



Somerset
MEDICAL CENTER

110 Rehill Avenue
Somerville, NJ 08876-2598
908.685.2200
somersetmedicalcenter.com

April 18, 2005

United States Nuclear Regulatory Commission
License Assistant Section
Region I
475 Allendale Road
King of Prussia, PA 19406-1415

Re: License No. 29-03089-01 *03002466*

To Whom It May Concern:

Somerset Medical Center would like to amend our radioactive material license to include the use of the GLIASITE RTS to deliver intracavity radiation therapy (brachytherapy) to patients with malignant brain tumors following tumor resection surgery.

I have attached detailed information regarding equipment and procedures we intend to use for the new clinical technique.

If you have any questions or require additional information, please contact me at (908)-685-2927.

Sincerely,

Michael A. Medina
Assistant Vice President

'05
APR 21
PM 2:58

RECEIVED
REGION 1

136909
NMSS/RGNI MATERIALS-002



Somerset

MEDICAL CENTER

110 Rehill Avenue
Somerville, NJ 08876-2598
908.685.2200
somersetmedicalcenter.com

Request for Amendment of the Hospital Radioactive Materials License To Add the Proxima Therapeutics GliSite® Brachytherapy Systems

Specifically, this licensee wishes to add the following line item to our license:

Material in 10CFR35.1000:

- **Radionuclide:** I-125
- **Physical Form:** an aqueous solution containing Na-3-[I-125] iodo-4-hydroxybenzenesulfonate (Iotrex®)
- **Inventory Limit:** as needed (or 8 Ci)
- **Purpose:** Brachytherapy with the GliSite catheter.

This line item amendment request follows the format and content of the NRC guidance published on the NRC web page (<http://www.nrc.gov/materials/miau/miau-reg-initiatives/liquid-brach.html>). The guidance was copied verbatim and responses to each point are given as applicable. Each specific regulatory requirement has been numbered to facilitate reference to the licensee's response. The NRC language is given in Arial font and the licensee response is provided in Times New Roman font.

Liquid Brachytherapy Sources and Devices

Licensing Guidance - I-125 Iotrex Liquid Brachytherapy Source in Proxima GliSite® Radiation Therapy System:

1. I-125 Iotrex liquid brachytherapy sources are manual brachytherapy sources used for temporary brachytherapy implantation therapy in the Proxima Therapeutics' GliSite Radiotherapy system.
2. The Proxima Therapeutics' GliSite Radiotherapy system (RTS) consists of the Proxima Therapeutics' GliSite Radiotherapy system balloon catheter and Iotrex liquid brachytherapy source.

The licensee is requesting a line item amendment to use the Proxima Therapeutics GliSite catheters and Iotrex. Iotrex is a liquid brachytherapy radioactive source and the GliSite catheters are used to temporarily contain the Iotrex during brachytherapy. The GliSite catheters are listed on the U.S. NRC Sealed Source and Device Registry (GA-1148-D-101-S).

3. Required training and experience for authorized users is specified in 10 CFR 35.490 or , until October 25, 2004, 10 CFR 35.940 for use with materials governed by 10 CFR 35.400, as well as vendor training in use of the Proxima Therapeutics' GliSite RTS.

4. An authorized user with experience in radiopharmaceutical therapy procedures should be on call to provide guidance in case of leakage of the implanted device.

The licensee have an authorized physician user with experience in radiopharmaceutical therapy procedures available “on call” to provide guidance and assistance in case of actual or suspected leakage of the implanted device.

The licensee shall follow all of the requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use, except where the following license conditions provide regulatory relief:

5. For brachytherapy using Proxima Therapeutics’ Gliasite RTS, “prescribed dose” means the total dose documented in the written directive.

Per our Written Directive for brachytherapy with the Gliasite, the “prescribed dose” is the prescribed radiation dose, in units of Gy delivered.

6. The written directive should include: (1) prior to implantation: the treatment site, the radionuclide (including the chemical/physical form (Iotrex)), and dose; and (2) after implantation but prior to completion of the procedure: the radionuclide (including the chemical /physical form (Iotrex)), treatment site, and the total dose.

Our Written Directive for brachytherapy with the Gliasite catheters includes the nuclide (I-125), the chemical/physical form (Iotrex), prescribed radiation dose (Gy), administered dosage of Iotrex (mCi) and dwell time (hours).

7. Procedures should specify how to confirm that the balloon does not leak prior to injection of the Iotrex or while Iotrex is implanted in the patient or human research subject.

Prior to afterloading the Iotrex, the integrity of the Gliasite catheter will be determined using one of a variety of imaging modalities such as MRI, CT or radiographs. The images will be obtained with the Gliasite catheter inflated, demonstrating the continued capability of the catheter to maintain its inflated fluid volume. The images used in this assessment will be kept in the patient’s medical records as required by state regulations.

