

Medical Necessity Guidelines Xofigo (radium Ra-223 dichloride)

Policy Number: 114

Contents

Overview.....	1
Medicare Advantage	1
Mass General Brigham ACO	2
One Care and Senior Care Options (SCO).....	2
Commercial and Qualified Health Plans.....	2
Codes	2
Summary of Evidence	3
Effective Dates.....	3
References.....	4

Overview

Xofigo (Radium Ra-223 Dichloride) is an alpha particle-emitting radioactive therapeutic agent indicated for the treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases, and no known visceral metastatic disease. Xofigo nonspecifically targets the DNA in the metabolically active areas of bone, such as metastatic disease.

Medicare Advantage

Prior Authorization Required	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
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Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for medical necessity determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan’s medical policies are used for medical necessity determinations. **At the time of Mass General Brigham Health Plan’s most recent policy review, CMS offered the following guidelines:**

- [Medicare Benefit Policy Manual Chapter 15 – Covered Medical and Other Health Services](#)

When CMS documentation references FDA labeling, Mass General Brigham Health Plan develops coverage criteria to clarify medical necessity of the requested services. Mass General Brigham Health Plan coverage criteria align with FDA labeling without contradicting existing determinations and enhance the clarity of medical necessity requirements, documentation requirements, and clinical indications.

Criteria

1. The member has metastatic, castration-resistant prostate cancer; and
2. The member has symptomatic bone metastases; and

- The member has no known visceral metastatic disease.

Exclusions

- The member has experienced disease progression on Xofigo.

Dosage and Administration

- One dose is 55 kBq (1.49 microcurie) per kg body weight
- Full course is one injection every four weeks for a total of six injections

Mass General Brigham ACO

Prior Authorization Required	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
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Mass General Brigham Health Plan uses guidance from MassHealth for medical necessity determinations for its Mass General Brigham ACO members. When there is no guidance from MassHealth for the requested service, Mass General Brigham Health Plan’s medical policies are used for medical necessity determinations. **At the time of Mass General Brigham Health Plan’s most recent policy review, MassHealth did not offer any guidelines for Xofigo.**

One Care and Senior Care Options (SCO)

Prior Authorization Required	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
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Mass General Brigham Health Plan uses guidance from CMS for medical necessity determinations for its One Care and SCO plan members. NCDs, LCDs, LCAs, and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, or the member does not meet all of the medical necessity criteria for the requested service, Mass General Brigham Health Plan uses medical necessity guidelines from MassHealth. **Refer to the Medicare Advantage section for medical necessity information.**

Commercial and Qualified Health Plans

Prior Authorization Required	Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>
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Mass General Brigham Health Plan covers a single course of Xofigo when all of the following criteria are met:

Criteria

- The member has metastatic, castration-resistant prostate cancer; and
- The member has symptomatic bone metastases; and
- The member has no visceral metastases; and
- The member has no bulky regional lymph nodes of greater than 3 cm; and
- The member will be using Xofigo in combination with a bone-protective agent (unless there is a documented contraindication or intolerance).

Dosage and Administration

- The recommended course of treatment of Xofigo is 55 kBq/kg (1.49 microcuries/kg) administered by slow intravenous injection over 1 minute every 4 weeks for 6 doses.

Exclusions



1. The member has already received a full treatment course of Xofigo.
2. The member experienced disease progression on Xofigo.
3. The member will be receiving concurrent chemotherapy, biologic therapy, or systemic radiotherapy.

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Authorized Code	Code Description
A9606	Radium ra-223 dichloride, therapeutic, per microcurie

Summary of Evidence

Radium-223 dichloride (Ra-223; Xofigo) is an alpha-emitting radiopharmaceutical approved for the treatment of metastatic, castration-resistant prostate cancer (mCRPC) in patients with symptomatic bone metastases and no known visceral metastatic disease. Its mechanism of action exploits the bone-seeking properties of radium, delivering targeted radiation to sites of osteoblastic activity while limiting systemic exposure (Xofigo package insert, 2019; symplr Evidence Analysis, 2013). According to NCCN Clinical Practice Guidelines (Version 5.2026) and updated American Society of Clinical Oncology guidelines (Garje et al. 2025), Ra-223 remains a recommended option in appropriately selected mCRPC patients, particularly those with bone-only metastatic disease. Real-world evidence supports its clinical utility: a systematic literature review by Lunan-Taylor et al. (2025) encompassing observational studies found consistent survival and disease control benefits across diverse patient populations, while a Japanese multicenter study by Matsumoto et al. (2023) reported meaningful reductions in bone pain and alkaline phosphatase levels in routine practice.

A critical safety concern with Ra-223 is an elevated risk of skeletal fractures, particularly when used in combination with newer hormonal agents (NHAs). Hijab et al. (2021) reported fracture rates at year 1 of 44% in mCRPC patients treated with Ra-223 as a single agent, and most of these fractures occurred in uninvolved bone, not the site of metastases. This concern prompted mandatory bone-protecting agent (BPA) use in the phase III EORTC 1333/PEACE-3 trial, which evaluated Ra-223 combined with enzalutamide versus enzalutamide alone. A safety analysis of PEACE-3 by Gillissen et al. (2025) demonstrated a marked decrease in fracture rates following implementation of mandatory BPA use, underscoring the importance of concurrent osteoclast inhibitor therapy. The results of PEACE-3, reported by Tombal et al. (2025), showed that the combination of Ra-223 plus enzalutamide significantly improved radiographic progression-free survival compared to enzalutamide alone. Supporting this, a network meta-analysis by Wang et al. (2023) and a systematic review and meta-analysis by Xiao et al. (2026) both confirmed that bone-protective therapy substantially reduced fracture risk and may improve survival outcomes in patients receiving Ra-223 combined with NHAs. Clinicians are therefore advised to co-administer denosumab or zoledronic acid, consistent with UpToDate recommendations from Van Poznak & Clemons (2026) and Sartor & DiBiase (2024).

Beyond fracture risk, real-world studies have also evaluated patient-centered outcomes and optimal treatment sequencing with Ra-223. A multicenter Japanese study by Urabe et al. (2025) found that administration of Ra-223 in the treatment sequence before significant decline in performance status was associated with greater therapeutic efficacy, with patients completing more of the six planned treatment cycles. The evidence supports Ra-223 as an effective, bone-targeted therapy that, when integrated thoughtfully into the mCRPC treatment continuum alongside mandatory BPA use, offers meaningful survival, quality of life, and palliative benefits.

Effective Dates



July 2026: Effective date.

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