Health Canada Endorsed Important Safety Information on INTELENCE* (etravirine)

October 15, 2009

Dear Healthcare Professional:

Subject: **New safety information regarding INTELENCE* (etravirine) and severe skin and hypersensitivity reactions**

Tibotec, a division of Janssen-Ortho Inc. ("Tibotec"), in collaboration with Health Canada, would like to inform you of important safety information regarding severe skin reactions in patients receiving combination therapy including INTELENCE (etravirine) tablets. Specifically, there have been post-marketing reports of severe hypersensitivity reactions sometimes accompanied by hepatic failure, and a report of a fatality due to toxic epidermal necrolysis.

- Severe, potentially life-threatening, and fatal skin reactions have been reported. These include cases of Stevens-Johnson syndrome, toxic epidermal necrolysis and erythema multiforme. Hypersensitivity reactions have also been reported and were characterized by rash, constitutional findings, and sometimes organ dysfunction, including hepatic failure.

- Discontinue INTELENCE immediately if signs or symptoms of severe skin reactions or hypersensitivity reactions develop (including, but not limited to, severe rash or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial edema, hepatitis, eosinophilia). Clinical status including liver transaminases should be monitored and appropriate therapy initiated. Delay in stopping INTELENCE treatment after the onset of severe rash may result in a life-threatening reaction.

The cases within clinical and post-marketing experience illustrate the importance of clinical vigilance and familiarity with the signs and symptoms of severe skin rash and hypersensitivity reactions. Additionally, they underscore the importance of immediate discontinuation of INTELENCE in cases where severe rash or hypersensitivity reaction is suspected.

In Phase 3 clinical trials, Grade 3 and 4 rashes were reported in 1.3% of subjects receiving INTELENCE compared to 0.2% of placebo subjects. A total of 2% of HIV-1-infected patients receiving INTELENCE discontinued from Phase 3 trials due to rash. Rash occurred most commonly during the first 6 weeks of therapy.

The most frequently reported adverse drug reaction (ADR) of at least Grade 2 in severity in the Phase 3 studies was rash (9.0%). Stevens-Johnson syndrome, severe hypersensitivity reaction, and erythema multiforme were reported in < 0.1% of subjects during clinical development with INTELENCE. In general, rash was mild to moderate, occurred primarily in the second week of therapy and was infrequent after Week 4. Rash generally resolved within 1-2 weeks on continued therapy.

Tibotec is currently working with Health Canada to incorporate this new safety information in the Canadian Product Monograph for INTELENCE.

Managing marketed health product-related adverse reactions depends on healthcare 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 skin reactions or hypersensitivity reactions, or other serious or unexpected adverse reactions in patients receiving INTELENCE should be reported to Tibotec or Health Canada at the following addresses:

Tibotec, a division of Janssen-Ortho Inc.
Drug Safety Department
19 Green Belt Drive
Toronto, Ontario M3C 1L9
Tel: (800) 567-3331 or Fax: (866) 767-5865
dsscan@its.jnj.com

Any suspected adverse reaction can also be reported to:
Canada Vigilance Program
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/_guide/2008-ar-ei_guide-ldir/index-eng.php

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: 613-941-2566
Fax: 613-941-1183

Sincerely,

original signed by

Cathy Lau, PhD.

Vice President
Regulatory Affairs
JANSSEN-ORTHO Inc.

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