

**REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF DEVICE**

(amended in its entirety)

CORRECTED PAGE – Change of Ownership, May 23, 2006

NO. GA-1148-D-101-S **DATE:** October 7, 2003 **PAGE:** 1 of 13

DEVICE TYPE: Low Dose Rate Brachytherapy

MODEL: GliaSite® RTS System, with catheter Models 1020, 1030, and 1040
 GliaSite® Spectrum System, with catheter Models 1520, 1530, and 1540

MANUFACTURER/DISTRIBUTOR: **Cytec Surgical Products II**
(previously Proxima Therapeutics) 2555 Marconi Drive
 Suite 220
 Alpharetta, Georgia 30005-2066

RADIONUCLIDE FORM AND DESCRIPTION:

Iotrex, a proprietary liquid solution, consisting of a combination of iodide and sodium 3-[I-125] iodo-4-hydroxybenzenesulfonate (I-HBS)

<u>ISOTOPE:</u>	<u>MAXIMUM ACTIVITY:</u>	<u>NOMINAL ACTIVITY:</u>
Iodine-125	1320 millicuries (48.84GBq),	[1200 mCi (44.4 GBq) ± 10%]

LEAK TEST FREQUENCY: Not Required – device is single use and is never implanted for greater than 6 months

PRINCIPAL USE: (V) General Medical Use

CUSTOM DEVICE: ___ YES X NO

NMSS12

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DEVICE TYPE: Low Dose Rate Brachytherapy

DESCRIPTION:

The GliaSite RTS System and GliaSite Spectrum System are single-use low-dose rate brachytherapy systems consisting of a double-wall balloon catheter filled with Iotrex, a solution containing organically bound I-125. The systems are intended to deliver intracavity radiation therapy in patients with malignant brain tumors following tumor resection surgery. Radiation therapy is delivered by inflating the balloon portion of the device with a combination of Iotrex solution and saline. After a patient-specific dwell time, the Iotrex solution is removed from the catheter, and the catheter is then removed from the patient. The GliaSite Spectrum is identical to the GliaSite RTS, except that it also has the capability to deliver chemotherapy agents (or other prescribed fluids) directly into the brain tumor resection cavity. This is accomplished via the Adjuvant Therapy (AT) infusion line.

The GliaSite catheter is constructed from common biocompatible materials and is configured similar to other currently marketed interstitial and intracavity brachytherapy applicators. The AT infusion line on the GliaSite Spectrum is constructed of the same materials as the GliaSite catheter.

The GliaSite catheter consists of a shaft with an inflatable dual silicon balloon configuration (balloon within a balloon) at the distal (treatment) end and an infusion port at the proximal end. The Spectrum catheter shaft is shorter than the RTS catheter to allow for the inclusion of the connection bifurcation for the AT infusion line. The three models of the GliaSite RTS catheter refer to different sized balloons, and thus, different fill volumes. The balloon diameters and maximum inflation volumes are contained in the table below. Note that the 3 models of the GliaSite Spectrum catheter are identical in size and volume as the RTS catheters.

Catheter Model	Balloon Diameter	Maximum Fill Volume
1020	2 cm	5 mL
1030	3 cm	15 mL
1040	4 cm	35 mL
1520	2 cm	5 mL
1530	3 cm	15 mL
1540	4 cm	35 mL

The inner balloon acts as a reservoir for the Iotrex solution. The outer balloon serves as the backup reservoir in the event the inner balloon ruptures. The RTS catheter shaft is constructed from radiopaque silicone, bi-lumen tubing and contains a malleable titanium element to assist in positioning of the balloon. The Spectrum catheter shaft is tri-lumen in order to accommodate the AT infusion line. This third lumen, separate from the other two lumens, is open-ended and positioned off-center of the catheter centerline, allowing the fluid to flow directly into the resection cavity. Both ends of the inner balloon have radiopaque markers along the catheter shaft. Additionally, the catheter shaft is equipped with positioning markers at 1 cm intervals beginning from the proximal end of the balloon.

