Evolent Clinical Guideline 3104 for Radiopharmaceuticals

Guideline Number: Evolent_CG_3104	**Applicable Codes**	
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STATEMENT

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.

INDICATIONS

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

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

Gastrointestinal and pancreatic neuroendocrine tumors (GEP-NET)

- 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.
- 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.

Non-Hodgkin’s Lymphoma (NHL)

- 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 **Evolent Pathways**.

Pheochromocytoma/Paraganglioma

- 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
- Azedra (iobenguane I-131) is being used as a primary treatment for members with a positive MIBG (meta-iodobenzylguanidine) scan.

Prostate Cancer

- Pluvicto (lutetium Lu 177 vipivotide tetraxetan) may be used as monotherapy in adult members with prostate-specific membrane antigen (PSMA) positive (confirmed on a PSMA PET/CT scan) metastatic castration-resistant prostate cancer who have been treated with an Androgen Receptor Pathway Inhibitor (e.g., enzalutamide, abiraterone) AND:
    - are considered appropriate to delay taxane-based chemotherapy (e.g., docetaxel), or
    - have received prior taxane-based chemotherapy.
- 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.
- Xofigo (radium Ra 223 dichloride) must not be combined with Zytiga (abiraterone) as detrimental outcomes have been noted in studies.

CONTRAINDICATIONS/WARNINGS

- Contraindications
    - None
- US Boxed Warning
    - Ibritumomab tiuxetan
        - Serious infusion reaction
            - Deaths have occurred within 24 hours of rituximab infusion, an essential component of the ibritumomab tiuxetan therapeutic regimen. These fatalities were associated with hypoxia, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, or cardiogenic shock. Most (80%) fatalities occurred with the first rituximab infusion. Discontinue rituximab and ibritumomab tiuxetan infusions in patients who develop severe infusion reactions.

- Ibritumomab tiuxetan administration results in severe and prolonged cytopenias in most patients. Do not administer the ibritumomab tiuxetan therapeutic regimen to patients with ≥25% lymphoma marrow involvement and/or impaired bone marrow reserve.
- Severe cutaneous and mucocutaneous reactions, some fatal, can occur with the ibritumomab tiuxetan therapeutic regimen. Discontinue rituximab and ibritumomab tiuxetan infusions in patients experiencing severe cutaneous or mucocutaneous reactions.
- The dose of ibritumomab tiuxetan should not exceed 32 mCi (1,184 MBq).

EXCLUSION CRITERIA

- 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)].
- 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
- For Xofigo (radium Ra 223 dichloride):
  - Use of Xofigo (radium Ra 223 dichloride) with Zytiga (abiraterone) is contraindicated
  - Concurrent use with other radioisotope or cytotoxic chemotherapy
  - The presence of visceral metastatic disease
- For Zevalin (ibritumomab tiuxetan):
  - Prior radioimmunotherapy or myeloablative therapy with autologous bone marrow transplant
  - The member has a platelet count less than 100,000/mcL
- Dosing exceeds single dose limit of:
  - Azedra (iobenguane I-131)
    - Weight greater than 62.5 kg: 18,500 Megabecquerel (MBq) (500 Millicuries (mCi) for a total of 2 doses
    - Weight 62.5 kg or less: 296 MBq/kg (8 mCi/kg) for a total of 2 doses
  - Lutathera (lutetium Lu 177 dotatate) 7.4 GBq (200 mCi) for a total of 4 doses
  - Pluvicto (lutetium Lu 177 vipivotide tetraxetan) 7.4 GBq (200 mCi).
    - Treatment exceeds the maximum duration limit of 36 weeks (or up to 6 doses).
  - Xofigo (radium Ra 223 dichloride) 55 kBq/kg (1.49 microcurie/kg)
    - Treatment exceeds the maximum duration limit of 6 cycles.
  - Zevalin (ibritumomab tiuxetan) 32 mCi (1184 MBq)

        - Treatment duration exceeds a single course of treatment.
- 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:
    - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    - 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.
    - 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).
    - 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.
    - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
    - 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.

CODING AND STANDARDS

Codes

- 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

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
May 2026	• Added total number of doses for Lutathera (lutetium Lu 177 dotatate) under exclusion criteria • Updated exclusion criteria details for Zevalin (ibritumomab tiuxetan) • Updated references
May 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1515 Radiopharmaceuticals • Updated prostate cancer indication for Pluvicto (lutetium Lu 177 vipivotide tetraxetan) • Updated references
December 2024	• New policy - consolidated five radiopharmaceutical policies [Azedra (iobenguane I-131), Lutathera (lutetium Lu 177 dotatate), Pluvicto (lutetium Lu 177 vipivotide tetraxetan), Xofigo (radium Ra 223 dichloride), Zevalin (ibritumomab tiuxetan)] into one policy

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

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