

Radiopharmaceutical Therapy: Agent/Protocol-Specific Procedure Radium 223 dichloride (Xofigo®)

Radiopharmaceutical Agent:

Radium (Ra-223) dichloride (Xofigo®)

Xofigo® is the brand name of a radiopharmaceutical, Radium 223 dichloride. Ra-223 has a half-life of 11.4 days and emits alpha, beta, and gamma radiation. The alpha radiation provides the therapeutic effects with its high Linear Energy Transfer. Gamma and Beta radiation can be detected with standard Nuclear Pharmacy and Nuclear Medicine instrumentation.

Xofigo® mimics calcium and forms complexes with the bone mineral hydroxyapatite at areas of increased bone turnover, such as bone metastases. The high linear energy transfer of alpha emitters leads to a high frequency of double-strand DNA breaks in adjacent cells, resulting in its anti-tumor effect. The alpha particle range from radium-223 is less than 100 micrometers (less than 10 cell diameters) which limits damage to the surrounding tissue.

Drug Information Source:

The FDA approved for the treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases and no known or insignificant visceral metastatic disease. For additional information regarding this agent, consult package insert or other standard references.

Applicability of Worksheet:

Clinical use of commercial product; standard of care

Target Patient Process:

Patients with castration-resistant prostate cancer (CRPC) with symptomatic bone metastases.

Prior to first administration of Xofigo®,

- 1) Absolute neutrophil count (ANC) should be $\geq 1.5 \times 10^9/L$
- 2) Platelet count $\geq 100 \times 10^9/L$
- 3) Hemoglobin ≥ 10 g/dL.

Prior to subsequent administrations:

- 1) Absolute neutrophil count (ANC) should be $\geq 1 \times 10^9/L$
- 2) Platelet count $\geq 50 \times 10^9/L$.

Safety and effectiveness of Xofigo® have not been established in children and adolescents below 18 years of age.

No dedicated pharmacokinetic study in patients with hepatic impairment has been conducted. However, since radium 223 is not metabolized and there is no evidence of hepatobiliary excretion based on imaging data, hepatic impairment is not expected to affect the pharmacokinetics of radium 223 dichloride.

No dedicated pharmacokinetic study in patients with renal impairment has been conducted. However, since excretion in urine is minimal and the major route of elimination is via the feces, renal impairment is not expected to affect the pharmacokinetics of radium 223 dichloride.

Contraindicated in pregnant or nursing women

Dose Range:

55 kBq (1.49 microcurie per kg body weight), given at 4 week intervals for 6 injections.

Written Directive and Validation: Authorized User or Authorized Medical Physicist will determine the appropriateness of the therapy based on the clinical presentation, perform the necessary calculations, and complete the written directive, as instructed on the **Radiopharmaceutical Therapy Dose Documentation Form specific for Ra-223**; no additional procedures required.

Scheduling Procedures: Once the referring physician identifies a prospective patient, a Ra-223 Written Directive is filled out and forwarded to the Nuclear Pharmacy via fax or in person by AU or AMP.
If dose is to be administered in Radiation Oncology, the Nuclear Pharmacy will order dose per the proper procurement procedures and have available for the planned day of administration.
If dose is to be administered in Nuclear Medicine, the Nuclear Pharmacy will forward information to the Senior Nuclear Medicine Technologists for scheduling in addition to procuring radiopharmaceutical.

Drug Procurement/Preparation: Written directive must be received by Nuclear Pharmacy at least 5 days before planned administration.

Upon receipt of written directive, Nuclear Pharmacy will order the radiopharmaceutical through Xofigo Access Services. This interfaces with a Cardinal Health central nuclear pharmacy that is currently the only distributor of Xofigo.