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DESCRIPTION: (continued)

The primary catheter lumen, which is used to access the inner balloon, is connected to the infusion port. To prevent leakage during insertion of the lotrex solution, the infusion port is equipped with a self-sealing silicone septum. To help differentiate the lotrex infusion port from the AT infusion line, an additional radiopaque marker band is added on the lotrex line, and the words, "IOTREX ONLY" are included on the line.

Refer to Figure 1a for a picture of an inflated, 3cm diameter GliaSite RTS catheter, and Figure 1b for an inflated, 2cm GliaSite Spectrum catheter. Note that Figure 1b shows one possible arrangement of the AT infusion line delivery system.

Refer to Figures 2-4 for a simplified step-by-step walk through of a typical GliaSite treatment, showing how the GliaSite is implanted and lotrex is inserted.

LABELING:

The GliaSite catheters do not require standard radioactive materials labeling since (1) the catheters, when shipped, do not contain radioactive material; (2) the only time the catheter contains radioactive material is when it is implanted in the patient; (3) radioactive material is removed from the catheter prior to removal from the patient; and (4) the catheter is disposed of as radioactive waste or decayed in storage.

The catheter itself is marked with "PROXIMA" and the model number of the catheter. The Spectrum catheters will also be marked "IOTREX ONLY" to clarify the lotrex line from the AT infusion line.

The tray in which the catheter is provided, as well as the box in which the catheter and its ancillary equipment is shipped, is labeled in accordance with FDA guidelines. A sample label for the GliaSite box is provided in Figure 5. A sample of the labels on the lotrex solution vial and shipping container is provided in Figures 6 and 7.

DIAGRAMS:

- | | | |
|-----------|----|------------------------------------------------------------|
| Figure 1a | -- | inflated GliaSite RTS catheter |
| Figure 1b | -- | inflated GliaSite Spectrum catheter |
| Figure 2 | -- | shows tumor resection cavity |
| Figure 3 | -- | shows placement of GliaSite catheter into resection cavity |
| Figure 4 | -- | shows infusion of lotrex solution |
| Figure 5 | -- | sample GliaSite box label |
| Figure 6 | -- | sample lotrex vial label |
| Figure 7 | -- | sample lotrex shipping container label |

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CONDITIONS OF NORMAL USE:

The GliaSite catheters are sterilized and stored in sealed containers prior to use. The catheter is inserted into the patient during surgery and the balloon is inflated. The entire catheter will be enclosed within the patient during the treatment time. The infusion port is located beneath the skin.

The Iotrex solution is received at the facility within 48 hours of its intended use in unit dose vials of not less than 150 millicuries. The Iotrex is withdrawn from the vials into a syringe and injected into the GliaSite catheter via the infusion port in the patient's private room or other secured location. Removal of the Iotrex is accomplished by reversing the insertion procedure.

Both the GliaSite catheter and the Iotrex solution are single use and are disposed of as radioactive waste upon removal from the patient.

Refer to the "Limitations and/or Other Considerations of Use" section for additional information regarding the use of the GliaSite Spectrum System.

PROTOTYPE TESTING:

The GliaSite catheter has been subjected to a battery of tests to confirm its integrity in typical use and expected accident conditions. These tests included bend and tensile testing of the catheter shaft, design pressure verification of the balloons, material interaction of the balloon (with x-ray contrast solution, saline, and Iotrex), and the ability to successfully image the catheter.

Since the GliaSite catheter must withstand gamma sterilization in the mega-Rad range prior to use, additional testing of the effects of the radiation emitted from the Iotrex is not required.

Standard leak test methods for sealed sources cannot be used on GliaSite. Instead, the GliaSite is evaluated based on the amount of pressure the balloon can withstand, and the amount of liquid that will permeate across the balloons over an extended period of time. It has been confirmed during animal and clinical trials that, because of silicon's permeability to small molecules, approximately 1% of the afterloaded activity will diffuse across the membrane into the body. This has been evaluated and determined to have no adverse effects on the patient. Uptake in the thyroid gland can be minimized by administering a thyroid-blocking agent to the patient prior to implantation.

