PUBLIC SUBMISSION

As of: 1/30/19 1:18 PM
Received: January 29, 2019
Status: Pending_Post
Tracking No. 1k3-97yp-yj8x
Comments Due: January 29, 2019
Submission Type: Web

Docket: NRC-2018-0230
Training and Experience Requirements for Different Categories of Radiopharmaceuticals

Comment On: NRC-2018-0230-0001
Training and Experience Requirements for Different Categories of Radiopharmaceuticals

Document: NRC-2018-0230-DRAFT-0133
Comment on FR Doc # 2018-23521

Submitter Information

Name: Al DeJesus

General Comment

Please see enclosed comment from Spectrum Pharmaceuticals.

Attachments

Spectrum Pharmaceuticals

SPECTRUM™
PHARMACEUTICALS
Redefining Cancer Care

January 29, 2019

Chairman Kristine L. Svinicki
U.S. Nuclear Regulatory Commission
Mail Stop O-16G4
Washington, DC 20555-0001

Re: Alpha- and Beta-Emitter Training and Experience Requirements

Dear Chairman Svinicki:

I am writing to follow up on past discussions and the most recent request from the Nuclear Regulatory Commission's (NRC's) for comments on the T&E requirements for the administration of therapeutic radiopharmaceuticals. As we have previously discussed, Spectrum Pharmaceuticals manufactures the biological product Zevalin® (ibritumomab tiuxetan) for non-Hodgkin's lymphoma, which has been approved by the Food and Drug Administration (FDA) and is also regulated by the NRC as a beta-emitter therapeutic radiopharmaceutical. We appreciate the time and attention that NRC and the ACMUI have devoted to the review of the appropriate training and experience requirements for Authorized Users (AUs). However, we are concerned that cancer patients are being denied access to an effective therapy because there a lack of a viable pathway for hematologists and oncologists to administer patient-ready doses of alpha- and beta-emitters to the cancer patients are in need. The current 700-hour "one size fits all" approach does not fit and is not well-suited to patient-ready doses of alpha- and beta-emitters. The current pathways for obtaining Authorized User status are neither reasonable nor access accessible for a majority of oncologists. Non-Hodgkin's lymphoma affects 72,400 people annually and accounts for about 4% of all cancers in the United States. I am of the opinion that therapeutic radiopharmaceuticals are highly under utilized in treatment due to the level of training required to become an Authorized User. Unfortunately, this has a disparate impact on rural cancer patients that are left untreated or receive less that optimal care due to a lack of access of created by these regulations due to a lacking of an Authorized Users within a reasonable distance.

Previously, as the Society of Nuclear Medicine and Molecular Imaging (SNMMI) noted in its January 24, 2017 letter to the NRC, the 700- hour requirement allows for the coverage of subjects including imaging and diagnostic radiology, which SNMMI believes appropriate for an authorization covering "all parenterals now and in the future." This comment demonstrates that the 700-hour requirement encompasses subjects which are in no way needed for the administration of patient-ready doses of alpha- and beta-emitters prepared at a licensed radiopharmacy. Rather than a broad authorization that seeks to cover many types, a tiered-based approach tailoring the training and experience requirements to the level of safety risk and complexity of administration would be more appropriate.

11500 South Eastern Ave. • Suite 240 • Henderson, NV 89052 • Tel: 702.835.6300 • Fax: 702.260.7405
www.sppirx.com • NASDAQ: SPPI

Current Regulatory Requirements Are Not Commensurate with Safety Profile

Spectrum first notified the NRC in 2011 of the overly broad requirement of 700 hours of training and experience for the administration of patient-ready dose therapies. Stakeholders throughout the current rulemaking process have advocated for a change to the training and experience requirements for the administration of patient-ready doses of alpha- and beta-emitters, which overly burdensome requirements are not commensurate with the safety profile of Zevalin and other patient-ready dose therapies. Spectrum and other stakeholders specifically recommended that the NRC reduce the 700-hour requirement framework as part of the current rulemaking.

As testified to by experienced training educators at prior ACMUI meetings, the current 700 hours of training and experience requirements for the administration of patient-ready doses of alpha and beta-emitter anti-cancer therapies are overly burdensome and not currently aligned with safety precautions needed to administer these doses. The doses are prepared for the individual patient at a licensed radiopharmacy and delivered to the physician on the day of administration in a pre-filled syringe. Unlike other radiolabeled products regulated under the same subpart of the regulations, patient-ready doses of alpha- and beta-emitters do not require mixing or direct handling of radioactive isotopes by the administering physician. NRC and ACMUI have acknowledged that alpha- and beta-emitters have an "exceptional" safety record for administration, and have had no effect of adverse affects on patients or risk to public health.

