

## Important Safety Information on ATARAX (hydroxyzine) and the Risk of QT Prolongation and Torsade de pointes



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### Audience

Health care professionals including cardiologists, general practitioners, pharmacists, and nurses.

### Key messages

- **ATARAX (hydroxyzine) is an antihistamine that can increase the risk of QT prolongation (QTP) and torsade de pointes (TdP) which may lead to dizziness, palpitations, syncope, seizures, and sudden cardiac death.**
- **ATARAX is now contraindicated in patients with a history of QTP and/or TdP; history of cardiac arrhythmias; significant electrolyte imbalance; significant bradycardia; family history of sudden cardiac death and concomitant use of other QT/QTc-prolonging drugs or of CYP3A4/5 inhibitors.**
- **ATARAX should be used for as short a duration as possible and at the lowest effective dose up to specified maximums. The revised daily maximum oral dose is a total of 100 mg in adults, 50 mg in the elderly (if use cannot be avoided) and 2 mg/kg/day in children and adolescent up to 40 kg, in divided doses.**

### What is the issue?

A Health Canada safety review has demonstrated that ATARAX (hydroxyzine) has the potential to block hERG channels and other types of cardiac channels, resulting in a potential risk of QT prolongation (QTP) and cardiac arrhythmia events including torsade de pointes (TdP).

### Products affected

ATARAX (Hydroxyzine hydrochloride) Syrup USP 10 mg/5 mL

Other products affected by this risk information include all generic formulations of hydroxyzine:

Hydroxyzine hydrochloride capsules 10 mg, 25 mg, 50 mg

Hydroxyzine hydrochloride syrup 10 mg/5 mL

Hydroxyzine hydrochloride injection, USP 50 mg/mL

## **Background information**

ATARAX (hydroxyzine) is an H1-antihistamine agent, and is indicated for use in the management of anxiety; for premedication, such as preparation for dental procedures; for the management of pruritus due to allergic conditions; and in the control of nausea and vomiting (except in pregnancy).

Health Canada has reviewed new safety information including a randomized controlled study provided by Erfa Canada 2012 Inc. and a clinical trial in elderly psychiatric patients. The results indicate that hydroxyzine may prolong the QT interval. Although the extent of QT prolongation with hydroxyzine is not clearly defined, non-clinical studies (live animals, perfused hearts, cell lines) have observed effects of hydroxyzine on cardiac repolarization currents consistent with those seen with terfenadine. The body of evidence for hydroxyzine and QTP/TdP, consists mostly of case reports and non-clinical data.

In Canadian and international reports of QTP/TdP with hydroxyzine, the adverse events were associated with QT-prolonging drug use, electrolyte imbalance, congenital long QT syndrome, daily doses over 100 mg, and/or inhibitors of hydroxyzine metabolism.

## **Information for consumers**

ATARAX (hydroxyzine) is a prescription antihistamine medication used to treat anxiety (for example in the preparation for dental procedures), itchiness due to allergic conditions and nausea and vomiting (except in pregnancy).

Hydroxyzine has been linked to changes in the electrical activity of the heart called QT prolongation. This can cause abnormal heart rhythms and in rare cases can be serious or life-threatening.

Patients should stop taking hydroxyzine and contact a health care professional immediately if they experience signs and symptoms of an abnormal heart rate or rhythm such as heart palpitations, dizziness, fainting, or seizures.

Before starting treatment with hydroxyzine, patients should speak to their health care professional if they or a family member have had any heart problems, if they are taking other medications, or if they have had low levels of potassium and/or magnesium in their blood.

Patients who are already taking hydroxyzine should consult their doctor or pharmacist to confirm they are taking the medication at the correct dose and for the correct duration.

## **Information for health care professionals**

ATARAX (hydroxyzine) is now contraindicated in patients with a history of QTP and/or TdP (including congenital long QT syndromes); history of cardiac arrhythmias; significant electrolyte imbalance (hypokalemia, hypomagnesemia);

significant bradycardia; family history of sudden cardiac death and concomitant use of other QT/QTc-prolonging drugs or of CYP3A4/5 inhibitors.

ATARAX should be used for as short a duration as possible and at the lowest effective dose up to specified maximums. The maximum daily oral dose should be a total of 100 mg in adults given in divided doses, 50 mg in the elderly given in divided doses (if use cannot be avoided) and 2 mg/kg/day in divided doses in children and adolescent up to 40 kg in weight. In children and adolescents over 40kg, the maximum daily dose should be the same as for adults.

### **Action taken by Health Canada**

Health Canada, in collaboration with Erfa Canada 2012 Inc., has updated the Canadian Product Monograph (CPM) for ATARAX (hydroxyzine). Health Canada is currently working with the manufacturers of the generic versions of hydroxyzine to update their respective CPMs. Health Canada is communicating this important safety information to health care professionals and to the public through its Healthy Canadians Web site and MedEffect™ e-Notice.

### **Report health or safety concerns**

Managing marketed health product-related side effects depends on health care professionals and consumers reporting them. Any case of serious QT prolongation and torsade de pointes or other serious or unexpected side effects in patients receiving ATARAX (hydroxyzine) should be reported to Erfa Canada 2012 Inc. or Health Canada.

#### **Erfa Canada 2012 Inc**

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Email: psq@eci2012.net

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

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on [Adverse Reaction Reporting](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

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E-mail: [mhpd\\_dpdc.public@hc-sc.gc.ca](mailto:mhpd_dpdc.public@hc-sc.gc.ca)  
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