Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lemsip Cough and Cold Capsules with CaffeineParacetamol 500mgGuaifenesin 100mgCaffeine 25mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredients mg/Capsule

Paracetamol 500.00
Caffeine anhydrous 25.00
Guaifenesin 100.00

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard.
Red and green hard gelatin capsule with 'Lemsip C&C' printed in white.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the relief of symptoms of cold and influenza, including the relief of aches and pains, sore throat, headache, lowering of temperature and chesty coughs and fatigue and drowsiness.

4.2 Posology and method of administration

The patient should consult a doctor, if symptoms persist or worsen, or if the product is required for more than 3 days.

Posology

Adults, the elderly and children aged 16 years and over: 2 capsules every 4-6 hours as required. Do not take more than 8 capsules (4 doses) in 24 hours.

Children: Ages 12 to 15 years: 1 capsule every 4-6 hours when necessary to a maximum of 4 capsules in 24 hours. Do not give to children under 12 years of age.

Method of administration
For oral administration. Swallow whole with water. Do not chew.

Paracetamol should be used at the lowest effective dose forthe shortest possible time. The maximum daily dose must not be exceeded.

In all patients over 16 years of age, the maximum daily dose of paracetamol should not exceed 60 mg/kg/day (up to a maximum of 2 g perday) in the following situations, unless directed by a physician: (see section4.4)

- Weight lessthan 50kg
- Dehydration
- Malnutrition
- Chronicalcoholism

Renal impairment

Paracetamol should be used with caution in patients with renal impairment as a reduced dose and/or prolonged dosing interval may be necessary (see section 4.4).

Hepatic impairment

Paracetamol should be used with caution in patients with hepatic impairment as a reduced dose or prolonged dosing interval may be necessary (see section 4.4).

The elderly

Experience has indicated that normal adult dosage of paracetamol is usually appropriate. However, in frail, immobile elderly subjects or in elderly patients with renal or hepatic impairment, a reduction in the amount or frequency of dosing may be appropriate (see section 4.4).

4.3 Contraindications

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

Do not take if suffering from porphyria.

Use in children under 12 years of age

4.4 Special warnings and precautions for use

Serious skin reactions, including Stevens-Johnson Syndrome, toxic epidermal necrolysis, and acute generalised exanthematous pustulosis, have been reported very rarely in association with paracetamol. These severe hypersensitivity reactions are potentially life threatening. The product should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Patients with hepatitis, non-cirrhotic alcoholic liver disease, hepatic insufficiency or renal insufficiency are at an increased risk of adverse reactions associated with paracetamol use. These patients should seek the advice of a doctor before taking this product.

Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if you feel well (see section 4.9).

Do not take if you are pregnant or breast feeding unless recommended by a health care professional (see section 4.6).

Due to the presence of caffeine, the product should be taken with care in patients with a history of peptic ulcers.

The product is particularly appropriate for day-time use due to the caffeine content.

Label: Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

Leaflet: Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

Do not exceed the stated dose. If symptoms persist, consult your doctor. Keep out of the sight and reach of children. If you are being prescribed medicine by your doctor, seek his advice before taking this product. Contains paracetamol (panel).

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

- Glucose-6-phosphate dehydrogenase deficiency
- Haemolytic anaemia
- Glutathione deficiency
- Dehydration

- Elderly Cases of paracetamol induced hepatotoxicity, including fatal cases, have been reported in patients taking paracetamol at doses within the therapeutic range. These cases were reported in patients with one or more risk factors for hepatotoxicity including low body weight (<50 kg), renal and hepaticimpairment, chronic alcoholism, concomitant intake of hepatotoxic drugs, and in acute and chronic malnutrition (low reserves of hepatic glutathione). Paracetamol should be administered with caution to patients with these risk factors. Caution is also advised in patients on concomitant treatment with drugs that induce hepatic enzymes and in conditions which may predispose to glutathione deficiency (see sections 4.2 and 4.9). Doses of paracetamol should be reviewed at clinically appropriate intervals and patients should be monitored for emergence of new risk factors for hepatotoxicity which may warrant dosage adjustment. 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 case medical assistance should be sought immediately. This medicine contains less than 1 mmol sodium (23mg) per dose, that is to say essentially 'sodium-free

4.5 Interaction with other medicinal products and other forms of interactions

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

Antiemetics: The speed of absorption of paracetamol may be increased by metoclopramide or domperidone.

Cholestyramine: Paracetamol absorption may be reduced by cholestyramine.

CYP Inhibitors: Caffeine undergoes extensive metabolism by hepatic microsomal cytochrome P450. Factors known to alter the activity of this enzyme system may influence caffeine clearance. For example, caffeine elimination is inhibited by cimetidine, disufiram, and oral contraceptive steroids.

Laboratory Interference: If urine is collected within 24 hours of a dose of the medicinal product, a metabolite of guaifenesin may cause a colour interference with laboratory determinations of urinary 5-hydroxyindoleacetic acid (5-HIAA) and vanillylmandelic acid (VMA).

Concurrent use of paracetamol and flucloxacillin is associated with an increased risk of metabolic acidosis, especially in patients with severe renal impairment, hepatic impairment, sepsis, malnutrition and chronic alcoholism

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.

There is limited data on the use of guaifenesin in pregnant women.

Breast-feeding
The product should be avoided during lactation unless recommended by a healthcare professional.

Whilst caffeine is excreted into breast milk at levels which are considered not to present a hazard to the infant, irritability and poor sleeping patterns have been reported.

Paracetamol is excreted in breast milk, but not in a clinically significant amount.

There is no information on the use of guaifenesin in lactation.

Fertility
No known effects.

4.7 Effects on ability to drive and use machines

Caffeine may have a minor influence on the ability to drive and use machines. Dizziness and agitation have been reported with caffeine use (see section 4.8): affected patients should not drive or use machinery.

