

**Health Canada Endorsed Important Safety Information on  
AVASTIN<sup>®</sup> (bevacizumab)**



December 16, 2008

Dear Health Care Professional:

**Subject: Reports of Eye Inflammation, Endophthalmitis, and Toxic Anterior Segment Syndrome (TASS) Following Off-label Intravitreal Use of AVASTIN<sup>®</sup> (bevacizumab)**

Hoffmann-La Roche Limited (Roche), in consultation with Health Canada, would like to inform you of important new safety information regarding off-label intravitreal use of AVASTIN (bevacizumab).

AVASTIN is a recombinant humanized monoclonal antibody that is directed against the vascular endothelial growth factor (VEGF). It is authorized for intravenous administration in the first-line treatment of patients with metastatic carcinoma of the colon or rectum in combination with fluoropyrimidine based chemotherapy.

- Use of AVASTIN in the ophthalmology setting has neither been reviewed nor authorized by Health Canada.
- As of November 26, 2008, Roche has been made aware of 25 spontaneously reported Canadian cases of eye inflammation, endophthalmitis, blurred vision, and floaters, some of which have been described as Toxic Anterior Segment Syndrome (TASS), in patients who were administered aliquots of AVASTIN Lot B3002B028 intravitreally. This is currently the subject of further investigations. All analytical release data has been reviewed by Roche for this manufactured lot and all test parameters were well within limits established for the authorized use of AVASTIN.
- A review of adverse event reports received in 2008 does not indicate any unusual reporting pattern associated with this lot or any other particular lot of AVASTIN distributed in Canada when used for the authorized indication.

TASS is a sterile postoperative inflammatory reaction caused by a non-infectious substance that enters the anterior segment of the eye and results in toxic damage to intraocular tissues<sup>1</sup>.

Roche has neither studied nor sought authorization for the use of Avastin in the ophthalmology setting. The current production methods, formulation and dosages for AVASTIN were developed specifically for intravenous use in the oncology setting.

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 AVASTIN 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](mailto: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*.

**For other inquiries related to this communication, please contact Health Canada at:**

Marketed Health Products Directorate (MHPD)  
E-mail: [mhpd\\_dpsc@hc-sc.gc.ca](mailto: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 from 8:30 a.m. to 4:30 p.m. Monday to Friday Eastern Standard Time.

Sincerely,

*original signed by*



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

**References:**

1. Mamalis N, Edelhauser H, Dawson D, Chew J, LeBoyer R, Werner L. Toxic anterior segment syndrome. *Journal of Cataract & Refractive Surgery* 2006; 32(2):324-333.