Corporate Medical Policy: Therapeutic Radiopharmaceuticals in Oncology **"Notification"** **POLICY EFFECTIVE JULY 1, 2026**

Restricted Product(s):

- lutetium Lu 177 dotatate (Lutathera®) intravenous infusion for administration by a healthcare professional
- lutetium Lu 177 vipivotide tetraxetan (Pluvicto®) intravenous injection or infusion for administration by a healthcare professional
- radium Ra 223 dichloride (Xofigo®) intravenous injection for administration by a healthcare professional

FDA Approved Use:

- Lutetium Lu 177 dotatate (Lutathera®)
  - For the treatment of adult and pediatric patients 12 years and older with somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors
- Lutetium Lu 177 vipivotide tetraxetan (Pluvicto®)
  - For the treatment of adults with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibitor (ARPI) therapy, and
    - are considered appropriate to delay taxane-based chemotherapy, or
    - have received prior taxane-based chemotherapy
- Radium Ra 223 dichloride (Xofigo®)
  - For the treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases, and no known visceral metastatic disease

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The request is for **Lutathera**; **AND**
   a. The patient is 12 years of age or older; **AND**
   b. The patient has a diagnosis of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs) (e.g., including those arising from the foregut [gastroduodenal], midgut [distal small intestine and proximal colon], hindgut [distal colorectal], and pancreas) or somatostatin receptor-positive bronchopulmonary or thymus neuroendocrine tumors; **AND**
   c. The patient has unresectable, locally advanced, or metastatic disease; **AND**
   d. The patient has documented over-expression of somatostatin receptors by the target lesions, as determined by an appropriate imaging study **[medical record documentation required]**; **AND**

e. The patient has well-differentiated disease with a Ki-67 index of 20% or less, as documented in a pathology report[1] **[medical record documentation required]**; **AND**
f. ONE of the following:
    i. The patient has had disease progression despite somatostatin analog therapy (e.g., octreotide long-acting release [LAR] or lanreotide) or molecularly targeted therapy (e.g., everolimus) **[medical record documentation required]**; **OR**
    ii. The patient has well-differentiated gastrointestinal or pancreatic NETs and BOTH of the following **[medical record documentation required]**:
        1. The patient has well-differentiated disease with a Ki-67 index of 10% to 20%, as documented in a pathology report; **AND**
        2. The patient has clinically significant tumor burden; **AND**
g. The patient will NOT be using the requested agent for treatment of pheochromocytomas or paragangliomas; **AND**
h. The patient will NOT receive more than 4 doses (one treatment course) total during a patient's lifetime; **OR**

[1]Well-differentiated neuroendocrine tumors include low-grade (G1) and intermediate-grade (G2) tumors, which correlate with a defined Ki-67 proliferation index, as determined by an immunohistochemical stain. Well-differentiated, low grade neuroendocrine tumors have a Ki-67 index of less than 3%, and well-differentiated, intermediate-grade neuroendocrine tumors have a Ki-67 index of 3-20%.

2. The request is for **Pluvicto**; **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The patient has a diagnosis of prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer; **AND**
    c. The patient has unresectable metastatic disease; **AND**
    d. The patient has at least one PSMA-positive lesion and/or predominantly PSMA-positive disease with no dominant PSMA-negative metastatic lesions, as determined by a gallium-68-labeled PSMA-11 positron emission tomographic-computed tomographic (PET/CT) scan **[medical record documentation required]**; **AND**
    e. The patient has had disease progression despite advanced androgen therapy with at least one androgen receptor pathway inhibitor (e.g., abiraterone [Zytiga, etc.], apalutamide [Erleada], darolutamide [Nubeqa], enzalutamide [Xtandi]), as demonstrated by prostate specific antigen (PSA) progression after at least 4 weeks **[medical record documentation required]**; **AND**
    f. ONE of the following **[medical record documentation required]**:
        i. The patient has had disease progression after at least one taxane-based chemotherapy regimen (e.g., docetaxel, cabazitaxel); **OR**
        ii. The patient is considered appropriate to delay taxane-based chemotherapy; **AND**

g. The patient has had a bilateral orchiectomy OR will be using the requested agent in combination with a luteinizing hormone-releasing hormone (LHRH) agonist (e.g., goserelin [Zoladex], leuprolide [Camcevi, Eligard, Lupron Depot], triptorelin [Trelstar]) or antagonist (e.g., degarelix [Firmagon], relugolix [Orgovyx]) **[medical record documentation required]**; **AND**
h. The patient will NOT receive more than 6 doses (one treatment course) total during a patient's lifetime; **OR**

