SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT: RONFIT COLD EXTRA

Generic Name of Product : Paracetamol, Phenylephrine, Caffeine with Chlorphenamine Tablets

Strength (formula) : Each uncoated tablet contains:

Paracetamol BP	500 mg
Phenylephrine HCL BP	20 mg
Chlorphenamine Maleate BP	4 mg
Caffeine (Anhydrous) BP	30 mg
Excipients	q.s.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

2.1 Qualitative & Quantitative Composition Declaration:

Approved name	Specifications	Label claim / Tablet (In mg)	Overages Added (In %)	Qty / tablet (in mg)
Paracetamol	BP	500.00	--	500.00
Caffeine Anhydrous	BP	30.00	--	30.00
Phenylephrine HCl	BP	20.00	--	20.00
Chlorpheniramine Maleate	BP	4.00	--	4.00
Microcrystalline Cellulose	BP	--	--	20.00
Maize Starch	BP	--	--	30.00
Maize Starch	BP	--	--	23.00
Povidone	BP	--	--	4.00
Sodium Methylparaben	BP	--	--	0.50
Sodium Propylparaben	BP	--	--	0.05
Purified Water*	BP	--	--	q.s.
Magnesium Stearate	BP	--	--	7.00
Sodium Starch Glycolate	BP	--	--	5.00
Maize Starch	BP	--	--	7.00

BP: - British Pharmacopoeia **IHS: -** In-House Specifications

3. PHARMACEUTICAL FORM:

White colour round shape uncoated tablet, having break line on one side and plain on other side.

RONAK EXIM PVT. LTD. INDIA

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications:

Pharmacotherapeutic Group: Other analgesics and antipyretics & other cold combination preparations.

RONFIT COLD EXTRA TABLETS is indicated for:

- Relief of nasal and sinus congestion.
- Relief of allergic symptoms of the nose or throat due to upper respiratory tract allergies.
- Relief of sinus pain and headache.
- Adjunct with antibacterial in sinusitis, tonsillitis and otitis media.

The product is recommended for the relief of sinus pain and the symptoms of colds and influenza, including fatigue and drowsiness.

4.2 Posology and Method of Administration:

Posology:

Adults and children 12 years of age and over
1 tablet twice or thrice daily. Or as directed by the physician.

Method of Administration:

Oral administration

4.3 Contra – Indications:

Hypersensitivity to paracetamol or any of the other constituents.
Should be given with care to patients with a history of peptic ulcer.
Severe coronary heart disease and cardiovascular disorders. Hypertension. Hyperthyroidism. Contraindicated in patients currently receiving or within two weeks of stopping therapy with monoamine oxidase inhibitors.
Not to be used in children under the age of 12 years.

4.4 Special Warning and Precautions for Use:

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
Use with caution in patients with Raynaud's phenomenon and diabetes mellitus.
The following warnings will appear on the pack:-
CONTAINS PARACETAMOL

- If symptoms persist consult your doctor.
- Do not exceed the stated dose.
- Keep all medicines out of the reach and sight of children.
- Do not take with any other paracetamol-containing products.

The Label shall say:

Immediate medical advice should be sought in the event of an overdose, even if you feel well.
The Leaflet shall say:
Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.
If you are pregnant or being prescribed medicine by your doctor, seek your doctor's advice before taking this product.

4.5 Interaction with other medicinal products and other forms of interaction

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.
Drugs which induce hepatic microsomal enzymes, such as alcohol, barbiturates, monoamine oxidase inhibitors and tricyclic antidepressants, may increase the hepatotoxicity of paracetamol, particularly after over dosage. Contraindicated in patients currently receiving or within two weeks of stopping therapy with monoamine oxidase inhibitors because of a risk of hypertensive crisis.
Phenylephrine may adversely interact with other sympathomimetics, vasodilators and beta blockers.

4.6 Pregnancy and lactation

Pregnancy

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use.
Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.
Taken during pregnancy, it appears that the half-life of caffeine is prolonged. This is a possible contributing factor in hyperemesis gravidarum (morning sickness).
Caffeine appears in breast milk. Irritability and poor sleeping pattern in the infant have been reported.
Due to the vasoconstrictive properties of phenylephrine the product should be used with caution in patients with a history of pre-eclampsia. Phenylephrine may reduce placental perfusion and the product should be used in pregnancy only if the benefits outweigh this risk. There is no information on use in lactation.

Lactation

Paracetamol, Caffeine, Phenylephrine HCl & Chlorphenamine maleate are excreted in breast milk May have a stimulating effect on breast fed infants. RONFIT COLD EXTRA should not be used during breast feeding.

4.7 Effects on ability to drive and use machine:

Not known.

