Effective February 26, 2018
Replaced by Article A54559

BlueCross BlueShield of Alabama

Effective for dates of service on or after November 1, 2015, *and prior to February 26, 2018* refer to:
Blue Cross and Blue Shield of Alabama Radiation Therapy Management – RTM Policies

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Name of Blue Advantage Policy:
Xofigo (Radium Ra 223 Dichloride)

Policy #: 529
Category: Pharmacology

Latest Review Date: February 2015
Policy Grade: B

Background:
Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

Description of Procedure or Service:

Xofigo is radium RA 223 dichloride, an alpha particle-emitting radioactive therapeutic agent. The active component is the alpha particle-emitting isotope radium 223, which mimics calcium and forms complexes with the bone mineral hydroxyapatite at areas of increased bone turnover, such as bone metastases. It binds with minerals in the bone to deliver radiation directly to bone tumors, limiting damage to the surrounding normal tissues.

Xofigo is used to treat patients with prostate cancer that is resistant to medical or surgical treatments that lower testosterone. This condition is otherwise known as metastatic castration-resistant prostate cancer, or mCRPC. Patients should also have symptomatic bone metastases and no known visceral metastatic disease.

Xofigo is given by slow IV injection over one minute. The dose regimen of Xofigo is 50 kBq (1.35 microcurie) per kg body weight, given at four week intervals for six injections. Safety and efficacy beyond six injections with Xofigo have not been studied.

The most common adverse drug reactions (≥10%) in patients receiving Xofigo were nausea, diarrhea, vomiting, and peripheral edema. The most common hematologic laboratory abnormalities (≥10%) were anemia, lymphocytopenia, leukopenia, thrombocytopenia, and neutropenia.

Bone marrow suppression may occur. Blood counts should be measured prior to treatment initiation and before every dose of Xofigo. Use of Xofigo should be discontinued if hematologic values do not recover within six to eight weeks after the last administration of Xofigo.

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Effective for dates of service prior to November 1, 2015:

Blue Advantage will treat **Xofigo®** as a **covered benefit** for the **treatment of prostate cancer** when the **all** following criteria are met:

- Patients have castration-resistant prostate cancer; **and**
- Patients have symptomatic bone metastases; **and**
- Patients have no known visceral metastatic disease.

FDA prescribing information states Xofigo is to be given at 4 week intervals for a total of 6 injections.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points

The efficacy and safety of Xofigo were evaluated in a double-blind, randomized, placebo-controlled Phase III clinical trial of patients with castration-resistant prostate cancer with symptomatic bone metastases. Patients with visceral metastases and malignant lymphadenopathy exceeding 3cm were excluded. The primary efficacy endpoint was overall survival. A key secondary efficacy endpoint was time to first symptomatic skeletal event (SSE) defined as external beam radiation therapy (EBRT) to relieve skeletal symptoms, new symptomatic pathologic bone fracture, occurrence of spinal cord compression, or tumor-related orthopedic surgical intervention. There were no scheduled radiographic assessments performed on study. All patients were to continue androgen deprivation therapy. At the cut-off date of the pre-planned interim analysis, a total of 809 patients had been randomized 2:1 to receive Xofigo 50kBq (1.35 microcurie)/kg intravenously every four weeks for six cycles (n=541) plus best standard of care or matching placebo plus best standard of care (n=268). Best standard of care included local EBRT, corticosteroids, antiandrogens, estrogens, estramustine or ketoconazole. Therapy was continued until unacceptable toxicity or initiation of cytotoxic chemotherapy, other systemic radioisotope, hemi-body EBRT or other investigational drug. Patients with Crohn's disease, ulcerative colitis, prior hemibody radiation or untreated imminent spinal cord compression were excluded from the study. In patients with bone fractures, orthopedic stabilization was performed before starting or resuming treatment in Xofigo.

The pre-specified interim analysis of overall survival revealed a statistically significant improvement in patients receiving Xofigo plus best standard of care compared with patients receiving placebo plus best standard of care.

The results showed men receiving Xofigo lived a median of 14 months compared to a median of 11.2 months for men receiving placebo. An exploratory updated analysis conducted later in the trial confirmed the ability of Xofigo to extend overall survival.

Key Words:

Xofigo, radium Ra 223 dichloride, prostate cancer, mCRPC

Approved by Governing Bodies:

On May 15, 2013, the U. S. Food and Drug Administration (FDA) approved Xofigo for the treatment of patients with symptomatic late-stage (metastatic) castration-resistant prostate cancer

that has spread to bones but not to other organs. It is intended for patients whose cancer has spread after receiving medical or surgical therapy to lower testosterone.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

Coding:

CPT Codes:

79101	Radiopharmaceutical therapy, by intravenous administration

HCPCS Codes:

A9699	Radiopharmaceutical, therapeutic, not otherwise classified

References:

1. Xofigo® full prescribing information: www.xofigo-us.com.

Policy History:

Adopted for Blue Advantage, July 2013
Available for comment July 3 through August 22, 2013
Medical Policy Group, January 2014
Medical Policy Group, February 2015
Medical Policy Group, September 2015
Medical Policy Group, November 2015
Medical Policy Group, February 2018