Summary of products characteristics (SmPC):

1. Name of the Medicinal Product: COLDEASE CAPSULES

2. Qualitative and Quantitative composition:
Each capsule contains Paracetamol BP 400mg, Caffeine Anhydrous BP 30mg, Chlorpheniramine Maleate BP 4mg, Pseudoephedrine Hydrochloride BP 30mg
For the full list of excipients, See section 6.1

3. Pharmaceutical form: Capsules
Pink coloured cap/pink coloured body '0' size capsule 'COLDEASE' imprinted on body and 'Rene Rene' imprinted on cap with black ink contains with off white colour powder.

4. Clinical particular's:
4.1 Therapeutic indication:
Symptomatic relief of symptoms of influenza, feverishness, chills and colds including feverish colds.
The symptomatic relief of nasal congestion and difficult breathing arising from this, sinusitis and its associated pain, acute nasal catarrh.

4.2 Posology and method of administration:
Adults and children over 12 years: One Coldease capsule three times a day in divided doses.
Method of Administration: Oral route.

4.3 Contraindication:
Contraindicated in the patients with known hypersensitivity to any of the ingredient in it.

4.4 Special warning and precaution for use:
It should be taken with caution in patients with impaired kidney and liver function. It may cause drowsiness.

4.5 Interactions with other medicinal products and other forms of interactions:
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.
Concurrent use of Chlorpheniramine and hypnotics or anxiolytics may cause an increase in sedative effects, therefore medical advice should be sought before taking Chlorpheniramine

concurrently with these medicines. Chlorpheniramine inhibits phenytoin metabolism and can lead to phenytoin toxicity.
Concomitant use of pseudoephedrine with tricyclic antidepressants, other sympathomimetic agents (such as decongestants, appetite suppressants and amfetamine-like psychostimulants) or with monoamine oxidase inhibitors (including furazolidone), which interfere with the catabolism of sympathomimetic amines, may occasionally cause a rise in blood pressure (see Contraindications).
The effect of antihypertensive agents, which interfere with sympathetic activity, may be partially reversed by this product, e.g. bretylium, betanidine, guanethidine, debrisoquine, methyldopa, alpha- and beta-adrenergic blocking agents.

Additional information on special populations:
Not Applicable
Pediatric population:
Not Applicable

4.6 Fertility, pregnancy and lactation:
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.

4.7 Effects on ability to drive and use machines:
Do not drive or operate machinery.

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, angiodema and Stevens Johnson syndrome, toxic epidermal necrolysis

Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary disorders	Hepatic dysfunction

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

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

Caffeine

Central Nervous system	Nervousness and anxiety Irritability, Restlessness and Excitability Dizziness

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.

Chlorpheniramine Maleate

Specific estimation of the frequency of adverse events for OTC products is inherently difficult (particularly numerator data). Adverse reactions which have been observed in clinical trials and which are considered to be common (occurring in 1% to <10% of subjects) or very common (occurring in ≥ 10% of subjects) are listed below by MedDRA Sytem Organ Class. The frequency of other adverse reactions identified during post-marketing use is unknown.

Blood and lymphatic system disorders:

Unknown: haemolytic anaemia, blood dyscrasias

Immune system disorders:

Unknown: allergic reaction, angioedema, anaphylactic reactions

Metabolism and nutritional disorders:

Unknown: anorexia

Psychiatric disorders:

Unknown: confusion*, excitation*, irritability*, nightmares*, depression

Nervous system disorders*:

Very common: sedation, somnolence

Common: disturbance in attention, abnormal coordination, dizziness headache

Eye Disorders:

Common: blurred vision

Ear and labyrinth disorders:

Unknown: tinnitus

Cardiac disorders:

Unknown: palpitations, tachycardia, arrhythmias

Vascular disorders:
Unknown: Hypotension
Respiratory, thoracic and mediastinal disorders:
Unknown: thickening of bronchial secretions
Gastrointestinal disorders:
Common: nausea, dry mouth
Unknown: vomiting, abdominal pain, diarrhoea, dyspepsia
Hepatobiliary disorders:
Unknown: hepatitis, jaundice
Skin and subcutaneous disorders:
Unknown: exfoliative dermatitis, rash, urticaria, photosensitivity
Musculoskeletal and connective tissue disorders:
Unknown: muscle twitching, muscle weakness
Renal and urinary disorders:
Unknown: urinary retention
General disorders and administration site conditions:
Common: fatigue
Unknown: chest tightness
*Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness).
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
Pseudoephedrine Hydrochloride
In clinical trials with this product, the incidence of somnolence and dizziness was no greater than that from placebo. Reports of drowsiness directly attributable to this product are extremely rare. For the great majority of patients, treatment with this product is not associated with clinically significant anticholinergic or sedative side effects.

