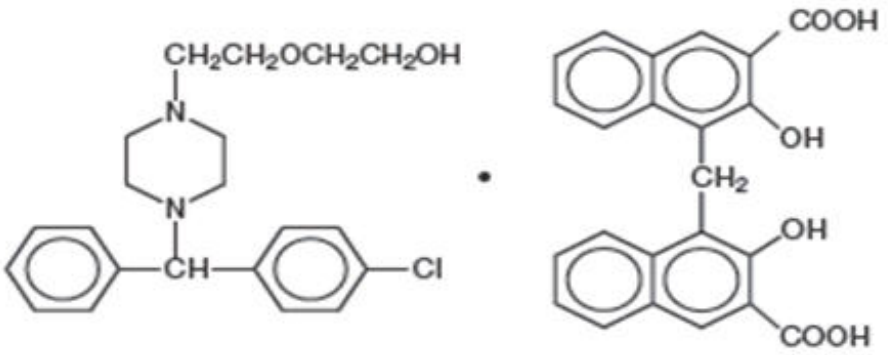
HYDROXYZINE PAMOATE- hydroxyzine pamoate capsule
Aphena Pharma Solutions - Tennessee, LLC

HydrOXYzine Pamoate Capsules, USP

Rx only

DESCRIPTION

Hydroxyzine pamoate is a light yellow, practically odorless powder practically insoluble in water and methanol and freely soluble in dimethylformamide. It is chemically designated as 1-(p-chlorobenzhydryl) 4-[2-(2-hydroxyethoxy) ethyl] diethylenediamine salt of 1,1'-methylene bis (2hydroxy-3-naphthalene carboxylic acid) and can be structurally represented as follows:



Chemical Formula: $C_{21}H_{27}ClN_2O_2 \cdot C_{23}H_{16}O_6$

Molecular Weight: 763.29

Each capsule, for oral administration, contains hydroxyzine pamoate equivalent to 25 mg or 50 mg of hydroxyzine hydrochloride. In addition, each capsule contains the following inactive ingredients: colloidal silicon dioxide, D&C yellow #10, FD&C blue #1, gelatin, magnesium stearate, pregelatinized starch, sodium lauryl sulfate, and titanium dioxide. The imprinting ink on the capsules contains synthetic black iron oxide.

CLINICAL PHARMACOLOGY

Hydroxyzine pamoate is unrelated chemically to the phenothiazines, reserpine, meprobamate, or the benzodiazepines. Hydroxyzine pamoate is not a cortical depressant, but its action may be due to a suppression of activity in certain key regions of the subcortical area of the central nervous system. Primary skeletal muscle relaxation has been demonstrated experimentally. Bronchodilator activity, and antihistaminic and analgesic effects have been demonstrated experimentally and confirmed clinically. An antiemetic effect, both by the apomorphine test and the veriloid test, has been demonstrated. Pharmacological and clinical studies indicate that hydroxyzine in therapeutic dosage does not increase gastric secretion or acidity and in most cases has mild antisecretory activity. Hydroxyzine is rapidly absorbed from the gastrointestinal tract and hydroxyzine pamoate's clinical effects are usually noted within 15 to 30 minutes after oral administration.

INDICATIONS

For symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested.

Useful in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses, and in histamine-mediated pruritus.

As a sedative when used as premedication and following general anesthesia, **Hydroxyzine may potentiate meperidine (Demerol ®) and barbiturates** , so their use in pre-anesthetic adjunctive therapy should be modified on an individual basis. Atropine and other belladonna alkaloids are not affected by the drug. Hydroxyzine is not known to interfere with the action of digitalis in any way and it may be used concurrently with this agent.

The effectiveness of hydroxyzine as an antianxiety agent for long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should reassess periodically the usefulness of the drug for the individual patient.

CONTRAINDICATIONS

Hydroxyzine, when administered to the pregnant mouse, rat, and rabbit, induced fetal abnormalities in the rat and mouse at doses substantially above the human therapeutic range. Clinical data in human beings are inadequate to establish safety in early pregnancy. Until such data are available, hydroxyzine is contraindicated in early pregnancy.

Hydroxyzine is contraindicated in patients with a prolonged QT interval.

Hydroxyzine pamoate is contraindicated for patients who have shown a previous hypersensitivity to any component of this medication.

Hydroxyzine is contraindicated in patients with known hypersensitivity to hydroxyzine products, and in patients with known hypersensitivity to cetirizine hydrochloride or levocetrizine hydrochloride.

WARNINGS

Nursing Mothers

It is not known whether this drug is excreted in human milk. Since many drugs are so excreted, hydroxyzine should not be given to nursing mothers.

PRECAUTIONS

THE POTENTIATING ACTION OF HYDROXYZINE MUST BE CONSIDERED WHEN THE DRUG IS USED IN CONJUNCTION WITH CENTRAL NERVOUS SYSTEM DEPRESSANTS SUCH AS NARCOTICS, NON-NARCOTIC ANALGESICS AND BARBITURATES. Therefore, when central nervous system depressants are administered concomitantly with hydroxyzine, their dosage should be reduced. Since drowsiness may occur with use of the drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery while taking hydroxyzine pamoate. Patients should be advised against the simultaneous use of other CNS depressant drugs, and cautioned that the effect of alcohol may be increased.

