PRODUCT MONOGRAPH

OncoScint® CR/OV (Satumomab Pendetide) Kit

Kit for the preparation of Indium In 111 Satumomab Pendetide

Radiodiagnostic Agent, Tumor Imaging Agent

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THERAPEUTIC CLASSIFICATION

OncoScint® CR/OV (Satumomab Pendetide) is a radiodiagnostic agent, Tumor Imaging Agent when radiolabelled with Indium In 111 chloride.

DESCRIPTION

Drug Substance: Satumomab Pendetide

Composition:

OncoScint® CR/OV vial contains:
1 mg Satumomab Pendetide
2 mL sodium phosphate buffered saline solution
hydrochloric acid, pH6

Sodium Acetate buffer vial contains:
136 mg of sodium acetate trihydrate
Water for Injection
Glacial acetic acid pH6

Kit contains:

Each OncoScint® CR/OV kit contains all of the non-radioactive ingredients necessary to produce a single unit dose of OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide), an immunoscintigraphic agent for use only by intravenous injection. Each OncoScint® CR/OV kit contains two vials. A single-dose vial of OncoScint® CR/OV, formulated with Water for Injection, contains 1 mg of Satumomab Pendetide in 2 mL of sodium phosphate buffered saline solution

adjusted to pH 6 with hydrochloric acid. OncoScint® CR/OV is sterile, pyrogen-free, clear, colourless and may contain some translucent particles (insoluble immunoglobulin aggregates). A vial of sodium acetate buffer contains 136 mg of sodium acetate trihydrate in 2 mL of Water for Injection adjusted to pH 6 with glacial acetic acid. It is sterile, pyrogen-free, clear, and colourless. Neither solution contains a preservative.

In accordance with the directions provided, the sodium acetate solution must be added to the Indium In 111 chloride solution to buffer it prior to radiolabelling Satumomab Pendetide. After radiolabelling with Indium In 111, the immunoscintigraphic agent OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) is formed.

Each kit also includes one sterile 0.22 µm Millex® GV filter, prescribing information, and two identification labels.

Physical Characteristics

Indium In 111 decays by electron capture with a physical half-life of 67.2 hours (2.8 days). The energies of the photons that are useful for detection and imaging studies are listed in TABLE 1.

TABLE 1- INDIUM In 111 PRINCIPAL RADIATION EMISSION DATA[1]

Radiation	Mean % per Disintegration	Mean Energy (keV)
Gamma 2	90.2	171.3
Gamma 3	94	245.4

External Radiation

The exposure rate constant for 37 MBq (1 mCi) of Indium In 111 is 8.3 x 10^{-4} C/kg/hr (3.21 R/hr). The first half-value thickness of lead (Pb) for Indium In 111 is 0.023 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from the interposition of various thicknesses of Pb is shown in TABLE 2. For example, the use of 0.834 cm of lead will decrease the external radiation exposure by a factor of about 1,000.

TABLE 2- INDIUM In 111 PRINCIPAL RADIATION ATTENUATION OF LEAD SHIELDING

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.023	0.5
0.203	10^{-1}
0.513	10^{-2}
0.834	10^{-3}
1.120	10^{-4}

These estimates of attenuation do not take into consideration the presence of longer-lived contaminants with higher energy photons, namely Indium-114m/114.

To allow correction for physical decay of Indium In 111, the fractions that remain at selected intervals before and after the time of calibration are shown in TABLE 3.

