# Medical Drug Clinical Criteria

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| **Subject:** | Xofigo (Radium Ra 223 Dichloride) | | |
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## Overview

This document addresses the use of radium Ra-223 dichloride (Xofigo) is an alpha particle-emitting radioactive therapeutic agent which mimics calcium to bind with bone minerals in areas of bone metastases primarily used to treat castration-resistant distant metastatic (M1) disease with symptomatic bone metastases and no visceral metastases.

The FDA approved indications for radium Ra-223 dichloride (Xofigo) include castration-resistant prostate cancer (CRPC), symptomatic bone metastases and no known visceral metastatic disease.

**Other Uses**

Radium Ra-223 dichloride has been investigated for other uses including treatment of osteosarcoma with relapse or progression after failure of chemotherapy and/or resection. While NCCN provides 2A recommendations for this off-label use, NCCN states that this is based on limited evidence in the form of a case report and review article. Currently there are ongoing phase I/II clinical trials evaluating use for breast cancer, breast cancer with bone metastases, osteosarcoma, and for use in combination with docetaxel for use in treatment of CRPC and bone metastases, but there currently is insufficient published literature to support safety and efficacy for these indications. UPDATE: NCCN Bone Cancer v1.2020 guidelines remove radium-223 as a regimen for second-line relapsed/refractory for metastatic osteosarcoma. UPDATE: NCCN Bone cancer guidelines added radium-223 as a regimen for relapsed or refractory disease beyond second-line therapy (useful in certain circumstances). The reference is a Subbiah et al. a phase I dose escalation trial. There is no discussion regarding the study within the NCCN Bone Cancer guidelines.

There are warnings for radium Ra-223 dichloride for myelosuppression and increase fractures and mortality when taken in combination with abiraterone plus prednisone or prednisolone. Radium Ra-223 dichloride is contraindicated in pregnancy.

**Definitions and Measures**

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 0 = Fully active, able to carry on all pre-disease performance without restriction
- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead

Gleason Grading system: A prostate cancer grading system. A primary and secondary pattern, the number range of each is from 1 to 5, are assigned and then summed to yield a total score.

Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.

Prostate: A gland in the male reproductive system; the small walnut sized structure which wraps around the urethra.

Radiotherapy: Systemic radiotherapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that travels in the blood to tissues throughout the body.

## Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

**Xofigo (radium Ra 223 dichloride)**

Requests for Xofigo (radium Ra-223 dichloride) may be approved if the following criteria are met (Label, NCCN Prostate Cancer Guideline):

I. Individual has a diagnosis of castration-resistant prostate cancer (CRPC) with symptomatic bone metastasis; **AND**
II. Individual is 18 years or older; **AND**
III. Individual has planned course of six monthly injections; **AND**
IV. Individual has a serum testosterone level is less than or equal to 50 ng per deciliter ([1.7 nmol per liter] after bilateral orchiectomy or during maintenance treatment consisting of androgen-ablation therapy with a luteinizing hormone-releasing hormone agonist or polyestradiol phosphate); **AND**
V. Individual has prostate-specific antigen (PSA) level is 5 ng per milliliter or higher with evidence of progressively increasing PSA values (two consecutive increases over the previous reference value) or objective evidence of progression of osseous metastases on imaging studies at time of initiation of Radium Ra 223 dichloride; **AND**
VI. Individual is using in combination with denosumab or zoledronic acid (NCCN Prostate Cancer Guidelines V4.2023); **AND**
VII. No known history or presence of visceral metastatic disease; **AND**
VIII. Individual does not have bulky lymph node metastases (>3-4 cm); **AND**
IX. Eastern Cooperative Oncology Group (ECOG) performance-status score of 0 to 2; **AND**
X. Individual will not use concurrently with other chemotherapy or biologic therapy (**Note:** this does not include androgen-ablation therapy or other hormonal therapy) for prostate cancer.

Requests for Xofigo (radium Ra-223 dichloride) may not be approved for the following (Label, NCCN Prostate Cancer Guideline):

I. Individual has imminent or established spinal cord compression; **OR**
II. Used in combination with Zytiga (abiraterone acetate) plus prednisone/prednisolone; **OR**
III. Individual has received systemic radiotherapy with radioisotopes within the previous 24 weeks; **OR**
IV. Individual was treated with chemotherapy or biologic therapy within the previous 4 weeks; **OR**
V. Used in combination with docetaxel or any other systemic therapy except androgen deprivation therapy (ADT); **OR**
VI. Individual has received a previous course of Radium Ra 223 dichloride; **OR**
VII. Individual being treated for a diagnosis other than CRPC; **OR**
VIII. When the above criteria are not met and for all other indications.

## Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

**HCPCS**

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| A9606 | Radium Ra-223 dichloride, therapeutic, per microcurie [Xofigo] |

**CPT**

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| 79101 | Radiopharmaceutical therapy, by intravenous administration [when specified as injection of Xofigo] |

**ICD-10 Diagnosis**

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| C61 | Malignant neoplasm of prostate |
| C79.51 | Secondary malignant neoplasm of bone |
| R97.21 | Rising PSA following treatment for malignant neoplasm of prostate |
| Z19.2 | Hormone resistant malignancy status |

## Document History

Revised: 02/21/2025
Document History:

- 02/21/2025 – Annual Review: No Changes. Coding Reviewed: No changes. 02/23/2024 – Annual Review: NCCN Prostate Cancer guidelines add concomitant therapy of denosumab or zoledronic acid with radium 223 dichloride for use in castration-resistant metastatic prostate cancer with symptomatic bone metastases without visceral metastases. Coding Reviewed: No changes.
- 02/24/2023 – Annual Review: No changes. Coding Reviewed: No changes.
- 02/25/2022 – Annual Review: Minor wording and formatting updates. Coding Reviewed: No changes.
- 02/19/2021 – Annual Review: Update Xofigo may not be approved criteria from the NCCN prostate cancer guideline. Coding Reviewed: No changes.
- 02/21/2020 – Annual Review: Update Xofigo with addition of lymph node metastases clinical criteria. Coding Reviewed: No changes
- 05/17/2019 – Annual Review: Initial review of Xofigo (radium Ra 223). Removal of duplicative criteria. Wording and formatting changes. Coding Reviewed: No changes.

## References


1. Anderson PM, Subbiah V, Rohren E. Bone-seeking radiopharmaceuticals as targeted agents of osteosarcoma: Samarium-153-EDTMP and Radium-223. Adv Exp Med Biol 2014; 804: 291-304.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2024. URL: http://www.clinicalpharmacology.com. Updated periodically.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 18, 2024.
    a. Prostate Cancer. V4.2023. Revised September 7, 2023.
    b. Bone Cancer. V1.2024. Revised August 7, 2023.
6. Subbiah V, Anderson PM, Kairemo K, et al. Alpha particle radium 223 dichloride in high-risk osteosarcoma: A phase I dose escalation trial. Clin Cancer Res 2019;25:3802- 3810.
7. Xofigo® (radium Ra 223 dichloride) [product information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc. August 2018.


Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.