Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Paralink Six Plus Paracetamol 250 mg/5 ml oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains paracetamol 250 mg.

Excipients

Each 5 ml also contains:
Liquid sorbitol (non-crystallising) (E420) 1300 mg
Propylene glycol 200 mg
Liquid maltitol (E965) 550 mg
Nipasept 5 mg
Nipasept is a mixture of methyl, ethyl and propyl parahydroxybenzoate (E218, E214, E216).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral Solution.
Colourless / straw coloured sugar free oral solution with a strawberry odour and taste.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Paralink Six Plus Paracetamol Oral Solution is indicated as an analgesic and antipyretic. It is used in the treatment of mild to moderate pain, including headache, migraine, neuralgia, toothache and pain associated with teething. It is also indicated for the relief of symptoms of colds and influenza and to reduce fever.

4.2 Posology and method of administration

Child's Age	How Much	How often (in 24 hours)
6 – 8 years	5mL	4 times
8 – 10 years	7.5mL	4 times
10 – 12 years	10mL	4 times
o Do not give more than 4 doses in any 24 hour period o Leave at least 4 hours between doses o Do not give this medicine to your child for more than 3 days without speaking to your doctor or pharmacist o Do not give to children under the age of 6 years.		

Children aged 12 – 16 years: 10 – 15mL up to 4 times a day.
Adults and children over 16 years: 10 – 20mL up to 4 times a day.

4.3 Contraindications

Hereditary fructose intolerance.
Hypersensitivity to paracetamol or to any of the other constituents.

4.4 Special warnings and precautions for use

Never take or give more medicine than shown in the table.
Always use the syringe supplied with the pack.
Do not take or give more than 4 doses in any 24-hour period.
Leave at least 4 hours between doses.
Prolonged use without medical supervision can be harmful.
Do not take or give this medicine for more than 3 days without speaking to your doctor or pharmacist.
If symptoms persist consult your doctor.
Do not take or give with any other paracetamol-containing products.
As with all medicines, if your child is currently taking any medicine consult your doctor or pharmacist before taking this product.
The product should be administered with caution to patients with known liver or renal impairment.
Immediate medical advice should be sought in the event of overdose, because of the risk of irreversible liver damage.
Keep out of the reach and sight of children.
Patients with rare hereditary problems of fructose intolerance should not take this medicine.
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.

4.5 Interaction with other medicinal products and other forms of interactions

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased bleeding; occasional doses have no significant effect.

The rate of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by coleystyramine.

Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose. 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 micosomel 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, 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 effective dose for the shortest possible time and at the lowest possible frequency.

Lactation
Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data does 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 but hypersensitivity including skin rash may occur. Very rare cases of serious skin reactions have been reported. There have been a few reports of blood dyscrasias including thrombocytopenia and agranulocytosis.

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 the disease improved after paracetamol withdrawal.

Nephrotoxic effects following therapeutic doses of paracetamol are 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 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

Symptoms
In many cases of paracetamol overdosage there are often no early symptoms. Pallor, nausea, vomiting, anorexia and abdominal pain are early symptoms of paracetamol overdosage. 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. As mentioned above symptoms may be limited to pallor, nausea, vomiting, anorexia and abdominal pain and may not reflect the severity of overdose or the risk of organ damage.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour.

Treatment with **acetylcysteine** is indicated in patients with paracetamol overdosage:

a) who have taken a staggered overdose irrespective of plasma paracetamol level. Staggered is defined as an overdose where the paracetamol was ingested over a period of 1 hour or more; or
b) where there is any doubt over the time of the overdose, irrespective of plasma paracetamol level; or
c) who present with a plasma paracetamol level on or above a line joining points of 100mg/L at 4h and 15mg/L at 15h (please refer to nomogram found in the acetyl cysteine SmPC)

N-acetylcysteine should be dosed based on weight-based acetylcysteine dosing tables for adults and children found in the N-acetylcysteine SmPC.

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.

The duration of administration of the first dose of intravenous acetylcysteine should be 60 minutes to minimise the risk of anaphylactoid reactions.

Hypersensitivity is not a contraindication to treatment with acetylcysteine.

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 24h from ingestion should be discussed with a liver unit.

Liver damage is possible in adults who have taken 10g or more of paracetamol. 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Analgesic, Antipyretic; N02 BE01.
Paracetamol is an antipyretic and analgesic. Paracetamol produces antipyresis through action on the hypothalamic heat-regulation centre and analgesia by elevation of the pain threshold. Paracetamol has analgesic and antipyretic actions similar to those of aspirin but it has no useful anti-inflammatory properties.

5.2 Pharmacokinetic properties

Paracetamol has analgesic and antipyretic actions but only weak anti-inflammatory properties.

Paracetamol is rapidly and almost completely absorbed from the gastro-intestinal tract. Peak plasma concentrations occur within 30 to 60 minutes, with slightly faster absorption of liquid preparations. Usual analgesic doses produce total serum concentrations of 5 to 20µg/ml. A good correlation between serum concentration and analgesic effect has not been found.

Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk.
Serum protein binding varies from 20% to 50% at toxic serum concentrations.

Paracetamol is metabolized predominantly in the liver and excreted in the urine mainly as glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 3 hours and is prolonged in neonates and in patients with hepatic impairment.

Total body clearance of paracetamol is reduced in neonates and increases with age.

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

Sorbitol (E420)
Liquid Maltitol (E965)
Propylene glycol
Macrogol 4000
Glycerol
Potassium sorbate
Nipasept (a mixture of the methyl, ethyl and propyl esters of hydroxybenzoic acid – E218, E214 and E216)
Citric acid

Neohesperidin-dihydrochalcone
Saccharin sodium
Strawberry flavour 221047
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 25°C.
Do not refrigerate.
Keep the bottle in the outer carton in order to protect from light.

6.5 Nature and contents of container

Amber glass bottles with child-resistant and tamper-evident closures. The closure is manufactured from polypropylene with a polyethylene liner and tamper evident band. A 5ml dosing syringe with markings at both 2.5ml and 5ml is provided with the bottle. Pack sizes 60 and 70 ml.
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

Phoenix Healthcare Ltd
Suite 12 Bunkilla Plaza
Bracetown Business Park
Clonee
Co Meath
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1721/006/004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31st July 2009
Date of last renewal: 31st July 2014

10 DATE OF REVISION OF THE TEXT

June 2022