

**PRESCRIBING INFORMATION  
PRODUCT MONOGRAPH**

**Pr HYDROXYZINE**

Hydroxyzine Hydrochloride Capsules

10, 25 and 50 mg

Anxiolytic - Antihistamine

AA Pharma Inc.  
1165 Creditstone Road, Unit #1.  
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Vaughan, Ontario  
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## **PRESCRIBING INFORMATION**

<sup>P</sup>rHYDROXYZINE

Hydroxyzine Hydrochloride Capsules

10 mg, 25 mg and 50 mg

### **THERAPEUTIC CLASSIFICATION**

Anxiolytic - Antihistamine

### **INDICATIONS**

#### **Adults**

HYDROXYZINE (hydroxyzine hydrochloride) is used to assist in the management of anxiety in adults.

#### **Adults and Children**

HYDROXYZINE is indicated for premedication, such as preparation for dental procedures. HYDROXYZINE is useful in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses.

HYDROXYZINE is useful in the control of nausea and vomiting, excluding nausea and vomiting of pregnancy (see CONTRAINDICATIONS section).

### **CONTRAINDICATIONS**

HYDROXYZINE is contraindicated in patients with:

- history of QT prolongation and/or torsade de pointes, including congenital long QT syndromes; history of cardiac arrhythmias; significant electrolyte imbalance (hypokalaemia, hypomagnesium); significant bradycardia; family history of sudden cardiac death; concomitant use of other QT/QTc-prolonging drugs, or of CYP3A4/5 inhibitors. (see also WARNINGS, and DRUG INTERACTIONS).
- known hypersensitivity to hydroxyzine hydrochloride, cetirizine, other piperazine derivatives, aminophylline or ethylenediamine, or any component of this medication.
- asthmatics who have previously experienced a serious anti-histamine induced adverse bronchopulmonary effect.
- porphyria
- early (first trimester) pregnancy

### **WARNINGS**

#### **Cardiovascular Effects**

Hydroxyzine has been associated with QT/QTc interval prolongation. Rare events of torsade de pointes, cardiac arrest, and sudden death have been reported with hydroxyzine during postmarket use.

Torsade de pointes is a polymorphic ventricular tachyarrhythmia. Generally, the risk of torsade de pointes increases with the magnitude of QT/QTc prolongation produced by the drug. Torsade de pointes may be asymptomatic or experienced by the patient as dizziness, palpitations, syncope, or seizures. If sustained, torsade de pointes can progress to ventricular fibrillation and sudden cardiac death.

Particular care should be exercised when administering hydroxyzine to patients who are suspected to be at an increased risk of experiencing torsade de pointes during treatment with a QT/QTc-prolonging drug. Risk factors for torsade de pointes in the general population include, but are not limited to, the following:

- female gender;
- age 65 years or older;
- baseline prolongation of the QT/QTc interval;
- presence of genetic variants affecting cardiac ion channels or regulatory proteins, especially congenital long QT syndromes;
- family history of sudden cardiac death at <50 years;
- cardiac disease (e.g., myocardial ischemia or infarction, congestive heart failure, left ventricular hypertrophy, cardiomyopathy, conduction system disease);
- history of arrhythmias (especially ventricular arrhythmias, atrial fibrillation, or recent conversion from atrial fibrillation);
- electrolyte disturbances (e.g., hypokalemia, hypomagnesemia, hypocalcemia) or conditions leading to electrolyte disturbances (e.g., gastrointestinal disease, eating disorders);
- bradycardia (<50 beats per minute);
- acute neurological events (e.g., intracranial or subarachnoid haemorrhage, stroke, intracranial trauma);
- diabetes mellitus;
- autonomic neuropathy

When drugs that prolong the QT/QTc interval are prescribed, healthcare professionals should counsel their patients concerning the nature and implications of the ECG changes, underlying diseases and disorders that are considered to represent risk factors, demonstrated and predicted drug-drug interactions, symptoms suggestive of arrhythmia, risk management strategies, and other information relevant to the use of the drug. (see also CONTRAINDICATIONS; DOSAGE AND ADMINISTRATION; and DRUG INTERACTIONS).

#### **Use in Pregnancy and Breast Feeding**

Hydroxyzine hydrochloride, 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 (hydroxyzine hydrochloride) is contraindicated in early pregnancy. (See also CONTRAINDICATIONS)

**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.

#### **Use in Elderly, Hepatic- or Renal-Impaired Populations:**

See DOSAGE AND ADMINISTRATION

## **PRECAUTIONS**

The potentiating action of hydroxyzine must be considered when the drug is used in conjunction with CNS depressants such as narcotics, non-narcotic analgesics, hypnotics, sedatives, psychotherapeutic agents, barbiturates or alcohol. Therefore, when CNS depressants are administered concomitantly with hydroxyzine, their dosage should be reduced.

