Health Canada Santé Canada

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# NOTICE OF DECISION for AVASTIN™

On September 9, 2005, Health Canada issued a Notice of Compliance to Hoffmann-La Roche Limited for the drug product Avastin (bevacizumab), an antiangiogenic agent for use in combination with fluoropyrimidine-based chemotherapy as first-line treatment for metastatic colorectal cancer. This submission was granted Priority Review due to a promising innovative approach to cancer treatment and possible extension of patient survival time.

Bevacizumab, the medicinal ingredient in Avastin, is a recombinant humanised monoclonal antibody (IgG1) which binds selectively to, and neutralizes the biologic activity of, human vascular endothelial growth factor (VEGF). Neutralizing the biologic activity of VEGF reduces the vascularization of tumours, inhibiting tumour growth.

The market authorization for Avastin was based on satisfactory review of quality (chemistry and manufacturing), non-clinical, and clinical data. The safety and efficacy evaluation of Avastin included a phase III, randomized, double-blind, controlled trial against an active control. Avastin was administered in combination with irinotecan, 5-fluorouracil and leucovorin (IFL) as first line treatment for metastatic carcinoma of the colon or rectum. The addition of Avastin to IFL resulted in a statistically significant increase in overall survival of 4.7 months. The data submitted demonstrate that Avastin can be administered safely when used under the conditions stated in the Product Monograph.

Avastin is supplied as either a 4 mL or 16 mL sterile solution contained in a single-use glass vial to deliver 100 mg or 400 mg of bevacizumab per vial, respectively. Dosing guidelines are available in the Product Monograph.

Serious side-effects associated with Avastin include gastrointestinal perforation, haemorrhage, arterial thromboembolism and impaired wound healing. The most frequently observed adverse events across all clinical trials in patients receiving Avastin with or without chemotherapy were asthenia, diarrhea, hypertension, nausea and pain NOS (Not Otherwise Specified). Detailed conditions for the use of Avastin are available in the Product Monograph.

Based on the Health Canada review of data on quality, safety, and effectiveness, Health Canada considers that the benefit/risk profile of Avastin is favourable when administered in combination with fluoropyrimidine-based chemotherapy, under the conditions stated in the Product Monograph, for first-line treatment of patients with metastatic carcinoma of the colon or rectum.



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