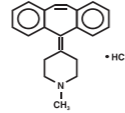


## CYPROHEPTADINE HYDROCHLORIDE TABLETS USP

Rx Only

### DESCRIPTION

Cyproheptadine HCl, is an antihistaminic and antiserotonergic agent. Cyproheptadine hydrochloride, USP is a white to slightly yellowish crystalline solid, with a molecular weight of 350.89, 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 4-(5H-dibenzo [a,d]cyclohepten-5-ylidene)-1-methylpiperidine hydrochloride. The molecular formula of the anhydrous salt is  $C_{21}H_{21}N \cdot HCl$  and the structural formula of the anhydrous salt is as follows:



Cyproheptadine hydrochloride, USP is available for oral administration in 4 mg tablets. Each tablet contains: **Inactives:** Lactose Monohydrate, Microcrystalline Cellulose, Sodium Starch Glycolate and Magnesium Stearate.

### CLINICAL PHARMACOLOGY

Cyproheptadine 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.

### Pharmacokinetics and Metabolism

After a single 4 mg oral dose of  $^{14}C$ -labeled cyproheptadine HCl in normal subjects, given as tablets, 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 detectable amounts of unchanged drug were present in the urine of patients on chronic 12 to 20 mg daily doses. The principle metabolite found in human urine has been identified as a quaternary ammonium glucuronide conjugate of cyproheptadine. Elimination is diminished in renal insufficiency.

### INDICATIONS AND USAGE

- 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.

### CONTRAINDICATIONS

#### 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 (See DRUG INTERACTIONS.)
- Angle-closure glaucoma
- Stenosing peptic ulcer
- Symptomatic prostatic hypertrophy
- Bladder neck obstruction
- Pyloroduodenal obstruction
- Elderly, debilitated patients

### 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 (see PRECAUTIONS, Geriatric Use).

### 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.

#### Drug Interactions

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.

#### 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 (see CONTRAINDICATIONS).

#### Pediatric Use

Safety and effectiveness in pediatric patients below the age of two have not been established (see CONTRAINDICATIONS, Newborn or Premature Infants, and WARNINGS, Pediatric Patients).

#### Geriatric Use

Clinical studies of cyproheptadine HCl tablets did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy (see WARNINGS, Activities Requiring Mental Alertness).

### ADVERSE REACTIONS

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.

#### Miscellaneous

Fatigue, chills, headache, increased appetite/weight gain.

### OVERDOSAGE

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 LD<sub>50</sub> of cyproheptadine is 123 mg/kg, and 295 mg/kg in the mouse and rat, respectively.

### DOSAGE AND 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 square meter of body surface (8 mg/m<sup>2</sup>).

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.

### HOW SUPPLIED

Cyproheptadine hydrochloride tablets USP, 4 mg are available as white to off-white color, round flat face tablet with debossed "B137" on one side and scored on the other, containing 4 mg of cyproheptadine HCl packaged in HDPE bottles of 100 and 1000 tablets.

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

Bottles of 100 tablets NDC 76385-130-01

Bottles of 1000 tablets NDC 76385-130-10

### STORAGE

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

To report SUSPECTED ADVERSE REACTIONS, contact Beximco Pharmaceuticals USA Inc. at 877-372-6093 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

Manufactured for  
**Beximco Pharmaceuticals USA Inc.**  
Suwanee, GA 30024, USA

Manufactured by  
**Beximco Pharmaceuticals Ltd.**  
126, Kathaldia, Tongi, Gazipur, 1711, Bangladesh

Distributed by  
**Bayshore Pharmaceuticals LLC**  
Short Hills, NJ 07078

3020007860

150120

Leaflet for Cyproheptadine Exp/USA

280x 300 mm

150120

FS 190120