Because of its potential antimuscarinic actions, HYDROXYZINE should be used with caution in patients suffering from angle closure glaucoma, urinary retention, prostatic hyperplasia, or pyloroduodenal obstruction.

Treatment should be stopped for one week before skin testing for allergy is undertaken, and for 96 hours prior to a methacholine test.

Caution is required in patients with the following conditions:

- seizure disorders, including epilepsy
- myasthenia gravis
- dementia
- decreased GI motility
- bladder outflow obstruction
- stenosing peptic ulcer
- patients with breathing problems (e.g. emphysema, chronic bronchitis)
- increased intraocular pressure
- hyperthyroidism
- cardiovascular disease
- hypertension

Since drowsiness may occur with use of this drug, patients should be cautioned against driving a car or operating dangerous machinery while taking hydroxyzine.

## **ADVERSE REACTIONS**

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

Anticholinergic: Dry mouth may be encountered at higher dosages.

Central Nervous System: Drowsiness.

Involuntary motor activity, including rare instances of tremor and convulsions, has been reported usually with doses considerably higher than those recommended.

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. Rare cases of cardiac arrest, cardio-respiratory arrest, electrocardiogram QT prolonged, and torsade de pointes, some fatal, have been reported following the use of hydroxyzine-containing products.

## DRUG INTERACTIONS

**QT/QTc-Prolonging Drugs:** The concomitant use of hydroxyzine with another QT/QTc prolonging drug is contraindicated. Drugs that have been associated with QT/QTc interval prolongation and/or torsade de pointes include, but are not limited to, the examples in the following list. Chemical/pharmacological classes are listed if some, although not necessarily all, class members have been implicated in QT/QTc prolongation and/or torsade de pointes:

- Class IA antiarrhythmics (e.g., quinidine, procainamide, disopyramide);
- Class III antiarrhythmics (e.g., amiodarone, sotalol, ibutilide);
- Class 1C antiarrhythmics (e.g., flecainide, propafenone);
- antipsychotics (e.g., chlorpromazine, pimozide, haloperidol, droperidol, ziprasidone, risperidone, olanzapine);
- antidepressants (e.g., fluoxetine, citalopram, venlafaxine, tricyclic/tetracyclic antidepressants e.g., amitriptyline, imipramine, maprotiline);
- opioids (e.g., methadone);
- macrolide antibiotics and analogues (e.g., erythromycin, clarithromycin, azithromycin, tacrolimus);
- quinolone antibiotics (e.g., moxifloxacin, levofloxacin, ciprofloxacin);
- pentamidine;
- antimalarials (e.g., quinine, chloroquine);
- azole antifungals (e.g., ketoconazole, fluconazole, voriconazole);
- domperidone;
- 5-hydroxytryptamine (5-HT)<sub>3</sub> receptor antagonists (e.g., ondansetron);
- arsenic trioxide
- tyrosine kinase inhibitors (e.g., vandetanib, sunitinib, nilotinib);
- histone deacetylase inhibitors (e.g., vorinostat);
- beta-2 adrenoceptor agonists (e.g., salmeterol, formoterol).

**CYP3A4/5 Inhibitors:** Hydroxyzine is a substrate for CYP3A4/5. Plasma levels of hydroxyzine can be increased by inhibitors of CYP3A4/5. Prolongation of the QT/QTc interval by hydroxyzine is anticipated to be increased in the presence of CYP3A4/5 inhibitors. Drugs that inhibit CYP3A4/5 include, but are not limited to, certain azole antifungals, macrolide antibiotics, and HIV protease inhibitors. The concomitant use of these drugs with hydroxyzine is contraindicated.

**Drugs that Cause Electrolyte Depletion:** The use of hydroxyzine with drugs that can disrupt electrolyte levels is not recommended. Such drugs include, but are not limited to, the following:

- loop, thiazide, and related diuretics;
- laxatives and enemas;
- amphotericin B;
- high dose corticosteroids

The above lists of potentially interacting drugs are not comprehensive. Current information sources should be consulted for newly approved drugs that prolong the QT/QTc interval, inhibit CYP3A4/5, or cause electrolyte disturbances, as well as for older drugs for which these effects have recently been established.

