

**Important Safety Information on
AVASTIN ▼[®] (bevacizumab)**



[REDACTED]

9th February 2009

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Subject:

Reports of severe eye inflammation and sterile endophthalmitis following off-label intravitreal use of AVASTIN[®] (bevacizumab) in Canada

Roche Products Limited 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).

Avastin in combination with fluoropyrimidine-based chemotherapy is indicated for treatment of patients with metastatic carcinoma of the colon or rectum. Avastin in combination with paclitaxel is indicated for first-line treatment of patients with metastatic breast cancer. Avastin, in addition to platinum-based chemotherapy, is indicated for first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer, other than predominantly squamous cell histology. Avastin in combination with interferon alfa-2a is indicated for first-line treatment of patients with advanced and/or metastatic renal cell cancer.

- As of November 26, 2008, Roche has been made aware of 2 clusters in Canada with a total of 25 spontaneously reported cases of adverse events in patients following off-label intravitreal administration of aliquots of AVASTIN Lot B3002B028. The symptoms included ocular irritation, photophobia, blurred vision and floaters associated with mild to moderate anterior and posterior cellular reaction with occasional findings of anterior chamber fibrin. No culture-positive cases of infectious endophthalmitis were confirmed.
- All analytical release data has been reviewed by Roche for this manufactured lot and all test parameters were well within limits established for the approved use of Avastin.
- Reports of adverse events associated with this particular lot following off-label intravitreal administration of Avastin were received from Canada only.
- There is no indication of any unusual adverse event reporting from oncology patients treated with this lot

- A small number of spontaneous reports of adverse events associated with the intravitreal administration of AVASTIN have been received from a number of countries, including those in the EU. These events have not been associated with specific batches of AVASTIN.
- A causal relationship between AVASTIN and the above-mentioned events has not been established, and reports are subject to ongoing analysis.
- The production methods, formulation and dosages for AVASTIN were specifically developed for intravenous use in the oncology setting.
- Roche has neither studied nor sought authorization for the use of AVASTIN in the ophthalmology setting.
- Use of AVASTIN in the ophthalmology setting has not been authorized by any Health Authority worldwide.

AVASTIN is packaged into single-use sterile preservative free vials; the practice of compounding single-use Avastin vials for intraocular use into multiple aliquots may be associated with the contamination of the product.

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:

Roche Products Limited, by phone on 01707 367554, by fax on 01707 367582 or e-mail at welwyn.uk_dsc@roche.com.

Any suspected adverse reaction should also be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) using a Yellow Card available directly from the MHRA, CHM Freepost, London SW8 5BR or electronically via the MHRA website at <http://www.yellowcard.gov.uk>

Should you have any questions or require additional information regarding the use of AVASTIN, please contact Roche Medical Information on 0800 3281629 or 01707 361 010 or e-mail at medinfo.uk@roche.com.

Yours sincerely,



Dr Michelle Rashford

Medical Director

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