

CYPROHEPTADINE HYDROCHLORIDE- cyproheptadine hydrochloride syrup

Tris Pharma Inc

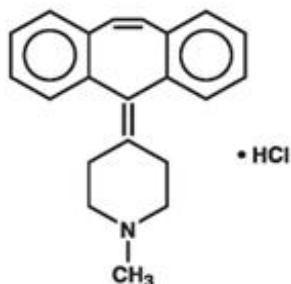
Cyproheptadine Hydrochloride Syrup (Cyproheptadine Hydrochloride Oral Solution, USP) Rx only

DESCRIPTION

Each 5 mL (one teaspoonful) contains: Cyproheptadine Hydrochloride 2 mg.

Inactive Ingredients: Alcohol 5% v/v, anhydrous citric acid, D&C yellow no. 10, edetate disodium, mint flavor, purified water, sodium benzoate, sodium citrate and sucrose.

Cyproheptadine HCl is an antihistaminic and antiserotonergic agent. Cyproheptadine hydrochloride is a white to slightly yellowish, crystalline solid, with a molecular weight of 350.89, which is slightly soluble in water, freely soluble in methanol, sparingly soluble in ethanol, soluble in chloroform and practically insoluble in ether. It is the sesquihydrate of 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:



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 ¹⁴C-labeled cyproheptadine HCl 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 detectable amounts of unchanged drug were present in the urine of patients on chronic 12 to 20 mg daily doses of cyproheptadine syrup. The principal 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 ciproheptadine 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

Children: Overdosage of antihistamines, particularly in infants and children, may produce hallucinations, central nervous system depression, convulsions 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.

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 years have not been established. (See **CONTRAINDICATIONS, Newborn or Premature Infants, and WARNINGS, Children.**)

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: 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.

To report SUSPECTED ADVERSE REACTIONS, contact Tris Pharma, Inc. at 1-732-940-0358 or FDA at 1-800-FDA-1088 or WWW.FDA.GOV/MEDWATCH.

OVERDOSAGE

Antihistamine overdose reactions may vary from central nervous system depression to stimulation especially in children. 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 the 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.

DOSAGE AND ADMINISTRATION

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

Although intended primarily for administration to children, the syrup is also used for administration to adults who cannot swallow tablets.

Children: The total daily dosage for children may be calculated on the basis of body weight or body area using approximately 0.25 mg/kg/day (0.11 mg/lb/day) or 8 mg per square meter of body surface (8 mg/m²).

Age 2 to 6 years: The usual dose is 2 mg (one teaspoonful) 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 (two teaspoonsful) 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 (0.23 mg/lb/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 (two teaspoonsful) three times a day and adjusted according to the size and response of the patient.

HOW SUPPLIED

Cyproheptadine Hydrochloride Syrup (Cyproheptadine Hydrochloride Oral Solution, USP, 2 mg/5 mL) is a pale yellow, mint-flavored syrup supplied as follows:

NDC 27808-099-01 (473 mL) in a plastic bottle

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Dispense in a tight, light-resistant container as defined in the USP.

Manufactured by:

Tris Pharma, Inc.

Monmouth Junction, NJ 08852

www.trispharma.com

LB8472

Rev. 00

December 2021

PRINCIPAL DISPLAY PANEL

NDC 27808-099-01

Cyproheptadine Hydrochloride Syrup

(Cyproheptadine Hydrochloride Oral Solution, USP)

2 mg/5 mL

Alcohol 5% (v/v)

Rx only

473 mL

NDC 27808-099-01

Cyproheptadine Hydrochloride Syrup

(Cyproheptadine Hydrochloride Oral Solution, USP)

2 mg/5 mL

Alcohol 5% (v/v)

Rx only

473 mL

Each 5 mL (one teaspoonful) contains:
Cyproheptadine Hydrochloride.....2 mg
Alcohol.....5%(v/v)

USUAL DOSAGE: See accompanying package outsert.

WARNING: Keep this and all drugs out of the reach of children.

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP Controlled Room Temperature].

Dispense in a tight, light-resistant container as defined in the USP.

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LB8471 Rev.00 12/2021

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LOT XXXXXXXXA
EXP XXXXXXXXX
SN XXXXXXXXXXXXX

CYPROHEPTADINE HYDROCHLORIDE

cyproheptadine hydrochloride syrup

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:27808-099
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CYPROHEPTADINE HYDROCHLORIDE (UNII: NJ82J0F8QC) (CYPROHEPTADINE - UNII:2YHB6175DO)	CYPROHEPTADINE HYDROCHLORIDE	2 mg in 5 mL

Inactive Ingredients

Ingredient Name	Strength
ALCOHOL (UNII: 3K9958V90M)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
MINT (UNII: FV98Z8GITP)	
SODIUM BENZOATE (UNII: OJ245FE5EU)	
SODIUM CITRATE (UNII: 1Q73Q2JULR)	
SUCROSE (UNII: C151H8M554)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	

Product Characteristics

Color	yellow (pale)	Score	
Shape		Size	
Flavor	MINT	Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:27808-099-01	473 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	12/30/2022	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA205431	12/21/2021	

Labeler - Tris Pharma Inc (947472119)