One method of assessing Gliasite integrity during brachytherapy that we may use (not exclusively though) is via radiation survey measurements. Upon completing the Iotrex afterloading periodic radiation exposure rate measurements will be used to monitor unexpected leakage of radioactive material from the Gliasite catheter. Radiation measurements will be performed over the injection site surface (at 20 to 30 centimeters from the injection site), at 1 meter from the injection site, and over the patient’s bladder. These measurements will be repeated periodically until the radioactive material is retrieved. Any significant changes from the initial readings (e.g., large decrease in cranial exposure rates concomitant with large increases in bladder exposure rates) will be documented and evaluated for further action as appropriate.

If patients are treated during brachytherapy on an outpatient basis, we will substantially follow the model guidance provided in US NRC NUREG –1556, vol. 9, Appendix U in releasing these patients for the duration of their brachytherapy treatment, making only the minor changes made necessary to satisfy 10 CFR 35.1000. Documentation demonstrating compliance with Section 35.75 requirements that the total effective dose equivalent to any other individual from exposure to the released individual is not likely to exceed 5 mSv is provided. Documentation includes forms describing the evaluation

process for determining which patients are suitable for outpatient treatment, patient release forms and appropriate patient instructions.

8. "Source leakage" for the Iotrex implanted in the GliaSite RTS means leakage of I-125 that results in a dose that exceeds 0.5 Sv (50 rem) dose equivalent to any individual organ other than the treatment site (based on definition of a medical event).

The licensee will evaluate all events which occur involving the unexpected loss of retained radioactivity in the catheter and assess the dose to the critical organ (bladder wall, per Iotrex Package Insert). If the dose to the critical organ exceeds 50 rem, the event will be handled and reported as a misadministration.

Per the manufacturer's product information, a small quantity of radioactivity diffuses from the catheter during normal operation.

In addition, there may be cases where in the medical opinion of the physician(s), the patient would best benefit from leaving the drained GliaSite in place (this is an "off-label" use of the GliaSite). Having said this, the federal food, drug and cosmetic act allows a practitioner to use a cleared device for an "off-label" use if the physician(s) believes that using the GliaSite is in the best interest of this patient (Practice of Medicine Clause).

Thus, GliaSite patients are expected to have some residual radioactivity present in their bodies after therapy is completed.

The licensee will evaluate each patient treatment to determine if the prescribed dose was successfully delivered to the treatment site. Specifically, a delivered radiation dose that differs by more than 20% from the prescribed radiation dose will be evaluated as a medical event.

9. The licensee shall retain a record of the leak test for 3 years (the period that 10 CFR 35.2067 requires for brachytherapy sources).

Diagnostic quality images will be obtained with the GliaSite catheter inflated, demonstrating the continued capability of the catheter to maintain its inflated fluid volume. The images used in this assessment will be kept in the patient's medical records as required by state regulations. The leak tests typically required of brachytherapy sources (e.g., removable contamination) are not possible as the GliaSite catheter is completely subcutaneous while the radioactive material resides within it. Also, the SDDR document states leak tests are not applicable to the GliaSite system.

10. The licensee shall report a leaking source to the NRC within 5 days of the leakage test to the locations specified and provide the information identified in 10 CFR 35.3067.

The GliaSite catheter is a single use device that will not be inflated with Iotrex if the integrity of the device is not demonstrated prior to afterloading Iotrex. In addition, leak tests are not required for the GliaSite as stated on Page 1 of the Sealed Source and Device Registry No. GA-1148-D-101-S.

11. The licensee shall provide instructions on how to safely handle contamination of unsealed materials, in addition to the instructions required by 10 CFR 35.410, "Safety instructions."

We will follow our policies and procedures for safe use of radioactive materials and provide instructions to the appropriate staff as necessary.

The following additional guidance applies when Iotrex™ is placed in vials, syringes, or radiation shields that are not labeled by the manufacturer:

12. Label syringes and syringe radiation shields with the radioisotope, form, and therapeutic procedure (i.e., I-125 Iotrex for brain brachytherapy).
13. Label vials and vial radiation shields with the radioisotope and form (i.e., I-125 Iotrex).

The licensee will label syringes, syringe shields, vials and vial shields with the form of the byproduct material (e.g., I-125 Iotrex). Syringes and syringe shields will also include the procedure (e.g. GliaSite or brain brachytherapy).

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

NO. GA-1148-D-101-S

DATE: September 11, 2001

PAGE: 1 of 12

DEVICE TYPE: Low Dose Rate Brachytherapy

MODEL: GliaSite® RTS System, with catheter Models 1020, 1030, and 1040

MANUFACTURER/DISTRIBUTOR: Proxima Therapeutics, Inc.
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)

ISOTOPE:

Iodine-125

MAXIMUM ACTIVITY:

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

NO

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES

SAFETY EVALUATION OF DEVICE

NO. GA-1148-D-101-S

DATE: September 11, 2001

PAGE: 2 of 12

DEVICE TYPE: Low Dose Rate Brachytherapy

DESCRIPTION:

The GliaSite RTS System is a single-use low-dose rate brachytherapy system consisting of a double-wall balloon catheter filled with lotrex, a solution containing organically bound I-125. The system is 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 lotrex solution and saline. After a patient-specific dwell time, the lotrex solution is removed from the catheter, and the catheter is then removed from the patient.

