SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lem Plus Capsules

Aspar Cold Relief Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredients:
Each capsules contains:-

Paracetamol E.P.	300mg
Caffeine E.P.	25mg
Phenylephrine Hydrochloride E.P.	5mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Hard gelatin green and yellow capsules.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of aches, pains, headache, sore throat, fever and nasal congestion
associated with colds and influenza.

4.2 Posology and method of administration

Posology

Adults, the elderly and children 16 years and over : two capsules to be taken every four to six hours, when necessary up to four times daily. Maximum dose of 8 capsules in 24 hours.

Do not take the medicine for more than 3 days without consulting a doctor.

Not recommended for children under 16 years of age:

Method of administration

Oral administration only.

4.3 Contraindications

Paracetamol: known hypersensitivity to paracetamol.

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

Phenylephrine hydrochloride: should be avoided or only used with great caution in hyper-susceptible patients or those with hyperthyroidism, aneurism, hypertension, arteriosclerosis and cardiovascular disorders. As an alpha-adrenoceptor stimulant it may provoke uterine changes which can result in foetal asphyxia.

4.4 Special warnings and precautions for use

Care is advised in the administration of paracetamol to patients with renal or hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

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 in patients with 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 underlying cause of HAGMA in patients with multiple risk factors.

Medical advice should be sought before using this product in patients with these conditions:

An enlargement of the prostate gland
Occlusive vascular disease (e.g. Raynaud's phenomenon)
Cardiovascular disease

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) (see interactions).

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

Keep out of sight and reach of children

Do not exceed the stated dose.

If symptoms persist, consult your doctor.

If you are under the care of your doctor or receiving prescribed medicines consult your doctor before taking this product.

Do not take other flu, cold or decongestant medicines or other paracetamol-containing medicines with this product.

Special Label Warnings
Contains Paracetamol.
Talk to a doctor at once if you take too much of this medicine, even if you feel well.
Do not take with any other paracetamol-containing products. Do not take with other flu, cold or decongestant products

Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Special Leaflet Warnings
Talk to a doctor at once if you take too much of this medicine, even if you feel well. This is because too much paracetamol can cause serious liver damage.

4.5 Interaction with other medicinal products and other forms of interaction

Enzyme-inducing drugs may increase hepatic damage, as does excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. These interactions are considered to be of unlikely clinical significance in acute usage at the dosage regimen proposed.

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 risk factors (see section 4.4).

Medical advice should be sought before taking paracetamol-caffeine phenylephrine in combination with the following drugs:

Monoamine oxidase inhibitors (including moclobemide)	Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine Oxidase inhibitors (see contraindications).

Sympathomimetic amines	Concomitant use of phenylephrine with other sympathomimetics amines can increase the risk of cardiovascular side effects (see warnings and precautions).
Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa)	Phenylephrine may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased (see contraindications).
Tricyclic antidepressants (e.g. amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine (see contraindications).
Digoxin and cardiac glycosides	Concomitant use of phenylephrine with digoxin or cardiac glycosides may increase the risk of irregular heartbeat or heart attack.
Ergot alkaloids	(ergotamine and methylsergide) increased risk of ergotism
Warfarin and other coumarins	The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with an increased risk of bleeding; occasional doses have no significant effect.

4.6 Fertility, pregnancy and lactation

This product is not recommended for use in pregnancy due to the phenylephrine and caffeine content. There is a potential increased risk of lower birth weight and spontaneous abortion associated with caffeine consumption during pregnancy.

This product should not be used while breast-feeding without medical advice. Caffeine in breast milk may have a stimulating effect on breast-fed infants. Phenylephrine may be excreted in breast milk.

4.7 Effects on ability to drive and use machines

Phenylephrine Hydrochloride: May cause drowsiness. If affected, do not drive or operate machinery. Avoid alcoholic drinks.

4.8 Undesirable effects

Adverse events of paracetamol from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class. The frequency of these adverse events is not known (cannot be estimated from available data).

Paracetamol

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis These are not necessarily causally related to paracetamol.
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angioedema and Stevens Johnson syndrome, toxic epidermal necrolysis
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary disorders	Hepatic dysfunction
Skin and subcutaneous tissue disorders	Very rare cases of serious skin reactions have been reported.

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

Caffeine

When the recommended paracetamol-caffeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects such as insomnia, restlessness, anxiety, irritability, headaches, gastrointestinal disturbances and palpitations.

Adverse reactions identified through post-marketing use with caffeine are listed below. The frequency of these reactions is unknown.

