Health Canada Endorsed Important Safety Information on TARCEVA® (erlotinib)

December 15, 2008

Subject: The use of TARCEVA® (erlotinib) in patients with moderate hepatic impairment and advanced solid tumours

Dear Health Care Professional,

Hoffmann-La Roche Limited, in consultation with Health Canada would like to inform prescribers of important new safety information regarding the use of TARCEVA® (erlotinib) in patients with moderate hepatic impairment and advanced solid tumors.

TARCEVA is a Human Epidermal Growth Factor Receptor Type 1/Epidermal Growth Factor Receptor (HER1/EGFR) tyrosine kinase inhibitor. It is authorized as monotherapy for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of at least one prior chemotherapy regimen, and whose EGFR expression status is positive or unknown.

Based on review of a pharmacokinetic study in patients with advanced solid tumours comparing patients with moderate hepatic impairment and those with normal hepatic function:

- Ten of the fifteen patients with moderate hepatic impairment died during treatment or within 30 days of the last dose of TARCEVA. Five of the ten subjects died within one month of initiating TARCEVA daily continuous treatment.
- Reduced TARCEVA doses should be considered for subjects with moderate hepatic impairment. Hepatic function should be closely monitored in patients with pre-existing liver disease or concomitant hepatotoxic medications. TARCEVA dosing should be interrupted if significant changes in liver function tests are observed.
- Safety of TARCEVA in subjects with severe hepatic dysfunction has not been studied.

A pharmacokinetic study was conducted in patients with advanced solid tumors comparing patients with moderate hepatic impairment (Child-Pugh Score 7-9) and patients with normal hepatic function. Ten of the fifteen patients with hepatic impairment died during treatment or within 30 days of the last TARCEVA dose. Two patients died from rapidly progressing liver failure including 1 patient with hepatorenal syndrome. Laboratory findings of hepatic failure and/or renal failure were also observed in at least 4 patients out of the remaining 8 patients. Six out of the 10 patients who died had baseline total bilirubin > 3 x ULN suggesting severe, rather than moderate, hepatic impairment, highlighting the limitations of utilizing the Child-Pugh criteria in an oncology patient population. All patients had hepatic impairment due to advanced cancer with liver involvement such as hepatocellular carcinoma, cholangiocarcinoma, or liver metastases.

The TARCEVA Product Monograph is currently being reviewed by Health Canada in conjunction with the sponsor regarding the information mentioned above, and will be updated accordingly.

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 occurrence of serious and/or unexpected adverse reactions in patients receiving Tarceva 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: 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/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 Metabolism, Oncology and Reproductive Sciences (BMORS)
E-mail: bmors_enquiries@hc-sc.gc.ca
Tel: (613) 941-3171
Fax: (613) 941-1365

Should you have any questions or require additional information regarding the use of Tarceva, 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