Health Canada Endorsed Important Safety Information on INVIRASE® (saquinavir mesylate)

27/10/2010

Dear Health Care Professional

Subject: Updated Prescribing Information for INVIRASE® (saquinavir mesylate) Regarding QT/PR Interval Prolongation and the Need for ECG Monitoring in the Treatment of HIV-infected Patients with ritonavir-boosted INVIRASE®

Hoffmann-La Roche Limited, in consultation with Health Canada, would like to inform healthcare professionals of updates to the Canadian Product Monograph (CPM) for INVIRASE. Additional cautionary language has been provided in the CPM to strengthen the warnings regarding QT/PR interval prolongation and to stress the need for electrocardiogram (ECG) monitoring in the treatment of HIV-infected patients **with ritonavir-boosted INVIRASE**.

INVIRASE is authorized for the treatment of HIV-1 infected adult patients. INVIRASE should only be given in combination with ritonavir and other antiretroviral products.

- An ECG should be completed prior to initiation of ritonavir-boosted INVIRASE;
- Patients with a QT interval greater than 450 msec should NOT use ritonavir-boosted INVIRASE;
- An on-treatment ECG is recommended after 3-4 days of treatment. If a patient's QT interval is greater than 20 msec above pre-treatment values, or greater than 480 msec, then ritonavir-boosted INVIRASE should be discontinued;
- Caution is advised when co-administering ritonavir-boosted INVIRASE and other therapies that may increase the QT interval. ECG monitoring should be performed in this patient population (see **WARNINGS AND PRECAUTIONS**, section, below).

The updated CPM can be found at: http://www.rochecanada.com or can be accessed by performing a search in Health Canada's Drug Product Database at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php. The main updates to the CPM include the following information:

WARNINGS AND PRECAUTIONS, Cardiovascular - Cardiac conduction *and* repolarisation abnormalities:

Patients initiating therapy with ritonavir-boosted INVIRASE: An ECG should be performed prior to initiation of treatment. Patients with a QT interval > 450 msec should not use ritonavir-boosted INVIRASE. For patients with a QT interval < 450 msec, an on-treatment ECG is suggested after approximately 3 to 4 days of therapy. Patients with a QT interval > 480 msec or prolongation over pre-treatment by > 20 msec on their on-treatment ECG should discontinue ritonavir-boosted INVIRASE.

Patients stable on ritonavir-boosted INVIRASE and requiring concomitant medication with potential to increase the QT interval or patients on medication with potential to increase the QT interval and requiring concomitant ritonavir-boosted INVIRASE where no alternative therapy is available and the benefits outweigh the risks: An ECG should be performed prior to initiation of the concomitant therapy, and patients with a QT interval > 450 msec should not initiate the concomitant therapy (see DRUG INTERACTIONS and CONTRAINDICATIONS). If baseline QT interval < 450 msec, an on-treatment ECG should be performed. For patients demonstrating a subsequent increase in QT interval to > 480 msec or increase by > 20 msec after commencing concomitant therapy, the physician should use best clinical judgment to discontinue either ritonavir-boosted INVIRASE or the concomitant therapy or both.

Ritonavir-boosted INVIRASE at a dose of 2000 mg once daily with ritonavir 100 mg once daily has not been studied with regard to the risk of QT prolongation and is not recommended.

Hoffman-La Roche Limited continues to monitor adverse events of QT and PR interval prolongation associated with INVIRASE and ritonavir-boosted INVIRASE and is committed to providing healthcare professionals with the most current information for its products.

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 prolongations of QT and PR intervals or other serious or unexpected adverse reactions in patients receiving INVIRASE should be reported to Hoffmann-La Roche Limited or Health Canada at the following addresses:

Hoffmann-La Roche Limited
Drug Safety Department
2455 Meadowpine Boulevard
Mississauga, Ontario, L5N 6L7
Or call toll free at: 1-888-762-4388
Or fax at: 905-542-5864
Or email to: Mississauga.drug_safety@roche.com

Any suspected adverse reaction can also be reported to:
Canada Vigilance Program
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701D
Ottawa, Ontario, K1A 0K9
Telephone: 613-957-0337 or Fax: 613-957-0335
CanadaVigilance@hc-sc.gc.ca

To report an Adverse Reaction, consumers and health professionals may call toll free:
Telephone: 1-866-234-2345
Fax: 1-866-678-6789

Postage paid labels, the Canada Vigilance Reporting Forms and the Adverse Reaction Reporting Guidelines can be found on the MedEffect™ Canada Web site in the Adverse Reaction Reporting section. The Reporting Form is also in the *Canadian Compendium of Pharmaceuticals and Specialties.*

http://hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php

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

To change your mailing address or fax number, contact the Market Authorization Holder.

Should you have any questions or require additional information regarding the use of INVIRASE, please contact the Drug Information Department at Hoffmann-La Roche Limited at 1-888-762-4388 from 8:30 a.m. to 4:30 p.m. Monday to Friday Eastern Standard Time.

Sincerely,

Lorenzo Biondi,
Vice President, Medical and Regulatory Affairs
Hoffmann-La Roche Limited