The GliaSite catheter is constructed from common biocompatible materials and is configured similar to other currently marketed interstitial and intracavity brachytherapy applicators.

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 three models of the GliaSite catheter refer to different sized balloons, and thus, different fill volumes. The balloon diameters and maximum inflation volumes are contained in the table below.

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

The inner balloon acts as a reservoir for the lotrex solution. The outer balloon serves as the backup reservoir in the event the inner balloon ruptures. The catheter shaft is constructed from radiopaque silicone, bi-lumen tubing and contains a malleable titanium element to assist in positioning of the balloon. 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.

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.

Refer to Figure 1 for a picture of an inflated, 3cm diameter GliaSite catheter.

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.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES SAFETY EVALUATION OF DEVICE

NO. GA-1148-D-101-S

DATE: September 11, 2001

PAGE: 3 of 12

DEVICE TYPE: Low Dose Rate Brachytherapy

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 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.

DIAGRAM:

- | | | |
|----------|----|--|
| Figure 1 | -- | inflated Gliasite 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 |

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 lotrex solution is received at the facility within 48 hours of its intended use in unit dose vials of not less than 150 millicuries. The lotrex 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 lotrex is accomplished by reversing the insertion procedure.

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

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES

SAFETY EVALUATION OF DEVICE

NO. GA-1148-D-101-S

DATE: September 11, 2001

PAGE: 4 of 12

DEVICE TYPE: Low Dose Rate Brachytherapy

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.

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 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.

The Iotrex solution has a shelf life of 19 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.

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.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES SAFETY EVALUATION OF DEVICE

NO. GA-1148-D-101-S

DATE: September 11, 2001

PAGE: 5 of 12

DEVICE TYPE: Low Dose Rate Brachytherapy

EXTERNAL RADIATION LEVELS: (continued)

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

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 System 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 System shall only be used under the supervision of an authorized user, or as approved by the U.S. Food and Drug Administration (FDA).
- Users of the GliaSite RTS System 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.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES

SAFETY EVALUATION OF DEVICE

NO. GA-1148-D-101-S

DATE: September 11, 2001

PAGE: 6 of 12

DEVICE TYPE: Low Dose Rate Brachytherapy

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

- 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 System.
- It is recommended that patients who will be administered Iotrex in the GliaSite RTS System also be administered a thyroid blocking agent in accordance with the precautions set out in the GliaSite RTS Instruction Manual.
- 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 System 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.

SAFETY ANALYSIS SUMMARY:

The GliaSite RTS System delivers a radiation therapy to the resected cavities of brain tumors. 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.

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES

SAFETY EVALUATION OF DEVICE

NO. GA-1148-D-101-S

DATE: September 11, 2001

PAGE: 7 of 12

DEVICE TYPE: Low Dose Rate Brachytherapy

SAFETY ANALYSIS SUMMARY: (continued)

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 System, and the information and test data cited below, we conclude that the device is acceptable for licensing purposes. Furthermore, we conclude that the Gliasite RTS System would be expected to maintain its containment integrity for normal conditions of use and accidental conditions that might occur during uses specified in this certificate.

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.

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

NO. GA-1148-D-101-S

DATE: September 11, 2001


PAGE: 8 of 12

DEVICE TYPE: Low Dose Rate Brachytherapy

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: September 11, 2001

Reviewer: 
Eric T. Jameson

Date: 11 September 2001

Concurrence: 
Elizabeth L. Drinnon

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

NO. GA-1148-D-101-S

DATE: September 11, 2001

Attachment 1



Figure 1. An inflated, 3-cm diameter GliaSite

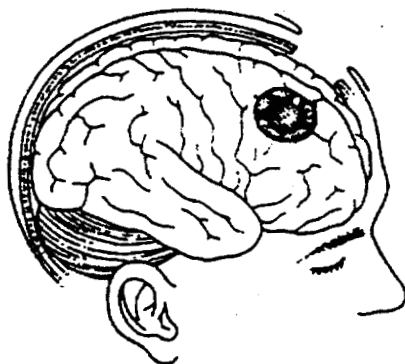


Figure 2 . Malignant tumor is resected leaving behind the resection cavity.

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

NO. GA-1148-D-101-S

DATE:

September 11, 2001

Attachment 2

Figure 3 . Surgical placement of the deflated GliaSite into the surgical resection cavity. The infusion port is also placed subcutaneously.

