol overdosage. Hepatic necrosis is a dose-related complication of paracetamol overdosage. Hepatic enzymes may become elevated and prothrombin time prolonged within 12-48 hours but clinical symptoms may not be apparent for 1 to 6 days after ingestion. Toxicity is likely in adults who have taken more than 10g. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias have been reported.

Prompt treatment is essential in the management of paracetamol overdosage. Any patient who has ingested about 7.5g or more of paracetamol in the preceding 4 hours should undergo gastric lavage or induced emesis. Specific therapy with an antidote such as acetylcysteine or methionine may be necessary. Acetylcysteine may be given intravenously or by mouth or methionine may be given by mouth within 10-12 hours of ingestion of the overdose. Generally treatment is required if the blood-paracetamol concentration is higher than a line (the ‘200’ line) drawn on semi-log/linear paper joining the points 200mg per litre (1.32mmol per litre) at 4 hours and 30mg per litre (0.20mmol per litre) at 15 hours following ingestion.

Determination of the concentration before 4 hours is not considered to give a reliable measurement. Liver function tests should be performed at 24 hour intervals for at least 96 hours post-ingestion if the plasma paracetamol concentration indicates a potential for hepatotoxicity. Renal and cardiac function should be monitored and supportive treatment should be directed at maintaining fluid and electrolyte balance and correcting hypoglycaemia. Haemodialysis and haemoperfusion have been used with some success but peritoneal dialysis is ineffective.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Paracetamol has analgesic and antipyretic properties similar to those of aspirin and is useful in the treatment of mild to moderate pain. It has only weak anti-inflammatory effects. It is only a weak inhibitor of prostaglandin biosynthesis although there is some evidence to suggest it may be more effective against enzymes in the central nervous system then in the periphery. This may in part account for its activity profile.

5.2. Pharmacokinetic Properties

Paracetamol is rapidly and almost completely absorbed from the gastro-intestinal 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

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Syrup
Sorbitol Solution
Glycerol
Dispersible Cellulose
Polysorbate 80
White Sugar Flavour FP731 (contains propylene glycol)
Orange Flavour 510652E
Methyl parahydroxybenzoate
F, D and C Yellow No. 6 Soluble
Sunset Yellow FCF, E110 (contains sodium)
Purified Water

6.2. Incompatibilities

None known.

6.3. Shelf Life

36 months

6.4. Special Precautions for Storage

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

6.5. Nature and Contents of Container

Amber glass bottle closed with a two-piece or three-piece child resistant, tamper evident closure fitted with a polyethylene/polyvinylidene chloride (PVDC)/polyethylene laminate faced wad.

Pack sizes: 100ml, 140ml, 200ml.

6.6. Instruction for Use/Handling

None applicable.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8. MARKETING AUTHORISATION NUMBER

MA192/03702

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

30th October 2006/22nd October 2014

10. DATE OF REVISION OF THE TEXT

12th April 2024