Health Canada Endorsed Important Safety Information on VIRACEPT (nelfinavir mesylate)

2007-09-10

Dear Healthcare Professional,

Subject: **Process-Related Impurity (ethyl methanesulfonate - EMS) in all strengths and formulations of VIRACEPT (nelfinavir mesylate)**

Pfizer and Health Canada wish to notify you of the presence of low levels of ethyl methanesulfonate (EMS), a process-related impurity in VIRACEPT (nelfinavir mesylate) and to provide guidance on the use of VIRACEPT in patients, including pregnant women and pediatric patients.

EMS is a potential human carcinogen. Data from animal studies indicate that EMS is teratogenic, mutagenic and carcinogenic. However, no data from humans exists. Animal studies do not necessarily predict human risk.

- At this time, physicians should consider the risks and benefits of prescribing VIRACEPT to their HIV-infected adult patients, given the information provided below. In general, Health Canada recommends that HIV-infected patients should be switched from VIRACEPT to an alternative therapy if this can be done safely. Health care professionals are requested to facilitate access for these patients.
- Patients should NOT stop taking VIRACEPT without first consulting with their physician.
- The following groups of patients may be more susceptible to harm from EMS and should be switched to alternative therapy as soon as medically feasible:

  - Pregnant women
  - Children

- VIRACEPT should NOT be used for post-exposure prophylaxis (occupational or non-occupational). (This use is not an approved indication in Canada.)
- VIRACEPT should NOT be prescribed for adults and children needing to initiate therapy.
- Pharmacists should notify the treating HIV physician when patients present for renewal of VIRACEPT prescriptions.

Patients taking VIRACEPT should contact their physician for discussion of whether they should continue or be switched to other treatment. For patients without other reasonable treatment options, Health Canada and Pfizer agree that there remains a positive benefit/risk for continued use of VIRACEPT.

VIRACEPT was removed by Roche Ltd from the European market in June 2007, due to detection of high levels of EMS in some product there. In the Canadian product (manufacturing source is different from that of the European formulations), the level of exposure is over 200 times less than that found in Europe.

The levels currently deemed acceptable for long-term exposure to EMS suggest a theoretical lifetime increased cancer risk in adults of less than 1 case per 100,000 patients exposed. While no data on the impact of high EMS levels in humans exist, estimates from in-vitro and animal data suggest that currently observed EMS levels in Canadian formulations may result in cancer risk in adults between 1 and 17 cases per 100,000 patients exposed for a lifetime. Current estimates of the background incidence of cancer in the HIV population are about 20 to 30 cases per 1000 patient-years. Toxicology experts generally agree that the lifetime risk associated with exposure to a carcinogen is about 3-fold greater among pediatric patients between 2 and 16 years of age, and even higher among pediatric patients younger than 2 years of age.

Pfizer is working with Health Canada to prospectively limit EMS levels in VIRACEPT while still considering the immediate needs of patients on therapy. Further relevant information will be provided as it becomes available.

Healthcare professionals and patients who have additional questions may contact Pfizer Canada's medical information line at 1-800-463-6001.

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 adverse reactions in patients receiving VIRACEPT should be reported to Pfizer Canada Inc. or Health Canada at the following addresses:

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

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:
Bureau of Gastroenterology, Infection and Viral Diseases (BGIVD)
E-mail: BGIVD_Enquiries@hc-sc.gc.ca
Tel: (613) 941-3207
Fax: (613) 941-1183

Sincerely,

Original Signed By

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Pfizer Canada Inc.