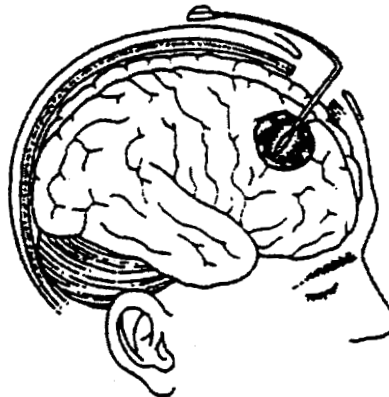
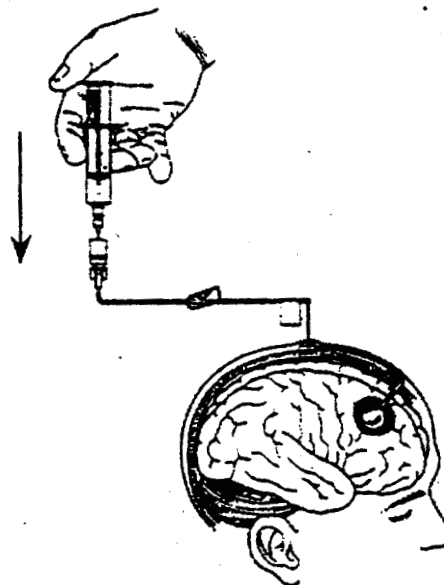


Figure 4. Iotrex is infused into a deflated GliaSite through the infusion set. An absorbent drape covers the patient's head during infusion and retrieval procedures (not shown).



REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF DEVICE

NO. GA-1148-D-101-S

DATE: September 11, 2001

Attachment 3

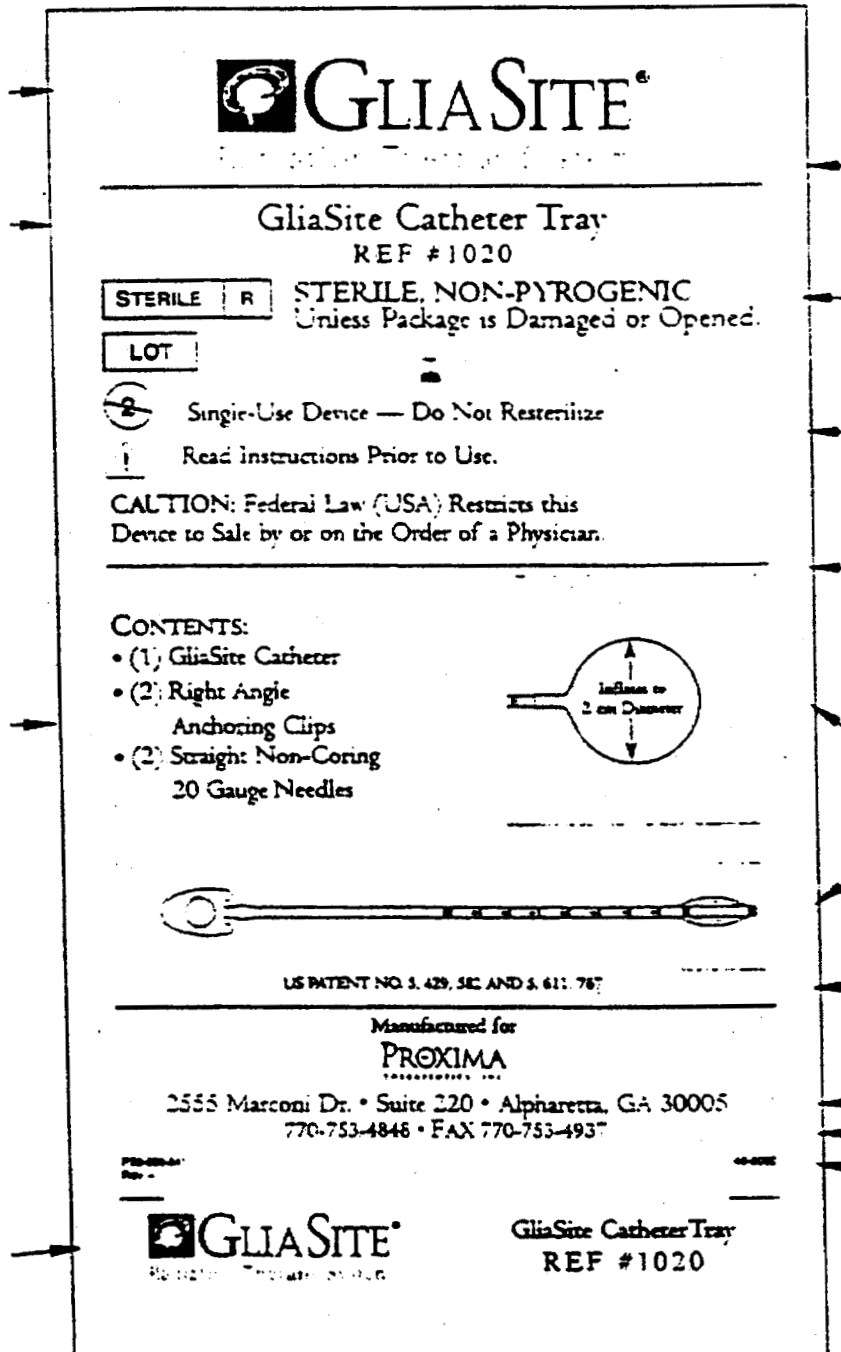


Figure 5 – GliSite box label


REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES
SAFETY EVALUATION OF DEVICE

