Xofigo®
radium Ra 223 dichloride
INJECTION

General Decontamination Procedures

Please see Important Safety Information on page 2
and click here for full Prescribing Information.

XOFIGO® IS INDICATED for the treatment of patients with castration-resistant prostate cancer (CRPC), symptomatic bone metastases and no known visceral metastatic disease.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions:

- **Bone Marrow Suppression:** In the phase 3 ALSYMPCA trial, 2% of patients in the Xofigo arm experienced bone marrow failure or ongoing pancytopenia, compared to no patients treated with placebo. There were two deaths due to bone marrow failure. For 7 of 13 patients treated with Xofigo bone marrow failure was ongoing at the time of death. Among the 13 patients who experienced bone marrow failure, 54% required blood transfusions. Four percent (4%) of patients in the Xofigo arm and 2% in the placebo arm permanently discontinued therapy due to bone marrow suppression. In the randomized trial, deaths related to vascular hemorrhage in association with myelosuppression were observed in 1% of Xofigo-treated patients compared to 0.3% of patients treated with placebo. The incidence of infection-related deaths (2%), serious infections (10%), and febrile neutropenia (<1%) was similar for patients treated with Xofigo and placebo. Myelosuppression–notably thrombocytopenia, neutropenia, pancytopenia, and leukopenia–has been reported in patients treated with Xofigo.

  Monitor patients with evidence of compromised bone marrow reserve closely and provide supportive care measures when clinically indicated. Discontinue Xofigo in patients who experience life-threatening complications despite supportive care for bone marrow failure
- **Hematological Evaluation:** Monitor blood counts at baseline and prior to every dose of Xofigo. Prior to first administering Xofigo, the absolute neutrophil count (ANC) should be ≥1.5 × 10^9/L, the platelet count ≥100 × 10^9/L, and hemoglobin ≥10 g/dL. Prior to subsequent administrations, the ANC should be ≥1 × 10^9/L and the platelet count ≥50 × 10^9/L. Discontinue Xofigo if hematologic values do not recover within 6 to 8 weeks after the last administration despite receiving supportive care
- **Concomitant Use With Chemotherapy:** Safety and efficacy of concomitant chemotherapy with Xofigo have not been established. Outside of a clinical trial, concomitant use of Xofigo in patients on chemotherapy is not recommended due to the potential for additive myelosuppression. If chemotherapy, other systemic radioisotopes, or hemibody external radiotherapy are administered during the treatment period, Xofigo should be discontinued
- **Increased Fractures and Mortality in Combination With Abiraterone Plus Prednisone/Prednisolone:** Xofigo is not recommended for use in combination with abiraterone acetate plus prednisone/prednisolone outside of clinical trials. At the primary analysis of the phase 3 ERA-223 study that evaluated concurrent initiation of Xofigo in combination with abiraterone acetate plus prednisone/prednisolone in 806 asymptomatic or mildly symptomatic mCRPC patients, an increased incidence of fractures (28.6% vs 11.4%) and deaths (38.5% vs 35.5%) have been observed in patients who received Xofigo in combination with abiraterone acetate plus prednisone/prednisolone compared to patients who received placebo in combination with abiraterone acetate plus prednisone/prednisolone. Safety and efficacy with the combination of Xofigo and agents other than gonadotropin-releasing hormone analogues have not been established
- **Embryo-Fetal Toxicity:** The safety and efficacy of Xofigo have not been established in females. Xofigo can cause fetal harm when administered to a pregnant female. Advise pregnant females and females of reproductive potential of the potential risk to a fetus. Advise male patients to use condoms and their female partners of reproductive potential to use effective contraception during and for 6 months after completing treatment with Xofigo

Administration and Radiation Protection: Xofigo should be received, used, and administered only by authorized persons in designated clinical settings. The administration of Xofigo is associated with potential risks to other persons from radiation or contamination from spills of bodily fluids such as urine, feces, or vomit. Therefore, radiation protection precautions must be taken in accordance with national and local regulations

Fluid Status: Dehydration occurred in 3% of patients on Xofigo and 1% of patients on placebo. Xofigo increases adverse reactions such as diarrhea, nausea, and vomiting, which may result in dehydration. Monitor patients' oral intake and fluid status carefully and promptly treat patients who display signs or symptoms of dehydration or hypovolemia

Injection Site Reactions: Erythema, pain, and edema at the injection site were reported in 1% of patients on Xofigo

