UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

December 9, 2022

ALL AGREEMENT STATES, CONNECTICUT, INDIANA

NOTIFICATION OF ISSUANCE OF REVISION OF LICENSING OF LUTETIUM-177 (STC-22-074)

Purpose: To inform Agreement States of the U.S. Nuclear Regulatory Commission (NRC) Lutetium-177 (Lu-177) PLUVICTO™ licensing decision and revision of 2018 memorandum transmitted via STC-18-042.

Background: On March 23, 2022, the Food and Drug Administration (FDA) approved lutetium-177 (Lu-177) vipivotide tetraxetan (PLUVICTO™) radiopharmaceutical for the treatment of prostate-specific membrane antigen positive metastatic castration-resistant prostate cancer. Similarly, the FDA approved Lu-177 dotatate (LUTATHERA®) radiopharmaceutical for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) on January 26, 2018. The NRC staff reviewed the use of PLUVICTO™ and found that all radiation safety considerations within the 2018 memorandum (Agencywide Documents Access and Management System Accession No. ML18136A824) and STC-18-042, dated June 21, 2018, apply to PLUVICTO™.

Lu-177 has a half-life of 6.7 days. Lu-177 beta emissions have a short penetration radius, which makes it suitable for radioimmunotherapy. Lu-177 has both gamma and beta emissions, allowing for the acquisition of images incidental to the intended therapeutic treatment. LUTATHERA® and PLUVICTO™, both Lu-177 radioimmunotherapy radiopharmaceuticals are delivered in a similar manner as other beta-emitting therapy parenteral administrations.

Discussion: The NRC staff reviewed radiation safety and regulatory aspects (e.g., radionuclide and progeny emissions, radiation detection, monitoring and measurements, authorized user training and experience needs, patient administration and release considerations, dose delivery, and handling and waste disposal) of medical uses of Lu-177 radioimmunotherapy radiopharmaceuticals (i.e., LUTATHERA® and PLUVICTO™) and determined that applicable licensing provisions are within Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, Subpart E, “Unsealed Byproduct Material – Written Directive Required.”

The NRC staff concluded that physicians approved for the use of any beta emitter or any photon-emitting radionuclide with a photon energy less than 150 keV under 10 CFR 35.390, “Training for use of unsealed byproduct material for which a written directive is required” may also be authorized for the medical use of Lu-177. Additionally, physicians authorized under 10 CFR 35.396, “Training for the parenteral administration of unsealed byproduct material requiring a written directive,” may also be authorized for the medical use of Lu-177.

The NRC staff evaluated waste and storage issues when handling Lu-177, LUTATHERA® and PLUVICTO™. Lu-177 waste may be decayed in storage under the performance-based rule in 10 CFR 35.92, “Decay-in-storage.” Small quantities of metastable Lu-177 (Lu-177m), with a half-life of 161 days, may be present as a contaminant generated from the production of Lu-177.

If present, Lu-177m may contribute approximately 0.02 percent of the total amount of Lu-177. Lu-177m emits low-energy photons and beta emissions that, even in low quantities, are detectable using standard scintillator detectors and Geiger counters. If Lu-177m is detected by survey methods, then it must be disposed as low-level radioactive waste in accordance with the requirements in 10 CFR Part 20 Subpart K, “Waste Disposal.” Furthermore, the licensee would need to develop safe handling and disposal procedures for detectable quantities of Lu-177m.

Additional radiation safety considerations for Lu-177 can be found using NRC’s Agencywide Documents Access and Management System Accession No. ML22318A150. If the NRC becomes aware of future developments related to the production, distribution, or medical uses of Lu-177 radiopharmaceuticals that may negatively impact radiation safety, the NRC staff will consider revisiting this licensing decision.

POINT OF CONTACT: Kenneth Brenneman EMAIL: ken.brenneman@nrc.gov
TELEPHONE: (301) 415-4094

Johnson, Robert signing on behalf of Anderson, Brian on 12/09/22

Brian C. Anderson, Chief
State Agreement and Liaison Programs Branch
Division of Materials Safety, Security, State and Tribal Programs
Office of Nuclear Material Safety and Safeguards

STC-22-074 - NOTIFICATION OF ISSUANCE OF REVISION OF LICENSING OF LUTETIUM-177 DATE December 9, 2022

ADAMS Accession No.: ML22318A151

OFFICE	NMSS/MSST/MSEB	NMSS/MSST	NMSS/MSST /MSEB	NMSS/MSST/SALB
NAME	KBrenneman *KB*	CValentin-Rodriguez *CV*	CEinberg *CE*	BAnderson RJohnson for *RJ*
DATE	Nov 15, 2022	Nov 16, 2022	Dec 8, 2022	Dec 9, 2022

OFFICIAL RECORD COPY