NO. GA-1148-D-101-S

DATE: September 11, 2001


Attachment 4

Iotrex™ 1mL
Sodium 3-(I-125) iodo-4-hydroxybenzenesulfonate 195mCi/mL
PROXIMA THERAPEUTICS INC.

CAUTION
RADIOACTIVE
MATERIAL 


Caution-Federal Law restricts this device to sale by or on the order of a physician.
995211.SPE(1) P30-000-341 Rev.-

Figure 6 – Iotrex vial label

Iotrex™  **GLIASITE®**
Radiation Therapy System

Lot: 195mCi/mL 1mL
Calibration Date: at 1200 ET
Exp. Date: at 1200 ET

No Refrigeration Required. Protect from Extreme Heat or Cold

 **CAUTION RADIOACTIVE MATERIAL**
Federal law restricts this device to sale by or on the order of a physician.

Manufactured for: PROXIMA THERAPEUTICS INC.
By: MDS Nordion Inc. 995211.SPE(1) P30-000-341 Rev. - Ref 00150

Figure 7 – Iotrex shipping container label



Somerset

MEDICAL CENTER

110 Rehill Avenue
Somerville, NJ 08876-2598
908.685.2200
somersetmedicalcenter.com

Proprietary and Confidential to Proxima Therapeutics, Inc.

Patient Monitoring

Introduction

The following information describes the recommended action for monitoring a patient during radiotherapy.

Radiation Survey of the patient's head and bladder

Upon completing the Iotrex afterloading and during radiotherapy, ambient radiation exposure rate measurements (with an appropriate survey meter) can be used to monitor for unexpected leakage of radioactive material from the GliaSite catheter. Radiation measurements should be performed at the injection site surface, 20 to 30 centimeters from the injection site, 1 meter from the injection site and over the patient's bladder. These measurements should be repeated daily until the radioactive material is retrieved. Any significant changes from the initial readings (e.g., large decrease in cranial exposure rates concomitant with large increases in bladder exposure rates) should be documented and evaluated for further action as appropriate.

Radiation Survey of Urine Collections

Another method for monitoring the function of the GliaSite catheter during radiotherapy is urine survey. This can be performed as surveys (with an appropriate survey meter) of 24-hour collections of individual urinations or of each urine collection. The action limit for 24-hour collections should be higher than that for an individual urine collection by a factor of approximately 5 (a typical person voids their bladder 5 times daily). This method applies equally well to urine collected in a foley catheter. Approximate calculations of the exposure rates at 1 foot from a large volume of urine containing ^{125}I (assumes inverse square law is valid) indicates that 1 mCi should give a meter reading of 1.6 mR/hr (assuming the meter is calibrated accurately). If the urine survey indicates proper function of the GliaSite, then the urine collected can be flushed down the toilet (verify this with the RSO). Detection of a high level of radiation should be documented and evaluated for further action as appropriate.

Detection of unexpected leakage of radioactive material from the GliaSite catheter (via either method) should be addressed as follows:

1. Notify the Radiation Safety Office and the Radiation Oncologist.
2. The remaining Iotrex should be retrieved.
3. Provide additional thyroid blocking to patient and hydrate orally or via intravenous line.
4. Monitor urine activity levels for 24-48 hours after retrieval of Iotrex.
5. When urine activity levels drop to acceptable levels, surgically remove GliaSite from patient, observing radioactive material precautions. (The external surfaces of the GliaSite and the resection cavity are most likely radioactive.)
6. Determine whether a misadministration has occurred. Upon discovery of a misadministration, follow all notification and reporting requirements as required by state and/or NRC regulations.

GliaSite® Radiation Therapy System

Summary of Treatment Procedure

This document contains partial information concerning the GliaSite RTS. For complete information concerning the device, contraindications, warnings and precautions, refer to the instruction manual.

This document is intended to be used as guidance for developing site-specific treatment procedures. The suggested content herein is considered controlled documentation by Proxima Therapeutics (P/N B30-100-017, Rev.-). Proxima is not responsible for modifications to or deviations from the original text.

