Health Canada Endorsed Important Safety Information on KETEK (telithromycin)

sanofi aventis
Because health matters

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Dear Health Care Professional:

Subject: **Updated safety information on KETEK (telithromycin) and hepatic events, aggravation of myasthenia gravis and syncope**

Sanofi-aventis Canada Inc. in consultation with Health Canada would like to inform you of important updated safety information regarding KETEK (telithromycin) tablets. Based on information in published case reports* and post-market adverse event reports, the Canadian Product Monograph has been revised to include information on severe and sometimes fatal hepatotoxicity in patients taking KETEK. The Product Monograph also includes updated information regarding syncope (loss of consciousness) and the use of KETEK in patients with myasthenia gravis.

- Acute liver failure including fulminant hepatitis and hepatic necrosis leading to liver transplant or death have been observed during or immediately after the completion of KETEK treatment.
- Exacerbations of myasthenia gravis have led to death or life-threatening acute respiratory failure with a rapid onset in patients taking KETEK.
- Syncope, usually associated with vagal syndrome, has been reported in patients taking KETEK.

Alterations in hepatic enzymes have been commonly observed in clinical studies with telithromycin. Hepatitis and hepatocellular injury were observed infrequently.

Most post-marketing cases of hepatic dysfunction were reversible after discontinuation of KETEK, however cases of severe hepatotoxicity, including necrosis, hepatic failure and death have occurred. In some of these cases liver injury occurred after administration of only a few doses of KETEK and progressed rapidly. The mechanism underlying severe hepatocellular injury is unknown. Severe reactions, in some but not all cases, have been associated with serious underlying diseases or concomitant medications.

In light of this safety information, the Product Monograph has been revised to include the

following recommendations:

- KETEK is contraindicated in patients with a previous history of hepatitis and/or jaundice associated with the use of this drug.
- KETEK is contraindicated in patients who are hypersensitive to telithromycin or to any macrolide antibiotic.
- Physicians and patients should monitor for symptoms of hepatitis, such as fatigue, malaise, anorexia, nausea, jaundice, bilirubinuria, acholic stools, liver tenderness, hepatomegaly, or pruritus.
- Patients with symptoms of hepatitis must be advised to discontinue KETEK and immediately seek medical evaluation, which should include liver function tests. If clinical hepatitis or transaminase elevations combined with other systemic symptoms of hepatocellular injury occur, KETEK should be permanently discontinued.

The Product Monograph has also been updated regarding the exacerbations of myasthenia gravis and regarding syncope, usually associated with vagal syndrome. These side effects and the following recommendations should be taken into consideration when prescribing KETEK:

- KETEK is not recommended for patients with myasthenia gravis, however if no other therapeutic alternatives are available then such patients must be closely monitored and advised to discontinue KETEK treatment and immediately seek medical attention if they experience any exacerbation of their symptoms.
- Patients should be cautioned about the potential effects of syncope on activities such as driving a vehicle, operating machinery or engaging in other potentially hazardous activities.

Complete product information is available in the official Canadian Product Monograph.

* Brief communication: severe hepatotoxicity of telithromycin: three case reports and literature review, K.D. Clay *et al.* (2006) Ann Intern Med 144:415-20

Reporting rates determined on the basis of spontaneously reported post-marketing adverse events are generally presumed to underestimate the risks associated with drug treatments.

The identification, characterization, and management of marketed health product-related adverse reactions are dependent on the active participation of health care professionals in adverse reaction reporting programmes. Any occurrence of hepatic events, exacerbations of myasthenia gravis, or syncope, or any other suspected adverse reactions in patients receiving KETEK should be reported to sanofi-aventis Canada Inc. or Health Canada at the following addresses:

Any suspected adverse reaction can be reported to:

sanofi-aventis Canada Inc.:
Toll-free telephone: 1-800-265-7927
Internet: www.sanofi-aventis.ca

Regular mail:
sanofi-aventis Canada Inc.
2150 St. Elzear Blvd. West
Laval, Quebec
H7L 4A8

Any suspected adverse reaction can also be reported to:
Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
OTTAWA, Ontario, K1A 0K9
Tel: (613) 957-0337 or Fax: (613) 957-0335
To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866 234-2345
Fax: 866 678-6789
cadrmp@hc-sc.gc.ca

The AR Reporting Form and the AR Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties.*

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/form/ar-ei_form_e.html
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

For other inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate (MHPD)
E-mail: MHPD_DPSC@hc-sc.gc.ca
Tel: (613) 954-6522
Fax: (613) 952-7738

Sincerely,

original signed by

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