Serious adverse effects associated with the use of pseudoephedrine are extremely rare. Symptoms of central nervous system excitation may occur including sleep disturbance, and, rarely, hallucinations.

Skin rashes, with or without irritation, have occasionally been reported with pseudoephedrine. Urinary retention has been reported occasionally in men receiving pseudoephedrine; prostatic enlargement could have been an important predisposing factor.

4.9 Overdose and Treatment:

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.

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.

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 and signs

Overdose of caffeine may result in epigastric pain, vomiting, diurese, tachycardia or cardiac arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions).

It must be noted that for clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol-related liver toxicity.

Treatment

No specific antidote is available, but supportive measures may be used.

Chlorpheniramine Maleate

Symptoms and signs

The estimated lethal dose of Chlorpheniramine is 25 to 50mg per kg body weight. Symptoms and signs include sedation, paradoxical excitation of the CNS, toxic psychosis, apnoea, convulsions, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias.

Treatment

Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions, and fluid and electrolyte balance.

If overdosage is by the oral route, treatment with activated charcoal should be considered provided there are no contraindications for use and the overdose has been taken recently (treatment is most effective if given within an hour of ingestion).

Hypotension and arrhythmias should be treated vigorously; CNS convulsions may be treated with I.V. diazepam. Haemoperfusion may be used in severe cases.

Pseudoephedrine Hydrochloride

There have been no reported cases of acute overdosage with this product. It may be expected that as with other sympathomimetic drugs, the symptoms and signs of overdosage may include irritability, restlessness, tremor, convulsions, palpitations, hypertension and difficulty with micturition.

Patients should receive necessary supportive treatment in the event of overdosage. Gastric lavage should be performed if indicated. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties:

Pharmacotherapeutic group: Antihistaminic, decongestant, analgesic

ATC Code: Paracetamol: N02BE01, Caffeine Anhydrous: N06BC01, Chlorpheniramine Maleate: R06AB04, Pseudoephedrine Hydrochloride: R01BA52

Paracetamol produces antipyresis by acting on the hypothalamic heat regulating centre and analgesia by elevating the pain threshold.
Chlorpheniramine Maleate is H1 antagonist (Antihistaminic)
Pseudoephedrine acts as a nasal and chest decongestant and caffeine is a central nervous system stimulant which there by also improves the physical performance.

5.2 Pharmacokinetic properties:

Paracetamol: is readily absorbed from the gastrointestinal tract. It is metabolised in the liver and excreted in the urine, mainly as glucoronide and sulphate conjugates.

Caffeine: is absorbed readily after oral administration, maximal plasma concentrations are achieved within one hour and the plasma half-life is about 3.5 hours. 65-80% of administered caffeine is excreted in the urine as 1-methyluric acid and 1-methylxanthine.

Chlorpheniramine Maleate: Chlorpheniramine is readily absorbed from the GI tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life is estimated to be 12 – 15 hours. There is significant plasma protein binding. The drug is largely inactivated in the liver and excreted as metabolites in the urine. Chlorpheniramine is metabolised to the monodesmethyl and didesmethyl derivative. About 22% of an oral dose is excreted unchanged in the urine. Only trace amounts have been found in the faeces.

Pseudoephedrine Hydrochloride

After the administration of one this product to healthy adult volunteers, the peak plasma concentration (C_{max}) for acrivastine is approximately 140 ng/ml, occurring at about 1.3 hours (T_{max}) after drug administration. The plasma half-life is approximately 1.6 hours. The peak plasma concentration for pseudoephedrine is approximately 210 ng/ml, with T_{max} approximately 2 hours after drug administration. The plasma half-life is approximately 5.5 hours (urine pH maintained between 5.0 - 7.0). The plasma half-life of pseudoephedrine is markedly decreased by acidification of urine and increased by alkalination. Renal excretion is the principal route of elimination of both acrivastine and pseudoephedrine.

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.

6. Pharmaceutical Particulars:

6.1 List of excipients

Coldease capsules contains the following excipients:
Colloidal silicone dioxide, Purified talc, Maize starch.

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6.4 Special precaution for storage

Do not store above 30°C. Protect from light. Keep out of reach of children

6.5 Nature and contents of container

Aluminium/ transparent PVC blister of 10 capsules and 10 of such blisters are packed in a unit box with pack insert.

6.6 Special precautions for disposal

No special precaution.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES:

Marketing Authorization Holder:
Rene Industries Ltd
Address: PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

Manufactured by:
Rene Industries Ltd
Address: PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

8. MARKETING AUTHORISATION NUMBER:

Not Applicable

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION:

Not Applicable

10. DATE OF REVISION OF THE TEXT:

Not Applicable

11. DOSIMETRY (IF APPLICABLE):
Not Applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE):
Not Applicable