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May 1, 2008

US Nuclear Regulatory Commission
Materials Licensing Section
2443 Warrenville Road Suite 210
Lisle, IL 60532-4352

License Number: 24-01565-01

Dear NRC Reviewer,

We are requesting the following changes to our current NRC license:

1) **We are requesting to add intracavitary brachytherapy using the GliaSite Radiation Therapy system to our current license.** The system uses liquid I-125 as "Iotrex" manufactured by Proxima Therapeutics. I have enclosed specific information for Iotrex, as well as, the Written Directive and Quality Management Program that will be followed.

2) **The following individuals currently listed on our license as Authorized Users are no longer performing duties under our license, and may be removed**:

   Hugh Jerry Murrell, M.D.
   Fishel Z. Liberman M.D.
   John Harold Bechtel, M.D.
   George Barber Dunn, M.D.

3) **Our facility no longer performs HDR procedures. The physicists listed on our license no longer perform duties under our license, and may be removed.**

   Joel Love, M.S.
   Keith Alan Hickey, Ph.D.

4) **Remove from Section 6 of our current license:**
   Iridium-192 seeds in nylon ribbon, manufactured by Best Industries,
   Model No. 81-01. This source was for use in the Cordis Checkmate System (Intravascular Brachytherapy). We no longer utilize this system.

Please contact me at (573) 815-3729 if you need additional information.

Sincerely, Liesje Myers

Liesje Myers, CNMT
Radiation Safety Officer

BJC HealthCare℠

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Iodine-125 as "Iotrex" for Use in the GliaSite Radiation Therapy System

1. ***The name and FDA approval number of the device used in the procedure.***

- Device Name: GliaSite Radiation Therapy System (RTS) Models 1020, 1030, 1040
- FDA 510(k) Number: K003206
- NRC Registration Number for device: GA 1148-D-101-S

2. ***The type of radioactive material used and model numbers.***

- Type of radioactive Material: I-125 bound in liquid (sodium-3-[I^{125}]iodo-4-hydroxybenzenesulfonate)
- Model Number: Iotrex (Proxima Therapeutics)

3. ***The maximum quantity of radioactive material we wish to possess.***

As needed or at least 5.0 Curies.

4. ***Facility***

All receiving and documentation procedures, described in our current license, will be followed. Only Authorized Users, Medical Physicists, and CNMT's will be authorized to order Iotrex. The Iotrex solution will be stored, prepared and assayed in the existing Nuclear Medicine Department Hot Lab or Hot Storage Room. The storage and handling room(s) are GL 1418 (Hot Lab) and GL 1403 (Hot/ Waste Storage) on our floor plan. The Authorized Users for this procedure are:

Authorized user(s):

Mark Bryer, M.D.
Steven Westgate, M.D.
Joseph Bean, MD
James Allen, M.D.
William Decker, M.D.

The Medical Physicist for this procedure is:
Steven Crooks, Ph.D.

Radioactive waste is stored in room GL 1403 (Hot/ Waste Storage), inside properly shielded and placarded containers. Existing procedures for Decay-In-Storage will be followed.

Radioactive Materials are secured from unauthorized removal by keeping the storage area locked at all times.

Following assay, the Iotrex solution will be transported by an Authorized User, a Physicist, or a CNMT in a shielded syringe carrier to treatment room 2107 (treatment room indicated on our current license), or other treatment room approved by the Radiation Safety Officer, for the afterloading procedure. Appropriate signage will be placed on the entry door to the patient's room. Following retrieval of the Iotrex solution at the conclusion of the radiotherapy, the liquid radioactive waste will be transported back to a secure RAM storage area by an Authorized User, a Medical Physicist or a CNMT. It may subsequently be transferred to an authorized rad waste vendor, or left to decay-in-storage.

5. ***Radiation Safety Committee***

Approval by the Radiation Safety Committee will be obtained prior to the use of radioactive I-125 (Iotrex®) to perform intracavitary brachytherapy procedures using the GliaSite.

6. ***Instrumentation***

A properly maintained dose calibrator will be used to assay the activity of the Iotrex dose prior to administration, and to determine residual activity in the syringe after administration. The measurement of Iotrex activity will be performed according to the manufacturer's recommended procedure for Iotrex assay.

7. ***Personnel Monitoring***

The existing personnel monitoring program will be followed.

8. ***Training Program***

All personnel involved with utilization of the Proxima GliaSite RTS radiation delivery system will be trained in the proper use of this device including radiation safety and relevant emergency procedures. Employees preparing Iodine-125 (Iotrex®) will be; licensed Nuclear Medicine Technologists, Authorized Users, or Medical Physicists. Proxima Therapeutics employees will provide training to those individuals involved in the assay and administration of Iotrex solution. Additional hospital personnel wishing to participate at a later date in such activities will observe/participate in at least two patient therapies, which will suffice as training in lieu of vendor training. Nursing personnel caring for patients undergoing GliaSite procedures receive radiation safety training as appropriate by institutional radiation safety personnel.

