

1. NAME OF THE MEDICINAL PRODUCT
APETAKRIS TABLETS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Cyproheptadine Hydrochloride BP

Eq. to anhydrous Cyproheptadine Hydrochloride 4mg

Excipients.....Q.S

Colour: Approved colour

Excipients with known effect:

Maize Starch, Dibasic Calcium Phosphate, Microcrystalline Cellulose, Sodium Starch Glycolate, P.V.P.K-90, Methyl Paraben, Propyl Paraben, Magnesium Stearate, Purified Talc, Colloidal Silicon Dioxide (Aerosil), Cross Carmelose Sodium.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet

Flat, white Colour, round shape tablet embossed with a break line on one side and other side plain.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cyproheptadine Hydrochloride Tablets 4mg is a serotonin and histamine antagonist with anticholinergic and sedative properties. In allergy and pruritus: Cyproheptadine Hydrochloride Tablets 4mg has a wide range of anti allergic and antipruritic activity, and can be used successfully in the treatment of acute and chronic allergic and pruritic conditions, such as dermatitis, including neurodermatitis and neurodermatitis circumscripta; eczema; eczematoid dermatitis; dermatographism; mild, local allergic reactions to insect bites; hay fever and other seasonal rhinitis; perennial allergic and vasomotor rhinitis; allergic conjunctivitis due to inhalant allergens and foods; urticaria; angioneurotic oedema; drug and serum reactions; anogenital pruritus; pruritus of chicken pox.

Cyproheptadine Hydrochloride Tablets 4mg is indicated as adjunctive therapy to adrenaline and other standard measures for the relief of anaphylactic reactions after the acute manifestations have been controlled.

In migraine and vascular headache Cyproheptadine Hydrochloride Tablets 4mg has been reported to have beneficial effects in a significant number of patients having vascular types of headache. Many patients who have responded inadequately to all other agents have reported amelioration of symptoms with Cyproheptadine Hydrochloride Tablets 4mg. The characteristic headache and feeling of malaise may disappear within an hour or two of the first dose.

4.2 Posology and method of administration

Posology

For the treatment of allergy and pruritus:

Dosage must be determined on an individual basis. The effect of a single dose usually lasts for four to six hours. For continuous effective relief, the daily requirement should be given in divided doses, usually three times a day, or as often as necessary, to provide continuous relief.

Adults: The therapeutic range is 4-20 mg (1 to 5 tablets) a day, most patients requiring 12-16 mg a day. It is recommended that dosage be initiated with 4 mg three times a day and then adjusted according to the weight and response of the patient up to a maximum of 32 mg a day.

Children aged 7-14 years: Usually 4 mg two or three times a day, according to the patient's weight and response. If an additional dose is required, it should be given at bedtime. Maximum 16 mg a day.

Children aged 2-6 years: Initially 2 mg two or three times a day, adjusted according to the patient's weight and response. If an additional dose is required, it should be given at bedtime. Maximum 12 mg a day.

For treatment of vascular headache and migraine

For both prophylactic and therapeutic use, an initial dose of 4 mg, repeated if necessary after half an hour. Patients who respond usually obtain relief with 8 mg, and this dose should not be exceeded within a 4- to 6-hour period.

Maintenance: 4 mg every four to six hours.

Use in the elderly: Cyproheptadine Hydrochloride Tablets 4mg should not be used in elderly, debilitated patients. Elderly patients are more likely to experience dizziness, sedation, and hypotension.

There is no recommended dosage for children under 2 years old. Cyproheptadine Hydrochloride Tablets 4mg is not recommended for elderly, debilitated patients

Method of administration

Tablet for oral administration

4.3 Contraindications

Cyproheptadine Hydrochloride Tablets 4mg 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..

4.4 Special warnings and precautions for use

Antihistamines should not be used to treat lower respiratory tract symptoms, including those of acute asthma.

The safety and efficacy of 'Cyproheptadine Hydrochloride 4 mg Tablets' is not established in children under 2 years old.

Overdosage of antihistamines, particularly in infants and 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.

Patients should be warned against engaging in activities requiring motor co-ordination and mental alertness, such as driving a car or operating machinery (see section 4.7 'Effects on ability to drive and use machines').

Rarely, prolonged therapy with antihistamines may cause blood dyscrasias.

Because 'Cyproheptadine Hydrochloride 4 mg Tablets' has an atropine-like action, it should be used cautiously in patients with a history of bronchial asthma, increased intra-ocular pressure, hyperthyroidism, cardiovascular disease, or hypertension.

Excipients Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 Pregnancy and Lactation

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 Cyproheptadine Hydrochloride Tablets 4mg is excreted in human milk, and because of the potential for serious adverse reactions in breast-feeding infants from Cyproheptadine Hydrochloride Tablets 4mg 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 (see Section 4.3 'Contra-indications') condition.

4.7 Effects on ability to drive and use machines

This product may cause drowsiness and somnolence. Patients receiving it should not drive or operate machinery unless it has been shown that their physical and mental capacity remains unaffected.

4.8 Undesirable effects

The side effects that appear frequently are drowsiness and somnolence. Many patients who initially complain of drowsiness may no longer do so after the first three to four days of continuous administration.