The makeup of the Iotrex compound is such that it precludes uptake into the body or its organs. To simulate a catheter failure (both balloons rupture and release the Iotrex), Iotrex was injected directly into the brain and tracked through the body. At 2 hours following injection, 93% had been excreted from the body; at 4 hours, 97.2% of the initial activity had been excreted. This shows that Iotrex is removed from the body quicker than standard radio-iodide, which has a biologic half-life of 8 hours.

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PROTOTYPE TESTING: (continued)

To date, clinical trials using the GliaSite RTS have utilized a maximum activity of 450 mCi of Iotrex. Data has shown that the GliaSite catheter can safely handle up to 1200 mCi of Iotrex.

The GliaSite RTS catheter has a shelf life of 5 years from the date of manufacture. It has undergone accelerated aging tests to validate that this shelf life will not adversely affect product performance or safety. **Extended use design validation testing has not been performed on the GliaSite Spectrum catheter. Thus, the GliaSite Spectrum catheter has a shelf life of 6 months.**

The Iotrex solution has a shelf life of 27 days based on the specification that no more than 20% of the I-125 can be in a non-bound (iodide) form at the time of afterloading. The amount of non-bound I-125 increases over time as the I-HBS compound breaks down.

The GliaSite Spectrum catheter is nearly identical to the GliaSite RTS catheter in terms of dimensions, materials of construction, and conditions of use. Thus, the original prototype testing results are still valid.

Since the GliaSite Spectrum System is constructed of the same materials as existing devices that deliver chemotherapy agents, it was only subjected to tests that correspond to the use of newer chemicals (i.e., it was not subjected to the entire original test sequence as its predecessor). These tests were conducted during the pre-clinical and design validation phases.

EXTERNAL RADIATION LEVELS:

The manufacturer provided calculated exposure rates from the head of a patient who received a GliaSite treatment with 1200 mCi of Iotrex. Additionally, the manufacturer provided actual data collected during trials for patients who received GliaSite treatments with up to 460 mCi of Iotrex. There is no direct correlation between administered activity and exposure rates around the patient because (1) the location of the GliaSite catheter with respect to the surface of the head varies from patient to patient; and (2) the physical makeup of the patient (i.e., skull thickness and skin thickness) varies, resulting in different levels of radiation attenuation.

The exposure rates around a patient are recorded in the table below.

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EXTERNAL RADIATION LEVELS: (continued)

Distance from Patient's Head	Exposure Rate, mR/hr [μ Sv/hr]		
	calculated (1200 mCi)	clinical range (up to 460 mCi)	typical expected (up to 460 mCi)
5 cm **	4310 [43,100]	20 – 650 [200 – 6500]	200 [2000]
30 cm	206 [2060]	not reported	not reported
100 cm	20 [200]	0.2 – 3.4 [2 – 34]	2 [20]
at room doorway	not calculated	0.02 – 0.6 [0.2 – 60]	< 0.1 [< 1]

** exposure rates were recorded at surface of head in clinical trials

QUALITY ASSURANCE AND CONTROL:

The manufacturer has implemented a Quality System that meets the qualifications of ISO 9001:1994, EN46001, and 21 CFR Part 820 (Quality Systems Regulations), which encompasses FDA's Current Good Manufacturing Practices.

Items that are provided by suppliers or subcontractors must conform to the design controls and specification requirements of the manufacturer's Quality System. The design controls provide evidence of device performance, verification and validation through all phases of use, and indicate the QC checkpoints during component construction.