TABLE 3 - INDIUM In 111 PHYSICAL DECAY CHART, HALF-LIFE 67.2 HOURS (2.8 DAYS)

Hours	Fraction Remaining
-48	1.64
-42	1.54
-36	1.44
-30	1.36
-24	1.28
-18	1.20
-12	1.13
-6	1.06
0*	1.00
6	0.94
12	0.88
18	0.83
24	0.78
30	0.74
36	0.69
42	0.65
48	0.61
54	0.58
60	0.54
66	0.51
72	0.48

* Calibration Time

ACTIONS AND CLINICAL PHARMACOLOGY

OncoScint® CR/OV (Satumomab Pendetide) is a conjugate produced from the murine monoclonal antibody, CYT-099 (MAb 72.3). MAb B72.3 is a murine monoclonal antibody of the IgG1, kappa subclass which is directed to a high molecular weight, tumor-associated glycoprotein (TAG-72). The differential expression of this glycoprotein has been demonstrated in a variety of adenocarcinomas. MAb B72.3 is produced by serum-free in vitro cultivation of cells and purification by sequential protein isolation and chromatographic separation procedures.

OncoScint® CR/OV is prepared by site-specific conjugation of the linker-chelator, glycyl-tyrosyl-(N-e-diethylenetriaminepentaacetic acid)-lysine hydrochloride (GYK-DTPA.HCl), to the oxidized oligosaccharide component of MAb B72.3 OncoScint® CR/OV retains the immunoreactivity of the unconjugated monoclonal antibody.

MAb B72.3 localizes or binds to a tumor associated antigen (TAG-72), a high molecular weight glycoprotein expressed differentially by adenocarcinomas. In *in vitro* immunohistologic studies, MAb B72.3 has been reported to be reactive with about 83% of colorectal adenocarcinomas, 97% of common epithelial ovarian carcinomas, and the majority of breast, non-small cell lung, pancreatic, gastric, and oesophageal cancers evaluated. MAb B72.3 is generally not immunoreactive with normal adult tissues, but it is reactive with salivary gland ducts, normal post-ovulatory endometria, some benign ovarian tumours, and fetal gastrointestinal tissues.

In clinical studies of patients with colorectal or ovarian carcinoma, OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) localised to primary and metastatic tumour sites. Non-antigen-dependent localisation, suspected to be secondary to catabolism, was observed in the liver, spleen, and bone marrow. Although there is variation among individuals, there may also be activity in the bowel, blood pool, kidneys, urinary bladder, male genitalia, and breast nipples in women.

Based on data obtained from 26 patient single-dose clinical studies, OncoScint® CR/OV labelled with Indium In 111 demonstrated either a monoexponential (n=17) or biexponential (n=9) elimination pattern with a terminal-phase half life of 56±14 hours. Pharmacokinetics were similar for men and women with colorectal (n=34) or women with ovarian (n=26) cancer. Approximately 10% of the administered radioisotope dose is excreted in the urine during the 72 hours following intravenous infusion. The pharmacokinetics of OncoScint® CR/OV-In are characterized by a slow plasma clearance rate (0.9 ±0.3 mL/hr/kg) and small volume of distribution (71 ± 32 mL/kg of ideal body weight).

CLINICAL TRIALS EXPERIENCE

The safety and imaging efficacy of OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) were evaluated in colorectal and ovarian carcinoma patients who received a single 1 mg intravenous dose. These clinical trials were performed in presurgical patients so that scan results could be scored positive or negative based upon tissue confirmation of disease at the site of the lesion shown on the scan.

Colorectal Carcinoma

One hundred fifty-five (155) colorectal cancer patients with surgically confirmed colorectal carcinoma were evaluated by both OncoScint® CR/OV-In imaging and computed tomography (CT). In patients with recurrent disease, OncoScint® CR/OV-In immunoscintigraphy detected a greater proportion of lesions in the pelvis (75% versus 55%; n=20) and the extrahepatic abdomen (67% versus 28%; n=18), while CT imaging detected a greater proportion of liver lesions (88% versus 38%; n=40). In patients with primary disease, the sensitivity of OncoScint® CR/OV-In immunoscintigraphy was higher than that of CT (77% versus 57%; n=82). In all patients with surgically confirmed disease, the aggregate sensitivity of the two diagnostic tests used in combination was 88%.