9. ***Spill Procedures***

Our existing Radioactive Spill Procedures will be followed. Personnel involved in the administration will wear appropriate protective clothing. A radioactive spill kit will be available in the patient's room in the event of a radioactive spill.

10. ***Area Surveys***

The existing Area Survey Procedures will be followed.

11. ***Waste***

Urine containing small amounts of radioiodine will be discarded down the patient's toilet, which will be flushed twice. After completion of the treatment, the recovered liquid iodine solution and explanted GliaSite will be handled in one of two ways, at the discretion of the Radiation Safety Officer.

1. The radioactive waste may be held to decay-in-storage for at least 10 half lives, along with the GliaSite catheter and any other contaminated objects. When the exposure rate from the solution is determined to be at background level, and 10 half-lives have passed, the solution will be disposed of in the sanitary system. Background exposure rate will be determined in a non-radiation area.

2. The retrieved Iotrex solution and the explanted GliaSite device may be transferred to an approved radioactive waste vendor, using an approved radwaste receptacle.

12. ***ALARA Program***

The existing ALARA Program will be followed.

13. ***Patient Monitoring***

The GliaSite device is carefully designed to minimize the possibility of a rupture. However, small amounts (< 0.8%) of radioiodine normally diffuse through the GliaSite balloon over a 7-day period, and become systemically distributed. Prior to afterloading the balloon, the patient's thyroid will be blocked using a potassium iodide solution. Upon completing the Iotrex afterloading and during radiotherapy, radiation exposure rate measurements will be used to monitor for unexpected leakage of radioactive material from the GliaSite catheter. Radiation measurements will be performed at the injection site surface, 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. The licensee will use an appropriate exposure rate survey meter to perform the ambient radiation level surveys.

14. Bioassay

Data from other institutions using the GliaSite RTS system demonstrate that air concentrations of radioiodine are below minimum detectable levels (see attachment – De Guzman 2002). In addition, no radioiodine uptake has been observed on thyroid bioassay at these facilities or during the initial safety and performance clinical trial (see attachment – Tatter 2003).

15. Patient Release

At the conclusion of radiotherapy, i.e., retrieval of Iotrex from the GliaSite catheter, some radioactivity will be in the patient's body from the small quantity of activity that diffused through the GliaSite balloon. 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. Thus, these patients are expected to have some radioactivity present in their bodies after therapy is complete. The licensee will release these patients in accordance with NRC NUREG 1556 vol. 9 or equivalent state guidance on the release of patient's administered radioactive materials.

The Authorized User will evaluate each patient for their ability and willingness to comply with outpatient release instructions for the GliaSite using the Patient Information and Release Determination form (see attachment A). Patients approved for outpatient therapy will be given written and verbal instructions stressing radiation safety and contamination prevention precautions as well as the date and time for return to the hospital for retrieval of the Iotrex (see attachments B-D). In addition, the licensee will call the patient and/or one of their caregivers or family members within 24 hours prior to the retrieval date and time, reminding the patient to return for the retrieval procedure.

16. Quality Management Program

See the attached Written Directive and QMP that will be used.

WRITTEN DIRECTIVE
FOR
THERAPEUTIC ADMINISTRATION
OF ^{125}I RADIOTHERAPY SOLUTION (IOTREX®)
FOR INTRACAVITARY RADIATION THERAPY

Patient Name: _____ Diagnosis: _____

Patient I.D. No.: _____ Treatment Site: *Brain Resection Cavity*

Route of Administration: *Temporary implant utilizing the GliaSite® RTS*

Dose Assessment Data:

1) GliaSite®catheter implanted: 2.0 cm GliaSite Catheter ☐
   3.0 cm GliaSite Catheter ☐
   4.0 cm GliaSite Catheter ☐

2) GliaSite Balloon Fill Volume _____ cc

3) Dose Prescription Point: _____ cm from inflated balloon surface

4) Prescribed Brachytherapy Dose (PBD): _____ Gy

5) a. Calculated Activity of Iotrex (I-125) needed to deliver PBD: _____ mCi
   (derived from Iotrex Calculation Booklet)
   b. Activity Ordered to ensure delivery of "5a" into the balloon: _____ mCi
   (taking into account the loss of activity left in the vial, syringe cap, syringe, etc)

   c. Labeled Activity on the delivered dose of Iotrex (I-125): _____ mCi

   d. Assayed Activity of the Iotrex (I-125) in the syringe w/red cap: _____ mCi

   e. Assayed Activity of the Iotrex (I-125) in the syringe with needle: _____ mCi

   f. Assayed Residual Activity remaining in the syringe post afterload: _____ mCi

   g. Net Afterloaded Activity Infused into the GliaSite Balloon (5e – f): _____ mCi Time: _____

