SUMMARY PRODUCT CHARACTERISTICS

1. Name of the medicinal product

COLDAMOL P SYRUP

2. Qualitative and quantitative composition

Active Constituents	**mg / 5mls**
Paracetamol	120.0 mg
Chlorpheniramine maleate	2.0 mg
Pseudoephedrine HCl	10.0mg

3. Pharmaceutical form

Syrup: A clear pink coloured syrup with a strawberry flavour and sweet taste free from any visible impurities

4. Clinical particulars

4.1 Therapeutic indications

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

Dosage and Administration

Notes: All doses at all ages may be repeated 3-4 times a day if needed, at intervals of not less than 4 hours between the doses. The product should not be administered more than 4 times in 24 hours.

COLDAMOL P SYRUP

For children under 6 years of age [under 22 kg (48 lbs.)] the physician should be consulted.

Adults and Children 12 Years of Age and over: 10 ml (2 teaspoonfuls), 3-4 times daily if needed.

Children 6-11 Years of Age [22 – 43 kg (48-95 lbs.)]

5-10 ml (1- 2 teaspoonfuls) 3-4 times daily if needed.

Recommended Dosage of COLDAMOL P Syrup When Prescribed by the Physician

Age	***Weight***	***Dose***
12-23 months Approx.	8-10 kg. (18-23 lbs)	3.75 ml.
2-3 years Approx.	11-16 kg (24-35 lbs.)	5 ml.
4-5 years Approx.	16-21 kg (36-47 lbs.)	7.5 ml.
6-8 years Approx.	22-27 kg (48-59 lbs.)	10 ml.
9-10 years Approx.	27-32 kg (60-71 lbs.)	12.5 ml
11 years Approx.	33-43 kg (72-95 lbs.)	15 ml.

Note: 1 lb = 0.4536 kg.

4.3 Contraindications

Contraindications Known hypersensitivity to any ingredient of the preparation. During lactation. Newborn and premature infants. Asthma or other lower respiratory tract conditions, narrow-angle glaucoma, stenosing peptic ulcer, symptomatic prostatic hypertrophy, bladder neck obstruction, pyloroduodenal obstruction. Concomitant use with monoamine oxidase (MAO) inhibitor therapy or within 14 days of discontinuation of such therapy (see Drug Interactions). Severe hypertension and severe coronary artery disease. Do not use in children under the age of 2 years.

4.4 Special warnings and precautions for use

Paracetamol can cause accidental poisoning in toddlers and infants. Paracetamol containing products should be kept well out of reach of children. Potentially fatal hepatotoxicity can result from paracetamol overdosage. However, in rare cases, hepatotoxicity has occurred in patients receiving high or excessive doses within therapeutic doses. Certain patients may be more susceptible to paracetamol hepatotoxicity, e.g., chronic alcoholics, patients with liver disease, or those who are malnourished or taking other drugs that induce hepatic enzymes. Because of the risk of hepatotoxicity, patients should be cautioned against the inadvertent administration of excessive doses of paracetamol by using multiple paracetamol-containing product at once, such as cough and cold remedies, analgesics or arthritic formulations, antipyretics or products for relief of menstrual symptoms or muscle spasm. Administration of paracetamol to children may be especially prone to error due to the many concentrations and strengths of products available. To avoid dosing errors, all product labels should be checked carefully to ensure calculation of the amount of paracetamol to be given.

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.

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 (eg amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine (see contraindications).
Digoxin and cardiac glycosides	Concimitant use of phenylephrine with digoxin or cardiac glycosides may increase the ris 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 Pregnancy and lactation
Use in Pregnancy Safety of use in pregnancy has not been established.

4.7 Effects on ability to drive and use machines
Patients should be advised not to drive or operate machinery if affected by dizziness.

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	Bromchospasm*
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.

Chloropheniramine maleate

The following adverse events have been observed in clinical trials with chloropheniramine maleate 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 is 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.