QT Prolongation/Torsade de Pointes (TdP): Cases of QT prolongation and Torsade de Pointes have been reported during post-marketing use of hydroxyzine. The majority of reports occurred in patients with other risk factors for QT prolongation/TdP (pre-existing heart disease, electrolyte imbalances or concomitant arrhythmogenic drug use). Therefore, hydroxyzine should be used with caution in patients with risk factors for QT prolongation, congenital long QT syndrome, a family history of long QT syndrome, other conditions that predispose to QT prolongation and ventricular arrhythmia, as well as recent myocardial infarction, uncompensated heart failure, and bradyarrhythmias.

Caution is recommended during the concomitant use of drugs known to prolong the QT interval. These include Class 1A (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmics, certain antipsychotics (e.g., ziprasidone, iloperidone, clozapine, quetiapine, chlorpromazine), certain antidepressants (e.g., citalopram, fluoxetine), certain antibiotics (e.g., azithromycin, erythromycin, clarithromycin, gatifloxacin, moxifloxacin); and others (e.g., pentamidine, methadone, ondansetron, droperidol).

Acute Generalized Exanthematous Pustulosis (AGEP): Hydroxyzine may rarely cause acute generalized exanthematous pustulosis (AGEP), a serious skin reaction characterized by fever and numerous small, superficial, non-follicular, sterile pustules, arising within large areas of edematous erythema. Inform patients about the signs of AGEP, and discontinue hydroxyzine at the first appearance of a skin rash, worsening of pre-existing skin reactions which hydroxyzine may be used to treat, or any other sign of hypersensitivity. If signs or symptoms suggest AGEP, use of hydroxyzine should not be resumed and alternative therapy should be considered. Avoid cetirizine or levocetirizine in patients who have experienced AGEP or other hypersensitivity reactions with hydroxyzine, due to the risk of cross-sensitivity.

Geriatric Use

A determination has not been made whether controlled clinical studies of hydroxyzine pamoate included sufficient numbers of subjects aged 65 and over to define a difference in response 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.

The extent of renal excretion of hydroxyzine pamoate has not been determined. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selections. Sedating drugs may cause confusion and over sedation in the elderly; elderly patients generally should be started on low doses of hydroxyzine pamoate and observed closely.

ADVERSE REACTIONS

Side effects reported with the administration of hydroxyzine pamoate are usually mild and transitory in nature.

Skin and Appendages: Oral hydroxyzine hydrochloride is associated with Acute Generalized Exanthematous Pustulosis (AGEP) and fixed drug eruptions in post-marketing reports.

Anticholinergic: Dry mouth.

Central Nervous System: Drowsiness is usually transitory and may disappear in a few days of continued therapy or upon reduction of the dose. Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually with doses considerably higher than those recommended. Clinically significant respiratory depression has not been reported at recommended doses.

Cardiac System: QT prolongation,Torsade de Pointes.

In post-marketing experience, the following additional undesirable effects have been reported: **Body as a Whole:** allergic reaction, **Nervous System:** headache, **Psychiatric:** hallucination, **Skin and Appendages:** pruritus, rash, urticaria.

To report SUSPECTED ADVERSE EVENTS, contact AvKARE, Inc. at 1-855-361-3993 or FDA at 1-800-FDA-1088 or http://www.fda.gov/ for voluntary reporting of adverse reactions.

To report SUSPECTED ADVERSE REACTIONS contact AvKARE, Inc. at 1-855-361-3993; email drugsafety@avkare.com; or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

The most common manifestation of overdosage of hydroxyzine pamoate is hypersedation. Other reported signs and symptoms were convulsions, stupor, nausea and vomiting. As in the management of overdosage with any drug, it should be borne in mind that multiple agents may have been taken.

If vomiting has not occurred spontaneously, it should be induced. Immediate gastric lavage is also recommended. General supportive care, including frequent monitoring of the vital signs and close observation of the patient, is indicated. Hypotension, though unlikely, may be controlled with intravenous fluids and vasopressors (**do not use epinephrine as hydroxyzine counteracts its pressor action.**) Caffeine and Sodium Benzoate Injection, USP, may be used to counteract central nervous system depressant effects.

Hydroxyzine overdose may cause QT prolongation and Torsade de Pointes. ECG monitoring is recommended in cases of hydroxyzine overdose.

There is no specific antidote. It is doubtful that hemodialysis would be of any value in the treatment of overdosage with hydroxyzine. However, if other agents such as barbiturates have been ingested concomitantly, hemo-dialysis may be indicated. There is no practical method to quantitate hydroxyzine in body fluids or tissue after its ingestion or administration.

