Health Canada-Endorsed Important Safety Information on ZITHROMAX® /ZMAX SR® (azithromycin)

May 14, 2013

Dear Healthcare Professional,

Subject: ZITHROMAX® /ZMAX SR® (azithromycin) and the Risk of potentially Fatal Cardiac Arrhythmias

Pfizer Canada Inc., in collaboration with Health Canada, would like to inform you of revisions to the Product Monographs for ZITHROMAX and ZMAX SR (azithromycin) regarding the risk of potentially fatal cardiac arrhythmias. A small absolute increase in the risk of cardiovascular deaths was observed in patients taking azithromycin as compared to those who took no antibiotics and those who took amoxicillin in a recent study by Ray et al.[1]. This risk mainly affected patients who were at a higher baseline risk for cardiovascular events.

Pfizer completed a review of all relevant available data, and has decided to update the Precautions section of the ZITHROMAX and ZMAX SR product monographs to include additional instructions.

- There have been rare reports of QT prolongation and *torsades de pointes* in patients receiving therapeutic doses of azithromycin.
- Caution is required when treating patients with congenital or documented QT prolongation; with electrolyte disturbance, particularly in cases of hypokalaemia and hypomagnesemia or with clinically relevant bradycardia, cardiac arrhythmia or cardiac insufficiency.
- Caution is also required when treating patients currently receiving treatment with other active substances known to prolong QT interval such as antiarrhythmics of classes IA and III, antipsychotic agents, antidepressants and fluoroquinolones.
- Elderly patients may be more susceptible to drug-associated effects on the QT interval.

Prolonged cardiac repolarization and QT interval have been seen in treatment with macrolides including azithromycin. Health care practitioners should consider the risk of fatal cardiac arrhythmias with azithromycin when prescribing antibacterial treatment for patients who are already at risk for cardiovascular events.

The profile of azithromycin is continually monitored and reassessed as new information becomes available through the literature, clinical studies, spontaneous reports, and safety data base searches.

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 serious QT prolongation and torsades de pointes or other serious or unexpected adverse reactions in patients receiving ZITHROMAX and ZMAX SR should be reported to Pfizer Canada Inc. or Health Canada.

If you have an inquiry of a medical nature related to **ZITHROMAX and ZMAX SR (azithromycin)**, please contact our Medical Information Services as per the contact information below

Pfizer Canada Inc.
17300 Trans-Canada Highway
Kirkland, QC H9J 2M5
1-800-463-6001.

This notice can be found on Pfizer Canada's website: www.pfizer.ca
To correct your mailing address or fax number, contact Pfizer Canada 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_dpsc@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

Sincerely,

Original signed by

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Pfizer Canada Inc.

References:

1. Ray WA, Murray KT, Hall K, Arbogast PG, Stein CM. Azithromycin and the Risk of Cardiovascular Death. The New England Journal of Medicine 2012;366:1881-90.