6) a. Initial Avg. Dose Rate Based on Pre-Treatment Plan Calculations Utilizing the Iotrex Calculation Booklet: _____ cGy/hour

   b. Actual Avg. Dose Rate Using "5g" as the Net Afterload Activity in the treatment plan calculations utilizing the Iotrex Calculation Booklet: _____ cGy/hour

7) a. Initial Dwell Time Based on pre-treatment plan calculations Utilizing the Iotrex Calculation Booklet: _____ hours

   b. Actual Dwell Time Using "5g" as the Net Afterload Activity in the treatment plan calculations utilizing the Iotrex Calculation Booklet: _____ hours

8) Thyroid blocked with what thyroid blocking agent: _____

9) If thyroid is not blocked, provide reason: _____

_____
Authorized Physician

_____
Date of Written Directive

_____
Date of Administration

Revised Dose Prescription: _____ **Gy** at a treatment distance of _____ cm from the inflated balloon surface

_____ _____

Authorized Physician Date

Reviewing Physicist's Signature: _____ Date: _____

Reviewing Physicist's Comments: _____

_____

VERIFICATION OF WRITTEN DIRECTIVE

Name: _____ **Patient ID No:** _____

Does the radiotherapy solution agree with that listed in the written directive? _____

Does the dosage (activity) agree with that ordered in the written directive? _____

Does the planned route of administration agree with the one identified in the written directive? _____

Assayed radiotherapy dosage: _____ mCi Date and Time of Assay: _____

Has the patient's thyroid been blocked with a thyroid blocking agent prior to therapeutic administration of the radiotherapy solution? _____

_____

Signature Title Date

VERIFICATION OF PATIENT IDENTITY

Name: _____ **Patient ID #:** _____ **Date:** _____

Before administering (afterloading) the prescribed radiotherapy dosage (activity), the authorized user shall verify the patients identity by verbally addressing the patient, and by at least one other confirmatory method selected from the following:

Physician addresses patient by name and the patient confirms. ☐

At least one of the below items must be checked off.

Date of Birth ☐

Address ☐

Social Security # ☐

Signature ☐

Name on patient's ID bracelet ☐

Name on patient's medical insurance card ☐

VERIFICATION OF RADIOACTIVE SOURCE AND BALLOON PLACEMENT

Is the information on the labeled syringe, i.e., the radiotherapy solution name, and either the patient's name or treatment procedure, consistent with the written directive? _____

Is the assayed radiotherapy dosage in agreement with the written directive? _____

Is the implanted balloon diameter in agreement with the written directive and has correct placement of the balloon into the resected cavity been verified by either radiographs or MR images? _____

_____ _____

Signature of Authorized User or qualified person Date of Administration

QUALITY MANAGEMENT PROGRAM
FOR
THERAPEUTIC ADMINISTRATION
OF ^{125}I RADIOTHERAPY SOLUTION (IOTREX®)
FOR INTRACAVITARY RADIATION THERAPY

This document is provided by Proxima Therapeutics, Inc. to hospitals using the GliaSite® RTS, and is intended for the explicit purpose of providing guidance for the preparation of a quality management program.

1. Written Directive

Prior to initiating radiation delivery using the ^{125}I radiotherapy solution (Iotrex®), a written directive shall be signed and dated by an Authorized User.

The Authorized User must be approved to administer radiation to patients and shall be listed on the facility's license or approved by the facility's Radiation Safety Committee. This treatment directive will be written for a specific patient.

If, in the authorized user's opinion, the patient may be harmed by delayed treatment, treatment may proceed on the basis of:

a) an *oral directive*, if documented immediately in the patient's record and a written directive is prepared within 24 hours of the oral directive;

b) an *oral modification to a written directive*, if documented immediately in the patient's record and a revised written directive is signed and dated by an authorized user within 48 hours of the oral directive.

A written modification to an existing written directive may be made provided the revision is dated and signed by an authorized user prior to completion of the existing brachytherapy dose prescription.

2. Verification of Patient Identity

Before administering (afterloading) the prescribed radiotherapy dosage (activity), the authorized user shall verbally ask the patient his or her name and confirm the response against the patient name on the written directive. The patient's name will be verified by at least two means before the ^{125}I radiotherapy solution (Iotrex®) is loaded.