LIMITATIONS AND/OR OTHER CONSIDERATIONS OF USE:

- The GliaSite RTS and Spectrum Systems shall be distributed to persons specifically licensed for the use of radioactive materials in the healing arts by the NRC or an Agreement State.
- Handling, storage, use, transfer, and disposal: To be determined by the licensing authority.
- The GliaSite RTS and Spectrum Systems shall only be used under the supervision of an authorized user, or as approved by the U.S. Food and Drug Administration (FDA).
- The GliaSite Spectrum System has not received full FDA approval (i.e., PMA, 510(k), etc.) and thus is currently NOT authorized for routine medical use. It may be used for investigational research under the auspices of a FDA- approved Investigational Device Exemption (IDE) study

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LIMITATIONS AND/OR OTHER CONSIDERATIONS OF USE: (continued)

- Users of the GliaSite RTS and Spectrum Systems shall have completed initial training by the manufacturer, or person specifically licensed by the NRC or an Agreement State to provide such training, prior to initial use.
- The Iotrex solution has not had a sealed source evaluation performed on it because, being a liquid, it cannot meet the requirements for a sealed source. Iotrex solution has been deemed acceptable for use in the GliaSite RTS and Spectrum Systems.
- It is recommended that patients who will be administered Iotrex in the GliaSite RTS and Spectrum Systems also be administered a thyroid blocking agent in accordance with the precautions set out in the respective Instruction Manual.
- The use of brachytherapy and chemotherapy at the same time has not been evaluated and therefore is not authorized for the GliaSite Spectrum System.
- In the GliaSite Spectrum System, the Iotrex solution must be afterloaded through the Iotrex infusion port – not through the AT infusion line. Afterloading Iotrex through the AT infusion line will result in the Iotrex directly entering the brain, which will result in a reportable event.
- REVIEWER NOTE: Care should be taken during insertion and removal of Iotrex to minimize the potential of surface contamination of the patient.
- REVIEWER NOTE: Patients who have been administered Iotrex in the GliaSite RTS and Spectrum Systems can be monitored and handled as if they were undergoing a thyroid ablation. For example, the product information insert for Iotrex recommends, "...all clothing, bandages or linens that come into contact with urine, sweat, or saliva should be surveyed for the presence of ¹²⁵I." Following those procedures will adequately protect workers and the general public from radiation coming from the patient.
- REVIEWER NOTE: Facilities might want to consider the placement of the bed in the patient's room so that doses emanating from patient's head do not have an impact on workers and unrestricted areas.
- REVIEWER NOTE: A radioactive spill kit should be available in the room in the event of a radioactive spill and personnel should be trained for its use.
- This registration sheet and the information contained within the references shall not be changed without the written consent of the Georgia Department of Natural Resources, Radioactive Materials Program.

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SAFETY ANALYSIS SUMMARY:

The GliaSite RTS and Spectrum Systems deliver a radiation therapy to the resected cavities of brain tumors. The GliaSite Spectrum System is also capable of delivering chemotherapy agents or other fluids directly into the tumor resection cavity. The GliaSite catheter remains in a sterile package until implanted in the patient following tumor resection. The system is radioactive only after the Iotrex solution is injected into the GliaSite catheter, which has been previously implanted and completely contained within the patient's body. The Iotrex solution, shipped within 48 hours of expected use, is contained within a double walled balloon catheter that has been shown to be compatible with the body and also to maintain its integrity while the therapy is delivered.

Both the GliaSite catheter and the Iotrex solution are single use and are disposed of as radioactive waste upon completion of treatment.

Under normal use, the GliaSite catheter is expected to release 1% of the loaded activity into the body because of the permeability of silicon to small molecules. This has been evaluated by the FDA and determined to have no adverse effects on the patient.

In the unlikely event that a GliaSite catheter fails during treatment and releases the Iotrex into the body, the Iotrex will be rapidly removed from the body primarily through the urine. Using the maximum dose administered to date, 460 mCi, doses to vital organs under this scenario are less than those received during a routine thyroid ablation using 150 mCi of I-131. To protect the patient in the event of device failure, a thyroid-blocking agent should be administered prior to implantation and during the course of treatment as outlined in the precautions in the GliaSite RTS Instruction Manual.

Based on review of the GliaSite RTS and Spectrum Systems, and the information and test data cited below, we continue to conclude that the device is acceptable for licensing purposes. Furthermore, we continue to conclude that the GliaSite RTS and Spectrum Systems would be expected to maintain their containment integrity for normal conditions of use and accidental conditions that might occur during uses specified in this certificate.

