

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lemsip Max Cold & Flu Lemon.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

<u>Active Ingredients</u>	<u>mg/Sachet</u>
Paracetamol	1000
Phenylephrine hydrochloride*	12.20

*Equivalent to phenylephrine base 10mg.

Excipient(s) with known effect:

Aspartame

Lactose

Sodium

Sucrose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral powder.

4.1 Therapeutic indications

For the short-term relief of the symptoms of colds and influenza, including the relief of aches and pains, sore throat, headache, nasal congestion and lowering of temperature.

4.2 Posology and method of administration

Duration of treatment should be limited to a maximum of 5 days. Patients should consult a doctor or pharmacist if symptoms persist for more than 5 days, or worsen.

Posology

Adults, the elderly and children 16 years and over: Content of one sachet dissolved by stirring in hot water and sweetened to taste.

Dose may be repeated in 4-6 hours as required.

Do not take more than 4 sachets in 24 hours.

Do not give to children under 16 years of age.

Elderly population:

Experience has indicated that normal adult dose 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.

Method of Administration

Oral administration after dissolution in water.

4.3 Contraindications

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

Due to the presence of phenylephrine, use of this product is contraindicated in:

- Patients with severe coronary heart disease or cardiovascular disorders.
- Patients with hypertension.
- Patients with hyperthyroidism.
- Patients currently receiving or within two weeks of stopping therapy with monoamine oxidase inhibitors (MAOIs) (see section 4.5).
- Patients using other sympathomimetic decongestants concomitantly.
- Patients with prostatic enlargement.
- Patients with phaeochromocytoma.
- Patients with closed-angle glaucoma.
- Patients with diabetes mellitus.

4.4 Special warnings and precautions for use

Use with caution in patients with Raynaud's phenomenon.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. These patients should seek the advice of a doctor before taking this product. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Patients should be advised not to take other paracetamol-containing products concurrently.

Immediate medical advice should be sought in the event of an overdose, even if the patient feels well because of the risk of delayed serious liver damage (see section 4.9).

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as, severe renal impairment and sepsis, or malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring, is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as an underlying cause of HAGMA in patients with multiple risk factors.

The product should not be used during pregnancy unless recommended by a healthcare professional (see section 4.6).

Use during breastfeeding should be avoided, unless recommended by a healthcare professional (see section 4.6).

Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Patients with rare hereditary problems of fructose intolerance, glucose- galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Each sachet contains approximately 2.2 g of carbohydrate.

This medicine contains 61.5mg aspartame in each sachet. Aspartame is a source of phenylalanine.. It may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

This medicinal product contains 128.71 mg sodium per dose, equivalent to 6.4 % of the WHO recommended maximum daily intake for sodium.

The maximum daily dose of this product is equivalent to 25.7 % of the WHO recommended maximum daily intake for sodium.

Lemsip Max Cold&Flu Lemon is considered high in sodium. This should be particularly taken into account for those on a low salt diet.”

Keep out of the sight and reach of children.

Do not exceed the stated dose.

If symptoms persist, consult your doctor.

4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol

Antiemetics: the rate of absorption of paracetamol may be increased by metoclopramide or domperidone.

Cholestyramine: paracetamol absorption may be reduced by cholestyramine.

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.

Flucloxacillin: caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).

Isoniazid: the toxicity of paracetamol may be increased by isoniazid.

Liver enzyme-inducing drugs: drugs which induce or regulate liver microsomal enzymes, such as, anticonvulsants (including phenytoin, barbiturates, carbamazepine) and alcohol, may increase the hepatotoxic potential of paracetamol.

Phenylephrine hydrochloride

Monoamine oxidase inhibitors (MAOIs) (including moclobemide): do not use in patients taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days. Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors (see section 4.3).

Sympathomimetic amines: concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects.

Oxytocic agents: the vasopressor effect of sympathomimetics, such as, phenylephrine, may be potentiated when used in conjunction with oxytocic drugs, such as, oxytocin and ergot alkaloids, which can increase risk of haemorrhagic stroke.

Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa): phenylephrine may reduce the efficacy of beta-blockers and antihypertensives. The risk of hypertension and other cardiovascular side effects may be increased (see section 4.3).

Tricyclic antidepressants (e.g. amitriptyline): may increase the risk of cardiovascular side effects with phenylephrine (see section 4.3).

Digoxin and cardiac glycosides: concomitant use of phenylephrine may increase the risk of irregular heartbeat or heart attack.

4.6 Pregnancy, Fertility and Lactation

Pregnancy

The product should not be used during pregnancy unless recommended by a healthcare professional.

The safety of this medicine during pregnancy and lactation has not been established but in view of a possible association of foetal abnormalities with first trimester exposure to phenylephrine, the use of the product during pregnancy should be avoided. In addition, because phenylephrine may reduce placental perfusion, the product should not be used in patients with a history of preeclampsia.

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage.

Breast-feeding

The product should be avoided during lactation unless recommended by a healthcare professional. There are limited data on the use of phenylephrine in lactation.

Paracetamol is excreted in breast milk, but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

Fertility

There are no available data regarding the effects of the active ingredients on fertility.

4.7 Effects on ability to drive and use machines

Lemsip Max Cold & Flu Lemon has no or negligible influence on ability to drive or use machinery.

