SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT: RONANUTRA

Generic Name of Product **:** CYPROHEPTADINE TABLETS BP 4 MG

Strength (formula) **:** Each uncoated tablet contains:
Cyproheptadine Hydrochloride (Anhydrous) BP 4 mg
Excipients…….. q.s.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

2.1 Qualitative & Quantitative Composition Declaration:

For, 1,00,000 TAB

Sr. No.	Ingredients	Spec.	Label Amount	% OA.	Qty. Req. / batch Kg
1	Cyproheptadine HCl	BP	4.0 MG	2.5%	4.45
2	Maize starch	BP	-	-	84.0
3	Dibasic Calcium Phosphate	BP	-	-	79.55
4	Maize starch	BP	-	-	7.00
5	Magnesium stearate	BP	-	-	5.00

Abbreviation:- USP:- Unite states Pharmacopoeia
BP:- British Pharmacopoeia
IHS:- In-House Specifications

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3. PHARMACEUTICAL FORM:

White coloured, round, flat, uncoated tablets, having break line on one side and plain on other side.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications:

Perennial and seasonal allergic rhinitis Vasomotor rhinitis Allergic conjunctivitis due to inhalant allergens and foods Mild, uncomplicated allergic skin manifestations of urticaria and angioedema. Amelioration of allergic reactions to blood or plasma Cold urticaria Dermatographism As therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

4.2 Posology and Method of Administration:

DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND THE RESPONSE OF THE PATIENT.

Each tablet contains 4 mg of cyproheptadine hydrochloride.

Pediatric Patients

Age 2 to 6 years

The total daily dosage for pediatric patients may be calculated on the basis of body weight or body area using approximately 0.25 mg/kg/day or 8 mg per 2 square meter of body surface (8 mg/m). The usual dose is 2 mg (1/2 tablet) two or three times a day, adjusted as necessary to the size and response of the patient. The dose is not to exceed 12 mg a day.

Age 7 to 14 years

The usual dose is 4 mg (1 tablet) two or three times a day adjusted as necessary to the size and response of the patient. The dose is not to exceed 16 mg a day.

Adults

The total daily dose for adults should not exceed 0.5 mg/kg/day. The therapeutic range is 4 to 20 mg a day, with the majority of patients requiring 12 to 16 mg a day. An occasional patient may require as much as 32 mg a day for adequate relief. It is suggested that dosage be initiated with 4 mg (1 tablet) three times a day and adjusted according to the size and response of the patient.

4.3 Contra – Indications:

Newborn or Premature Infants This drug should not be used in newborn or premature infants.

Nursing Mothers

Because of the higher risk of antihistamines for infants generally and for newborns and prematures in particular, antihistamine therapy is contraindicated in nursing mothers.

Other Conditions

Hypersensitivity to cyproheptadine and other drugs of similar chemical structure.

Monoamine oxidase inhibitor therapy.

Angle-closure glaucoma, Stenosing peptic ulcer, Symptomatic prostatic hypertrophy, Bladder neck obstruction, Pyloroduodenal obstruction, Elderly, debilitated patients.

4.4 Special Warning and Precautions for Use:

WARNINGS

Pediatric Patients

Overdosage of antihistamines, particularly in infants and young children, may produce hallucinations, central nervous system depression, convulsions, respiratory and cardiac arrest, and death. Antihistamines may diminish mental alertness; conversely, particularly, in the young child, they may occasionally produce excitation.

CNS Depressants

Antihistamines may have additive effects with alcohol and other CNS depressants, e.g., hypnotics, sedatives, tranquilizers, antianxiety agents.

Activities Requiring Mental Alertness

Patients should be warned about engaging in activities requiring mental alertness and motor coordination, such as driving a car or operating machinery. Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

PRECAUTIONS

General

Cyproheptadine has an atropine-like action and, therefore, should be used with caution in patients with:

History of bronchial asthma

Increased intraocular pressure

Hyperthyroidism

Cardiovascular disease

Hypertension.

Information for Patients

Antihistamines may diminish mental alertness; conversely, particularly, in the young child, they may occasionally produce excitation. Patients should be warned about engaging in activities requiring mental alertness and motor coordination, such as driving a car or operating machinery.

4.5 Interaction with other medicinal products and other forms of interaction

Drug Interaction

MAO inhibitors prolong and intensify the anticholinergic effects of antihistamines.

Antihistamines may have additive effects with alcohol and other CNS depressants, e.g., hypnotics, sedatives, tranquilizers, antianxiety agents.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenic studies have not been done with cyproheptadine.
Cyproheptadine had no effect on fertility in a two-litter study in rats or a two generation study in mice at about 10 times the human dose.
Cyproheptadine did not produce chromosome damage in human lymphocytes or fibroblasts in vitro; high doses (10^{-4} M) were cytotoxic. Cyproheptadine did not have any mutagenic effect in the Ames microbial mutagen test; concentrations of above 500 mcg/plate inhibited bacterial growth.