4.8 Undesirable effects

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur.
There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

Nausea and insomnia have been noted.
Phenylephrine hydrochloride may elevate blood pressure with headache, vomiting and rarely palpitations; tachycardia or reflex bradycardia; tingling and coolness of the skin. There have been rare reports of allergic reactions.

4.9 Overdoses:

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, 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 British National Formulary (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 National Poisons Information Service (NPIS) or a liver unit.

CAFFEINE

Doses over 1g are probably necessary to induce toxicity, 2 – 5g to produce severe toxicity and 5 – 10g is likely to be lethal.

Symptoms include: epigastric pain, vomiting, diuresis, tachycardia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors, convulsions).

No specific antidote is available, reduce or stop dosage and avoid excessive intake of coffee or tea.

PHENYLEPHRINE HYDROCHLORIDE

Severe overdosage may produce hypertension and associated reflex bradycardia. Treatment measures include early gastric lavage and symptomatic and supportive measures. The hypertensive effects may be treated with an alpha-receptor blocking agent (such as phentolamine mesylate 6 – 10 mg) given intravenously, and the bradycardia treated with atropine, preferably only after the pressure has been controlled.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties

Mechanism of Action:

Pharmacotherapeutic Group: Other analgesics and antipyretics & Other cold combination preparations

ATC code: N02BE51

PARACETAMOL

Analgesic:

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting a prostaglandin synthesis in the central nervous system (CNS) and to a lesser extent through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.

Antipyretic:

Paracetamol probably produces antipyresis by acting on the hypothalamic heat-regulating centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

CAFFEINE

Central nervous system stimulant – Caffeine stimulates all levels of the CNS, although its cortical effects are milder and of shorter duration than those of amfetamines.

Analgesia Adjunct:

Caffeine constricts cerebral vasculature with an accompanying decrease in cerebral blood flow and in the oxygen tension of the brain. It is believed that caffeine helps to relieve headache by providing a more rapid onset of action and/or enhanced pain relief with lower doses of analgesic. Recent studies with ergotamine indicate that the enhancement of effect by the addition of caffeine may also be due to improved gastrointestinal absorption of ergotamine when administered with caffeine.

PHENYLEPHRINE HYDROCHLORIDE

Sympathomimetic amines, such as phenylephrine, act on alpha-adrenergic receptors of the respiratory tract to produce vasoconstriction, which temporarily reduces the swelling associated with inflammation of the mucous membranes lining the nasal and sinus passages. This allows the free drainage of the sinusoidal fluid from the sinuses.

In addition to reducing mucosal lining swelling, decongestants also suppress the production of mucus, therefore preventing a buildup of fluid within the cavities which could otherwise lead to pressure and pain. Chlorpheniramine in provides prompt relief of itchy watery eyes, runny nose, sneezing, itching of the nose or throat due to respiratory allergies.

5.2 Pharmacokinetic properties

PARACETAMOL

Absorption and Fate

Paracetamol is rapidly absorbed from the gastro-intestinal tract with peak plasma concentrations occurring between 10 and 120 minutes after oral administration. It is metabolised in the liver 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 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 overdose and cause liver damage.

CAFFEINE

Absorption and Fate

Caffeine is absorbed readily after oral administration and is widely distributed throughout the body. Caffeine is metabolised almost completely via oxidation, demethylation, and acetylation, and is excreted in the urine as 1-methyluric acid, 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine), 5-acetylamino-6-formylamino-3-methyluracil (AFMU), and other metabolites with only about 1% unchanged.

PHENYLEPHRINE HYDROCHLORIDE

Absorption and Fate

Phenylephrine has reduced bioavailability from the gastro-intestinal tract owing to irregular absorption and first-pass metabolism by monoamine oxidase in the gut and liver.

CHLORPHENAMINE MALEATE

Chlorphenamine Maleate is an alkylamine derivative with a plasma half-life of up to 42 hours which is extensively metabolised in the liver and excreted almost exclusively in the urine.

5.3 Preclinical safety data

Not available

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients

Maize Starch, Microcrystalline Cellulose, Povidone, Sodium Methylparaben, Sodium Propylparaben, Purified Water*, Magnesium Stearate, Sodium Starch Glycolate.

6.2 Incompatibilities:

Not Applicable.

6.3 Shelf – life:

36 Months.

6.4 Special Precautions for Storage:

Store below 30°C. Protected from light & moisture.

6.5 Nature and Contents of Container:

1 X 4 Tablets are packed in a blister & such 48 blister are placed in a carton with pack insert.

6.6 Special Precautions for disposal:

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Manufacturer

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8. DATE OF PUBLICATION OR REVISION:

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