Treatment Summary

The GliaSite® Radiation Therapy System is a brachytherapy catheter designed to deliver a spherically uniform dose of radiation to the tissue surrounding a brain tumor resection cavity. By delivering a conformal dose of radiation to the tumor cavity, the intent is to improve tumor control and minimize damage to healthy tissue for patients with malignant brain tumors. The device consists of a catheter that is implanted in a tumor cavity with a distal inflatable balloon, which is accessed through a subcutaneous injection port. The liquid radioactive I-125 source (Iotrex) will be placed inside the balloon via a shielded syringe and needle several days after implant. The procedure will be done under the supervision of a radiation oncologist, certified medical physicist and radiation safety officer. Following completion of radiation therapy, the Iotrex will be retrieved and the GliaSite catheter removed. The GliaSite RTS may be used in patients with newly diagnosed or recurrent malignant brain tumors, as well as metastatic tumors.

FDA Clearance

The GliaSite RTS was cleared by FDA for commercial distribution on April 25, 2001.

Indication

- The GliaSite RTS is intended to deliver intracavitary radiation therapy (brachytherapy) in patients with malignant brain tumors following tumor resection surgery.

Authorized Users

- Only Radiation Oncology or Nuclear Medicine physicians approved by the Radiation Safety Committee as authorized users for this procedure will be allowed to deliver radiation treatment to the patient.
- Trained Medical Physicist or Certified Nuclear Medicine Technician approved by the Radiation Safety Committee (RSC) as source handler will be responsible for source preparation and calibration.

Location of Use

- Source preparation and calibration should be done inside a ventilation hood approved by the Radiation Safety Committee for use with radioactive material.
- This may be done in Nuclear Medicine hot lab or in another suitable hot lab.
- Procedure will be performed in the patient's room or other room as designated by the Radiation Safety Department.

GliaSite RTS System Description

- GliaSite® catheter
 - The infusion port has self-sealing silicone septum at proximal end for injection.
 - Shaft is an 18 cm length of bilumen, radiopaque, silicone tubing with a malleable titanium element to assist in positioning the balloon.
 - The dual silicone configuration balloon at the distal end comes in diameters of 2, 3 or 4 cm.
 - Inner balloon acts as a reservoir for the liquid I-125 source (Iotrex).
 - Radiopaque markers mark the proximal and distal side of the inner balloon.
 - Outer balloon acts as a backup in the event that the integrity of the inner balloon is compromised.
 - A safety lumen is incorporated into the catheter shaft to allow access to the outer balloon.
 - Positioning markers are provided on the catheter shaft at 1 cm intervals beginning at the proximal end of the balloon.
 - A right-angle anchoring clip is used to secure the catheter where it exits the burr hole.

- Iotrex®
 - A sterile, non-pyrogenic solution containing sodium 3-(I¹²⁵) iodo-4-hydroxybenzenesulfonate (I¹²⁵-HBS) that is intended for use with the GliaSite catheter.
 - It is delivered in nominal 1.0 ml unit dose conical vials containing a minimum of 150 mCi at the time of calibration by the licensee.
 - Net afterloaded activity ranges from 75 mCi to 1200 mCi. Required activity is dependent on prescribed radiation dose, treatment depth and balloon diameter.
 - All Iotrex™ solution shall remain in a secured facility in the Radiation Oncology Department or other designated area approved by the RSC until the actual procedure time.
 - “*Safe Use of Radiopharmaceuticals*” practice will be followed when handling the source.

- GliaSite RTS Access Tray
 - Infusion set with 20 gauge non-coring needle, clamp and pre-attached injection site
 - Two 20 cc syringes with pre-attached 21-gauge needle
 - Three 5 cc syringes with pre-attached 21-gauge needle
 - Fenestrated drape with hole
 - Transparent dressing
 - Three gauze pads
 - Steri-strips
 - Safety lumen accesses supplies
 - Surgical marking pen

Treatment Procedure

- A) *Catheter Placement*
- B) *Final Balloon Fluid Volume Determination and Placement Verification*
- C) *Iotrex® Radiotherapy Solution Infusion*
 - 1) *Injection Site Access*
 - 2) *Fluid Removal*
 - 3) *Iotrex® Solution Afterloading Procedure*
- D) *Final Balloon Fluid Volume Determination and Placement Verification*
- E) *Patient Treatment*
- F) *Iotrex® Solution Retrieval*
- G) *GliaSite Catheter Removal*

Considerations with Catheter Placement:

- Placement of the GliaSite balloon is done by the neurosurgeon at the completion of tumor resection.
- Balloon size is determined by the neurosurgeon based on the cavity volume.
- System integrity has to be confirmed by OR nurses prior to use, (See attached IM section 1.2.0 for details.).
- Once in place, the balloon is filled with saline and contrast agent to secure position in the resection cavity.
- The amount of fluid infused into or withdrawn from the balloon is recorded on the Fluid Status Chart.
- The dura and the bone flap are closed. The following considerations need to be made:
 - An adequate pathway for future removal of the GliaSite catheter should be incorporated;
 - Rough edges can damage the GliaSite catheter;
 - Thread the catheter shaft through the burr hole that allows for a more direct removal pathway and lay the infusion port off to the side, on top of the skull;
 - Suture or screw the right-angle anchoring clip, provided in the GliaSite RTS tray, to the skull or bone flap at the outer edge of the burr hole in order to minimize movement of the GliaSite;
 - Select a site for the placement of the infusion port, and to avoid kinks in the catheter, suture or screw the infusion port into position.

