

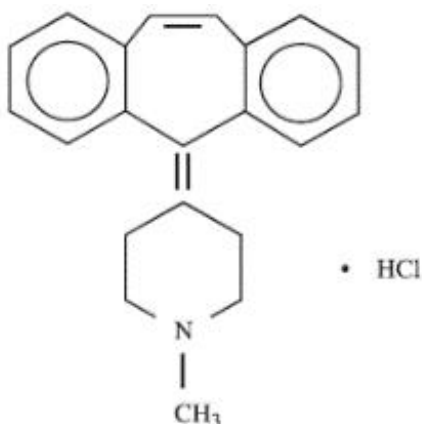
**CYPROHEPTADINE HYDROCHLORIDE- cyproheptadine hydrochloride tablet**  
**Heritage Pharmaceuticals Inc. d/b/a Avet Pharmaceuticals Inc.**

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**Rx only**

**DESCRIPTION**

Cyproheptadine hydrochloride, USP 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 of 4-(5*H*-dibenzo[*a,d*]cyclohepten-5-ylidene)-1-methylpiperidine hydrochloride. The molecular formula of the anhydrous salt is C<sub>21</sub>H<sub>21</sub>N•HCl and the structural formula of the anhydrous salt is:



Molecular Formula: C<sub>21</sub>H<sub>21</sub>N•HCl      Molecular Weight: 350.89

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

**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 <sup>14</sup>C-labelled cyproheptadine hydrochloride 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 mg 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 hydrochloride 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.

**To report SUSPECTED ADVERSE REACTIONS, contact Avet Pharmaceuticals Inc. at 1-866-901-DRUG (3784) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

## **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 ½ 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 (½ 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, round, flat-faced, bevel-edged tablets, debossed **703** on one side and bisect on the other side. They are available as follows:

Bottles of 100: NDC 23155-703-01

Bottles of 500: NDC 23155-703-05

Bottles of 1000: NDC 23155-703-10

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].**

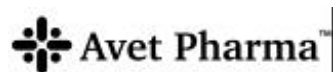
**KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.**

Distributed by:

**Avet Pharmaceuticals Inc.**

East Brunswick, NJ 08816

1.866.901.DRUG (3784)



51U000000331US01

**Revised: 10/2019**

**PACKAGE LABEL.PRINCIPAL DISPLAY PANEL**

**NDC 23155-703-01**

**Cyproheptadine Hydrochloride Tablets, USP**

**4 mg**

**100 Tablets**

**Rx only**

The image shows a rectangular principal display panel for a medication package. The panel is divided into several sections. On the left, there is a dark blue header with the Avet Pharma logo and name. Below this, the text "NDC 23155-703-01" is printed. The main product name "Cyproheptadine Hydrochloride Tablets, USP" is prominently displayed in large, bold, black letters. Below the product name, the strength "4 mg" is shown in white text on a dark blue background. Further down, "100 Tablets" and "Rx only" are printed in white on a dark blue background. The central part of the panel contains detailed information: "Each tablet contains 4 mg Cyproheptadine Hydrochloride, USP." followed by "Usual Dosage: See package insert for full prescribing information." and "Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]." Below this, it states "Dispense in a well-closed container as defined in the USP, with a child-resistant closure (as required)." and "KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN." The bottom right section of the panel includes the distributor information: "Distributed by: Avet Pharmaceuticals Inc. East Brunswick, NJ 08816 1.866.901.DRUG (3784) 51U000000328US01 Rev. 10/2019". A barcode is located in the bottom right corner, with the numbers "N 3" and "23155-703-01" printed below it. To the right of the barcode, the text "Non Varnished Area" is printed vertically in orange.

**CYPROHEPTADINE HYDROCHLORIDE**

cyproheptadine hydrochloride tablet

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:23155-703
<b>Route of Administration</b>	ORAL		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CYPROHEPTADINE HYDROCHLORIDE (UNII: NJ82J0F8QC) (CYPROHEPTADINE - UNII:2YHB6175DO)	CYPROHEPTADINE HYDROCHLORIDE	4 mg

### Inactive Ingredients

Ingredient Name	Strength
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

### Product Characteristics

<b>Color</b>	WHITE	<b>Score</b>	2 pieces
<b>Shape</b>	ROUND	<b>Size</b>	7mm
<b>Flavor</b>		<b>Imprint Code</b>	703
<b>Contains</b>			

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:23155-703-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	01/09/2020	
2	NDC:23155-703-05	500 in 1 BOTTLE; Type 0: Not a Combination Product	01/09/2020	
3	NDC:23155-703-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	01/09/2020	

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA087056	01/09/2020	

**Labeler** - Heritage Pharmaceuticals Inc. d/b/a Avet Pharmaceuticals Inc. (780779901)

**Registrant** - Heritage Pharmaceuticals Inc. d/b/a Avet Pharmaceuticals Inc. (780779901)

### Establishment

Name	Address	ID/FEI	Business Operations
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Heritage Pharma Labs Inc. d/b/a Avet Pharmaceuticals Labs Inc.	189630168	ANALYSIS(23155-703) , LABEL(23155-703) , MANUFACTURE(23155-703) , PACK(23155-703)
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Revised: 1/2020

Heritage Pharmaceuticals Inc. d/b/a Avet Pharmaceuticals Inc.