Xofigo®
radium Ra 223 dichloride
INJECTION

Therapeutic Use of Xofigo® Procedure Checklist

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

Indication

Xofigo is indicated for the treatment of patients with castration-resistant prostate cancer, 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 $\geq 1.5 \times 10^9$/L, the platelet count $\geq 100 \times 10^9$/L, and hemoglobin ≥10 g/dL. Prior to subsequent administrations, the ANC should be $\geq 1 \times 10^9$/L and the platelet count $\geq 50 \times 10^9$/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%)

Please click here for full Prescribing Information.

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

Xofigo®
radium Ra 223 dichloride
INJECTION

I. PURPOSE

To outline the therapeutic administration of Xofigo protocol established by the facility's Radioactive Materials (RAM) License.

II. DEFINITIONS

The Authorized User (AU) of Xofigo is a physician who is approved and listed on the RAM License for therapeutic use of radium Ra 223 dichloride.

III. REQUIREMENTS AND PROTOCOLS FOR USE

A. Xofigo therapy involves a slow intravenous injection over 1 minute.

B. Xofigo therapy requires the use of universal precaution practices to control administration and prevent contamination of the patient and injection area.

C. Certified Nuclear Medicine or Radiation Oncology staff may assist the AU in performing the Xofigo therapy protocol.

D. The Radiation Safety Officer is responsible for ensuring Xofigo therapy is performed in accordance with the RAM License and applicable state and federal regulations.

E. In the event of contamination, decontamination instructions are detailed in the facility Decontamination Protocol.

Radiation protection
The administration of Xofigo is associated with potential risks to other persons (eg, medical staff, caregivers, and patient's household members) 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.

For drug handling
Follow the normal working procedures for the handling of radiopharmaceuticals and use universal precautions for handling and administration such as gloves and barrier gowns when handling blood and bodily fluids 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 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.

F. Radiation levels in unrestricted areas will be maintained in accordance with the limits specified in state and federal regulations.

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

IU. PROCEDURE CHECKLIST (Complete and initial each requirement.)

ORDERING

1. ☐ Procedure Information

   Therapy Date: _____ Time: _____ Activity: _____ µCi

   Patient Name: _____ AU: _____

   Referring Physician Contact Info: _____

   Facility Shipping Address: _____

2. ☐ Verify the AU Physician is listed on RAM License for radium Ra 223 dichloride use
3. ☐ Verify the RAM License authorizes the requested quantity and the facility possession limits are not exceeded
4. ☐ RSO-approved Nuclear Medicine/Radiation Oncology staff orders Xofigo
5. ☐ Instruct radiopharmacy delivery staff to deliver Xofigo directly to the RAM License approval area

RECEIPT AND ADMINISTRATION

6. ☐ Upon receipt of the Xofigo package:
   - Survey package per RAM License conditions
   - Assay Xofigo dose and document into inventory
7. ☐ Prepare injection area for injection procedure (cover surfaces with protective material [eg, plastic-backed absorbent paper]). Appropriate aseptic precautions should be taken
8. ☐ AU verifies the dose (activity per the written directive) and patient name prior to administration
9. ☐ Administer dose per Xofigo prescribing information
10. ☐ Assay syringe after administration per prescribing information. Any unused product or materials used in connection with the preparation or administration are to be treated as radioactive waste and should be disposed of in accordance with local regulations

In keeping with the **A**s **L**ow **A**s **R**easonably **A**chievable (ALARA) principle for minimization of radiation exposure, it is recommended to minimize the time spent in radiation areas, to maximize the distance to radiation sources, and to use adequate shielding

PATIENT DISCHARGE

11. ☐ Discharge Survey (at patient umbilicus) _____ mR/hr Date: _____ Time: _____ Technologist: _____

    Survey Instrument: _____ Serial Number: _____ Instrument Calibration Date: _____

12. ☐ Provide patient instructions/radiopharmaceutical administration release card per institutional protocol
13. ☐ Perform survey of injection area and assess for possible contamination

This procedure is provided as a guide only. Please ensure compliance with all facility requirements as well as local rules and regulations applicable to use of Xofigo.

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

PP-XOF-US-2041-1 06/25

Xofigo® radium Ra 223 dichloride INJECTION