Health Canada Santé Canada

Date issued December 13, 2005

NOTICE OF DECISION for ZEVALIN®

On May 10, 2005, Health Canada issued a Notice of Compliance to Berlex Canada Inc. for the drug product Zevalin, a therapeutic radiopharmaceutical. Zevalin contains the medicinal ingredient ibritumomab tiuxetan that is radiolabeled with Yttrium-90 (^{90}Y).

Zevalin is indicated for the treatment of patients with relapsed or refractory low-grade or follicular, CD20+, B-cell non-Hodgkin's lymphoma, including patients with rituximab-refractory follicular non-Hodgkin's lymphoma. Zevalin is composed of the murine monoclonal antibody ibritumomab that is linked to the chelator tiuxetan, which binds the ^{90}Y radioisotope. Ibritumomab is a murine IgG_1 monoclonal antibody directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes. When administered intravenously, Zevalin selectively targets tumor cells with the delivery of the radiation dose resulting in significant tumor shrinkage.

This submission was granted Priority Review due to the unmet medical need for an innovative therapy in the treatment of non-Hodgkin's lymphoma.

The market authorization for Zevalin was based on satisfactory review of quality (chemistry and manufacturing), non-clinical, and clinical data. The safety and efficacy of the Zevalin therapeutic regimen were evaluated in two multi-centre trials enrolling a total of 197 subjects. Patients treated with Zevalin exhibited adequate evidence of efficacy for the authorized indication. The data submitted demonstrate that Zevalin can be administered safely when used under the conditions stated in the Product Monograph.

Zevalin (3.2 mg/2 mL ibritumomab tiuxetan) is supplied as a kit that contains all of the non-radioactive components necessary to prepare a single dose of Zevalin for labelling with ^{90}Y for intravenous use. The therapeutic regimen of Zevalin is administered in a two step process. Step 1 includes a single infusion of rituximab. Step 2 is initiated seven to nine days following step 1 and consists of a second infusion of rituximab followed by ^{90}Y- Zevalin. Dosing guidelines are available in the Product Monograph.

Zevalin is contraindicated for patients with known hypersensitivity to ibritumomab tiuxetan, to Yttrium (^{90}Y) chloride, to other murine proteins or to any component of the Zevalin regimen. Detailed conditions for the use of Zevalin 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 Zevalin is favourable for the treatment of patients with relapsed or refractory low-grade or follicular, CD20+, B-cell non-Hodgkin's lymphoma, including patients with rituximab-refractory follicular non-Hodgkin's lymphoma.

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