Ordering flow:

- Nuclear Pharmacy calls Xofigo Access Services at 1-855-6XOFIGO (1-855-696-3446) to order dose
- Xofigo Access Services Access Counselor will collect initial information for the patient order:
 - Pharmacy generated patient identification number and patient weight.
 - This information is forwarded electronically, as well as the telephone call to Cardinal Health in Denver or Indianapolis where the order is placed from UW Hospital to Cardinal Health. This includes the actual patient name, weight, dose, and date of administration.
- Cardinal Health central distribution pharmacy delivers a patient-ready unit dose to the UWHC Nuclear Pharmacy by 0800 am.
- Xofigo is available for delivery Monday through Friday

Pharmacy Product Validation: As instructed on the **Radiopharmaceutical Therapy Dose Documentation Form specific for Ra-223**.

The verification of a product from the outside vendor will include placement of the dose into the UWHC dose calibrator calibrated with an NIST traceable Ra-223 source, and comparison of the UWHC assay to the vendor's radiopharmaceutical label to ensure that both the label and the UWHC dose calibrator demonstrate that the dose is within 10% of the prescribed activity.

Patient Instructions/Education Validation:

- 1) Be compliant with blood cell count monitoring appointments.
 - a. Instruct patients to report signs of bleeding or infections.
- 2) Stay well hydrated and to monitor oral intake, fluid status, and urine output.
- 3) Report signs of dehydration, hypovolemia, urinary retention, or renal failure/insufficiency.
- 4) There are no restrictions regarding contact with other people after receiving therapy.
- 5) Follow good hygiene practices while receiving Xofigo and for at least 1 week after the last injection.
 - a. Patients should use a toilet and the toilet should be flushed several times after each use.
 - b. Clothing soiled with patient fecal matter or urine should be washed promptly and separately from other clothing.
- 6) 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.

- 7) Those who are sexually active should use condoms and their female partners of reproductive potential should use a highly effective method of birth control during treatment and for 6 months following completion of treatment.

The most common adverse reactions ($\geq 10\%$) in patients receiving Xofigo were nausea, diarrhea, vomiting, and peripheral edema

The most common hematologic laboratory abnormalities in Xofigo-treated patients ($\geq 10\%$) were anemia, lymphocytopenia, leukopenia, thrombocytopenia, and neutropenia

Administration/Treatment Schedule:

- 1) Written directive is completed; dose is prepared and administered as directed on the **Radiopharmaceutical Therapy Dose Documentation Form specific for Ra-223**.
- 2) Administration of Ra-223 is to be via peripheral IV (PIV) which is placed by Nuclear Medicine or Radiation Oncology.
NOTE: Indwelling catheters are not to be used (e.g. Hickman catheter, infuse-port etc)
- 3) For patients with difficult peripheral IV (PIV) placement page IV Access Team (Pager 4876) for assistance. In text message note that peripheral IV is need for start of therapy and to bring ultrasound unit.
- 4) Prior to administration of Ra-223 flush the peripheral IV with at least 10 ml of isotonic saline to check patency.
- 5) Administer Xofigo by slow intravenous injection over 1 minute and flush IV system with at least 10 ml of isotonic saline.

Administration Validation:

Immediately after administration, the net patient dose of administered Xofigo should be determined by measurement of the empty syringe and tubing in a suitable dose calibrator that has been calibrated with a NIST traceable Ra-223 standard and decay corrected.

Only appropriately trained individuals may administer this product. Complete and document administration as instructed on the **Radiopharmaceutical Therapy Dose Documentation Form specific for Ra-223**.

Exposure Calculations/Release Criteria:

External radiation exposure associated with handling of patient doses is expected to be low, because the typical treatment activity will be below 8,000 kBq (216microcurie).

Other information/instructions:

Patients admitted to the hospital within two days following this therapy will be assessed for the need for radiation isolation with standard radiation isolation orders issued, regardless of whether or not radiation precautions are required. Refer to UWHC Policy for Patients who Received Therapeutic Radiopharmaceuticals and Need to be Admitted to the Hospital.

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