Public Communication -
Health Canada Endorsed Important Safety Information on
ZOFRAN® (ondansetron hydrochloride dihydrate, ondansetron)

October 9, 2012

Subject: ZOFRAN® (ondansetron hydrochloride dihydrate, ondansetron) - Important new safety information: Association of ZOFRAN® with changes in electrical activity in the heart

GlaxoSmithKline Inc., in collaboration with Health Canada, would like to notify you of new safety information regarding the use of ZOFRAN® (ondansetron). ZOFRAN® is a prescription drug given for the prevention of nausea and vomiting in patients receiving chemotherapy and radiation for cancer, and in patients who have had surgery.

A recent study showed that ZOFRAN® can affect the "QT interval" (a measure of the heart's electrical activity) when used at high doses. The QT interval is read from an electrocardiogram (ECG), and is an indicator of how the heart electrically resets itself after each beat. When the QT interval is too long, abnormal heart beats can arise, which could result in dizziness, a sensation of rapid, pounding, or irregular heartbeat, fainting or death.

The prescribing information for ZOFRAN® has been revised to include updated safety information on the risk of QT prolongation and intravenous (IV, given by needle into a vein) dosing instructions, as described below:

- At high doses, ZOFRAN® can affect electrical activity in the heart which in turn could cause dizziness, rapid, pounding, or irregular heartbeat, fainting or death.
- The 32 mg intravenous dose of ZOFRAN® should not be used. In adults, the new **maximum** recommended intravenous dose of ZOFRAN® is 16 mg.
- Avoid ZOFRAN® if you have congenital long QT syndrome (ask your doctor if you are not sure).
- If you have problems with your heart or are taking any medications, tell your doctor before using ZOFRAN®.
- Tell your doctor immediately if you experience dizziness, abnormal heartbeat, or fainting during treatment with ZOFRAN®.

In adults, there are no recommended dosing changes for ZOFRAN® given by mouth.

In children, there are no recommended dosing changes for ZOFRAN® given intravenously or by mouth.

Although these serious heart-related effects of ZOFRAN® have been reported rarely, some people may be at higher risk. Doctors are being advised to consider each patient's risks before treatment. GSK has sent a letter to healthcare professionals informing them of this new safety information. Further information may be obtained on the Canadian website of GlaxoSmithKline (www.gsk.ca) or on the Health Canada website.

If you have any questions regarding your ZOFRAN® prescription, contact your doctor.

For media inquiries, please contact GlaxoSmithKline Communications at (905) 819-3363.

Managing marketed health product-related side effects depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing side effects are generally presumed to underestimate the risks associated with health product treatments. Any serious or unexpected side effects in patients receiving ZOFRAN® should be reported to GlaxoSmithKline Inc. or Health Canada.

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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, please contact Health Canada at:
Marketed Health Products Directorate
E-mail: mhpd_dpsc@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

Sincerely,

Original signed by

Dr. Glenn Crater,
Vice-President, Medical and Chief Medical Officer
GlaxoSmithKline Inc.