In patients found to be surgically free of disease who were imaged by both modalities, the specificities of OncoScint® CR/OV-In immunoscintigraphy and CT were identical (76.9%, n=13).

OncoScint® CR/OV-In detected malignant lesions that were not demonstrated by other diagnostic tests in 17 of 174 with histopathologically confirmed colorectal cancer. These occult tumour deposits were detected in patients with primary synchronous lesions (ie, colonic sites anatomically separate from the index primary lesion); primary disease patients at high risk of regional extension or metastatic spread; patients with rising serum CEA levels and otherwise negative diagnostic evaluations; patients with presumed isolated, resectable recurrences; and patients with equivocal findings on other diagnostic tests.

Seven radiolocalizations on the OncoScint® CR/OV-In scans were evaluated histopathologically and found to correspond to non-malignant tissues. Of these seven false positive findings, four corresponded to sites of inflammation, two were benign colonic polyps, and one was normal colonic tissue.

In this trial, 120 of 124 positive OncoScint® CR/OV-In scans were confirmed at surgery resulting in a positive predictive value of 97%. Thirteen of 67 negative OncoScint® CR/OV-In scans were confirmed at surgery for a negative predictive value of 19% in colorectal cancer patients. **Therefore, a negative antibody scan result is not informative about disease and negative scan results should not be used to guide clinical practice.**

Secondary evaluations of efficacy consisted of assessments by the clinical investigators of the impact of antibody imaging on these management of colorectal cancer patients. Based on these assessments OncoScint® CR/OV-In assisted in decision-making by detecting occult recurrence, by determining the extent and resectability of disease in patients with known lesions, and by clarifying equivocal results of other diagnostic evaluations.

Ovarian Carcinoma

The sensitivity of OncoScint® CR/OV-In imaging was significantly higher than that of CT scanning (57% versus 31%) in 83 patients with surgically confirmed ovarian cancer recurrences who were evaluated by both imaging modalities. In 51 patients with diffuse miliary disease or carcinomatosis OncoScint® CR/OV-In imaging was also more sensitive than CT scanning for the detection of carcinomatosis (65% versus 43%).

OncoScint® CR/OV-In immunoscintigraphy detected histopathologically confirmed malignant lesions that were not demonstrated by other diagnostic tests in 27% of patients with recurrent ovarian cancer. Detection of these occult ovarian tumour deposits, including diffuse miliary disease or carcinomatosis, was reported to be clinically useful for directing restaging surgical procedures.

There were 15 false positive OncoScint® CR/OV-In images among 38 patients who were found

surgically free of recurrent ovarian carcinoma. There were five false positive results among ten patients evaluated for primary ovarian carcinoma who were found to have benign ovarian tumours. **Because some benign ovarian tumours express the TAG-72 antigen, OncoScint® CR/OV-In imaging cannot distinguish benign from malignant primary ovarian tumours and is therefore not recommended for the evaluation of patients with suspected primary ovarian cancer.**

In patients evaluated for recurrent ovarian cancer, 47 of 62 positive OncoScint® CR/OV-In scans were confirmed at surgery resulting in a positive predictive value of 76%. Twenty-three (23) of 60 negative OncoScint® CR/OV-In scans were confirmed at surgery for a negative predictive value of 38%. **Therefore, a negative antibody scan is not informative about disease and should not be used to guide clinical practice.**

Secondary evaluations of efficacy consisted of assessments by the clinical investigators of the impact of antibody imaging on the management of recurrent ovarian cancer patients. Based on these assessments OncoScint® CR/OV-In assisted in decision-making by detecting occult recurrence, by determining the extent and resectability of disease in patients with known lesions, and by clarifying equivocal results of other diagnostic evaluations.

INDICATIONS AND CLINICAL USES

OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) is a diagnostic imaging agent indicated for aiding in the determination of the location and extent of extrahepatic malignant disease in patients with known colorectal or ovarian cancer. Single use only.