Side effects reported with antihistamines are:

Blood and lymphatic system disorders:

Haemolytic anaemia, leucopenia, agranulocytosis, thrombocytopenia

Immune system disorders:

Allergic manifestation of rash and oedema, anaphylactic shock

Metabolism and nutrition disorders:

Anorexia, increased appetite

Psychiatric disorders:

Confusion, restlessness, excitation, irritability, nervousness, insomnia, aggressive behaviour, hallucinations, hysteria and euphoria

Nervous system disorders:

Sedation, sleepiness (often transient), dizziness, disturbed coordination, tremor, paraesthesiae, neuritis, convulsions, faintness, headache

Eye disorders:

Blurred vision, diplopia Ear and labyrinth disorders: Acute labyrinthitis, tinnitus, vertigo

Cardiac disorders:

Palpitation, tachycardia, extrasystolesloss.

Vascular disorders:

Hypotension

Respiratory, thoracic and mediastinal disorders:

Thickening of bronchial secretions, dryness of nose and throat, tightness of chest and wheezing, nasal stuffiness, epistaxis

Gastrointestinal disorder:

Dryness of mouth, epigastric distress, nausea, vomiting, diarrhoea, constipation

Hepato-biliary disorders:

Cholestasis, hepatic failure, hepatitis, hepatic function abnormality, jaundices

Skin and subcutaneous tissue disorders:

Urticaria, photosensitivity, excessive perspiration

Renal and urinary disorders:

Frequency and difficulty of micturition, urinary retention Reproductive system and breast disorders: Early menses

General disorders and administration site conditions:

Fatigue, rigors

Investigations:

Weight gain

4.9 Overdose

Antihistamine overdosage reactions may vary from CNS depression or stimulation to convulsions respiratory and cardiac arrest and death, especially in infants and children. Atropine-like and gastrointestinal symptoms may occur.

If vomiting has not occurred spontaneously, it should be induced in the conscious patient with syrup of ipecac. If the patient cannot vomit, gastric lavage with isotonic or half isotonic saline is indicated,

followed by activated charcoal. Precautions against aspiration must be taken, especially in infants and children.

Life-threatening CNS signs and symptoms should be treated appropriately.

Saline cathartics usefully draw water into the bowel by osmosis to dilute bowel content rapidly.

Central stimulants must not be used, but vasopressors may be used to counteract hypotension.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Cyproheptadine hydrochloride is a serotonin and histamine antagonist with anticholinergic and sedative effects. Antiserotonin and antihistamine drugs appear to compete with serotonin and histamine, respectively, for receptor sites.

Cyproheptadine hydrochloride antagonises the following effects of serotonin in laboratory animals: Bronchoconstrictor (guinea-pig)

Vasopressor (dog)

Spasmogenic (isolated rat uterus)

Oedema (rat)

Lethal (hemophilus petussis-treated mouse)

In these effects it equals or surpasses the activity of many of the activities of specific serotonin antagonists, such as 1-Benzyl-2-methyl-5-methoxy-tryptamine (BAS) and 1-Benzyl-2-methyl-5-hydroxy-tryptamine (BMS), in contrast, specific anti-histamines, even the most potent, show little or no serotonin antagonism.

Cyproheptadine hydrochloride antagonises or blocks the following effects of histamine in laboratory animals: Bronchoconstrictor (guinea-pig)

Vasopressor (dog)

Spasmogenic (isolated rat uterus)

Anaphylactic shock, active and passive (guinea-pig and mouse)

Increased gastric secretion (Heidenhain pouch dog)

It is unusual that cyproheptadine hydrochloride protects both the guinea-pigs and mice against anaphylactic shock. In guinea-pigs, the pulmonary aspects of anaphylactic shock are attributable to the release of endogenous histamine and can be controlled by substances with specific anti-histamine activity. In mice however, where histamine release seems to be less important and serotonin release may be involved, specific anti-histamines are of little value in protecting against anaphylaxis. Thus, the protective effect of cyproheptadine hydrochloride in mice may be an antiserotonin effect.

The inhibitory effect of cyproheptadine in histamine-induced gastric secretion is also unusual as specific anti-histamines do not influence this effect.

Cyproheptadine has appetite stimulation properties in laboratory animals.

5.2 Pharmacokinetic properties

After a single 4 mg oral dose of ¹⁴C-labelled cyproheptadine hydrochloride in normal subjects given as tablets 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. No detectable amounts of unchanged drug were present in the urine of patients on chronic 12-20 mg daily doses of Periactin syrup. The principle metabolite found in human urine has been identified as a quaternary ammonium glucuronide conjugate of cyproheptadine. Elimination is diminished in renal insufficiency.

5.3 Preclinical safety data

No relevant information.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch, Dibasic Calcium Phosphate , Microcrystalline Cellulose, Sodium Starch Glycolate, P.V.P.K 90, Methyl Paraben, Propyl Paraben, Magnesium Stearate, Purified Talc, Colloidal Silicon Dioxide (Aerosil), Cross Carmelose Sodium.

6.2 Incompatibilities

Not Known

6.3 Shelf-life

Blisters: 36 Months

6.4 Special precautions for storage

Store below 30°C. Protect from light.

6.5 Nature and contents of container

The tablets are packed in Alu/PVC blister in a mono carton.

Pack sizes: 1x10 Tablet

6.6 Special precautions for disposal and other handling

No special requirements

7.0 Manufactured by:

Krishat Pharma Industries Limited
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