Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2018
Document Type: USP Monographs
DocId: GUID-560A332F-4F03-46CB-A198-B0E8DE7DD778_3_en-US
DOI: https://doi.org/10.31003/USPNF_M89430_03_01
DOI Ref: 40yjd

Yttrium Y 90 Ibritumomab Tiuxetan Injection

» Ibritumomab Tiuxetan is the immunoconjugate resulting from a stable thiourea covalent bond between the monoclonal antibody ibritumomab and the linker-chelator tiuxetan [*N*-[2-bis(carboxymethyl)amino]-3-(*p*-isothiocyanatophenyl) propyl]-[*N*-[2-bis(carboxymethyl)amino]-2-(methyl)ethyl)glycine. This chelate provides a high-affinity, conformationally restricted chelation site for ^{90}Y and ^{111}In. The approximate molecular weight of Ibritumomab Tiuxetan is 148 kD.

Ibritumomab is a murine IgG_1 kappa monoclonal antibody directed against the CD20 antigen, which is found on the surface of normal and malignant B lymphocytes. Ibritumomab is produced in Chinese hamster ovary cells and is composed of two murine gamma 1 heavy chains of 445 amino acids each and two kappa light chains of 213 amino acids each.

Yttrium Y 90 Ibritumomab Tiuxetan Injection is a sterile, nonpyrogenic preparation of the immunoconjugate of ibritumomab and tiuxetan that is labeled with ^{90}Y and is suitable for intravenous administration. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ^{90}Y as the ibritumomab complex, expressed in megabecquerels (or millicuries) per mL at the time indicated in the labeling. It may contain buffers and stabilizers. It contains no antimicrobial agents. Other chemical forms of radioactivity do not exceed 5 percent of the total radioactivity. The immunoreactive fraction, as determined by a validated method, is not less than 90 percent.

Packaging and storage—Preserve in single-dose containers, and store in a refrigerator for not more than 8 hours. [Note—Translucent protein particles may develop, which are removed by filtration prior to administration using a 0.22-µm low-protein-binding filter.]

Labeling—Label it to include the following in addition to the information specified for *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*: the time and date of calibration; the amount of Yttrium Y 90 ibritumomab tiuxetan as total MBq (or mCi) and concentration of yttrium ^{90}Y ibritumomab tiuxetan, in MBq (or mCi) per mL, at the time of calibration; the expiration date and time; the storage temperature; and the statement, "Caution—Radioactive Material." The labeling indicates that, in making dosage calculations, correction is to be made for radioactive decay, and also indicates that the radioactive half-life of ^{90}Y is 64.1 hours.

Radionuclide identification (see *Radioactivity ⟨821⟩*)—

A: The beta radiation of the Injection shows a mass absorption coefficient within 5% of the value found for a known standard of the ^{90}Y when tested under the same counting conditions.

B: The beta-ray spectrum, obtained on an energy calibrated beta spectrometer, is identical to that of the spectrum of ^{90}Y of known purity, showing a maximum beta particle energy (E_{max}) at about 2280 keV. [Note—Because of the inherent difficulty in measuring beta radiation, a second comparative test should be performed.]

Bacterial Endotoxins Test ⟨85⟩—The limit of endotoxin content is not more than 175/*V* USP Endotoxin Units per mL of the Injection, when compared with the USP Endotoxin RS, in which *V* is the maximum recommended total dose, in mL, at the expiration date or time.

pH ⟨791⟩: between 5.5 and 7.5.

Radiochemical purity—

Adsorbent: 1- × 8-cm instant silica gel strip.

Test solution: the Injection.

Application volume: 10 µL.

Developing solvent system: 0.9% sodium chloride solution.

Procedure—Proceed as directed for *Thin-Layer Chromatography* under *Chromatography ⟨621⟩* by ascending chromatography. Determine the distribution of radioactivity on the chromatogram by scanning with a suitable collimated radiochromatogram strip scanner, and determine the percentage of radiochemical purity of the test specimen. Not less than 95% of the ^{90}Y activity is present as a band between the R_F values of 0.0 and 0.1.

Radionuclidic purity (Content of ^{90}Sr in an yttrium Y 90 chloride solution) (see *Radioactivity ⟨821⟩*)—Prepare a strontium/yttrium carrier solution containing 0.34 mg of yttrium chloride ($YCl_3 \cdot 6H_2O$) and 0.30 mg of strontium chloride ($SrCl_2 \cdot 6H_2O$) per mL of 0.1 N hydrochloric acid. Apply about 50 µL of this solution at the origin of a 2- × 19-cm cellulose phosphate chromatographic strip (see *Chromatography ⟨621⟩*), and allow to dry. Apply about 5 µL of the yttrium Y 90 chloride radiolabeling solution at the origin, and develop the chromatogram by ascending

chromatography over a period of about 1.25 hours, using 3 N hydrochloric acid as the developing solvent, until the solvent front migrates to the 15-cm mark. Allow to dry. Cut the strip at the 8-cm mark, and place the upper section (solvent front) in a suitable liquid scintillation solvent. Using a suitable counting assembly, determine the radioactivity, in KBq (or µCi) per mL of yttrium Y 90 chloride solution. The total radioactivity of ^{90}Sr is not greater than 740 KBq per 37 GBq (or 20 µCi per Ci) of ^{90}Y at the expiration date as stated on the labeling.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*, except that the radioactive component may be distributed or dispensed prior to completion of the test for *Sterility,* the latter test being started on the date of manufacture.

Assay for radioactivity (see *Radioactivity⟨821⟩*)—Using a suitable counting assembly, determine the total radioactivity, in MBq (or µCi), of the unshielded Injection, using a calibrated system.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
YTTRIUM Y 90 IBRITUMOMAB TIUXETAN INJECTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 29(3)

Current DocID: GUID-560A332F-4F03-46CB-A198-B0E8DE7DD778_3_en-US
Previous DocID: GUID-560A332F-4F03-46CB-A198-B0E8DE7DD778_1_en-US
DOI: https://doi.org/10.31003/USPNF_M89430_03_01
DOI ref: 40yjd