Health Canada Endorsed Important Safety Information on fosamprenavir (PrTELZIR®)

GlaxoSmithKline

2009/07/17

Dear Health Care Professional:

Subject: **Potential association of myocardial infarction in patients treated with PRTELZIR®(fosamprenavir).**

GlaxoSmithKline, in consultation with Health Canada, would like to inform you of important safety information regarding a potential association between myocardial infarction and exposure to fosamprenavir (PRTELZIR®) in HIV-infected patients.

Fosamprenavir is a protease inhibitor (PI) used in combination with low-dose ritonavir and other antiretrovirals in the treatment of HIV-1 infection.

- A nested case-control study conducted in the French Hospital Database on HIV has reported an association between exposure to fosamprenavir and an increased risk of myocardial infarction (Odds Ratio (OR) 1.55 per additional year of exposure; 95% Confidence Interval (CI), 1.20-1.99)[1].
- This may be related to the propensity for this drug class to raise blood lipids. Triglyceride and cholesterol levels should therefore be checked prior to initiating therapy with fosamprenavir and at periodic intervals during therapy. Appropriate clinical management of lipid disorders should be initiated as required.
- Other modifiable risk factors for cardiovascular disease (such as hypertension, diabetes and smoking) should also be monitored in HIV-infected subjects and managed as clinically appropriate.

Recent data presented at the 16th Conference on Retroviruses and Opportunistic Infections (CROI 2009) suggested a potential association between fosamprenavir and myocardial infarction in HIV infected adults. The nested case-control study reported an increased risk of myocardial infarction in association with cumulative exposure to fosamprenavir (OR, 1.55 per additional year of exposure; 95% CI, 1.20-1.99)[1]. Myocardial infarction has already been identified as being potentially associated with the PI class in the ongoing Data Collection on Adverse Events of Anti-HIV Drugs (DAD)[2].

Suppression of viral replication in HIV disease with antiretroviral therapy is of the utmost importance. Physicians should monitor a patient's cardiovascular risk as part of the follow-up and seek to adjust modifiable risk factors. Combination antiretroviral therapy is associated with redistribution of body fat (lipodystrophy) in HIV-infected patients. Clinical examination should include evaluation for physical signs of fat distribution. HIV infection itself has been associated with lipid disorders and ischaemic heart disease.

GSK will be working with Health Canada on this issue to integrate new safety information in the Canadian Product Monograph.

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 myocardial infarction or other serious or unexpected adverse reactions in patients receiving **TELZIR® Tablets and Oral Solution** should be reported to GlaxoSmithKline or Health Canada at the following addresses:

GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4
Tel.: 1-800-387-7374
www.gsk.ca

Any suspected adverse reaction can also be reported to:
Canada Vigilance National Office
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
CanadaVigilance@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/ar-ei_form-eng.php
http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_fs-if/2009-ar-ei-guide-prof/index-eng.php

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

Sincerely,

original signed by

Dr. Tjark Reblin, MD, MBA
Vice President, Medical Division and Chief Medical Officer
GlaxoSmithKline Inc.

REFERENCES

1. Lang S, Mary-Krause M, Cotte L et al. Impact of Specific NRTI and PI Exposure on the Risk of Myocardial Infarction: A Case-Control Study Nested within FHDH ANRS CO4. 16th Conference on Retroviruses and Opportunistic Infections (CROI 2009) February 8 - 11, 2009, Montreal, Canada. Abstract #43LB. (Slides and audio from the oral presentation by D Costagliola in session "Oral Abstract: Pharmacogenetics, Pharmacoenhancement, and Complications of ART" on Monday, Feb 9, 2009 10:00 AM available from the CROI webpage at: *http://app2.capitalreach.com/esp1204/servlet/tc?c=10164&cn=retro&e=10649&m=1&s=20415&&espmt=2&mp3file=10649&m4bfile=10649&br=80&audio=false)*

2. DAD Study Group. Class of antiretroviral drugs and the risk of myocardial infarction. N Engl J Med. 2007;356(17):1723-35.