GlaxoSmithKline (MALTA) Ltd
1, 1st floor, De la Cruz Avenue,
Qormi, QRM 2458, Malta
Tel +356 21238131

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Direct Healthcare Professional Communication on ondansetron (Zofran) and dose-dependent QT interval prolongation – updated information on posology for intravenous use

Dear Healthcare Professional,

I am writing to inform you of 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.

This new guidance is in addition to a previous communication sent to you in July 2012, which stated a new maximum dose for a single intravenous dose of ondansetron in adult patients.

Summary

Elderly 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 less 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).

Repeat dosing in all adult patients (including elderly patients):

- Repeat intravenous doses of ondansetron should be given no less than 4 hours apart.

Dilution and administration in elderly patients aged 65 years or older:

- All intravenous doses should be diluted in 50–100mL saline or other compatible fluid and infused over at least 15 minutes.

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
- use of medicines which lower heart rate

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.

There are no changes in the recommended intravenous or oral dosing for any indication in the paediatric population.

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 submitted in July 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.

This letter is not a comprehensive presentation of the risk profile of ondansetron.

PLEASE NOTE: the current, local prescribing information is currently in the process of being updated.

Further advice for healthcare professionals
Please share the information in this letter with relevant colleagues and health care personnel.

Call for reporting
Please report any suspected adverse reactions and medication errors via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Any suspected adverse reactions with ondansetron may also be reported to GlaxoSmithKline at GlaxoSmithKline (Malta) Limited, 1, 1st floor, de la Cruz Avenue, Qormi, QRM 2458; by phone to 21238131; or e-mail at mt.info@gsk.com, as appropriate.

When reporting, please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

Further Information
If you have any questions about this new information, please contact GlaxoSmithKline at GlaxoSmithKline (Malta) Limited, 1, 1st floor, de la Cruz Avenue, Qormi QRM 2458, Malta (Tel. 21 238131).

Yours sincerely

Ruth Gatt
Medical Lead - Malta & Gibraltar
Europe

Email ruth.m.gatt@gsk.com
Mobile +356 7903 2498
Tel +356 2567 5113