4.6 Pregnancy and lactation

Pregnancy:

Pregnancy Category B Reproduction studies have been performed in rabbits, mice, and rats at oral or subcutaneous doses up to 32 times the maximum recommended human oral dose and have revealed no evidence of impaired fertility or harm to the fetus due to cyproheptadine. Cyproheptadine has been shown to be fetotoxic in rats when given by intraperitoneal injection in doses four times the maximum recommended human oral dose. Two studies in pregnant women, however, have not shown that cyproheptadine increases the risk of abnormalities when administered during the first, second and third trimesters of pregnancy. No teratogenic effects were observed in any of the newborns. Nevertheless, because the studies in humans cannot rule out the possibility of harm, cyproheptadine should be used during pregnancy only if clearly needed.

Nursing Mothers:

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from cyproheptadine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machine:

Not applicable.

4.8 Undesirable effects

Adverse reactions which have been reported with the use of antihistamines are as follows:

Central Nervous System :

Sedation and sleepiness (often transient), dizziness, disturbed coordination, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, paresthesias, neuritis, convulsions, euphoria, hallucinations, hysteria, faintness.

Integumentary :
Allergic manifestation of rash and edema, excessive perspiration, urticaria, photosensitivity.

Special Senses :
Acute labyrinthitis, blurred vision, diplopia, vertigo, tinnitus.

Cardiovascular :
Hypotension, palpitation, tachycardia, extrasystoles, anaphylactic shock.

Hematologic :
Hemolytic anemia, leukopenia, agranulocytosis, thrombocytopenia.

Digestive System :
Cholestasis, hepatic failure, hepatitis, hepatic function abnormality, dryness of mouth, epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation, jaundice.

Genitourinary :
Urinary frequency, difficult urination, urinary retention, early menses.

Respiratory :
Dryness of nose and throat, thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

4.9 Overdose

Antihistamine overdosage reactions may vary from central nervous system depression to stimulation especially in pediatric patients. Also, atropine-like signs and symptoms (dry mouth; fixed, dilated pupils; flushing, etc.) as well as gastrointestinal symptoms may occur. If vomiting has not occurred spontaneously, the patient should be induced to vomit with syrup of ipecac. If patient is unable to vomit, perform gastric lavage followed by activated charcoal. Isotonic or 1/2 isotonic saline is the lavage of choice. Precautions against aspiration must be taken especially in infants and children.

When life threatening CNS signs and symptoms are present, intravenous physostigmine salicylate may be considered. Dosage and frequency of administration are dependent on age, clinical response, and recurrence after response. (See package circulars for physostigmine products.) Saline cathartics, as milk of magnesia, by osmosis draw water into the bowel and, therefore, are valuable for their action in rapid dilution of bowel content. Stimulants should not be used.

Vasopressors may be used to treat hypotension. The oral LD50 of cyproheptadine is 123 mg/kg, and 295 mg/kg in the mouse and rat, respectively.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistaminic.

ATC code: R06AX02

Mode of action

Serotonin and histamine antagonist; competitively inhibits H1 receptor, mediating bronchial constriction, smooth-muscle contraction, edema, hypotension, CNS depression, and cardiac arrhythmias; prevents histamine release in blood vessels and is more effective in preventing histamine response than in reversing it; may be useful in patients with syndromes sustained by histamine-producing tumors.

Moderate anticholinergic activity with low sedative effect
May have anti-5HT2 effects
May have some calcium-channel blocking activity.

5.2 Pharmacokinetic properties

Absorption

Peak plasma time: 6-9 hr

Metabolism

Metabolized by glucuronidation via UGT1A
Metabolites: Quaternary ammonium glucuronide conjugate

Elimination

Excretion: Urine (40%), feces (2-20%)

5.3 Preclinical safety data

The results of the preclinical tests do not add anything of further significance to the prescriber.

6. Pharmaceutical particulars

6.1 List of excipients

Maize Starch, Dibasic calcium phosphate, Magnesium stearate

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a dry place below 30°C. Protect from light, heat & moisture.

6.5 Nature and contents of container

10 Tablet is packed in Alu-PVC blister and such 50 blisters are packed in a printed carton along with package insert.

6.6 Special precautions for disposal and other handling

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7. Marketing authorization holder

(Company) Name: RONAK EXIM PRIVATE LIMITED

Address: Sant Kabir Road, Behind Gendi Gate,

Police Station, Baroda – 390 001, GUJARAT

Country: INDIA

Phone: +91 265 2428444
Fax: +91-265-2565162
e-Mail: ahmedi@ronakoverseas.com

8. Marketing authorization number(s)

Not applicable.

9. Date of first authorization/renewal of the authorization

Not applicable.

10. Date of revision of the text

Not applicable.

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