Cyproheptadine Hydrochloride Syrup
(Cyproheptadine Hydrochloride Oral Solution, USP)

2 mg / 5 mL

473 mL (ONE PINT)  Rx only

EACH 5 mL (ONE TEASPOONFUL) CONTAINS:
Cyproheptadine Hydrochloride 2 mg, Alcohol 5%, Sorbic Acid 0.1% added as preservative.

USUAL DOSAGE:
See accompanying package insert.

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

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

Distributed by: Rising Pharmaceuticals, Inc.
Allendale, NJ 07401

Manufactured by: Lyne Laboratories, Inc.
Brockton, MA 02301

PROOF DATE: 11/12/10
CUSTOMER: LYNE LABS
JOB NUMBER: 50522
LABEL SIZE: 3.0" x 6.5"
LEAFLET FLAT SIZE: 3.0" x 14.25"
LEAFLET FOLDED SIZE: 3.0" x 3.0"
LABEL COLORS: BLACK  PMS 123  PMS 279
LEAFLET "IN" COLORS: BLACK
LEAFLET "OUT" COLORS: BLACK
DIELINE DOES NOT PRINT
Job #50522

Each 5 mL (one teaspoonful) contains:
Cyproheptadine Hydrochloride 2 mg, Alcohol 5%, Sorbic Acid 0.1% added as preservative.

Usual Dosage:
See accompanying package insert.

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

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

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Nursing Mothers:
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in 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.

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, irritability, muscle weakness, 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, 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 children. If the patient is unable to vomit, perform gastric lavage followed by scheduled charcoal (40 g). If the patient vomits, the lavage is of little value. Purgatives against aspiration must be taken immediately in infants and children. When antihistamines are used and symptoms are present, serious physostigmine salicylate may be considered. Dosage and frequency of administration depend on age, clinical response and recurrence after response (see package circulars for physostigmine products).

Saline cathartics, a milk of magnesia, by enema displace water into the bowel and are not valuable for their action in rapid dilution of off-color 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 depending on 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 teaspoonfuls) two or three times a day, adjusted according to the size and response of the patient. The dose is not to exceed 16 mg a day.

Adults: The adult 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 4 to 12 mg a day. A occasional patient may require as much as 32 mg a day under special circumstances. It is suggested that dosage be initiated with 4 mg (two teaspoonfuls) and should be made 3 to 4 days a week 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) in a yellow, mint-flavored vehicle, is supplied in a pint (473 mL) container.

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

Distributed by:
Rising Pharmaceuticals, Inc.
Allendale, NJ 07401

Manufactured by:
Lyne Laboratories, Inc.
Brockton, MA 02301

Each 5 mL contains 2 mg of Cyproheptadine Hydrochloride 2 mg. Alcohol 5%, Sorbic Acid 0.1% added as preservative.

Usual Dosage:
See accompanying package insert.

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

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

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Lyne Laboratories, Inc.
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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%, citric acid, D&C Yellow #10, flavoring water, purified water, sodium citrate, sorbic acid (0.1% as preservative) and sucrose syrup.

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 mollinol, sparingly soluble in ether, soluble in chloroform and in most organic solvents containing uncharged drugs such as alkylamines, e.g., the isopropeylate of 4-methylbenzoic acid, diethylamino-1-propanol and methyl parahydroquinone. The molecular formula of the anhydrous salt is C21H21NCl. The structural formula of the anhydrous salt is:

CLINICAL PHARMACOLOGY

Cyproheptadine is a serotonin and histamine antagonist with anticholinergic and sedative effects. Antiserotonin and antihistaminic 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 tablets or syrup, 2-20% of the radioactivity was excreted in the stools. Only about 34% of the stool radioactivity was unchanged drug. The remainder was excreted in the urine. No detectable amounts of unchanged drug were present in the urine of patients on chronic 12-20 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
NHL uncomplicated allergic skin manifestations of urticaria and angioedema
Amelioration of allergic reactions to blood or plasma
Cold urticaria
As therapy for anaphylactic reactions

CONTRAINDICATIONS

Newborn or Premature Infants: This drug should not be used in newborn or premature infants, infants up to 2 months of age.

Nursing Mothers: Because of the higher risk of antihistamines for infants generally and for newborns and premature in particular, antihistamine therapy is contraindicated in nursing mothers. Oral forms should not be used to treat colds in infants or children.

Other Contraindications:

Impaired ability to cytochrome P450 and other drugs of similar chemical structure

CNS Depressants: Antihistamines may have additive effects with alcohol and other CNS depressants, e.g., hypnotics, sedatives, tranquillizers, antidepressants, and anxiolytics.

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 may be 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 excitement. 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, tranquillizers, antidepressants, and anxiolytics.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Long-term carcinogenicity studies have not been done with cyproheptadine. Cyproheptadine may have effects similar to other antihistamines in studies in rats or in hamsters. In one study of male rats, the highest dose tested was 25 mg/kg of body weight, and in one of female rats, the highest dose tested was 12.5 mg/kg of body weight; in hamsters, it was 24 mg/kg of body weight. Cyproheptadine was administered from the 5th week of life to the 12th week of life, in these studies, no significant increase in the incidence of tumors was noted. In two species of mice, concentrations of above 500 mcg/g inhibited both growth and fertility.

Pregnancy:

Pregnancy Category B. Reproduction studies have been performed in rabbits, mice and rats, and no substantial adverse effects on fertility or neonatal development were observed in any of the species. Cyproheptadine has not been shown to produce congenital anomalies when administered to laboratory animals at doses which are up to 24 times the recommended human oral dose. Two studies in pregnant women, however, have not shown that cyproheptadine increases the risk of abnormal birth or of abortion when administered before the third trimester. However, since there is no evidence of human metabolic enzyme elaboration in any of the newborn. Nevertheless, because the studies in humans cannot rule out the possibility of harm, cyproheptadine should be used during pregnancy only if clearly needed.