Pseudoephedrine HCl.
Common adverse drug reactions (ADRs) associated with pseudoephedrine therapy include central nervous system stimulation, insomnia, nervousness, excitability, dizziness and anxiety. Infrequent ADRs include tachycardia or palpitations. Rarely, pseudoephedrine therapy may be associated with mydriasis (dilated pupils), hallucinations, arrhythmias, hypertension, seizures and ischemic colitis;[17] as well as severe skin reactions known as recurrent pseudo-scarlatina, systemic contact dermatitis, and nonpigmenting fixed drug eruption.[18] Pseudoephedrine, particularly when combined with other drugs including narcotics, may also play a role in the precipitation of episodes of paranoid psychosis.[19] It has also been reported that pseudoephedrine, among other sympathomimetic agents, may be associated with the occurrence of stroke.[20]

4.9 Overdose
Overdosage For Paracetamol Manifestations Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia, and abdominal pain. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported. In massive overdosage, paracetamol may cause hepatic toxicity. In adults and adolescents, hepatic toxicity has been rarely reported following ingestion of acute overdose of less than 7.5 –10 g. Fatalities are infrequent (less than 3-4% of untreated cases) and have been rarely reported with overdoses of less than 15 g. Early symptoms following a potentially hepatotoxic overdose may include nausea, vomiting, stomach pain, diaphoresis, and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48-72 hours post-ingestion. Serious toxicity or fatalities are extremely infrequent in children, possibly due to differences in the way they metabolize paracetamol. An acute overdosage of less than 150 mg/kg bodyweight in children has not been associated with hepatic toxicity.

Treatment Adults and Adolescents Regardless of the quantity of paracetamol reported or assumed to have been ingested, N-acetylcysteine should be administered immediately, if 24 hours or less have elapsed from the time of ingestion. An initial dose of 150 mg N-acetylcysteine/kg body weight is infused I.V. in 200 ml of 5% Dextrose Injection over 15 minutes. This is followed by I.V infusion of 50 mg N-acetylcysteine/kg body weight in 500 ml of 5% Dextrose Injection over the next 4 hours, and 100 mg N-acetylcysteine/kg body weight in 1 liter of 5% Dextrose Injection over the next 16 hours (providing a total dose of 300 mg/kg body weight of N-acetylcysteine over 20 hours). In addition to N-acetylcysteine administration, it is recommended that the stomach be emptied promptly by lavage, or by induction of emesis with syrup of ipecac. A serum paracetamol assay should be obtained as early as possible, but not less than 4 hours following ingestion. If plasma level falls above the lower treatment line on the paracetamol overdose nomogram, acetylcycteine therapy should be continued. Liver function tests should be performed initially, and repeated at 24-hour intervals. Children Induce emesis using syrup of ipecac. A serum paracetamol assay should be obtained as soon as possible, but not less than 4 hours following ingestion. If more than 150 mg/kg body weight or an unknown amount was ingested, plasma paracetamol level should be obtained. The plasma paracetamol level should be obtained as soon as possible, but no sooner than 4 hours following ingestion. If plasma level falls above the lower treatment line on the paracetamol overdose nomogram, the acetylcysteine therapy should be initiated and continued for a full course of therapy. If a paracetamol assay is not available and the paracetamol ingestion exceeds 150 mg/kg body weight, N-acetylcysteine therapy should be initiated and continued for a full course. The dosage and administration of N-acetylcysteine in children is the same as recommended for adults and adolescents. However, the quantity of I.V. fluid used in children should be modified, taking into account both age and weight.

For Chlorpheniramine Maleate Manifestations Antihistamine overdosage reactions may vary from central nervous system depression to stimulation, especially in children. Atropine-like signs and symptoms such as dry mouth, fixed dilated pupils and flushing, as well as gastrointestinal symptoms, may occur. Treatment There is no specific therapy for acute overdosage with antihistamines. General symptomatic and supportive measures should be instituted promptly and maintained for as long as necessary. Conscious Patients Vomiting should be induced even though it may have occurred spontaneously. If the patient is unable to vomit, gastric lavage is indicated. Isotonic saline is the lavage of choice. Adequate precautions must be taken to protect against aspiration, especially in infants and children. Charcoal slurry or another suitable agent should be instilled into the stomach after vomiting or lavage. Saline cathartics or milk of magnesia may be of additional benefit.