3. The request is for **Xofigo**; **AND**
   a. The patient is 18 years of age or older; **AND**
   b. The patient has a diagnosis of castration-resistant prostate cancer; **AND**
   c. The patient has symptomatic bone metastases; **AND**
   d. The patient does NOT have any known visceral metastatic disease; **AND**
   e. The patient has had a bilateral orchiectomy OR will be using the requested agent in combination with a luteinizing hormone-releasing hormone (LHRH) agonist (e.g., goserelin [Zoladex], leuprolide [Camcevi, Eligard, Lupron Depot], triptorelin [Trelstar]) or antagonist (e.g., degarelix [Firmagon], relugolix [Orgovyx]) **[medical record documentation required]**; **AND**
      i. The patient has had disease progression despite castrate levels of serum testosterone less than 50 ng/dL **[medical record documentation required]**; **AND**
   f. The requested agent will NOT be used in combination with abiraterone (e.g., Zytiga, etc.) plus prednisone/prednisolone, cytotoxic chemotherapy (e.g., docetaxel, cabazitaxel), other systemic radioisotopes, or hemibody external radiotherapy (NOTE: use in combination with androgen deprivation therapy and denosumab or zoledronic acid is permitted); **AND**
   g. The patient will NOT receive more than 6 doses (one treatment course) total during a patient's lifetime; **OR**

4. The patient has an indication that is supported by ALL requirements in NCCN (National Comprehensive Cancer Network) 1 or 2A recommended use for the requested agent (i.e., the indication must be supported by ALL requirements in the NCCN "Recommended Use" box [e.g., performance status, disease severity, previous failures, monotherapy vs combination therapy]); **AND**

5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., oncologist, radiation oncologist, nuclear medicine physician) or has consulted with a specialist in the area of the patient's diagnosis; **AND**
6. The requested quantity (dose) and treatment duration are within FDA labeled dosing for the requested indication or NCCN 1 or 2A compendia supported dosing for the requested indication AND do not exceed the maximum units allowed for the duration of approval (see table below).

Duration of Approval: 365 days (1 year); one treatment course per lifetime
Lutathera: 4 doses per lifetime
Pluvicto: 6 doses per lifetime

Xofigo: 6 doses per lifetime

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
lutetium Lu 177 dotatate (Lutathera®) intravenous (IV) infusion	Somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in patients ≥ 12 years old	IV: 7.4 GBq (200 mCi) every 8 weeks (± 1 week) for a total of 4 doses Prior to treatment initiation: Discontinue long-acting somatostatin analogs (e.g., long-acting octreotide) at least 4 weeks prior to initiating treatment. Administer short-acting octreotide as needed, and discontinue at least 24 hours prior to initiating treatment. During treatment: Administer long-acting octreotide 30 mg intramuscularly (IM) between 4 to 24 hours after each dose. Do not administer long-acting octreotide within 4 weeks prior to each subsequent dose. Short-acting octreotide may be given for symptomatic management during treatment but must be withheld at least 24 hours before each dose. Following treatment: Continue long-acting octreotide 30 mg IM every 4 weeks after completing treatment until disease progression or for 18 months following treatment initiation at the discretion of the physician.	A9513	800 (4 doses per lifetime)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
lutetium Lu 177 vipivotide tetraxetan (Pluvicto®) intravenous (IV) injection or infusion	PSMA-positive metastatic castration-resistant prostate cancer in adults who have been treated with androgen receptor pathway inhibitor therapy, and have received prior taxane-based chemotherapy or are considered appropriate to delay taxane-based chemotherapy	IV: 7.4 GBq (200 mCi) every 6 weeks for up to 6 doses	A9607	1,200 (6 doses per lifetime)
radium Ra 223 dichloride (Xofigo®) intravenous (IV) injection	Castration-resistant prostate cancer in adults with symptomatic bone metastases and no known visceral metastatic disease	IV: 55 kBq (1.49 microcurie) per kg body weight every 4 weeks for 6 doses	A9606	894 (6 doses per lifetime)

***Maximum units allowed for duration of approval**

References: all information referenced is from FDA package insert unless otherwise noted below.