3. Verification of Written Directive by Administering Physician/Physicist/Nuclear Medicine Tech

The authorized user must verify, before administering (afterloading) the prescribed radiotherapy dosage (activity), that the details of the administration (afterloading) are in accordance with the written directive. Specifically, the radiotherapy solution, dosage (activity), and route of administration should be confirmed by the person administering (afterloading) the radiotherapy solution to verify agreement with the written directive; that is, the dosage (activity) should be measured in the dose calibrator and the results compared with the prescribed radiotherapy dosage (activity) in the written directive.

4. Seek Guidance

All personnel involved in delivery of the brachytherapy dose shall seek guidance if they do not understand how to carry out the written directive. Workers having any question or confusion about specific details of the treatment shall not administer the dosage until the question is resolved.

5. Radioactive Source Verification

The authorized user, or a qualified person under the supervision of the authorized user, shall ensure that the treatment plan is in agreement with the signed written directive. Specifically, verify that the radiotherapy solution, dosage, and balloon size/volume are in agreement with the written directive before infusing the radiotherapy solution.

6. Verification of Balloon Placement in Resected cavity

After implantation of the GliaSite catheter and before administration (afterloading) of the radiotherapy dosage (activity), a dilute solution of a non-ionic contrast agent must be used to inflate the balloon to its desired fill volume as determined by a physician. Radiographs or MR images shall be taken to verify that correct placement of the balloon into the resected cavity has been achieved.

7. Recording Actual Activity Used and Dose

As soon as practical after administration (afterloading) of the radiotherapy dosage (activity), the authorized user shall record the actual activity infused (the net activity in the GliaSite balloon, taking into consideration residual activity in the afterloading syringe), the corresponding dose rate, and the dwell time necessary to deliver the prescribed brachytherapy dose. This information shall be recorded in the patient's record and the authorized user shall sign or initial this record.

8. Dose Calculation Check

Before the brachytherapy treatment is completed, the authorized user or another qualified individual (preferably a person who did not perform the original calculations) shall check the dose calculations. Calculations should be checked for arithmetic errors, accurate transcription and use of all dosimetry data, and the proper use of nomograms and formulas. Computer calculations may also be checked by manually calculating dose to one key point. Additionally, all treatment planning systems must be thoroughly acceptance tested before using with patients. If, in the authorized user's opinion, delaying treatment may harm the patient, a second check of the calculations may be delayed up to within two working days prior to completion of the brachytherapy treatment.

9. Routine Review of Written Directive

All written directives will be reviewed by a qualified physicist. This review is indicated by the reviewing physicist signing or initialing in the assigned space at the bottom of the appropriate written directive. The physicist shall review the written directive for any unintended deviation.

10. Unintended Deviations from the Written Directive

If an unintended deviation from the written directive is found, the following shall occur as soon as is practical:

a. Recalculate doses to the patient if necessary.
b. Determine if any detriment to the patient has occurred.
c. Conduct a review of the event to determine a root cause for the deviation.
d. Determine if the current practice is appropriate.
e. Make changes as determined by c. and d. above.

11. Actions Taken When a Medical Event Is Found during Routine Written Directive Reviews.

All medical events will be thoroughly reviewed and corrective actions devised. In doing this, the hospital will: a) assemble the relevant facts including the cause, b) identify what, if any, corrective actions may be required to prevent recurrence, and c) retain a record, in an auditable form, for three years, of the relevant facts and what corrective action was taken.

12. Annual Review

On an annual basis, random selection of brachytherapy treatments shall be reviewed. The patient records for the preceding year shall be reviewed for conformance of the given treatments to the corresponding written directives. A written summary of this review shall be transmitted to the Radiation Safety Committee.

13. Effectiveness of the QMP

The effectiveness of the QMP will be based on the following:

a. Trends in the number of medical events.
b. Trends in the type of records errors
c. Trends in the number of records errors
d. Unintended deviations from the written directive

Modifications to the underlying programs will be made based on root cause analysis of the event or error being considered. All suggested modifications will be submitted to the Radiation Oncologist and Medical Physicist in the form of an audit report. Final implementation will be determined by the Radiation Oncologist, the Medical Physicist and the Radiation Safety Officer.

14. Modifications to the Quality Management Program

Modifications made to the QMP will be submitted to the appropriate regulatory body within 30 days after the modification has been implemented.

15. Records Retention

All written directives will be retained for a minimum of 3 years after the date of administration. All QMP reviews will be retained for a minimum of 3 years after the date they are reviewed by the Radiation Safety Committee. All records will be maintained in an auditable form.

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Boone Hospital Center

L. Myers, R.S.O.

BJC HealthCare™

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