NRC Should Propose a New Tiered-Based Framework

A broad cross-section of stakeholders agrees that the current training and experience requirements for alpha- and beta-emitters far exceed the levels needed to ensure safety. The regulations requiring 700 hours of training and experience are outdated, and do not recognize that patient-ready doses are prepared by licensed radiopharmacies and delivered to the physician as a pre-filled syringe on the day the treatment is administered. This point was made clear when neither the NRC nor the ACMUI were able to demonstrate why the training and experience requirements for AU certification to administer patient-ready doses of alpha- and beta-emitters need to be 700 hours. In point of fact, no one has been able to document how the 700-hour threshold was established as a requirement in the first instance. Additionally, there have been no safety incidents with the AUs who became authorized under the previous 80-hour training and experience requirements have been administering alpha- and beta-emitters for years.

There is a growing recognition that a competency-based framework is better suited to assessing training and experience than a strict hours-based requirement. At its October 2016 meeting, the ACMUI heard from leading academic experts in the field of radiation safety education and training, who presented this view.

Recommendations

As was testified to at the October 2016 ACMUI meeting, the issue impacts other alpha and beta-emitters beyond Zevalin. There are numerous alpha- and beta-emitter products in the pipeline. The success of these products in development and innovation for new products is jeopardized by

the 700-hour training and experience requirement limiting which physicians can administer the products.

Our specific recommendations are as follows:

1. **NRC Staff Should Develop Competency-Based Training & Experience Framework**

We appreciate that a subcommittee has been established under the ACMUI to re-evaluate training and experience for all modalities with a focus on competencies. While this is a positive step, it is likely that this process will be lengthy, and the new framework could not be implemented without another full rulemaking process. Because of the negative impact that the current training and experience regulations have on patient access to patient-ready doses of alpha- and beta-emitting radiopharmaceuticals, we recommend that the NRC present to the ACMUI a tiered framework to evaluate the specific category of patient-ready doses of alpha- and beta-emitters first among modalities. The tiered approach should link the safety profile and complexity of administration of the radioimmunotherapy with the appropriate level of training and experience required to administer the therapy safely. This framework should be based closely on the competencies required to administer patient ready doses of these radionuclides.

The NRC could lay out a process and timeline in its current Final Rule by which the Commission staff will develop this framework. This approach would be well within the scope of the ongoing rulemaking.

2. **NRC Staff Should Develop Guidance on Interpretation of Training & Experience Requirements**

The current 700-hour pathway is essentially a bar on practicing medical oncologists and hematologists becoming AUs, as evidenced by the fact that nobody has ever been certified as an AU through the 700-hour pathway. Because the need to address this issue is imminent for cancer patients, we recommend that the NRC take interim steps to make it possible for medical oncologists and hematologists to become AUs under the existing regulatory framework. Specifically, the NRC should issue guidance providing for the application of the training and experience requirements set out in the current regulations at 10 C.F.R. § 35.390 in a manner that reflects the competencies needed to administer alpha- and beta-emitters in patient-ready doses.

Clinicians such as Dr. Jennifer Cultrera of Florida Cancer Specialists, who has presented to the ACMUI about her considerable experience in radioimmunotherapy and the impossibility of becoming an AU under the current training and experience requirements, should be afforded a pathway to demonstrate that they have training and experience equivalent to that which the regulations require. Applying the existing training and experience requirements in a manner focused on patient-ready doses as an interim measure would allow Dr. Cultrera and other experienced clinicians to administer Zevalin and other patient-ready therapies. This guidance would also help to assist the Agreement States in applying their own regulations to patient-ready doses, which are based upon the NRC regulations.

3. **NRC Should Modify Training & Experience Requirements for Patient-Ready Doses of Alpha- and Beta-Emitters Through Rulemaking**

We recommend that once the tiered competency based requirements are set, NRC should undertake an expedited rulemaking and promulgate those changes without further delay. We feel that that NRC should recognize the T&E requirements as imposed by other regulatory and licensing bodies as sufficient. We respectfully request that the Commission make this a high priority.

*****

In conclusion, we believe that there is no justification for the 700-hour training and experience requirement for the administration of alpha- and beta-emitter patient-ready doses. The NRC has the regulatory authority to modify these outdated requirements and needs to act now.

Thank you for your ongoing attention to this issue.

Sincerely,

Francois Lebel, MD, FRCPC
Chief Medical Officer
Spectrum Pharmaceuticals, Inc.

11500 South Eastern Ave. • Suite 240 • Henderson, NV 89052 • Tel: 702.835.6300 • Fax: 702.260.7405
www.sppirx.com • NASDAQ: SPPI