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REFERENCES:

The following supporting documents for the GliaSite RTS System are hereby incorporated by reference and are made a part of this registry document.

- Proxima Therapeutics, Inc.'s application with enclosures dated March 6, 2001, and signed by James B. Stubbs, Ph.D., Vice President, Scientific Affairs.
- Letter with enclosures dated August 6, 2001 and, signed by James B. Stubbs, Ph.D., Vice President, Scientific Affairs.
- Letters with enclosures dated November 13, 2002, January 22, 2003, and October 1, 2003, all signed by James B. Stubbs, Ph.D., Vice President, Scientific Affairs.

ISSUING AGENCY: Georgia Department of Natural Resources
Radioactive Materials Program

This document is not a license to receive, possess or distribute radioactive material. Receipt, possession and distribution of radioactive material, sources and devices containing radioactive material, are subject to the terms and conditions of applicable regulations and licenses issued by NRC or Agreement States.

Date: October 7, 2003

Reviewer: 
Eric T. Jameson

Date: October 7, 2003

Concurrence: 
Cynthia Sanders

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Attachment 1

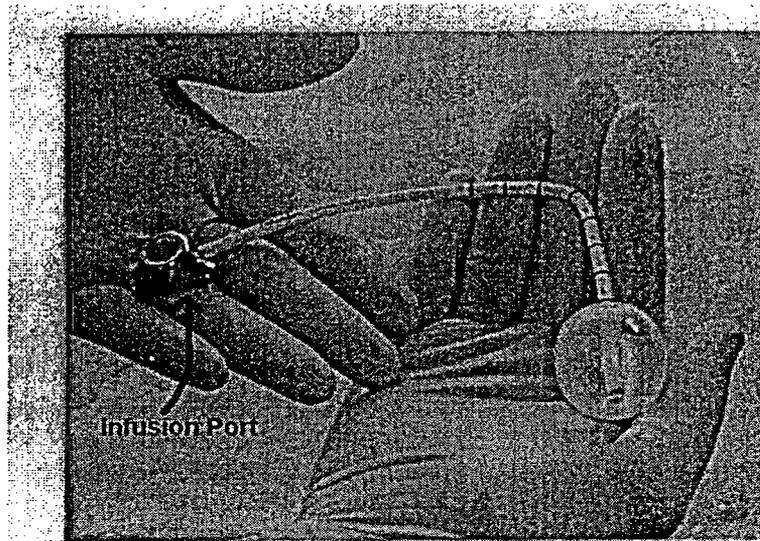


Figure 1a An inflated, 3-cm diameter Gliasite

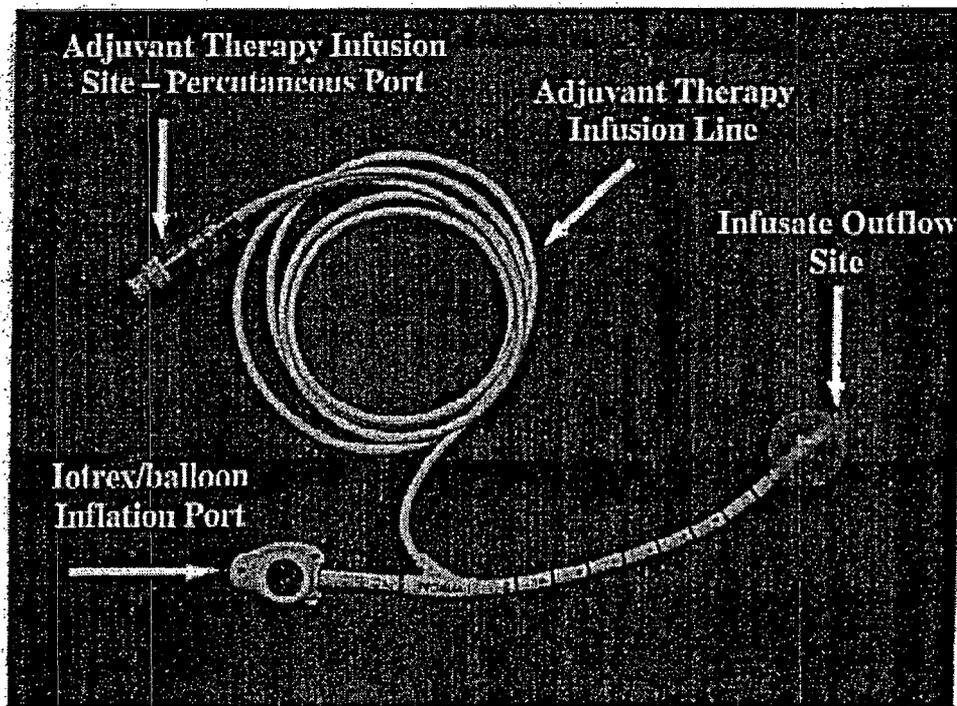


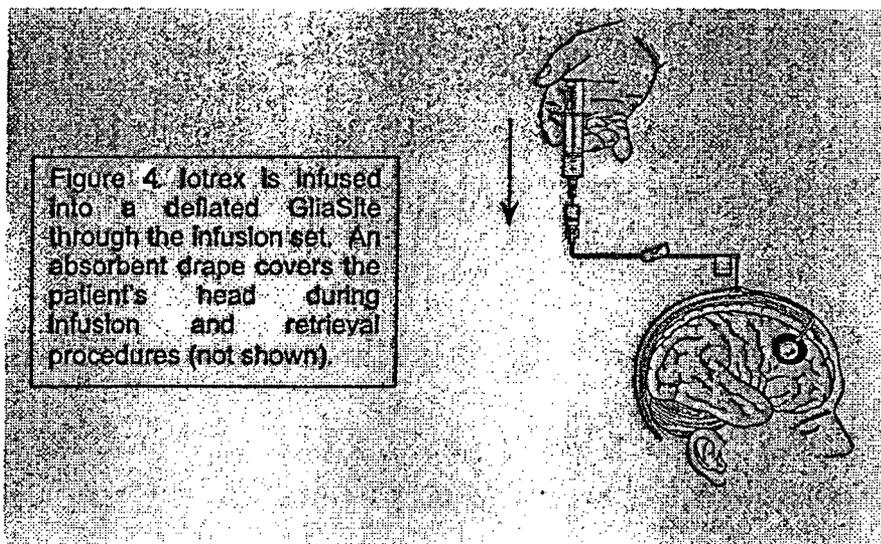
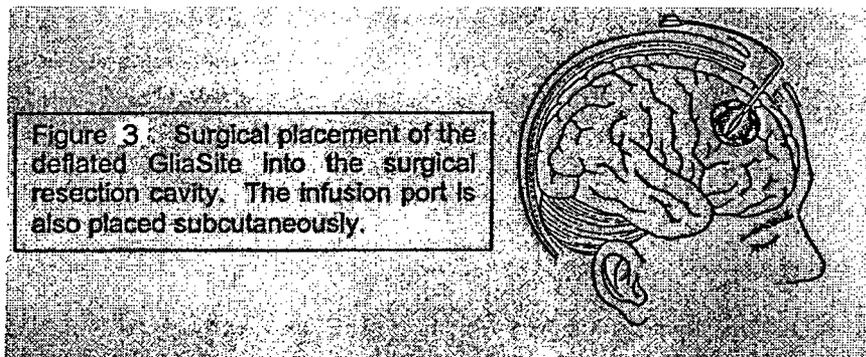
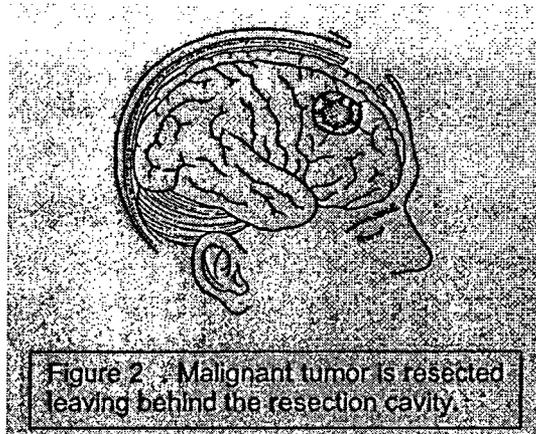
Figure 1b -- inflated, 2 cm diameter Gliasite Spectrum