This diagnostic agent should be used only after completion of standard diagnostic tests when additional information regarding disease extent could aid in patient management. The diagnostic images acquired with the OncoScint® CR/OV-In should be interpreted in conjunction with a review

of the information obtained from other appropriate diagnostic tests. It has to be noted that a negative antibody scan result is not informative about disease and should not be used to guide clinical practice.

False positive localization of radiolabeled antibodies is a recognized phenomenon. Malignant lesions may demonstrate nonspecific antibody localization, though this nonspecific localization occurs at a lower rate than specific localization to tumor antigen. Benign ovarian tumors may express the TAG-72 antigen targeted by OncoScint®. Such lesions can be inadvertently classified as malignancy. It has also been reported that Indium In 111 labeled antibodies may localize non-specifically in colostomy sites, degenerative joint disease, abdominal aneurysms, postoperative bowel adhesions, and local inflammatory lesions, including those typically associated with inflammatory bowel disease or secondary to surgery or radiation. Potential localization of OncoScint® CR/OV-In in the normal liver, spleen, bone marrow, bowel, blood pool, kidneys, urinary bladder, male genitalia, and breast nipples in woman has also been observed. Careful review of the patient's medical history and other diagnostic information should aid in the interpretation of the images.

CONTRAINDICATIONS

OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) should not be used in patients who are hypersensitive to this or any other product of murine origin or to Indium In 111 chloride.

Caution should be exercised in patients with pre-existing HAMA titres. (Refer to PRECAUTION section).

The safety and effectiveness of OncoScint® CR/OV-In in children have not been establish.

WARNINGS

Allergic reactions, including anaphylaxis, can occur in patients who receive murine antibodies. Although serious reactions of this type have not been observed in clinical trials after OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) administration, medications for the treatment of hypersensitivity reactions should be available during administration of this agent.

Each OncoScint® CR/OV kit is a unit of use package. The contents of the kit are to be used only to prepare OncoScint® CR/OV-In; unlabelled OncoScint® CR/OV should NOT be administered directly to the patient. After radiolabelling with Indium In 111, the entire OncoScint® CR/OV-In dose must be administered to the patient for whom it was prescribed. **Reducing the dose of either component may adversely impact imaging results, and, therefore, is not recommended**.

False positive localization of radiolabeled antibodies is a recognized phenomenon.(see Action and Clinical Pharmacology)

It has been reported that Indium In 111 labeled antibodies may localize non-specifically in colostomy sites, degenerative joint disease, abdominal aneurysms, postoperative bowel adhesions, and local inflammatory lesions, including those typically associated with inflammatory bowel disease or secondary to surgery or radiation. Potential localization of OncoScint® CR/OV-In in the normal liver, spleen, bone marrow, bowel, blood pool, kidneys, urinary bladder, male genitalia, and breast nipples in woman has also been observed.

PRECAUTIONS

General

The components of the kit are sterile and pyrogen free and contain no preservative. OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) should be used within 8 hours after radiolabelling. It is essential to follow the directions for preparation carefully and to adhere to strict aseptic procedures during preparation of the radiolabelled product.

The contents of the kit are not radioactive. However, after the Indium In 111 chloride is added, appropriate shielding of OncoScint® CR/OV-In must be maintained. Care should be taken to

minimize radiation exposure to patients and medical personnel, consistent with proper hospital and patient management procedures.

Radiopharmaceuticals should be used only by those medical practitioners who are appropriately qualified in the use of radioactive prescribed substances in or on humans.

Patients should be informed that the use of this product could affect the future use of other murine-based products, including OncoScint® CR/OV-In, and should be advised to discuss prior use of murine-antibody based products with their physicians.

