Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lemsip Cold & Flu Capsules with Caffeine
Paracetamol 500mg
Caffeine 65mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains paracetamol 500 mg and caffeine 65 mg.

Excipients: Contains Tartrazine

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard capsules.

A red and yellow hard gelatine capsule printed “Lemsip”.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the relief of symptoms associated with the common cold and influenza, including relief of aches and pains, fever, sore throat, headache, fatigue and drowsiness and lowering of temperature.

4.2 Posology and method of administration

Duration of treatment should be limited to a maximum of 3 days. 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.

The product is particularly appropriate for day-time use.

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 per day) in the following situations, unless directed by a physician: (see section 4.4)

- Weight less than 50kg
- Dehydration
- Malnutrition
- Chronic alcoholism

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).

Paediatric population under 16 years
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.

4.3 Contraindications

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

Caffeine: Should be given with care to patients with a history of peptic ulcer.

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.
Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment.

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).

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

Excessive intake of caffeine (e.g. coffee, tea and some soft drinks) should be avoided while taking this product.

Tartrazine is present in this product and may cause allergic reactions.

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 hepatic impairment, 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.

4.5 Interaction with other medicinal products and other forms of interactions

The hepatotoxicity of paracetamol may be potentiated by other drugs that affect the liver.

Antiobiotics: Paracetamol is reported to increase the half-life of chloramphenicol.

Anticoagulants: The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding.

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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Paracetamol:

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.

Caffeine: Taken during pregnancy, it appears that the half-life of caffeine is prolonged. This is a possible contributing factor in hyperemesis gravidarum.
Paracetamol-caffeine is not recommended for use during pregnancy due to the possible increased risk of spontaneous abortion associated with caffeine consumption.

Therefore this product is not recommended during pregnancy.

Breast-feeding

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

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

Therefore this product should not be used during breast feeding.

Fertility

No known effects.

4.7 Effects on ability to drive and use machines

The product contains caffeine, a central nervous stimulant which helps counteract drowsiness and restore alertness. These effects are usually considered to have a positive influence on the ability to drive or operate machinery. However, 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 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, agranulocytosis [1]
Immune System Disorders	Not known	Hypersensitivity
Psychiatric Disorders	Not known	Insomnia, restlessness, anxiety, agitation
Nervous System Disorders	Not known	Dizziness
Gastrointestinal Disorders	Not known	Gastric ulcer, epigastric discomfort, nausea, 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).

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:

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 measured 4 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.

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.

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.

Caffeine: Caffeine is absorbed readily after oral, rectal or parenteral 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, 1-methylxanthine 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

Maize starch
Croscarmellose sodium
Magnesium stearate
Sodium laurilsulfate
Gelatin
Titanium dioxide

Quinoline yellow
Erythrosine
Patent blue V
Shellac
Tartrazine (E102)
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

Twelve capsules in PVC/aluminium blisters, cartons containing one or two blister strips.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special precautions for use.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA0979/024/001

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10 DATE OF REVISION OF THE TEXT

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