Secondary Malignant Neoplasms: Xofigo contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure may be associated with an increased risk of cancer and hereditary defects. Due to its mechanism of action and neoplastic changes, including osteosarcomas, in rats following administration of radium -223 dichloride, Xofigo may increase the risk of osteosarcoma or other secondary malignant neoplasms. However, the overall incidence of new malignancies in the randomized trial was lower on the Xofigo arm compared to placebo (<1% vs 2%; respectively), but the expected latency period for the development of secondary malignancies exceeds the duration of follow-up for patients on the trial

Subsequent Treatment With Cytotoxic Chemotherapy: In the randomized clinical trial, 16% of patients in the Xofigo group and 18% of patients in the placebo group received cytotoxic chemotherapy after completion of study treatments. Adequate safety monitoring and laboratory testing was not performed to assess how patients treated with Xofigo will tolerate subsequent cytotoxic chemotherapy

Adverse Reactions: The most common adverse reactions (≥10%) in the Xofigo arm vs the placebo arm, respectively, were nausea (36% vs 35%), diarrhea (25% vs 15%), vomiting (19% vs 14%), and peripheral edema (13% vs 10%). Grade 3 and 4 adverse events were reported in 57% of Xofigo-treated patients and 63% of placebo-treated patients. The most common hematologic laboratory abnormalities in the Xofigo arm (≥10%) vs the placebo arm, respectively, were anemia (93% vs 88%), lymphocytopenia (72% vs 53%), leukopenia (35% vs 10%), thrombocytopenia (31% vs 22%), and neutropenia (18% vs 5%)

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For further information, please visit www.hcp.xofigo-us.com.

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GENERAL GUIDELINES

Follow the normal working procedures for the handling of radiopharmaceuticals, and use universal precautions, such as gloves and barrier gowns, when handling blood and bodily fluids, in order to avoid contamination. In case of contact with skin or eyes, the affected area should be flushed immediately with water. In the event of spillage of Xofigo®, the local radiation safety officer (RSO) should be contacted immediately to initiate the necessary measurements and required procedures to decontaminate the area. A complexing agent such as 0.01 M ethylene-diamine-tetraacetic acid (EDTA) solution is recommended to remove contamination.

IN THE EVENT OF A SPILL:

1. **Know your responsibilities**

   All users are responsible for conducting surveys and promptly decontaminating all items and surfaces

2. **Reviewed by:**

   Lead Technologist: _____ Phone: _____

   RSO: _____ Phone: _____

3. **Follow decontamination protocols identified below:**

   - **NOTIFY** persons in the area that a spill has occurred
   - **Assess the need for personnel decontamination**

     If needed, follow established **GUIDELINES FOR PERSONNEL DECONTAMINATION**. Radioactive contamination should be removed from the skin as soon as possible to reduce radiation exposure
   - **Use protective apparel and measures**

     Minimum requirements include wearing a lab coat and 2 pairs of disposable gloves. Gloves must be worn to prevent the spread of radioactive contamination to the hands during decontamination procedures
   - **Use approved cleaning solutions and methods**

     Cover the spill with disposable absorbent paper or pads to prevent further spread of contamination

     Use approved decontamination materials as indicated above

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- **Survey the area frequently**

  Monitor surfaces during decontamination with either thin window GM or scintillation survey meter or swipe tests to determine the effectiveness of the procedures being used

  Check the area around the spill, hands, and clothing for contamination

  Continue decontamination as necessary

  Items and surfaces that cannot be successfully decontaminated must be identified and controlled as radioactive material

- **Manage waste**

  Ensure that all waste is properly collected and disposed of in radioactive solid and liquid waste containers

  Carefully fold and place all used disposable absorbent materials and other contaminated disposables into a plastic bag

  Once decontamination procedures are complete, remove gloves and wash hands thoroughly

  Monitor hands, body, lab coat, clothing, etc., for radioactive contamination

  If needed, follow established **GUIDELINES FOR PERSONNEL DECONTAMINATION**

Regulatory References:

Title 10 Code of Federal Regulations: 10 CFR 19.11(a)(3), 10 CFR 20.1101,10 CFR 20.1406, 10 CFR 20.2202, 10 CFR 20.2203, 10 CFR 30.32, 10 CFR 30.35(g), 10 CFR 30.50, 10 CFR 30.51, 10 CFR 35.27

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