### **Drug-Food Interactions**

CYP3A4 can be inhibited by certain foods, including, but not limited to, grapefruit, grapefruit juice, and grapefruit-containing products, which could lead to increased plasma concentrations of hydroxyzine. Patients should be instructed not to consume these foods during treatment with hydroxyzine because the risk of QT/QTc prolongation may be increased.

### **SYMPTOMS AND TREATMENT OF OVERDOSAGE**

For management of a suspected drug overdose, contact your regional Poison Control Center immediately.

The most common manifestation of HYDROXYZINE overdose is hypersedation. Other reported signs and symptoms were convulsions, stupor, nausea and vomiting. QT prolongation and torsade de pointes have been observed with excessive blood concentrations of hydroxyzine in a context of overdose or impaired drug metabolism. As in the management of overdose with any drug, ingestion of multiple agents may have occurred.

General supportive care, including frequent monitoring of the vital signs and close observation of the patient, is indicated. Electrocardiogram monitoring is recommended in the event of overdose.

Hypotension, though unlikely, may be controlled with intravenous fluids and vasopressors (such as norepinephrine). Do not use epinephrine as HYDROXYZINE counteracts its pressor action. There is no specific antidote. It is doubtful that hemodialysis would be of any value in the treatment of overdose with hydroxyzine. However, if other agents have been ingested concomitantly, hemodialysis may be indicated.

## **DOSAGE AND ADMINISTRATION**

In order to help mitigate the potential risk of QT interval prolongation HYDROXYZINE should be used for as short a duration as possible, at the lowest effective dose up to specified maximums (see below). See also CONTRAINDICATIONS; WARNINGS; and DRUG INTERACTIONS.

### Usual Dosage

Adults: The maximum total daily dose in adults is 100 mg (50ml), given in divided doses.

Children and Adolescents:

- In children and adolescents up to 40kg in weight, the maximum daily dose is 2 mg /kg /day, given in divided doses. (Therefore, at the maximum weight of 40 kg, the maximum daily dose is 80 mg or 40 ml).
- In children and adolescents over 40 kg, the maximum daily dose is the same as for adults: 100 mg per day (50 ml), given in divided doses.

Elderly: Use should generally be avoided, but if judged to be an appropriate option in an individual case, the maximum daily dose is 50 mg (25 ml), given in divided doses.

Hepatic impairment: The total daily dose should be reduced by 33%. Use in patients with severe liver impairment should be avoided

Renal impairment: For patients with moderate or severe renal impairment, it is recommended that the total daily dosage should be reduced by 50%

### **AVAILABILITY OF DOSAGE FORMS**

Hydroxyzine capsules 10 mg: an off-white paste in an orange opaque soft gel shell printed “10” in white ink.

Hydroxyzine capsules 25 mg: an off-white to yellow paste in a green opaque soft gel shell printed “25” in white ink.

Hydroxyzine capsules 50 mg: an off-white to light pink paste in a red opaque soft gel shell printed “50” in white ink.

Available in bottles of 100 and 500.



## PHARMACEUTICAL INFORMATION

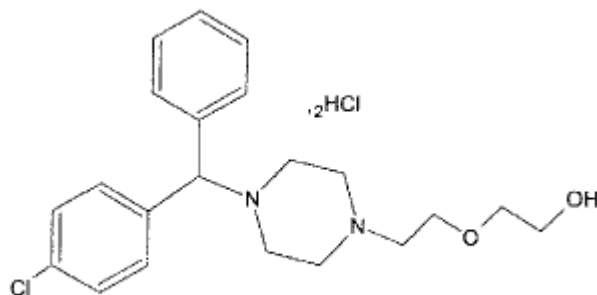
### CHEMISTRY

(I) Drug Substance:

Proper Name(s): Hydroxyzine hydrochloride

Chemical Name(s): Ethanol, 2-[2- [(4-chlorophenyl) phenylmethyl] -1 -piperaziny] ethoxy], dihydrochloride, ( $\pm$ ).

Structural Formula:



Molecular Formula:  $C_{21}H_{27}ClN_2O_2 \cdot 2HCl$

Molecular Weight: 447.83 g/mol

Description: Hydroxyzine hydrochloride is a white powder. Melts at 200°C with decomposition. Very soluble in water, soluble in chloroform, slightly soluble in acetone, practically insoluble in ether.

(II) Composition:

Each capsule contains the active ingredient: hydroxyzine hydrochloride  
Non-medicinal ingredients (in alphabetical order): Beeswax-yellow, ethyl vanillin, FD&C Blue No. 1 (25 mg), FD&C Red No. 2 (50 mg), FD&C Yellow No. 6 (10 mg and 50 mg), FD&C Yellow No. 10 (25 mg), gelatin, glycerine, hydrogenated vegetable oil type II, lecithin, methylparaben, propylparaben, soybean oil, soybean oil flakes and titanium dioxide.

