1 NAME OF THE MEDICINAL PRODUCT

INKRETIN TABLET 4mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Cyproheptadine hydrochloride	4 mg
Excipients	q.s.

3 PHARMACEUTICAL FORMS

Oral Tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic Indication.

Cyproheptadine provides quick recovery from allergic disorders, treatment of inflammation of nasal mucosa such as rhinitis. Nutritional deficiencies, diet regulation in the course of treatment are corrected.

Cyproheptadine is indicated in the treatment of

* 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

4.2 Posology and method of administration.

Posology

Dosage should be individualized according to the needs and the response of the patient. Each tab let contains 4mg of Cyproheptadine Hydrochloride

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 0.25mg/kg/day or 8mg per 2 square meter of body surface (8 mg/m). The usual dose is 2mg (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 4mg (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 16mg a day.

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

Method of administration

For oral administration.

4.3 Contraindications
INKRETIN is contraindicated in:

• Patients undergoing therapy for an acute asthmatic attack;

• Newborn or premature infants; use in infants has been associated with apnoea, cyanosis and respiratory difficulty;

• Breast-feeding mothers;

• Patients with known sensitivity to cyproheptadine hydrochloride or drugs with similar chemical structure;

• Concurrent use with monoamine oxidase inhibitors;

• Glaucoma;

• Patients with pyloroduodenal obstruction, stenosing peptic ulcer, symptomatic prostatic hypertrophy, predisposition to urinary retention or bladder neck obstruction;

• Elderly, debilitated patients.

Known hypersensitivity to any of the active constituents.

4.4 Special warnings and precautions for use
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
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, tranquillisers and anti-anxiety agents.

Drugs with anti-serotonin activity, such as cyproheptadine, may interfere with serotonin enhancing anti-depressants including selective serotonin re-uptake inhibitors (SSRI's). This may result in possible recurrence of depression and related symptoms.

Cyproheptadine may cause a false positive test result for tricyclic antidepressant drugs (TCA) when evaluating a drug screen (e.g. urine, serum). Because cyproheptadine and TCAs may produce similar overdose symptoms, physicians should carefully monitor patients for TCA toxicity in the event of combined overdose.

4.6 Fertility, pregnancy and lactation
Pregnancy

The use of any drug in pregnancy or in women of child-bearing age requires that the potential benefit of the drug should be weighed against possible hazards to the embryo and fetus.

It is not known whether INKRETIN is excreted in human milk, and because of the potential for serious adverse reactions in breast-feeding infants from INKRETIN, a decision should be made whether to discontinue breast-feeding or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effect on the ability to drive and use machine.
In clinical trials that assessed driving ability, no impairment occurred in patients receiving Cyproheptadine Hydrochloride. However, patients should be informed that very rarely some people experience drowsiness, which may affect their ability to drive or use machines.

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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.

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

After a single 4 mg oral dose of 14C-labelled Cyproheptadine Hydrochloride in normal subjects given as Syrup or syrup, 2 to 20% of the radioactivity was excreted in the stools. Only about 34% of the stool radioactivity was unchanged drug, corresponding to less than 5.7% of the dose. At least 40% of the administered radioactivity was excreted in the urine.

No significant difference in the mean urinary excretion exists between the tablet and syrup formulations. The principle metabolite found in human urine has been identified as a quaternary ammonium glucuronide conjugate of cyproheptadine. Elimination is diminished in renal insufficiency.

Nicotinamide is readily absorbed from the GI tract following oral administration and is widely distributed in the body tissues. Small amounts of nicotinamide are excreted unchanged in urine

following therapeutic doses, however, the amount excreted unchanged is increased with larger doses.

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%)

In reproductive toxicity studies, no teratogenic effects were observed. However, prolonged parturition and reduced viability of offspring were observed in rats at plasma levels (AUC) 10 times higher than those achieved with clinical doses.

5.3 Preclinical safety data

Non-clinical data reveal.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipient

Lactose monohydrate,
maize starch,

Povidone

Gelatine

Methyl paraben

Propyl paraben

Aerosil

Sodium starch glycolate

6.2 Incompatibilities

unknown

6.3 Shelf-life

36 months

6.4 Special precautions for storage

Do not store above 30 C. Store in a dry place.

6.5 Nature and composition of immediate packaging

Blisters of 1 x 30 tablets with INKRETIN written on the foil on one side and plain PVC on the other.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

None.

7.0 APPLICANT/MANUFACTURER

7.1 Name and Address

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