



**Health Canada Endorsed Important Safety Information on Intravenous
ZOFRAN® (ondansetron hydrochloride dihydrate)**

June 12, 2014

Dear Healthcare Professional:

Subject: New safety information regarding the dosage and administration of intravenous ondansetron (ZOFRAN®) in geriatrics (>65 years of age).

GlaxoSmithKline Inc., in consultation with Health Canada, would like to provide you with important new safety information regarding the dosing and administration of intravenous (IV) ondansetron (ZOFRAN®) in geriatrics. New dosing restrictions are recommended to mitigate the risk of QT prolongation in elderly patients (>65 years of age). In geriatrics, ZOFRAN® is indicated for the prevention of nausea and vomiting associated with emetogenic chemotherapy, including high dose cisplatin, and radiotherapy. Please note that ZOFRAN® is not approved for the prevention and treatment of post-operative nausea and vomiting in elderly patients.

- There is a risk of dose dependent QT interval prolongation, which is expected to be greater with faster rate of infusion and larger doses for the IV administration.
- The Dosage and Administration section of the ZOFRAN® Product Monograph has been updated with the new safety information.
- Healthcare professionals should use the new dosage and administration recommendations to mitigate the risk of QT prolongation in elderly patients.

The dosing restrictions for geriatrics are summarized below:

- In patients ≥ 75 years of age, the initial IV dose must not exceed **8 mg**.
- In patients < 75 years of age, the initial IV dose must not exceed **16 mg**.
- Subsequent IV doses must not exceed 8 mg and may be given 4 and 8 hours after the initial dose.
- All IV doses must be diluted in 50–100 mL of saline or other compatible fluid.
- All IV doses must be infused over no less than **15 minutes**.

These additional recommendations follow a previous risk communication (October 3, 2012), which detailed that ondansetron causes a dose-dependent prolongation of the QT interval, which can lead to Torsade de Pointes (TdP), a potentially life-threatening heart arrhythmia. Caution must be used if administering ondansetron to patients with risk factors for QT interval prolongation or cardiac arrhythmias and electrolyte imbalances should be corrected prior to ondansetron administration.

There are no changes to the recommended oral dosing.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of QT interval prolongation, ventricular dysrhythmia, cardiac arrest, sudden death, or other serious or unexpected adverse reactions in patients receiving ZOFRAN® should be reported to GlaxoSmithKline Inc. or Health Canada.

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Tel: 1-800-387-7374

To correct your mailing address or fax number, contact GlaxoSmithKline Inc.

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>) 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:
Marketed Health Products Directorate
E-mail: mhpd_dpssc@hc-sc.gc.ca
Telephone: 1-613-954-6522
Fax: 1-613-952-7738

Should you have any questions or require additional information regarding the use of ZOFRAN[®], please contact GlaxoSmithKline Inc., Medical Information Department at 1-800-387-7374.

Sincerely,

Original signed by

Dr. Sally Taylor
Country Medical Director, Canada
GlaxoSmithKline Inc.