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Attachment 2



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Attachment 3

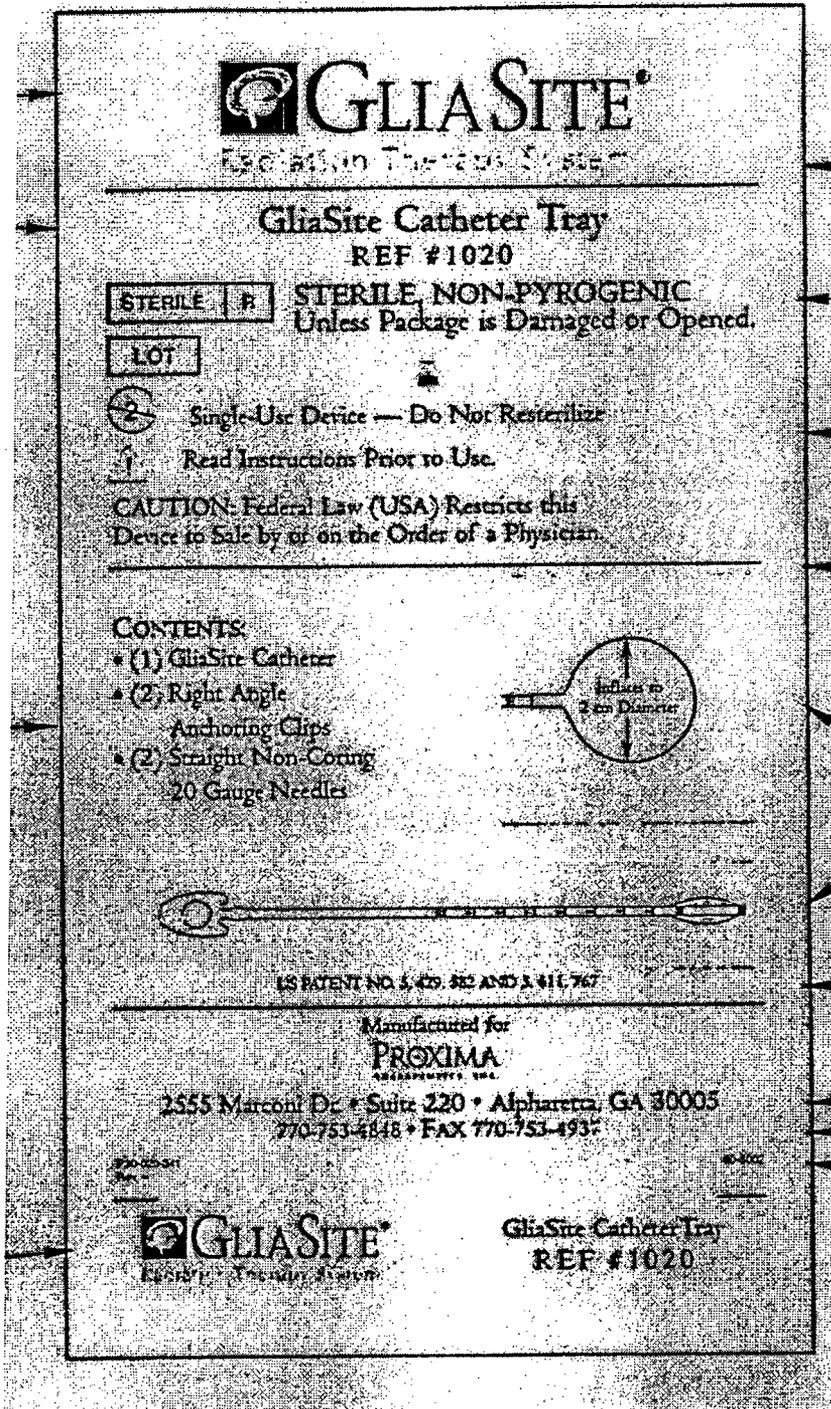


Figure 5 – GliaSite box label