Unconscious Patients The airway should be secured with a cuffed endotracheal tube before attempting to evacuate the gastric contents. Intensive supportive and nursing care are indicated, as for any comatose patient. Do not administer CNS stimulants. Hypotension is an early sign of impending cardiovascular collapse. If a vasopressor agent is needed, noradrenaline, phenylephrine or dopamine is indicated. Use of adrenaline should be avoided since it may worsen hypertension. In case of convulsions, diazepam may be used and repeated as necessary. When life-threatening CNS signs and symptoms are present, intravenous physostigmine salicylate may be considered. Ice packs and cooling sponge baths, but not alcohol, can help in reducing the fever commonly observed in children. Hemoperfusion may be used in severe cases. For Pseudoephedrine Manifestations: As with other sympathomimetic agents, symptoms of

overdosage include: mild anxiety, irritability, restlessness, tremor, convulsions, palpitations, hypertension, and difficulty in micturition. Symptoms usually appear within 4-8 hours of ingestion and are transient, usually requiring no treatment. Treatment Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed if indicated. Catheterization of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Paracetamol: An analgesic and antipyretic.

Chlorpheniramine maleate: Antihistamine action: Antihistamines compete with histamine for H_1-receptor sites on smooth muscle of the bronchi, GI tract, uterus, and large blood vessels; they bind to cellular receptors, preventing access of histamine, thereby suppressing histamine-induced allergic symptoms. They don't directly alter histamine or its release.

Pseudoephedrine is a sympathomimetic amine. Its principal mechanism of action relies on its direct action on the adrenergic receptor system.[9][10] The vasoconstriction that pseudoephedrine produces is believed to be principally an α-adrenergic receptor response.[11]

The active ingredients are not known to cause sedation.

Chlorpheniramine is an antihistamine that reduces the effects of natural chemical histamine in the body. Histamine can produce symptoms of sneezing, itching, **watery eyes**, and **runny nose**.

Pseudoephedrine is a decongestant that shrinks blood vessels in the nasal passages. Dilated blood vessels can cause **nasal congestion** (stuffy nose).

Chlorpheniramine and pseudoephedrine is a combination medicine used to treat symptoms of the **common cold** or seasonal **allergies**, including sneezing, runny or stuffy nose, and itchy, watery eyes.

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.

Chlorpheniramine maleate:
Absorption: Well absorbed from the GI tract. Food in the stomach delays absorption but doesn't affect bioavailability.
Distribution: Distributed extensively into the body; drug is about 72% protein-bound.
Metabolism: Metabolized largely in GI mucosal cells and liver (first-pass effect).
Excretion: Half-life is 12 to 43 hours in adults and 10 to 13 hours in children; drug and metabolites are excreted in urine.

Pseudoephedrine acts on α- and β2-adrenergic receptors, to cause vasoconstriction and relaxation of smooth muscle in the bronchi, respectively.[9][10] α-adrenergic receptors are located

on the muscles lining the walls of blood vessels. When these receptors are activated, the muscles contract, causing the blood vessels to constrict (vasoconstriction). The constricted blood vessels now allow less fluid to leave the blood vessels and enter the nose, throat and sinus linings, which results in decreased inflammation of nasal membranes, as well as decreased mucus production. Thus, by constriction of blood vessels, mainly those located in the nasal passages, pseudoephedrine causes a decrease in the symptoms of nasal congestion. Activation of β2-adrenergic receptors produces relaxation of smooth muscle of the bronchi,[9] causing bronchial dilation and in turn decreasing congestion (although not fluid) and difficulty breathing.

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.

6. Pharmaceutical particulars:

6.1 List of excipients:

- Propylene glycol
- Rectified spirit
- Methyl paraben sodium
- Propyl paraben sodium
- Sucrose
- Saccharin sodium
- Celocell
- Strawberry (Inhouse)
- ponceau 4R colour (inhouse)

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

3 years

6.4 Special precautions for storage:

Do not store above 30°C, Protect from direct sunlight.

6.5 Nature and contents of the container:

Pack: 100mls in amber coloured bottles inserted in unit cartons.

6.6 Special precautions for disposal:

No special requirements.

7. Marketing authorization holder:

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8. Marketing authorization number(s)

H200B/8843/932

9. Date of first authorization/renewal of the authorization

19.04.2009

10. Date of revision of the text