4.8 Undesirable effects

Adverse events which have been associated with paracetamol and phenylephrine hydrochloride are given below, tabulated by system organ class and frequency. Frequencies are defined as: Very common ($\geq 1/10$); Common ($\geq 1/100$ and $< 1/10$); Uncommon ($\geq 1/1000$ and $< 1/100$); Rare ($\geq 1/10,000$ 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, leucopenia, pancytopenia, neutropenia, agranulocytosis ¹ •
Immune System Disorders	Not known	Hypersensitivity•▪
Nervous System Disorders	Not known	Headache▪
Cardiac Disorders	Not known	Palpitations▪
Vascular Disorders	Not known	Hypertension▪
Metabolism and Nutrition Disorders	Not known	High anion gap metabolic acidosis ²
Gastrointestinal Disorders	Not known	Abdominal discomfort, nausea, vomiting
Skin and Subcutaneous Tissue Disorders	Very rare	Cases of serious skin reactions have been reported•
	Not known	Skin rash•
Renal and Urinary Disorders	Not known	Urinary retention ³ ▪

Description of Selected Adverse Reactions

¹ There have been reports of blood dyscrasias including thrombocytopenia, leucopenia, pancytopenia, neutropenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

² High anion gap metabolic acidosis: Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

³ Especially in males.

•Paracetamol; ▪Phenylephrine Hydrochloride

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Paracetamol

Immediate medical advice should be sought in the event of an overdose, even if you feel well. Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk factors

An increased risk of liver damage from paracetamol overdosing has been associated with: (a) Patients on long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

Or

(b) Patients who regularly consume ethanol in excess of recommended amounts.

Or

(c) Patients likely to be glutathione depleted, e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Or

(d) Patients taking isoniazid.

Symptoms

Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. 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. Overdose may also result in disseminated intravascular coagulation.

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. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines. See BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). 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. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage

schedule. 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 24 hours from ingestion should be discussed with the NPIS or a liver unit.

Phenylephrine hydrochloride

Features of severe overdose of phenylephrine include haemodynamic changes and cardiovascular collapse with respiratory depression, seizures and arrhythmias. However, smaller amounts of the paracetamol and phenylephrine hydrochloride combination product would be required to cause paracetamol related liver toxicity than to cause serious phenylephrine-related toxicity. Treatment includes symptomatic and supportive measures. Hypertensive effects may be treated with an i.v. alpha-receptor blocking agent.

Phenylephrine overdose is likely to result in: nervousness, headache, dizziness, insomnia, increased blood pressure, nausea, vomiting, reflex bradycardia, mydriasis, acute angle closure glaucoma (most likely to occur in those with closed angle glaucoma), tachycardia, palpitations, allergic reactions (e.g. rash, urticaria, allergic dermatitis), dysuria, urinary retention (most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy).

Additional symptoms may include, hypertension, and possibly reflex bradycardia. In severe cases confusion, seizures and arrhythmias may occur. However the amount required to produce serious phenylephrine toxicity would be greater than that required to cause paracetamol-related liver toxicity.

Treatment should be as clinically appropriate. Severe hypertension may need to be treated with alpha blocking medicinal products such as phentolamine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Analgesics, Anilides;
ATC Code: N02BE51. Paracetamol, combinations excl. psycholeptics

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.

Phenylephrine hydrochloride: Phenylephrine is sympathomimetic post-synaptic α_1 -adrenergic receptor agonist with low cardioselective beta receptor affinity and minimal central nervous stimulant activity. It is a recognised decongestant and acts by vasoconstriction to reduce oedema and nasal swelling.

5.2. Pharmacokinetic properties

Paracetamol: Paracetamol is absorbed rapidly and completely mainly from the small intestine producing peak plasma levels after 15-20 minutes following oral dosing.

In a study of healthy controls fasted overnight the T_{max} for an equivalent product compared to two tablets of standard paracetamol was 20 minutes

versus 35 minutes (p=0.0865). However, the speed to achieve 10 µg/ml for the product was faster than a standard paracetamol (17 minutes versus 30 minutes).

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 T_{1/2} of approximately 2 hours. The major metabolites are glucuronide and sulphate conjugates (>80%) which are excreted in urine.

Phenylephrine: Phenylephrine is absorbed from the gastrointestinal tract, but has reduced bioavailability by the oral route due to first-pass metabolism. It retains activity as a nasal decongestant when given orally, the drug distributing through the systemic circulation to the vascular bed of nasal mucosa. When taken by mouth as a nasal decongestant phenylephrine is usually given at intervals of 4 – 6 hours.

5.3 Preclinical safety data

No preclinical findings of relevance have been reported.

6.1 List of excipients

Sodium citrate,
Citric acid,
Curcumin (curcumin (E100), Lactose, Polysorbate 80 (E433) and Silica (E551)).
Lemon flavour,
Aspartame,
Saccharin sodium,
Pulverised sucrose,
Caster sugar and
Ascorbic acid.

6.2 Incompatibilities

None known.

6.3 Shelf life

Two years.

6.4 Special precautions for storage

Store below 25°C in a dry place.

6.5 Nature and contents of container

Heat-sealed laminate sachet of 40 gsm paper, 12 gsm PE extrusion, 8 micron aluminium foil and ethylene/methacrylic acid copolymer. In a cardboard outer carton.

Pack size: 5, 6, 7, 8, 9, 10, 12, 14, and 16 sachets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Healthcare (UK) Limited, Dansom Lane, Hull, HU8 7DS, East Yorkshire.

8 MARKETING AUTHORISATION NUMBER(S)

PL 00063/0069.

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/03/2009

10 DATE OF REVISION OF THE TEXT

23/02/2026