Body System	**Undesirable effect**
Central nervous system	Dizziness Headache

Cardiac disorders	Palpitation
Psychiatric disorders	Insomnia Restlessness Anxiety and irritability
Gastrointestinal disorders	Gastrointestinal disturbances

Phenylephrine

The following adverse events have been observed in clinical trials with phenylephrine and may therefore represent the most commonly occurring adverse events.

Body System	**Undesirable effect**
Psychiatric disorders	Nervousness
Nervous system disorders	Headache, dizziness, insomnia
Cardiac disorders	Increased blood pressure
Gastrointestinal disorders	Nausea, vomiting, diarrhoea

Adverse reactions identified during post-marketing use are listed below. The frequency of these reactions are unknown.

Eye disorders	Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma
Cardiac disorders	Tachycardia, palpitations
Skin and subcutaneous disorders	Allergic reactions (e.g. rash, urticaria, allergic dermatitis). Hypersensitivity reactions – including that cross-sensitivity may occur with other sympathomimetics
Renal and urinary disorders	Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Metabolism and nutrition disorders

High anion gap metabolic acidosis with frequency “Not known” (cannot be estimated from the available data)

Description of selected adverse reactions

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.

Reporting of suspected adverse reactions:

Reporting of suspected adverse reactions after authorization 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:

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, phenobarbital, 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.

Symptoms

Symptoms of paracetamol overdosage 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.

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

Caffeine: Symptoms – emesis and convulsions may occur. No specific antidote. However, treatment is usually fluid therapy. Fatal poisoning is rare. If symptoms become apparent or overdose is suspected, consult a doctor immediately.

Phenylephrine Hydrochloride: Not Known – if overdose is suspected consult a doctor immediately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesic and antipyretic.

ATC code: N02BE51

Paracetamol: An analgesic and antipyretic.

Caffeine: A mild stimulant

Phenylephrine hydrochloride: A sympathomimetic decongestant. The active ingredients are not known to cause sedation.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver (90-95%) and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours.

Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite (n-acetyl-p-benzoquinoneimine) which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage. The time to peak concentrations of paracetamol is 0.5 to 2 hours, the time to peak effect I to 3 hours and the duration of action 3 to 4 hours.

Caffeine: is readily absorbed 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. Caffeine is metabolised almost completely and is excreted in the urine as 1-methyluric acid, 1-methylxanthine and other metabolites with only about 1% unchanged.

Phenylephrine hydrochloride: has reduced bioavailability from the gastro-intestinal tract owing to first pass metabolism by monoamine oxidase in the gut and liver. When injected intramuscularly it takes 10 to 15 minutes to act and subcutaneous and intramuscular injections are effective for about an hour. Intravenous injections are effective for about 20 minutes.

5.3 Preclinical safety data

Pre-clinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use of the product and which have not already been mentioned elsewhere in this Summary.

The toxicity of paracetamol has been extensively studied in numerous animal species. Pre-clinical studies in rats and mice have indicated single dose oral LD_{50} values of 3.7 g/kg and 338 mg/kg, respectively. Chronic toxicity in these species at large multiples of the human therapeutic dose, occurs as degeneration and necrosis of hepatic, renal and lymphoid tissue, and blood count changes. The metabolites believed responsible for these effects have also been demonstrated in man. Paracetamol should not, therefore, be taken for long periods of time, and in excessive doses. At normal therapeutic doses, paracetamol is not associated with genotoxic or carcinogenic risk. There is no evidence of embryo-or foetus-toxicity from paracetamol in animal studies. 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

Starch BP
Colloidal
Anhydrous Silica
EP
(Aerosil 200)
Magnesium
Stearate EP

Empty Hard Gelatin Capsule Shell contains:
Indigotine-FD & C Blue2 (E132)
Yellow Iron Oxide (E172)
Titanium Dioxide (E171)
Gelatin

6.2 Incompatibilities

Paracetamol: None known

Caffeine: Iodine, silver salts, tannins and strong solution of caustic alkalis.

Phenylephrine Hydrochloride: Butacaine, alkalis, ferric salts and oxidising agents.

6.3 Shelf life

3 Years from the date of manufacture.

6.4 Special precautions for storage

Store in a diy place below 25°C.
Protect from light.
Keep out of reach of children.

6.5 Nature and contents of container

Blister Pack

Capsules are packed individually in pre-moulded PVC film and sealed with aluminium foil.

Pack sizes of 10, 12, 20 and 24 capsules.

6.6 Special precautions for disposal

Return unused capsules to the Pharmacist.

7 MARKETING AUTHORISATION HOLDER

Aspar Pharmaceuticals Limited
Acrewood Way
St Albans,
AL4 0JY
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 08977/0037

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27 June 2000

10 DATE OF REVISION OF THE TEXT

26/03/2025