Hypersensitivity

Patients who have been previously exposed to mouse proteins may develop hypersensitivity reactions following injection of this murine monoclonal product, due to the induction of a human anti-mouse antibody (HAMA) response. Rarely, patients may show the presence of an immunoglobulin (or immunoglobulin-like substance) that binds to the injected monoclonal antibody, even when there is no history of exposure to mouse antibody or mouse proteins.

Anaphylactic and other hypersensitivity reactions are possible whenever mouse protein materials are administered to patients. Full cardiopulmonary resuscitation facilities and trained personnel should be immediately available. Adrenaline (epinephrine), antihistamines and corticosteroids should be available for immediate use in the event of an adverse reaction.

Human anti-mouse antibody (HAMA)

Murine monoclonal antibodies are heterologous proteins, and their administration can induce human anti-murine antibodies (HAMA).

While limited data exist concerning the clinical significance of HAMA, detectable serum levels can alter the clearance and tissue biodistribution of MAbs. The development of persistently elevated serum HAMA levels could compromise the efficacy of diagnostic or therapeutic murine antibody-

based agents.

When considering the administration of OncoScint® CR/OV-In to patients who have previously received antibody-based products, physicians should be aware of the potential for assay interference and increased clearance and altered biodistribution, which may interfere with the quality or sensitivity of the imaging study. Therefore, prior to administration of murine antibodies, including OncoScint® CR/OV-In, the physician should review the patients history to determine whether the patient has previously received such products.

OncoScint® CR/OV-In has been shown to induce HAMA to murine IgG after single administration in about 40% of patients in tumour imaging trials. HAMA levels became negative (undetectable or <400 ng/mL) in approximately half of such patients at 4 to 12 months after infusion.

With respect to HAMA levels in patients who may have previously received a murine antibody-based product and given the potential for effects on efficacy of OncoScint® CR/OV-In, if HAMA values are <50 ng/ml, most subjects may image normally. Altered biodistribution may occur in 3 - 4 % of cases for unknown reasons unrelated to HAMA level. If HAMA values are between 50 - 400 ng/mL, there may be a higher incidence of altered biodistribution and, hence, compromised efficacy. Because of the possibility of infusional reactions and uniformly altered biodistribution and poor quilaity imaging, OncoScint® CR/OV-In should not be given if the HAMA level is > 400 ng/mL.

Interactions with other medicines and other forms of interactions

Administration of OncoScint® CR/OV-In may result in falsely elevated values from *in vitro* immunoassays, including tests for carcinoembryonic antigen (CEA) and CA 125. Because this interference may persist for months, the clinical laboratory should investigate for assay interference in patients who develop elevated CEA or CA 125 subsequent to imaging with OncoScint® CR/OV-In, and appropriate measures be taken to avoid this interference. Methods include the use of non-murine immunoassays, or HAMA removal by adsorption, blocking, or heat inactivation.

Carcinogenicity, Mutagenicity, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic or mutagenic potential of OncoScint® CR/OV-In or to evaluate its effect on fertility in males or females.

Reproduction and Teratology

Animal reproduction studies have not been conducted with OncoScint® CR/OV-In. It is also not known whether OncoScint® CR/OV-In can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. OncoScint® CR/OV-In should not be administered to a pregnant woman unless, in the opinion of the physician, the information to be gained outweighs the potential risks. MAb B72.3 is the monoclonal in OncoScint® CR/OV and has been shown to react with fetal gastrointestinal tissues.

In general, examinations using radiopharmaceuticals in women of childbearing potential should be performed during the first few days (approximately 10) following the onset of menses. Women of childbearing potential should practice birth control.

Nursing Mothers and/or Lactating Women

It is not known whether OncoScint® CR/OV-In is excreted in human milk and, if so, for how long. Because many drugs are excreted in human milk, caution should be exercised when OncoScint® CR/OV-In is administered to a nursing woman. OncoScint® CR/OV-In has not been administered to lactating females and therefore should not be administered to nursing mothers unless, in the opinion of the physician, the information to be gained outweighs the potential risk. In such cases, formula feedings should be substituted for breast feedings.