DOSAGE

For symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in organic disease states in which anxiety is manifested: in adults, 50 mg to 100 mg q.i.d.; children under 6 years, 50 mg daily in divided doses; and over 6 years, 50 mg to 100 mg daily in divided doses.

For use in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses, and in histamine-mediated pruritus: in adults, 25 mg t.i.d. or q.i.d.; children under 6 years, 50 mg daily in divided doses; and over 6 years, 50 mg to 100 mg daily in divided doses.

As a sedative when used as a premedication and following general anesthesia: 50 mg to 100 mg in adults, and 0.6 mg/kg in children. When treatment is initiated by the intramuscular route of administration, subsequent doses may be administered orally.

As with all medications, the dosage should be adjusted according to the patient's response to therapy.

HOW SUPPLIED

Hydroxyzine pamoate capsules, USP (hydroxyzine pamoate equivalent to hydroxyzine hydrochloride) are supplied as follows:

25 mg capsules: Dark green opaque cap/light green opaque body filled with yellow powder. Imprinted in black "IX" on the capsule cap and "657" on the capsule body, in bottles of 90 (NDC 42291-406-90) and 500 (NDC 42291-406-50).

50 mg capsules: Dark green opaque cap/white opaque body filled with yellow powder. Imprinted in black "IX" on the capsule cap and "658" on the capsule body, in bottles of 90 (NDC 42291-407-90) and 500 (NDC 42291-407-50).

Store below 30°C (86°F) [See USP].

Dispense in a tight, light resistant container as defined in USP/NF.

BIBLIOGRAPHY

Available on request.

Manufactured by:

Manufactured for:
AvKARE, Inc.
Pulaski, TN 38478

Mfg. Rev. 03/18
AV 04/18 (P)

Repackaging Information

Please reference the ***How Supplied*** section listed above for a description of individual tablets. This drug product has been received by Aphena Pharma - TN in a manufacturer or distributor packaged configuration and repackaged in full compliance with all applicable cGMP regulations. The package configurations available from Aphena are listed below:

Count	25 mg
90	71610-095-60

Store between 20°-25°C (68°-77°F). See USP Controlled Room Temperature. Dispense in a tight light-resistant container as defined by USP. Keep this and all drugs out of the reach of children.

Repackaged by:

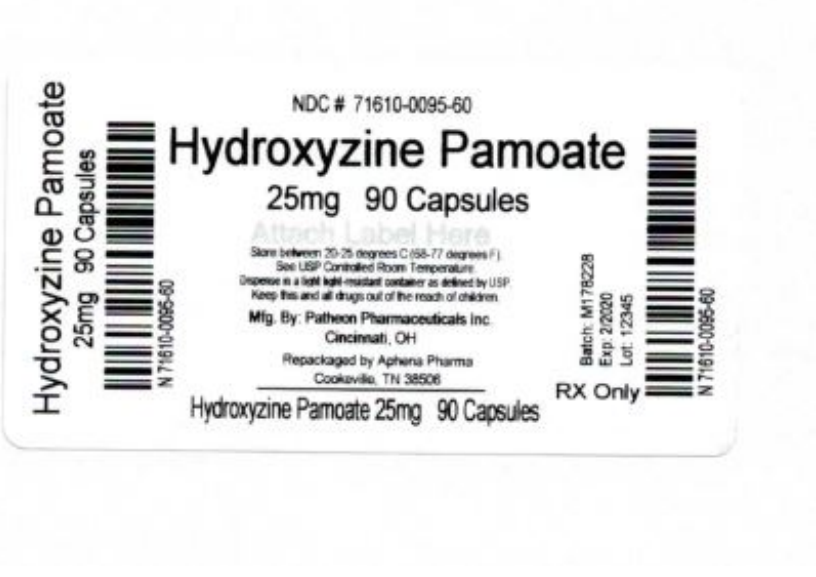
Aphena Pharma Solutions

Cookeville, TN 38506

20180717JH

PRINCIPAL DISPLAY PANEL - 25 mg

NDC 71610-095 - Hydroxyzine Pamoate 25 mg - Rx Only



HYDROXYZINE PAMOATE

hydroxyzine pamoate capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:71610-095(NDC:42291-406)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HYDROXYZINE PAMOATE (UNII: M20215MUFR) (HYDROXYZINE - UNII:30S50YM8OG)	HYDROXYZINE HYDROCHLORIDE	25 mg

Inactive Ingredients

Ingredient Name	Strength
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
GELATIN (UNII: 2G86QN327L)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
STARCH, CORN (UNII: O8232NY3SJ)	

Product Characteristics

Color	green (dark green opaque/light green opaque)	**Score**	no score
Shape	CAPSULE	**Size**	16mm
Flavor		**Imprint Code**	IX;657
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:71610-095-60	90 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	07/13/2018	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA040156	04/12/2018	

Labeler - Aphena Pharma Solutions - Tennessee, LLC (128385585)

Establishment

Name	Address	ID/FEI	Business Operations
Aphena Pharma Solutions - Tennessee, LLC		128385585	REPACK(71610-095)