PRESCRIBING INFORMATION
PRODUCT MONOGRAPH

ATARAX SYRUP, 2MG/ML

Hydroxyzine Hydrochloride Syrup USP 10 mg/5 ml

Anxiolytic - Antihistamine Agent

Date of preparation: 06 Sep 2005

Date of revision: 10th of May 2016

Control No:183332

ERFA
Canada 2012 Inc.

8250 Décarie Blvd, suite 110
Montréal, QC
Canada, H4P 2P5

PRODUCT INFORMATION

ATARAX*

Hydroxyzine Hydrochloride Syrup USP 10 mg/5 ml

Anxiolytic - Antihistamine Agent

INDICATIONS

Adults

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

Adults and Children

Atarax is indicated for premedication, such as preparation for dental procedures.

ATARAX is useful in the management of pruritus due to allergic conditions such as chronic urticaria and atopic and contact dermatoses.

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

CONTRAINDICATIONS

ATARAX (hydroxyzine hydrochloride) 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, **ATARAX** (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, ATARAX (hydroxyzine hydrochloride) 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 hydrochloride must be considered when the drug is used in conjunction with central nervous system (CNS) depressants such as narcotics, non-narcotic analgesics, hypnotics, sedatives, psychotherapeutic agents, barbiturates or alcohol. Therefore when central nervous system depressants are administered concomitantly with ATARAX (hydroxyzine hydrochloride) their dosage should be reduced.
Because of its potential antimuscarinic actions, Atarax should be used with caution in patients suffering from angleclosure 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 methocholine 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 ATARAX (hydroxyzine hydrochloride).

ADVERSE REACTIONS

Side effects reported with the administration of ATARAX (hydroxyzine hydrochloride) 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/QTcprolonging 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)3 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: ***(bolding added)*** 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: ***(bolding added)*** 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

The most common manifestation of **ATARAX** overdosage 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 overdosage 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 overdosage. Hypotension, though unlikely, may be controlled with intravenous fluids and vasopressors (such as norepinephrine). Do not use epinephrine as **ATARAX** counteracts its pressor action.
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 have been ingested concomitantly, hemodialysis may be indicated.

DOSAGE AND ADMINISTRATION

In order to help mitigate the potential risk of QT interval prolongation ATARAX 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 Oral 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%

DOSAGE FORMS

Availability:

Pr **ATARAX** Syrup: Each 5 ml of mint-flavored syrup contains: hydroxyzine hydrochloride 10 mg, sodium benzoate 1.5 mg. Also contains sucrose, water, alcohol, menthol, spearmint oil, peppermint oil and sodium hydroxide or hydrochloric acid (for pH adjustment). Energy: 67 kJ (16 kcal). Tartazine-free. Available in bottles of 473 ml.

PHARMACEUTICAL INFORMATION

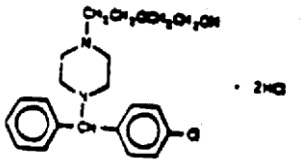
CHEMISTRY

(I) Drug Substance:

Proper Name(s): Hydroxyzine hydrochloride

Chemical Name(s): 1-(p-chlorobenzhydryl) 4-2-(2-hydroxy-ethoxy)-ethylpiperazine dihydrochloride.

Structural Formula:



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

Molecular Weight: 447.83

Description: Hydroxyzine hydrochloride is a white odorless powder with bitter taste. M.p. 196° to 204° with decomposition. Soluble 1 in 1 of water, 1 in 4.5 of alcohol and 1 in 13 of chloroform, slightly soluble in acetone.

(ii) Composition: **ATARAX** Syrup: Each 5 ml of mint- flavored syrup contains: hydroxyzine hydrochloride 10 mg. Also contains sodium benzoate 1.5 mg, sucrose, water, alcohol, menthol, spearmint oil, peppermint oil and sodium hydroxide or hydrochloric acid (for pH adjustment).

Energy: 67 kJ (16 kcal).

Tartrazine-free.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

ATARAX®
Hydroxyzine hydrochloride Syrup

Read this carefully before you start taking ATARAX 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 ATARAX.

What is ATARAX used for?

ATARAX is used:
In Adults and children:
- 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 ATARAX work?

ATARAX 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 ATARAX?

Medicinal ingredients: hydroxyzine hydrochloride

Non-medicinal ingredients: alcohol, menthol, sodium benzoate, spearmint oil, sodium hydroxide or hydrochloric acid (for pH adjustment), sucrose, peppermint oil and water. Tartazine –free.

ATARAX comes in the following dosage form:

- Syrup: 2mg/ml.

Do not use ATARAX if you:

- are allergic to:
  - hydroxyzine hydrochloride
  - cetirizine
  - other piperazine derivatives
  - aminophylline
  - ethylenediamine
- are allergic to any of the other ingredients in ATARAX (see: **"What are the ingredients in ATARAX?"**)
- 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 ATARAX. 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. ATARAX 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: ATARAX 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 ATARAX, 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 ATARAX should be stopped.

Test results: Since ATARAX 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 methocholine test (a test to diagnose asthma)

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

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 ATARAX:

- 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 ATARAX such as drugs used in the treatment of:
  - HIV (protease inhibitors)
  - fungal infections (such a 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 ATARAX. It may increase the sedative effects of the alcohol.

- Grapefruit, grapefruit juice and products that contain grapefruit. It may increase the levels of ATARAX in your blood.

How to take ATARAX:

ATARAX 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 Dose:
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)
ATARAX should generally be avoided in the elderly. When ATARAX is 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. ATARAX 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 ATARAX, 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 ATARAX?

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

Side effects may include:

- dry mouth
- flushing
- drowsiness
- itching
- rash

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
UNCOMMON			
• **Allergic reactions**: rash, swelling of the lips, face or neck, difficulty breathing or speaking			✓
• **Heart conduction disorders**: feeling lightheaded, dizzy, or passing out			✓

• **Irregular heart beat or heart palpitations (skipped beats)**			✓
• **Seizures**			✓
• **Severe skin reactions:** 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 help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.
3 ways to report:
Online at MedEffect;
By calling 1-866-234-2345 (toll-free);
By completing a Consumer Side Effect Reporting Form and sending it by:
- Fax to 1-866-678-6789 (toll-free), or
- Mail to: Canada Vigilance Program
  Health Canada, Postal Locator 0701E
  Ottawa, ON
  K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

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 – 30°C). Protect from freezing.

Keep out of reach and sight of children.

If you want more information about ATARAX:
- 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; the manufacturer's website www.eci2012.net or by calling 1-888-922-3133.

This leaflet was prepared by ERFA Canada 2012 Inc.

Last Revised May 10th, 2016