Pediatric Use

The safety and effectiveness of OncoScint® CR/OV-In in children have not been established.

ADVERSE REACTIONS

After administration of 1188 doses of OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) to 1041 patients, adverse reactions were observed in approximately 4% of patients.

OncoScint® CR/OV (Satumomab Pendetide) is generally well tolerated. No deaths attributable to OncoScint® CR/OV-In administration were reported. The most common adverse reaction was fever, which occurred in less than 1% of patients. Other adverse reactions, each of which occurred in less than 1% of patients, are listed in order of decreasing frequency: hypotension, hypertension, nausea, chills, rash, injection site reactions, pruritus, allergic reactions, sweating, abdominal pain, asthenia, chest pain, headache, hypothermia, pain, bradycardia, vasodilatation, flushing, diarrhea, arthralgia, confusion, dizziness, nervousness, crying, and angioedema. Although causality was not determined, an isolated occurrence of reversible thrombocytopenia was observed in a patient who received OncoScint® CR/OV-In in clinical trials.

OVERDOSAGE

The maximum amount of OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) that can be safely administered has not been determined. In clinical trials, single doses of 20 mg of OncoScint® CR/OV labelled with 5 mCi-Indium In 111 were administered to 64 patients with various types of epithelial carcinomas; the type and frequency of adverse reactions at this dose were similar to those observed with lower doses.

DOSAGE AND ADMINISTRATION

The dose of OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) is 1 mg radiolabelled with 5 mCi of Indium In 111 chloride. Each dose is administered intravenously over 5 minutes and should not be mixed with any other medication during its administration. The patient dose of the radiolabel should be measured in a dose calibrator prior to administration.

Each OncoScint® CR/OV kit is a single unit dose package. After radiolabelling with Indium In 111, the entire OncoScint® CR/OV-In dose should be administered to the patient. **Reducing the dose of either component may adversely impact imaging results, and is, therefore, not recommended**.

The safety and effectiveness of OncoScint® CR/OV-In in children have not been established.

Image Acquisition and Interpretation

For optimal results, images should be acquired using a large field of view gamma camera equipped with a parallel hole medium energy collimator. The camera should be calibrated using the 171 and 245 keV photopeaks and a 20% symmetric window.

In order to obtain adequate counting statistics, planar images should be acquired in anterior and posterior views for 10 minutes per view. Because of the uptake of OncoScint® CR/OV-In by the liver, images obtained with the liver in the field of view must be acquired with adequate counts to allow the detection of lesions in the extrahepatic abdomen. Clinical trial results indicate that optimal diagnostic images are routinely obtained between 48 and 72 hours after injection. However, variability occurs and interpretable images have been obtained as early as 24 hours and as late as 120 hours post-infusion.

Following OncoScint® CR/OV-In administration, some of the radiolabel localizes to normal liver, spleen, and bone marrow. Although there is variation among individuals, there may also be activity observed in the bowel, blood pool, kidneys, urinary bladder, male genitalia, and breast nipples in women.

Imaging studies may also show activity in the large bowel because of the presence of radiolabel in stool. Therefore, the administration of a cathartic prior to obtaining initial or follow-up images may be useful.

Follow-up imaging sessions can be performed on subsequent days. These may be useful to resolve ambiguities resulting from activity in blood pool, stool or urinary bladder, which may be increased in some patients at earlier imaging sessions, or to clarify equivocal findings seen on initial images. Single photon emission computed tomographic (SPECT) images also may be useful to clarify equivocal findings seen with planar imaging.

It has been reported that Indium In 111 labelled antibodies may localize non-specifically in colostomy sites, degenerative joint disease, abdominal aneurysms, post-operative bowel adhesions, and local inflammatory lesions, including those typically associated with inflammatory bowel disease or secondary to surgery or radiation.[5] Careful review of the patient's medical history and other diagnostic information should aid in the interpretation of the images.