The capsule imprinting ink contains (in alphabetical order): propylene glycol, shellac, simethicon and titanium dioxide.

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE  
PATIENT MEDICATION INFORMATION**

**PrHYDROXYZINE**

Hydroxyzine hydrochloride Capsules

Read this carefully before you start taking HYDROXYZINE and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about HYDROXYZINE.

**What is HYDROXYZINE used for?**

HYDROXYZINE is used:

**In Adults**

- as a pre-surgery medication (such as in preparation for a dental procedure)
- in the treatment of itching with rash or eczema that is caused by an allergic reaction
- in the treatment of nausea and vomiting (such as from chemotherapy or after surgery)

**In Adults:**

- to help in managing anxiety

**How does HYDROXYZINE work?**

HYDROXYZINE works by:

- blocking a substance called histamine. Your body produces this when you have an allergic reaction.
- affecting how certain chemicals work in your brain, such as serotonin.

**What are the ingredients in HYDROXYZINE?**

Each capsule contains the active ingredient: hydroxyzine hydrochloride

Non-medicinal ingredients (in alphabetical order): Beeswax-yellow, ethyl vanillin, FD&C Blue No. 1 (25 mg), FD&C Red No. 2 (50 mg), FD&C Yellow No. 6 (10 mg and 50 mg), FD&C Yellow No. 10 (25 mg), gelatin, glycerine, hydrogenated vegetable oil type II, lecithin, methylparaben, propylparaben, soybean oil, soybean oil flakes and titanium dioxide.

The capsule imprinting ink contains Propylene glycol, shellac, simethicon and titanium dioxide.

**HYDROXYZINE comes in the following dosage form:**

Bottles of 100 and 500 capsules

**Do not use HYDROXYZINE if you:**

- are allergic to:
  - hydroxyzine hydrochloride

- cetirizine
  - other piperazine derivatives
  - aminophylline
  - ethylenediamine
- are allergic to any of the other ingredients in HYDROXYZINE (see: **“What are the ingredients in HYDROXYZINE?”**)
  - have had an ECG (electrocardiogram) that showed that you have or had a heart rhythm problem called “QT interval prolongation.”
  - have or had heart disease
  - have or had a heart rate that is very slow
  - have had anyone in your family die suddenly from heart problems
  - have a low levels of potassium or magnesium in your blood
  - have asthma and have had an allergic reaction to another antihistamine in the past
  - have porphyria (a rare inherited disease where there is a problem with proteins in the blood).
  - are pregnant or planning to become pregnant

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take HYDROXYZINE. Talk about any health conditions or problems you may have, including if you:**

- have kidney disease or are on dialysis
- have liver disease or liver failure. HYDROXYZINE is not suitable for use in these patients
- have glaucoma or an increase in pressure of the eye
- have digestive system or stomach problems
- have myasthenia gravis (a muscle weakness disorder)
- have dementia
- have seizure disorders including epilepsy
- have breathing problems such as:
  - emphysema
  - chronic bronchitis
- have trouble emptying your bladder
- have hyperthyroidism. This is also known as an “overactive thyroid”
- have high blood pressure (hypertension)
- have an ulcer in your stomach
- are breast-feeding

**Other warnings you should know about:**

**Heart problems:** HYDROXYZINE may be linked with an increase in the risk of heart rhythm disorder. This may be life-threatening. Therefore, tell your doctor if you have any heart problems. While taking HYDROXYZINE, seek immediate medical attention if you have any symptoms of a possible heart rhythm problem, such as:

- dizziness
- palpitations (feeling of rapid pounding or skipped heartbeat or “fluttering”)
- fainting
- seizures

Treatment with HYDROXYZINE should be stopped.

**Test results:** Since HYDROXYZINE may affect the test results of an allergy and asthma test, treatment should be stopped for:

- 1 week before a skin test for allergies
- 96 hours before a methacholine test (a test to diagnose asthma)

**Driving and using machines:** Before doing tasks that require special attention, wait until you know how you respond to HYDROXYZINE.