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Attachment 4

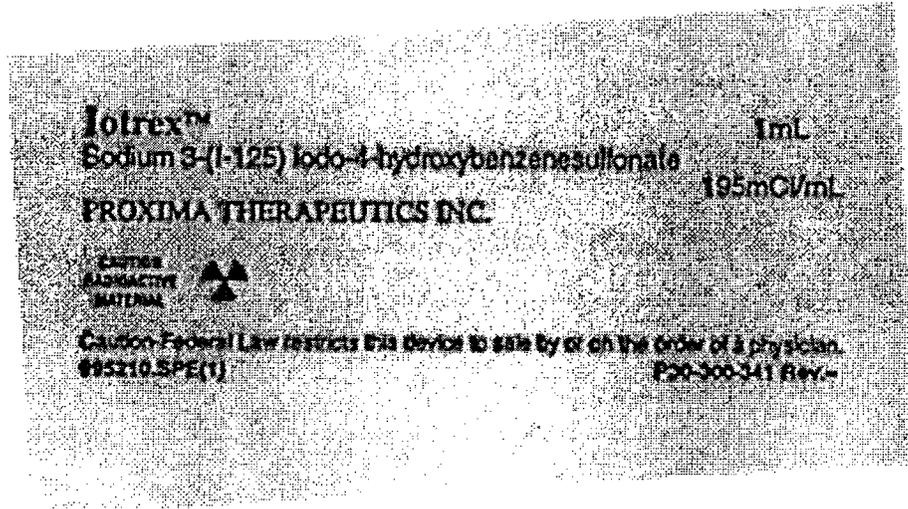


Figure 6 – Iotrex vial label

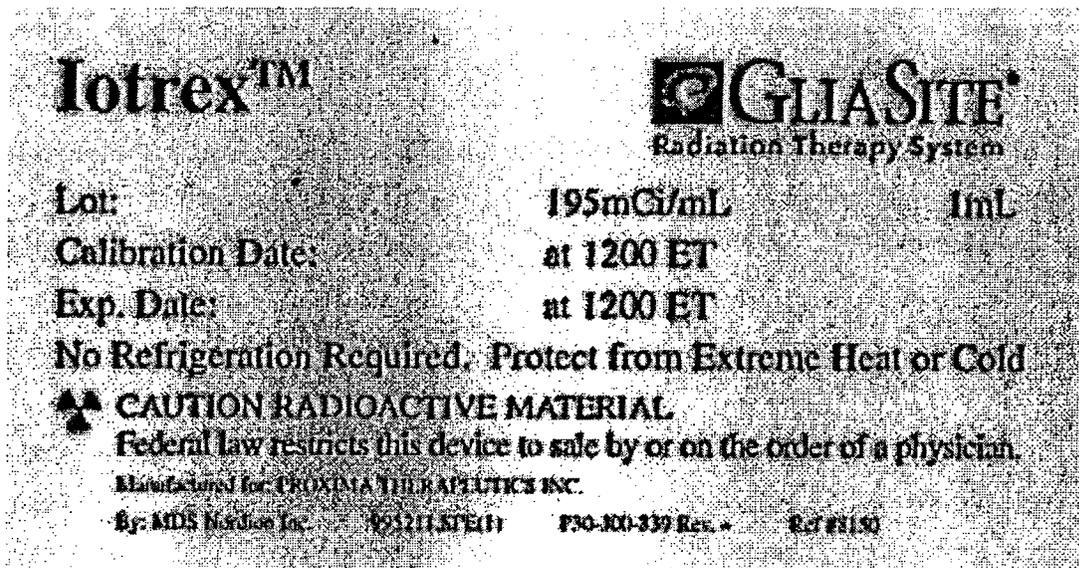


Figure 7 – Iotrex shipping container label