In order to establish optimal patient management plans and in accordance with standard medical practice, the diagnostic images acquired with OncoScint® CR/OV-In should be interpreted in conjunction with a review of the information obtained from other appropriate diagnostic tests.

INSTRUCTIONS FOR PREPARATION AND USE

Directions for Radiolabelling OncoScint® CR/OV with Indium In 111 Chloride

Proper aseptic techniques and precautions for handling radioactive materials should be employed. Waterproof gloves should be worn during the radiolabelling procedure. The preparation of the product should be done by the following procedure.

1. Sterile, pyrogen-free Indium In 111 chloride solution must be utilized in the preparation of OncoScint® CR/OV-In. The use of high purity Indium In 111 chloride manufactured by an approved (licensed) supplier is required. Indium In 111 chloride should be used only to radiolabel OncoScint® CR/OV and should not be injected directly into the patient. Indium In 111 chloride should not be utilized after its expiration date.

2. Before radiolabelling bring the refrigerated OncoScint® CR/OV to room temperature. Note: OncoScint® CR/OV is a protein solution which may develop particulates. These particulates will be removed by filtration.

3. Clean the rubber closure of each vial such as with an alcohol wipe. With a sterile disposable syringe add 0.5 mL of sodium acetate buffer solution to the Indium In 111 chloride and mix.

4. Withdraw not less than 5.0 mCi nor more than 6.0 mCi of the buffered Indium In 111 chloride and add to the OncoScint® CR/OV vial. Swirl gently to mix. Assay contents in a

dose calibrator, 5 or 6 mCi of Indium In 111 (radioactivity) must be present in the 2 mL. On one of the labels provided, record the patient's identification, the date, time of preparation and activity in the vial. Affix the label to the vial shield.

5. Allow to react at room temperature for 30 minutes.

6. Attach the 0.22 µm Millex® GV sterile filter (provided) and a sterile hypodermic needle to a 10 mL sterile disposable syringe and withdraw the radiolabelled OncoScint® CR/OV-In through the filter into the syringe. Keep the needle immersed in the solution to avoid air-locking the filter.

7. Remove the filter and needle. Attach a fresh sterile hypodermic needle to the syringe.

8. Assay syringe and contents in a dose calibrator. The final product should contain not less than 4.0 mCi. Doses less than 4 mCi should not be administered. (See "Directions for OncoScint® CR/OV-In Quality Control" section). NOTE that this test has to be performed before administration to the patient.

9. On the second label provided in the kit, record the patient's identification, the date, time of assay, and activity in the syringe. Affix this label to the syringe shield.

10. After preparation, the OncoScint® CR/OV-In dose should be placed in a **syringe shield** (to shield from radiation) and stored at room temperature until administration. OncoScint® CR/OV-In should be used within 8 hours of radiolabelling.

11. Discard vials, needles, and syringes in accordance with municipal, provincial, and federal regulations governing radioactive and biohazardous waste.

Directions for OncoScint® CR/OV Quality Control:

1. Add 1 mL sterile water to a "cold" DTPA kit. Mix equal drops of the OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) (previously reserved in the test tube) with the DTPA solution.

2. Prepare a 1 x 8 cm Silica gel ITLC strip. Mark the origin 1 cm from the bottom of the ITLC strip using a water soluble marker.

