MEDICAL POLICY

Excellus

SUBJECT: RADIUM-223 (Xofigo) FOR TREATMENT OF CASTRATION-RESISTANT PROSTATE CANCER **POLICY NUMBER: 6.01.44** **CATEGORY: TAC Assessment**	**EFFECTIVE DATE: 08/21/14** **REVISED DATE: 04/16/15, 04/21/16, 4/20/17, 04/19/18** **PAGE: 1 OF: 4**

- ***If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.***
- ***If a commercial product, including an Essential Plan product, covers a specific service, medical policy criteria apply to the benefit.***
- ***If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.***

POLICY STATEMENT:

Based upon our criteria and assessment of peer-reviewed literature, radium-223 (Xofigo, Bayer HealthCare Pharmaceuticals Inc) is considered **medically necessary** for the treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastatic disease.

POLICY GUIDELINES:

I. The dose regimen of radium-223 (Xofigo) is 55 kBq (1.49 microcurie) per kg body weight, given at 4 week intervals for 6 injections. Safety and efficacy beyond 6 injections with Xofigo have not been studied.

II. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

DESCRIPTION:

Radium-223 (Ra-223) is an alpha-emitting agent for treatment of men with symptomatic bone-metastatic castration resistant prostate cancer (CRPC). Radium-223 has a half-life of 11.4 days, and releases 94% of its energy as alpha-particles with very little beta or gamma-emission. Radium-223 mimics calcium and forms complexes with the bone mineral hydroxyapatite at areas of increased bone turnover, such as bone metastases. Alpha-emission consists of particles with high energy and a short range, causing non-repairable breakage of double-strand DNA in adjacent cells, resulting in a highly localized cytotoxic effect in the target areas and causing an anti-tumor effect on bone metastases. The alpha particle range from radium-223 dichloride is less than 100 micrometers (less than 10 cell diameters) which limits damage to the surrounding normal tissue and reduces marrow toxicity.

Radium-223 is administered intravenously once a month for 6 months by an appropriately licensed facility, usually in nuclear medicine or radiation therapy departments. Hematologic evaluation of patients must be performed at baseline and prior to every dose of radium-223. Prior to the initial dose, patients must have absolute neutrophil count (ANC) greater than or equal to 1.5×10^9/L, platelet count greater than or equal to 100×10^9/L, and hemoglobin greater than or equal to 10 g/dL. Before subsequent administrations of radium-223, the absolute neutrophil count (ANC) should be greater than or equal to 1×10^9/L and the platelet count greater than or equal to 50×10^9/L. Radium-223 should be discontinued if a delay of 6 to 8 weeks does not result in the return of blood counts to these levels. Non-hematologic side effects are generally mild, and include nausea, diarrhea, and vomiting. These symptoms are likely related to the fact that radium-223 is predominantly eliminated by fecal excretion. Whenever possible, patients should use a toilet and the toilet should be flushed several times after each use. When handling bodily fluids, simply wearing gloves and hand washing will protect caregivers. Clothing soiled with radium-223 or patient fecal matter or urine should be washed promptly and separately from other clothing. Caregivers should use universal precautions for patient care such as gloves and barrier gowns when handling bodily fluids to avoid contamination. When handling bodily fluids, wearing gloves and hand washing will protect caregivers.

RATIONALE:

On May15, 2013, the U. S. Food and Drug Administration approved radium Ra-223 dichloride marketed as Xofigo Injection (Bayer HealthCare Pharmaceuticals Inc).

The National Comprehensive Cancer Network (NCCN) Guidelines for Prostate Cancer (2017) principles of radiopharmaceutical therapy states that Radium-223 is an alpha-emitting radiopharmaceutical that has been shown to extend survival in men who have castration-resistant prostate cancer (CRPC) with symptomatic bone metastases, but no visceral metastases. Radium-223 alone has not been shown to extend survival in men who have visceral metastases or bulky nodal disease greater than 3 to 4 cm. Radium-223 differs from beta-emitting agents, such as samarium-153 and strontium-89, which are palliative and have no survival advantage. Radium-223 causes double-strand DNA breaks and has a short radius of activity. Grade 3-4 hematologic toxicity (2% neutropenia, 3% thrombocytopenia, 6% anemia) occurs at a low frequency. At the present time, except on a clinical trial, radium-223 is not intended to be used in combination with chemotherapy due to the potential for additive myelosuppression. Concomitant use of denosumab or zoledronic acid does not interfere with the beneficial effects of radium-223 on survival.

The Alpharadin in Symptomatic Prostate Cancer Patients (ALSYMPCA) trial was a phase 3, randomized, double-blind, placebo-controlled study which randomized 921 men with symptomatic bone-metastatic CRPC to six injections every weeks of either radium-223(50 kBq/kg) or placebo. Patients were symptomatic with two or more bone metastases, without visceral metastases and had received docetaxel or were ineligible for doxcetaxel treatment. Median overall survival in the radium-223 arm was 14.9 months compared to 11.2 months in the placebo arm. Median time-time-to-first skeletal related event was significantly improved in the treatment arm (13.6 months) compared to placebo (8.4 months). Time-to-alkaline-phosphatase-progression and time-to-PSA-progression was also improved in the treatment group. More adverse events were observed in the radium-223 group with discontinuation of treatment due to adverse events occurring in 13% of the men in the radium-223 and 20% of the men in the placebo arm. The significantly improved overall survival in the treatment group met the predetermined boundary for discontinuing the study early and the trial was terminated due to evidence of significant treatment benefit of radium-223.

CODES: Number Description

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

CPT: There is no specific CPT code for Radium (Ra-223) dichloride (Xofigo).

HCPCS:	A9606	Radium Ra 223 dichloride, therapeutic, per microcurie
	A9699	Radiopharmaceutical, therapeutic, not otherwise classified
	C9399	Unclassified drugs or biologicals
ICD10:	C61	Malignant neoplasm of prostate
	D40.0	Neoplasm of uncertain behavior of prostate
	Z85.46	Personal history of malignant neoplasm of prostate

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* key article

KEY WORDS:

XoFigo, Ra-223, radium-223, radiopharmaceutical

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently no National Coverage Determination (NCD) or Local Coverage Determination (LCD) for Radium-223 (Xofigo) for the treatment of castration-resistant prostate cancer.