Considerations with Final Balloon Fluid Volume Determination and Placement Verification:

- Prior to closing the scalp incision site (skin flap), the physician must determine the fluid volume that will reside in the balloon during the surgical recovery period. A 75% sterile normal saline to 25% non-ionic contrast agent mixture is recommended.
- The final volume and type of fluid residing in the balloon on the Fluid Status Chart is to be recorded.
- Confirm the GliaSite catheter placement with a post-operative MRI or x-ray.
- A copy of the final MRI and the Fluid Status Chart are to be sent to the Radiation Oncology Dept. for treatment planning and to determine the amount of Iotrex to be ordered.

Considerations with Iotrex[®] Radiotherapy Solution Infusion:

- Radiation Oncology will schedule patient for Iotrex treatment. Infusion of the Iotrex is typically initiated between 3 days and 3 weeks (and completed within 29 days) post-catheter implantation.
- Once the Radiation Oncologist decides to use the GliaSite RTS, dose planning is performed using an MRI with the balloon inflated to the desired volume. The Iotrex calculation booklet is used to determine the prescription parameters.
- Based on the prescription, the authorized user or designate will calculate and order the appropriate amount of Iotrex solution needed for the procedure. A written directive will be provided.
- Twenty-four hours prior to, and continuing throughout brachytherapy, the patient will receive Lugol's solution or SSKI to block the thyroid as prescribed by the Radiation Oncologist.
- Depending on the prescribed dose, patient will be kept in a private room for the duration of the radiation delivery (approximately 3 to 7 days). During that time patient will be under strict radiation precautions with all radiation placarding in place. Standard procedures for therapeutic use of radiopharmaceuticals will be followed for use with this treatment modality. Since radioactive I-125 solution is a low energy x-ray and γ -emitter, no external shielding is necessary.
- Source preparation and calibration will be done under the direct supervision of the Medical Physicist. A running inventory of the liquid source will be maintained for each case.
- The syringe dose is to be delivered to the Authorized User in the patient room with the assistance of the Medical Physicist and/or Radiation Safety personnel.
- Room preparation, room surveys, in-service for the nursing staff, radiation waste disposal and release of patient will be done by the Radiation Safety staff in a manner consistent with U.S. NRC Regulatory Guide 10.8, rev. 2, 1987.
- For personnel handling the Iotrex and for other support staff in the same room where Iotrex is being manipulated, a thyroid bioassay between 6 and 72 hours after the procedure is recommended (Follow standard procedure).

Considerations for Iotrex Delivery:

There are three main steps to the afterloading of the Iotrex: injection site access, fluid removal, and Iotrex afterloading. Iotrex fluid insertion is done with the GliaSite RTS Access tray. In addition to the GliaSite RTS Access Tray, the following items are required:

- Sterile gloves (recommend that the physician wear 2 pairs for the procedure);
- Sterile normal saline;
- Radioactive waste container;
- Radiation decontamination kit.

• Considerations for Injection Site Access:

- Perform standard aseptic site preparation;
- Palpate the scalp to locate the infusion port and mark the location for needle entry into the infusion port with the surgical marking pen;
- Locate and unfold the fenestrated drape and place drape over the patient's head, centering the drape hole over the infusion site;
- The transparent dressing is placed over the infusion site to cover skin and edges of drape hole;
- The pouch containing the infusion set with the noncoring needle provided in the tray should be opened and primed with saline;

- The clamp on the infusion set should be closed and then a non-coring needle inserted into the infusion port, secure the noncoring needle with the steri-strips provided in the tray.
- **Considerations with Fluid Removal:**
 - Fluid is to be removed with the 20 cc syringe;
 - The non-coring needle of the syringe is inserted into the infusion set injection site and then the clamp opened;
 - The clamp should be closed prior to withdrawing the needle from the infusion site;
 - The catheter and balloon should be flushed with saline after fluid removals using a 5 cc syringe;
 - Syringe should be disposed of in accordance with hospital procedure.
- **Considerations with Iotrex® Solution Afterloading Procedure:**
 - Two fluid-filled syringes, one containing the prescribed Iotrex solution and the other containing normal saline solution, are to be prepared in advance;
 - The needle of the syringe containing the Iotrex solution is inserted into the infusion set injection site;
 - After it is confirmed that the needle is completely inserted into the injection site, the clamp is opened and the Iotrex is slowly infused;
 - The used needle and syringe containing the Iotrex should be measured for residual activity;
 - The needle of the syringe containing the saline is inserted into the infusion set injection site and infused;
 - Once all fluid has been delivered, the needle and syringe are removed from the infusion set injection site and disposed of as radioactive waste;
 - All of the dressings and drapes should be handled as radioactive waste;
 - The volume of Iotrex solution and saline infused is to be recorded on the patient's Fluid Status Chart.

