Ondansetron (Zofran) IV: Drug Safety Communication - QT prolongation

[Posted 06/29/2012]

AUDIENCE: Oncology, Surgery, Gastroenterology

ISSUE: The U.S. Food and Drug Administration (FDA) is informing healthcare professionals and the public that preliminary results from a recently completed clinical study suggest that a 32 mg single intravenous dose of ondansetron (Zofran, ondansetron hydrochloride, and generics) may affect the electrical activity of the heart (QT interval prolongation), which could pre-dispose patients to develop an abnormal and potentially fatal heart rhythm known as Torsades de Pointes.

GlaxoSmithKline (GSK) has announced changes to the Zofran drug label to remove the 32 mg single intravenous dose. The updated label will state that ondansetron can continue to be used in adults and children with chemotherapy-induced nausea and vomiting at the lower intravenous dose recommended in the drug label, a dose of 0.15 mg/kg administered every 4 hours for three doses; however, no single intravenous dose should exceed 16 mg. Information from the new clinical study will be included in the updated drug label.

BACKGROUND: Zofran (ondansetron) is in a class of medications called 5-HT3 receptor antagonists. It is used to prevent nausea and vomiting caused by cancer chemotherapy, radiation therapy and surgery. FDA will evaluate the final study results when available, and will work with GSK to explore an alternative single dose regimen that is both safe and effective for the prevention of chemotherapy-induced nausea and vomiting in adults.

RECOMMENDATION: The new information on QT prolongation does not change any of the recommended oral dosing regimens for ondansetron. It also does not change the recommended lower dose intravenous dosing of ondansetron to prevent post-operative nausea and vomiting.

- The use of a single 32 mg intravenous dose of ondansetron should be avoided. New information indicates that QT prolongation occurs in a dose-dependent manner, and specifically at a single intravenous dose of 32 mg.
- Patients who may be at particular risk for QT prolongation with ondansentron are those with congenital long QT syndrome, congestive heart failure, bradyarrhythmias, or patients taking concomitant medications that prolong the QT interval
- Electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia) should be corrected prior to the infusion of ondansetron.
- The lower dose intravenous regimen of 0.15 mg/kg every 4 hours for three doses may be used in adults with chemotherapy-induced nausea and vomiting. However, no single intravenous dose of ondansetron should exceed 16 mg due to the risk of QT prolongation.

- The new information does not change any of the recommended oral dosing regimens for ondansetron, including the single oral dose of 24 mg for chemotherapy induced nausea and vomiting.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of this product to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm[1]
- Download form[2] or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

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