Health Canada Endorsed Important Safety Information on AVASTIN® (bevacizumab)

29 April 2013

Dear Healthcare Professional:

Subject: Cases of Necrotizing Fasciitis Reported with the Use of AVASTIN® (bevacizumab)

Hoffmann-La Roche Limited (Roche), in consultation with Health Canada, would like to inform you of an important update to the safety information regarding the use of AVASTIN.

- Necrotizing fasciitis, including fatal cases, has been reported in patients receiving AVASTIN in both clinical trials and in the post-marketing setting.
- It is recommended that AVASTIN is discontinued and appropriate therapy initiated promptly upon diagnosis of necrotizing fasciitis.

Further information

Necrotizing fasciitis is a rare but life-threatening infection of the soft tissue, characterized by rapidly spreading necrosis of superficial fascia and subcutaneous tissue. Immunocompromised and diabetic patients are at a higher risk of developing necrotizing fasciitis.

Roche has conducted a comprehensive safety review that has identified 52 serious case reports of necrotizing fasciitis that occurred between November 1997 and September 2012, worldwide. Two of these reports occurred in Canada. A total of 17 of the global cases reported a fatal outcome, including 1 Canadian death.

The reported cases of necrotizing fasciitis occurred in patients treated with AVASTIN in several cancer indications. Approximately two thirds of the cases occurred in patients treated for colorectal cancer. Twenty-one (21) patients had gastrointestinal perforation, fistula formation or wound healing complications preceding the development of necrotizing fasciitis. All patients were receiving additional chemotherapies other than AVASTIN and some patients did not have any other risk factors.

Roche will be working with Health Canada to implement appropriate revisions to the AVASTIN Product Monograph.

AVASTIN Indication Information

AVASTIN is a recombinant humanised monoclonal antibody that selectively binds to

and neutralises the biologic activity of human vascular endothelial growth factor A (VEGF-A).

It is currently authorized for use in the treatment of metastatic colorectal cancer (mCRC) and locally advanced, metastatic or recurrent non-squamous non-small cell lung cancer (NSCLC). Roche also holds a Notice of Compliance with Conditions (NOC/c) for use as a single agent in the treatment of patients with glioblastoma after relapse or disease progression, following prior therapy.

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 necrotizing fasciitis or other serious or unexpected adverse reactions in patients receiving AVASTIN should be reported to Roche or Health Canada.

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

To correct your mailing address or fax number, contact Hoffmann-La Roche Limited.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax

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

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

Original signed by

Lorenzo Biondi, R.Ph.,C.Dir
Vice President, Medical and Regulatory Affairs
Hoffmann-La Roche Limited