Considerations with Patient Treatment:

- Final dwell (treatment) time is to be determined by the Medical Physicist, based on the net activity injected and the prescribed dose.
- Patient is to remain in room. Visitors are allowed during designated times and at designated area to be determined by the Radiation Safety Officer in a manner consistent with state and NRC requirements.
- During a course of treatment, small quantities of I^{125} diffuse through the GliaSite catheter and are excreted in the urine. Therefore, all clothing, bandages or linens that come into contact with body fluids are to be kept for survey by Radiation Safety staff. All contaminated articles should be disposed of as radioactive waste.
- To ensure balloon catheter integrity, RSO and/or Medical Physicist should survey patient's head and bladder daily. If measurement is above baseline value, Physics, Radiation Safety and Neurosurgery need to be notified immediately. All measurements are maintained in patient record.

Considerations with Iotrex® Solution Retrieval:

- This is to be performed by an authorized user only.
- In addition to the GliaSite RTS Access Tray, the following items are required:
 - Sterile gloves (recommend that the physician wear 2 pairs for the procedure);
 - 20 cc leaded syringe shield (2 needed for a 4 cm GliaSite catheter);
 - Sterile normal saline;

- Fluid Status Chart of the patient;
 - Standard supplies for aseptic infusion site preparation;
 - Radioactive waste container;
 - Radiation decontamination kit.
- Prepare site as described above (see “Considerations for Injection Site Access”).
 - Insert the needle of the empty 20 cc syringe housed in a lead syringe shield into the infusion set injection site.
 - Open the clamp on the infusion set.
 - Pull back slowly on the syringe plunger to remove all fluid from the GliSite catheter.
 - When fluid flow stops or the syringe is full, close the clamp on the infusion set.
 - Remove the 20 cc syringe and set aside for disposal as radioactive waste.
 - Repeat until all fluid is withdrawn.
 - Compare the volume of fluid withdrawn to the amount expected per the Fluid Status Chart to verify that all fluid has been removed.
 - The injection site is flushed with the 5 cc syringe filled with saline and flushing should be repeated a second time.
 - The infusion set and any dressings/drapes should be disposed of as radioactive waste.
 - The volume of Iotrex/saline solution retrieved should be recorded on the patient’s Fluid Status Chart.

Considerations with GliSite Catheter Removal:

- Explanted GliSite catheter is radioactive and will be disposed of by Radiation Safety Office in accordance with NRC requirement.
- Radiation Safety staff should be present during the explant procedure for disposal of catheter and for patient room survey.
- Radiation survey will be done on patient before release from the hospital.

Emergency Procedures

- In the event of a patient emergency, notify Radiation Oncologist, Radiation Safety Office and Neurosurgeon in charge immediately.
- Prepare liquid radioactive I¹²⁵ Access Tray.
- Retrieve the Iotrex from the patient.
- Recover all radioactive material and all contaminated items.
- Schedule patient for an operating room procedure as soon as practical to remove the implanted balloon catheter.
- Follow instructions in the instruction manual for accessing the safety lumen.

This is to acknowledge the receipt of your letter/application dated

4/18/2005, and to inform you that the initial processing which includes an administrative review has been performed.

Amendment 29-03089-01 There were no administrative omissions. Your application was assigned to a technical reviewer. Please note that the technical review may identify additional omissions or require additional information.

Please provide to this office within 30 days of your receipt of this card

A copy of your action has been forwarded to our License Fee & Accounts Receivable Branch, who will contact you separately if there is a fee issue involved.

Your action has been assigned **Mail Control Number** 136909.
When calling to inquire about this action, please refer to this control number.
You may call us on (610) 337-5398, or 337-5260.

BETWEEN: : (FOR LFMS USE)
 : INFORMATION FROM LTS
 : -----
 :
 License Fee Management Branch, ARM : Program Code: 02120
 and : Status Code: 0
 Regional Licensing Sections : Fee Category: 7C
 : Exp. Date: 20050731
 : Fee Comments: _____
 : Decom Fin Assur Reqd: N
 :

LICENSE FEE TRANSMITTAL

A. REGION I

1. APPLICATION ATTACHED

Applicant/Licensee: SOMERSET MEDICAL CENTER
 Received Date: 20050421
 Docket No.: 3002466
 Control No.: 136909
 License No.: 29-03089-01
 Action Type: Amendment

2. FEE ATTACHED

Amount: /
 Check No.: /

3. COMMENTS

Signed Rebecca J. Wood
 Date 4/26/05

B. LICENSE FEE MANAGEMENT BRANCH (Check when milestone 03 is entered /__/)

1. Fee Category and Amount: _____

2. Correct Fee Paid. Application may be processed for:

Amendment _____
 Renewal _____
 License _____

3. OTHER _____

Signed _____
 Date _____