Cyproheptadine Hydrochloride Tablets, USP

DESCRIPTION
Cyproheptadine HCl, USP, is an antihistaminic and anti-serotinergic agent.

Cyproheptadine hydrochloride USP is a white to slightly yellowish crystalline solid, with a molecular weight of 359.87, which is soluble in water, freely soluble in methanol, sparingly soluble in ethanol, soluble in chloroform, and practically insoluble in ether. It is the sesquihydrate of (4H-Dibenzo[f,h]cyclohepten-5-ylidene)-1-methylpiperidine hydrochloride. The molecular formula of the sesquihydrate salt is C21H21N.HCl.2.H2O and the structural formula of the anhydrous salt is:

![Structural formula of Cyproheptadine](attachment:image.png)

Cyproheptadine hydrochloride USP is available for oral administration in 4 mg tablets. Inactive ingredients include lactose monohydrate, magnesium stearate, microcrystalline cellulose, and Pregelatinized starch.

CLINICAL PHARMACOLOGY
Cyproheptadine is a serotonin and histamine antagonist with antihistaminic and serotonergic effects. Antihistaminic and antiserotonergic drugs appear to compete with serotonin and histamine, respectively, for receptor sites.

Pharmacokinetics and Metabolism
After a single 4 mg dose of 14C-labeled cyproheptadine HCl in normal subjects, given as tablets, 7.2% of the radioactivity was recovered in the stools. Only about 0.09% of the dosed radioactive drug was recovered in the urine. No detectable amounts of unchanged drug were present in the urine of patients on chronic dosing. No metabolites of the administered drug were present in the urine of patients on chronic dosing. The principles metabolized in normal urine have not been identified in a quantitative manner. Glomerular filtration or tubular secretion are not important, and no conjugates were identified in the urine. The drug has been shown to be extensively metabolized in the mammalian small intestine, where it is inactivated by the cytochrome P-450 monooxygenase system. Only about 5% of the radioactivity recovered in the stools was in the form of unchanged cyproheptadine. Elimination is predominantly renal, with about 70% of the administered dose being recovered in the urine and about 15% in the stools. The administration of probenecid to patients receiving cyproheptadine increased the area under the serum concentration-time curve for cyproheptadine by about 50%, indicating that cyproheptadine is eliminated by competition with probenecid for tubular secretion.

INDICATIONS AND USAGE
Paroxysmal and seasonal allergic rhinitis
Vasomotor rhinitis
Perennial and seasonal allergic rhinitis
Cold urticaria
Dermatographism
Angioedema
Vasomotor rhinitis
Allergic manifestations of rhinoconjunctivitis
Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.
Symptomatic prostatic hypertrophy
Urinary frequency, difficult urination, urinary retention, early menses.

CONTRAINDICATIONS
Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.
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WARNINGS

OVERDOSAGE

Children
Cyproheptadine has been shown to be generally well tolerated in children when used in appropriate dose ranges. However, parents should be advised to report any unusual behavior or reactions to cyproheptadine in children so that appropriate dosage adjustments can be made. The total daily dosage for pediatric patients may be calculated on the basis of body weight. Doses for children aged 6 years and over are determined on the basis of body weight (8 mg/m2).

Pregnancy
Cyproheptadine did not produce teratogenic damage in mice. Prewings (10-4M) were cytotoxic. Cyproheptadine did not have any mutagenic effect in the Ames microbial mutagen test; concentrations of above 300 mg/ml inhibit microbial growth.

Diabetes Mellitus
Hyperglycemia
Hypopituitarism
Gastrointestinal
Diarrhea, nausea, vomiting

dosage should be increased after the acute manifestations have been controlled.

An occasional patient may require as much as 32 mg a day for adequate relief. It is

DOSAGE AND ADMINISTRATION
The total daily dose for adults should not exceed 0.5 mg/kg/day. The therapeutic

for severe obstructive diseases caused by carcinomatous, inflammatory, or cicatricial factors and by obstruction of unconsolidated disease or other drug therapy (see WARNINGS, Activities Requiring Mount Alarms). ADVERSE REACTIONS

information for patients

Antihistamines may have additive effects with alcohol and other CNS depressants, e.g.,

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Symptomatic prostatic hypertrophy
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OVERDOSE

Antihistamines overdose reactions may vary from central nervous system depression to stimulation especially in pediatric patients. Also, atropine-like signs and symptoms (dry mouth, blurred vision, flushing, etc.) as well as gastrointestinal symptoms may occur.

If symptoms do not occur 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. Barbiturates or 15 to 20% sodium bicarbonate in the lower end of the grade. Procedures 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.)

Sedation and sleepiness (often transient), dizziness, disturbed coordination, confusion, restlessness, excitement, nervousness, tremor, irritability, insomnia, paresthesias, flushing, tachycardia, palpitations, arrhythmias, hypotension, palpitation, tachycardia, extrasystoles, anaphylactic shock.

Allergic manifestation of rash and edema, excessive perspiration, urticaria, angioedema, pseudotumor cerebri, keratitis, conjunctivitis, meningitis, encephalitis, convulsions, euphoria, hallucinations, hysteria, faintness.

Respiratory:
- Drowsiness, nausea, vomiting, headache, dizziness, hallucinations, confusion, fatigue, tachycardia, tachypnea, urinary retention, urinary frequency, dysuria.

Miscellaneous:
- Fatigue, chills, headache, increased appetite/weight gain.

DOSAGE AND ADMINISTRATION

THERAPEUTIC INDICATIONS

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 12 mg a day.

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 square meter of body surface (8 mg/m2).

The usual dose is 2 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 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 12 mg a day.

Adults
The total daily dosage for adults should not exceed 12 mg a day. The therapeutic ranges 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 22 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.

HOW SUPPLIED

Cyproheptadine Hydrochloride Tablets USP, 4 mg are available as White to off-white round, flat face, beveled edge tablets, "A7" imprinted on one side and bisect on the other side, containing 4 mg of cyproheptadine HCl packaged in bottles of 100 (NDC 0059-112-01) and 1000 (NDC 0059-112-10) tablets.

Pharmacist: Dispense in a well-closed container as defined in the USP, with a child-resistant closure (as required).

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

Manufactured By:
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