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2. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines). Neuroendocrine and Adrenal Tumors, Version 3.2025. Revised October 1, 2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Last accessed March 31, 2026.
3. Singh S, Halperin D, Myrehaug S, et al. [^{177}Lu]Lu-DOTA-TATE plus long-acting octreotide versus high-dose long-acting octreotide for the treatment of newly diagnosed, advanced grade 2-3, well-differentiated, gastroenteropancreatic neuroendocrine tumours (NETTER-2): an open-label, randomised, phase 3 study. *Lancet*. 2024 Jun 29;403(10446):2807-2817.
4. Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 trial of ^{177}Lu-dotatate for midgut neuroendocrine tumors. *N Engl J Med*. 2017 Jan 12;376(2):125-135.

5. Strosberg JR, Caplin ME, Kunz PL, et al. ^{177}Lu-Dotatate plus long-acting octreotide versus high-dose long-acting octreotide in patients with midgut neuroendocrine tumours (NETTER-1): final overall survival and long-term safety results from an open-label, randomised, controlled, phase 3 trial. *Lancet Oncol*. 2021 Dec;22(12):1752-1763. Erratum in: *Lancet Oncol*. 2022 Feb;23(2):e59.
6. Morris MJ, Castellano D, Herrmann K, et al. ^{177}Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naive patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): a phase 3, randomised, controlled trial. *Lancet*. 2024 Sep 28;404(10459):1227-1239. Erratum in: *Lancet*. 2025 Dec 21;404(10471):2542.
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8. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. *N Engl J Med*. 2021 Sep 16;385(12):1091-1103.
9. Sartor O, Castellano Gauna DE, Herrmann K, et al. LBA$_{13}$ Phase III trial of [^{177}Lu]Lu-PSMA-617 in taxane-naive patients with metastatic castration-resistant prostate cancer (PSMAfore). *Annals of Oncology*. 2023;34(Supplement 2):S1324-S1325.
10. Hoskin P, Sartor O, O'Sullivan JM, et al. Efficacy and safety of radium-223 dichloride in patients with castration-resistant prostate cancer and symptomatic bone metastases, with or without previous docetaxel use: a prespecified subgroup analysis from the randomised, double-blind, phase 3 ALSYMPCA trial. *Lancet Oncol*. 2014 Nov;15(12):1397-1406.
11. Parker C, Nilsson S, Heinrich D, et al. Alpha emitter radium-223 and survival in metastatic prostate cancer. *N Engl J Med*. 2013 Jul 18;369(3):213-223.
12. Sartor O, Coleman R, Nilsson S, et al. Effect of radium-223 dichloride on symptomatic skeletal events in patients with castration-resistant prostate cancer and bone metastases: results from a phase 3, double-blind, randomised trial. *Lancet Oncol*. 2014 Jun;15(7):738-746.
13. Smith M, Parker C, Saad F, et al. Addition of radium-223 to abiraterone acetate and prednisone or prednisolone in patients with castration-resistant prostate cancer and bone metastases (ERA 223): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2019 Mar;20(3):408-419.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q3 annually.

July 2026: Original medical policy criteria issued. Added Xofigo (radium Ra 223 dichloride) and associated criteria to policy for treatment of castration-resistant prostate cancer in patients with symptomatic bone metastases and no known visceral metastatic disease. For Lutathera, extended age to 12 years and older for treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs) according to FDA label. For Pluvicto, added requirement that the patient has had a bilateral orchiectomy or will be using the requested agent in combination with a LHRH agonist or antagonist. Added requirement to be prescribed by or in consultation with a specialist; added maximum units; medical policy formatting change. **Policy notification given 4/2/2026 for effective date 7/1/2026**. *Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.