Drug Policy:
Radiopharmaceuticals

POLICY NUMBER UM ONC_1515	**SUBJECT** Radiopharmaceuticals: Azedra (iobenguane I-131), Lutathera (lutetium Lu 177 dotatate), Pluvicto (lutetium Lu 177 vipivotide tetraxetan), Xofigo (radium Ra 223 dichloride), Zevalin (ibritumomab tiuxetan)	**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 5**
DATES COMMITTEE REVIEWED 12/12/24	**APPROVAL DATE** December 12, 2024	**EFFECTIVE DATE** December 27, 2024	**COMMITTEE APPROVAL DATES** 12/12/24
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Evolent Specialty Services Clinical Guideline Review Committee	
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**	**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

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I. PURPOSE

To define and describe the accepted indications for Radiopharmaceuticals [Azedra (iobenguane I-131), Lutathera (lutetium Lu 177 dotatate), Pluvicto (lutetium Lu 177 vipivotide tetraxetan), Xofigo (radium Ra 223 dichloride), Zevalin (ibritumomab tiuxetan)] usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical

Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The member has not experienced disease progression on the requested medication AND
2. The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
3. Additional medication(s) are not being added to the continuation request.

B. Gastrointestinal and pancreatic neuroendocrine tumors (GEP-NET)

1. Lutathera (lutetium Lu 177 dotatate) may be used in pediatric and adult members 12 years of age and older who have metastatic, locally advanced, or unresectable gastrointestinal OR pancreatic neuroendocrine tumors (GEP-NET), AND have the confirmed presence of somatostatin receptors on metastatic lesions documented by peptide receptor scintigraphy e.g., Ga-DOTA scan or similar test
2. Lutathera (lutetium Lu 177 dotatate) may be used in members who have previously received Octreotide LAR and/or Lanreotide and experienced disease progression on either of the above agents.

C. Non-Hodgkin's Lymphoma (NHL)

1. NOTE: Zevalin (ibritumomab tiuxetan) is not supported by Evolent Policy for the treatment of relapsed or refractory Follicular Lymphoma, primary cutaneous diffuse large B-cell lymphoma leg type, Nodal Marginal Zone Lymphoma, Splenic Marginal Zone Lymphoma, Gastric and Non-gastric MALT Lymphoma. This policy position is based on the lack of Level 1 Evidence (randomized clinical trials and/or meta-analyses) to show superior outcomes compared to Evolent recommended alternative agents/regimens available at: https://www.evolent.com/pathways.

D. Pheochromocytoma/Paraganglioma

1. Azedra (iobenguane I-131) may be used in adult or pediatric members 12 years of age and older who have unresectable, locally advanced, or metastatic pheochromocytoma or paraganglioma AND
2. Azedra (iobenguane I-131) is being used as a primary treatment for members with a positive MIBG (meta-iodobenzylguanidine) scan.

E. Prostate Cancer

1. Pluvicto (lutetium Lu 177 vipivotide tetraxetan) may be used as monotherapy in members with prostate-specific membrane antigen (PSMA) positive (confirmed on a PSMA PET/CT scan) metastatic castration-resistant prostate cancer following disease progression on or after 2 prior lines of therapy including an Androgen Receptor Pathway Inhibitor (e.g., enzalutamide, abiraterone) AND a taxane-based chemotherapy (e.g., docetaxel).
2. Xofigo (radium Ra 223 dichloride) may be used in members with metastatic castrate-resistant prostate cancer who have symptomatic bone metastases (e.g., bone pain) and do not have visceral metastases.

3. Xofigo (radium Ra 223 dichloride) must not be combined with Zytiga (abiraterone) as detrimental outcomes have been noted in studies.

III. EXCLUSION CRITERIA

A. Disease progression while taking any one of the aforementioned Radiopharmaceuticals [Azedra (iobenguane I-131), Lutathera (lutetium Lu 177 dotatate), Pluvicto (lutetium Lu 177 vipivotide tetraxetan), Xofigo (radium Ra 223 dichloride), Zevalin (ibritumomab tiuxetan)].

B. For Azedra (iobenguane I-131), the member has a platelet count less than 80,000/mcL or absolute neutrophil count less than 1,200/mcL

C. For Xofigo (radium Ra 223 dichloride):
   a. Use of Xofigo (radium Ra 223 dichloride) with Zytiga (abiraterone) is contraindicated
   b. Concurrent use with other radioisotope or cytotoxic chemotherapy
   c. The presence of visceral metastatic disease

D. For Zevalin (ibritumomab tiuxetan), prior radioimmunotherapy or myeloablative therapy with autologous bone marrow transplant

E. Dosing exceeds single dose limit of:
   a. Azedra (iobenguane I-131)
      i. Weight greater than 62.5 kg: 18,500 Megabecquerel (MBq) (500 Millicuries (mCi) for a total of 2 doses
      ii. Weight 62.5 kg or less: 296 MBq/kg (8 mCi/kg) for a total of 2 doses
   b. Lutathera (lutetium Lu 177 dotatate) 7.4 GBq (200 mCi)
   c. Pluvicto (lutetium Lu 177 vipivotide tetraxetan) 7.4 GBq (200 mCi).
      i. Treatment exceeds the maximum duration limit of 36 weeks (or up to 6 doses).
   d. Xofigo (radium Ra 223 dichloride) 55 kBq/kg (1.49 microcurie/kg)
      i. Treatment exceeds the maximum duration limit of 6 cycles.
   e. Zevalin (ibritumomab tiuxetan) 32 mCI of Zevalin
      i. Treatment duration exceeds a single course of treatment

F. Investigational use of Radiopharmaceuticals [Azedra (iobenguane I-131), Lutathera (lutetium Lu 177 dotatate), Pluvicto (lutetium Lu 177 vipivotide tetraxetan), Xofigo (radium Ra 223 dichloride), Zevalin (ibritumomab tiuxetan)] with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
   1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
   2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
   3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by

ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.

4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. CODING INFORMATION

HCPCS Code	Description
A9590	Iodine i-131, iobenguane, 1 millicurie
A9513	Lutetium lu 177, dotatate, therapeutic, 1 millicurie
A9607	Lutetium lu 177 vipivotide tetraxetan, therapeutic, 1 millicurie
A9606	Radium ra-223 dichloride, therapeutic, per microcurie
A9543	Yttrium y-90 ibritumomab tiuxetan, therapeutic, per treatment dose, up to 40 millicuries

V. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

VI. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VII. ATTACHMENTS

A. None

VIII. REFERENCES

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C. Pluvicto prescribing information 2022. Advanced Accelerator Applications USA, Inc. Millburn, NJ

D. Xofigo prescribing information 2019. Bayer Healthcare pharmaceuticals, Whippany, New Jersey

E. Zevalin prescribing information 2023. Acrotech Biopharma LLC East Windsor, NJ

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Q. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.

R. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

S. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.