4.8 Undesirable effects

Adverse events which have been associated with paracetamol, guaifenesin and caffeine are given below, tabulated by system organ class and frequency. Frequencies are defined as: Very common (≥1/10); Common (≥1/100 and <1/10); Uncommon (≥1/1000 and <1/100); Rare (≥1/10,000 and <1/1000); Very rare (< 1/10,000); Not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

System Organ Class	Frequency	Adverse Events
Blood and Lymphatic System Disorders	Not known	Thrombocytopenia[a] agranulocytosis [a1] leukopenia[a1]
Immune System Disorders	Not known	Hypersensitivity[abc]
Psychiatric Disorders	Not known	Insomnia, restlessness, anxiety, agitation
Nervous System Disorders	Not known	Dizziness
Gastrointestinal Disorders	Not known	Gastric ulcer, abdominal discomfort, nausea and vomiting
Skin and Subcutaneous Tissue Disorders	Not known	Stevens-Johnson Syndrome, toxic epidermal necrolysis, acute generalised exanthematous pustulosis[2] Skin rash

Description of Selected Adverse Reactions

[1] There have been occasional reports of blood dyscrasias, including thrombocytopenia and agranulocytosis.

[2] Serious hypersensitivity reactions have been reported (see section 4.4).

Active ingredients

[a] Paracetamol

[b] Guaifenesin

[c] Caffeine

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

Immediate medical advice should be sought in the event of an overdose, even if you feel well.
The main cause for concern in overdosage with this product is paracetamol intake.
Paracetamol overdose can result in liver damage which may be fatal.

Symptoms generally appear within the first 24 hours and may comprise: nausea, vomiting, anorexia, pallor, and abdominal pain, or patients may be asymptomatic.
Overdose of paracetamol can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death.
Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.
Liver damage is likely in patients who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite become irreversibly bound to liver tissue.

Some patients may be at increased risk of liver damage from paracetamol toxicity:
Risk factors include;

- Patients with liver disease
- Elderly patients
- Young children

- Patients receiving long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- Patients who regularly consume ethanol in excess of recommended amounts
- Patients with glutathione depletion e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Acute renal failure with acute tubular necrosis may also develop.

Cardiac arrhythmias and pancreatitis have also been reported.

Emergency Procedure:

Immediate transfer to hospital.

Blood sampling to determine initial paracetamol plasma concentration. In the case of a single acute overdose, paracetamol plasma concentration should be measured4 hours post ingestion. Administration of activated charcoal should be considered if the overdose of paracetamol has been ingested within the previous hour.

The antidote N-acetylcysteine, should be administered as soon as possible in accordance with national treatment guidelines.

Symptomatic treatment should be implemented.

Guaifenesin overdose may cause nausea and vomiting.

Symptoms of caffeine overdose are rare but may include emesis and convulsions

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, Anilides; **ATC Code:** N02BE51

Paracetamol: Paracetamol has both analgesic and antipyretic activity, which is believed to be mediated principally through its inhibition of prostaglandin synthesis within the central nervous system.

Guaifenesin: Guaifenesin is an expectorant which increases the volume of mucous that can be expelled by mucocilliary action due to a reduction in the adhesiveness and viscosity of tenacious sputum.

Caffeine: Caffeine is a central nervous system stimulant. It inhibits the enzyme phosphodiesterase and has an antagonistic effect at central adenosine receptors. Its action on the central nervous system is mainly on the higher centres and it produces a condition of wakefulness and increased mental activity.

5.2 Pharmacokinetic properties

Paracetamol: Paracetamol is absorbed rapidly and completely from the small intestine, producing peak plasma levels after 15-20 minutes following oral dosing. The systemic availability is subject to first-pass metabolism and varies with dose between 70% and 90%. The drug is rapidly and widely distributed throughout the body and is eliminated from plasma with a T½ of approximately 2 hours. The major metabolites are glucuronide and sulphate conjugates (>80%) which are excreted in urine.

Guaifenesin: Guaifenesin is absorbed from the gastrointestinal tract after oral administration and rapidly metabolised by oxidation to beta-(2-methoxyphenoxy)-lactic acid. Within 3 hours, approximately 40% of a single dose is excreted in the urine as this metabolite. The half-life in plasma is approximately 1 hour. Guaifenesin may increase the rate of absorption of paracetamol.

Caffeine: Caffeine is absorbed readily after oral, rectal or parental administration, but absorption from the gastrointestinal tract may be erratic. There is little evidence of accumulation in any particular tissue. Caffeine passes readily into the central nervous system and into saliva. Concentrations have also been detected in breast milk. It is metabolised almost completely and is excreted in the urine as 1-methyluric acid and other metabolites, with only about 1% unchanged. Elimination half-life can vary between 2-10 hours.

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

Capsule contents
Maize starch
Croscarmellose sodium
Sodium laurilsulfate
Magnesium stearate
Talc sterilised

Capsule body
Gelatin
Patent blue V (E131)
Quinoline yellow (E104)
Erythrosin – FD&C red 3 (E127)
Titanium dioxide (E171)

Capsule cap
Gelatin
Erythrosin (E127)
Quinoline yellow (E104)
Patent blue V (E131)
Titanium dioxide (E171)

Printing Ink contains shellac,
Titanium dioxide (E171) and Aluminium hydroxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

6,8 and 12 capsules in a 250 micron opaque uPVC blister with foil/paper laminate, 35gsm paper / 9 micron soft-temper foil and heat-sealed coated, contained in an outer cardboard carton.
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

Reckitt Benckiser Ireland Ltd
7 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0979/029/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22nd June 2007
Date of last renewal: 22nd June 2012

10 DATE OF REVISION OF THE TEXT

October 2021