3. Using a Tuberculin syringe, place a small dot of the OncoScint® CR/OV-In DTPA solution at the origin.

4. Fill the developing chamber with normal saline to a depth of 0.5 cm. Place the ITLC strip in the developing chamber. Allow the solution to migrate 6 cm from the origin (approximate time 2-4 minutes). **NOTE: AVOID ALLOWING THE ITLC STRIP TO ADHERE TO THE SIDE OF THE CHAMBER OR TO BECOME IMMERSED IN THE DEVELOPING SOLUTION.**

5. Cut the ITLC strip in half, placing each portion in a separate test tube. Count the room background and each half of the ITLC strip in an accurate counter. Calculate radiopharmaceutical purity as:

$$\%RCP = \frac{\text{Bottom Half Counts - Background}}{\text{Bottom Half Counts + Top Half Counts - 2 x Background}} \times 100\%$$

6. If percent is <90%, then this should be repeated. RCP should be ≥95% for the preparation to be infused.

RADIATION DOSIMETRY

The estimated absorbed radiation doses to an average adult patient from an intravenous injection of OncoScint® CR/OV labelled with 5 mCi of Indium In 111 are shown on Table 1. Total dose estimates include absorbed radiation doses from both Indium In 111 and the Indium-114m

radiocontaminant. The maximum permissible level (0.16% at the expiration date) of the Indium-114m was utilised for the dose estimates presented in TABLE 4

TABLE 4- ESTIMATED AVERAGE ABSORBED RADIATION DOSE IN ADULT PATIENTS FROM INTRAVENOUS ADMINISTRATION OF OncoScint® CR/OV LABELLED WITH 5 mCi OF INDIUM In 111 chloride

Tissue/Organs	Average Dose (Rad/5 mCi)	mGy/185 MBq
Total Body	2.7	27
Liver	15	150
Spleen	16	160
Kidney	9.7	97
Lungs	4.9	49
Red Marrow	12	120
Adrenal	4.5	45
Bladder	2.8	28
Heart Wall	3.2	32
Bone	3.3	33
Stomach Wall	3.2	32
Small Intestine	3.0	30
Upper Large Intestine Wall	3.1	31
Lower Large Intestine Wall	2.5	25
Other Tissues	2.3	23
Ovaries[a]	2.9	29
Pancreas	3.7	37
Skin	1.6	16
Thyroid	1.5	15
Uterus[a]	2.7	27
Testes[a]	1.4	14

[a] Results weighted by actual number of males and females studied.

Table of Dose Estimates
CYT 103 Effective Dose/Effective Dose Equivalent (ED/EDE) Values

		rad/mCi				mSv/MBq		
ED		In-111	In-114m	In-total		In-111	In-114m	In-total
	Male	0.970	0.028	0.998	Male	0.26	0.01	0.27
	Female	1.120	0.031	1.151	Female	0.30	0.01	0.31
EDE								
	Male	1.090	0.037	1.127	Male	0.29	0.01	0.30
	Female	1.310	0.045	1.355	Female	0.35	0.01	0.37

The data included blood, urine and whole body and organ counts over many days, some out to over 7 days. The data were fit by a compartmental model using the SAAM analysis system in which all compartments share the same best fit exponential terms. For the urinary bladder compartment, a 4.8 hour voiding interval was employed. The area under the curve out to the last measurement time for all patients was used in the determination of residence times. The slowest clearance component was extrapolated out to infinity and the dose was computed using the MIRDOSE package distributed by Oak Ridge (RIDIC), using the S-factors for In-111 and In-114m as a contaminant.

HOW SUPPLIED

The OncoScint® CR/OV kit for the preparation of OncoScint® CR/OV-In (Indium In 111 Satumomab Pendetide) includes one vial containing 1 mg of Satumomab Pendetide per 2 mL of sodium phosphate buffered saline and one 2 mL vial of sodium acetate solution, 0.5 M. These solutions are sterile and pyrogen free and contain no preservative. Each kit also includes one sterile 0.22 µm Millex® GV filter, prescribing information, and two identification labels.

STORAGE

Store at 2^0C to 8^0C. Do not freeze. Store upright.

After preparation the OncoScint® CR/OV-In should be stored at room temperature until administration, within 8 hours of radiolabelling.

EXPIRY

Do not use the kit beyond the expiration date stamped on the box.

After preparation the OncoScint® CR/OV-In should be stored at room temperature until administration, within 8 hours of radiolabelling.

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