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

**The following may interact with HYDROXYZINE:**

- Medications that can affect the rhythm of your heart. These include some drugs used in the treatment of:
  - heart rhythm problems (such as quinidine, amiodarone)
  - schizophrenia (such as haloperidol)
  - depression (such as citalopram)
  - fungal infections (such as ketoconazole)
  - bacterial infections (such as erythromycin and ciprofloxacin)
  - cancer (such as toremifene and arsenic trioxide)
  - pain (opioid medications such as methadone)
  - malaria (such as quinine and chloroquine)
  - nausea and vomiting (such as domperidone, ondansetron)
  - asthma and chronic obstructive pulmonary disorder (COPD) (such as salmeterol)
  - pneumonia (such as pentamidine)
- Medications that can increase the levels of HYDROXYZINE such as drugs used in the treatment of:
  - HIV (protease inhibitors)
  - fungal infections (such as ketoconazole)
  - bacterial infections (such as erythromycin and ciprofloxacin)
- Medications that can cause low levels of electrolytes in your blood such as:
  - drugs used to relieve constipation (laxatives and enemas)
  - high dose corticosteroids
  - drugs used to help your body get rid of water (diuretics)
- Alcohol. You should not drink alcohol while you are taking HYDROXYZINE. It may increase the sedative effects of the alcohol.
- Grapefruit, grapefruit juice and products that contain grapefruit. It may increase the levels of HYDROXYZINE in your blood.

**How to take HYDROXYZINE:**

HYDROXYZINE should be used at the lowest effective dose. The treatment period should be as short as possible.

Take this medicine exactly as your healthcare provider has told you to. Do not take more than the maximum daily dose

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HYDROXYZINE should be used at the lowest effective dose. The treatment period should be as short as

possible.

Take this medicine exactly as your healthcare provider has told you to. Do not take more than the maximum daily dose.

#### Usual Dosage

Adults: the maximum daily dose is 100 mg (50 mL), given in divided doses throughout the day.

Children and Adolescents who are **over** 40 kg in weight: the maximum daily dose is 100 mg (50 mL), given in divided doses throughout the day.

Children and Adolescents **up to** 40 kg in weight: the maximum daily dose is 2 mg/ kg, given in divided doses throughout the day.

#### Elderly patients (> 65 years of age)

HYDROXYZINE should generally be avoided in the elderly. When HYDROXYZINE recommended by a healthcare professional, the maximum daily dose for the elderly is 50 mg per day.

#### Patients with liver disease

Your healthcare professional will reduce your dose by about 1/3 if you have liver disease. HYDROXYZINE is not suitable for patients with severe liver disease or liver failure.

#### Patients with kidney disease

Your healthcare provider will reduce your dose by about 1/2 if you have kidney disease.

#### **Overdose:**

If you think you have taken too much HYDROXYZINE, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

#### Symptoms of an overdose can vary and may include:

- enlarged pupils of the eye
- uncontrolled and fast eye movements
- nausea and vomiting
- slurred speech
- feeling restless
- uncontrolled or slow movements
- problems with your vision
- fast or pounding heartbeat
- seizures
- shaking
- hallucinations
- feeling unusually drowsy
- slowing of your breathing and heart rate
- losing consciousness
- hot dry skin
- fever
- fast or pounding heartbeat
- problems with coordination
- confused or disturbed thinking

#### **Missed dose:**

If you forget to take a dose, you should take it as soon as you remember. If it is close to the time of your

next dose when you remember, skip the missed dose and take your next dose at the usual time. DO NOT take a double dose.

**What are possible side effects from using HYDROXYZINE?**

These are not all the possible side effects you may feel when taking HYDROXYZINE. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- dry mouth
- flushing
- drowsiness
- itching
- rash

<b>Serious side effects and what to do about them</b>			
<b>Symptom / effect</b>	<b>Talk to your healthcare professional</b>		<b>Stop taking drug and get immediate medical help</b>
	<b>Only if severe</b>	<b>In all cases</b>	
<b>UNCOMMON</b>			
<b>Allergic reactions:</b> rash, swelling of the lips, face or neck, difficulty breathing or speaking			✓
<b>Heart conduction disorders:</b> feeling lightheaded, dizzy, or passing out			✓
Irregular heart beat or heart palpitations (skipped beats)			✓
<b>Seizures</b>			✓
<b>Severe skin reactions:</b> such as rash, blistering of the skin			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

**Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

**Storage:**

Store at controlled room temperature 15°C to 30°C.

**More Information:**

If you want more information about HYDROXYZINE:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website;

<https://www.canada.ca/en/health-canada.html>; the manufacturer's website  
<https://www.aapharma.ca/en/>, or by contacting the sponsor AA Pharma Inc. at: 1-877-998-9097

This leaflet was prepared by AA Pharma Inc.

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