GlaxoSmithKline
Scientific Office

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المكتب العلمي

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**August 29th, 2013**

**Title: ZOFRAN® (ondansetron) – updated information on posology for intravenous use and dose dependant QT interval prolongation.**

**Dear Healthcare Professional,**

GlaxoSmithKline in agreement with the Saudi Food and Drug Authority would like to inform you about updated information on posology for intravenous ondansetron for the management of chemotherapy induced nausea and vomiting (CINV). This includes new guidance for repeat dosing and for use in elderly patients.

**Summary:**

The new advice on dilution and administration in patients age 65 years or older refers only to the indication for prevention of chemotherapy-induced nausea and vomiting; there has been no change to the dosing, dilution, or administration instructions for the indication of postoperative nausea and vomiting.

Patients aged 75 years or older:

- A single dose of intravenous ondansetron given for the prevention of chemotherapy-induced nausea and vomiting (CINV) must not exceed 8mg (infused over at least 15 minutes).

Adult patients aged younger than 75 years:

- A single dose of intravenous ondansetron given for the prevention of CINV in adults (aged less than 75 years) must not exceed 16mg (infused over at least 15 minutes).

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Dilution and administration in patients age 65 years or older (refers only to the indication for prevention of chemotherapy-induced nausea and vomiting)

- All intravenous doses (For prevention of CINV) should be diluted in 50–100 ml saline or other compatible fluid and infused over at least 15 minutes.

Repeat dosing in all adults (including elderly patients):

- Repeat intravenous doses of ondansetron must not exceed 8 mg and should be given no less than 4 hours apart.

Ondansetron causes a dose-dependent prolongation of the electrocardiographic-corrected QT interval (QTc), which can lead to Torsade de Pointes a potentially life-threatening heart arrhythmia. Therefore the above new dose restrictions are in place for use of intravenous ondansetron.

**Further information on the safety concern**

Ondansetron should be avoided in patients with congenital long QT syndrome.

Caution must be used if administering ondansetron to patients with risk factors for QT interval prolongation or cardiac arrhythmias. These include:

- electrolyte abnormalities
- congestive heart failure
- bradyarrhythmias
- use of other medicines that prolong the QT interval (including cytotoxic drugs), or that may lead to electrolyte abnormalities

Hypokalaemia and hypomagnesaemia should be corrected prior to ondansetron administration.

There are no changes to the recommended oral and rectal dosing for CINV in adult and elderly patients.

There are no changes to the recommended intravenous and oral dosing for the prevention and treatment of post-operative nausea and vomiting (PONV) in adult and elderly patients Maximum recommended dose in this setting is a single dose of 4 mg.

There are no changes in the recommended intravenous or oral dosing for any indication in the paediatric population (age > 6 months and adolescents).

**Background:**

The risk of prolongation of QTc interval and cardiac arrhythmia, including Torsade de Pointes, with ondansetron use is already included in the product information for ondansetron.

The communication dated June 2012 was based on the results of a study which demonstrated that ondansetron causes a dose-dependent prolongation of the QTc.

Further analysis of the results of this study together with other data sources demonstrated a concentration-dependent relationship and now allows for additional specific guidance for repeat intravenous dosing and for use in elderly patients.

Call for reporting

GlaxoSmithKline will continue to monitor the safety of ZOFRAN® **(ondansetron)** and update SFDA of any serious adverse event for evaluation. You can assist us in monitoring the safety of ZOFRAN® **(ondansetron)** by reporting adverse reactions to fax: +966 12 6536660 or by email to GlaxoSmithKline safety email: faisal.m.shujrah@gsk.com Or to the National Pharmacovigilance and Drug Safety Center at Fax: +966 11 2057662 or by email to: npc.drug@sfda.gov.sa

If you have any question about the new information, please contact GSK medical information department at GlaxoSmithKline Saudi Arabia by phone: +966 12 6536666 or fax: +966 12 6536660.

**The letter is sent in agreement with the Saudi Food and Drug Authority**

Best regards;

Mohammed Hany Soliman

Country Medical Director
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**References**:


- ZOFRAN® (Ondansetron) SPC.
- ZOFRAN® (Ondansetron) PSUR.
- MHRA – DrugSafetyUpdate - Volume 6, Issue 12 July 2013
- Zofran DHCPL ( Dated April 14th , 2012)