

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

Radiopharmaceutical Agent:	<p>Radium (Ra-223) dichloride (Xofigo®)</p> <p>Xofigo® is a novel 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.</p> <p>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</p>
Drug Information Source:	<p>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.</p>
Applicability of Worksheet:	<p>Clinical use of commercial product; standard of care</p>
Target Patient Process:	<p>Patients with castration-resistant prostate cancer (CRPC) with symptomatic bone metastases</p> <p>Prior to first administering Xofigo®,</p> <ol style="list-style-type: none">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. <p>Prior to subsequent administrations:</p> <ol style="list-style-type: none">1) Absolute neutrophil count (ANC) should be $\geq 1 \times 10^9/L$2) Platelet count $\geq 50 \times 10^9/L$. <p>Safety and effectiveness of Xofigo® have not been established in children and adolescents below 18 years of age.</p> <p>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.</p> <p>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.</p> <p>Contraindicated in pregnant or nursing women</p>
Dose Range:	<p>50 kBq (1.35 microcurie) per kg body weight, given at 4 week intervals for 6 injections.</p>

Written Directive and Validation:

Authorized User 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, the Nuclear Pharmacy is notified via phone or e-mail. (263-9982 or SKnishka@UWHealth.org **AND** GKlasek@UWHealth.org)

A Ra-223 Therapy form 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:
 - Patients name, patients weight, facility shipment address, dosage, administration time and date, referring physician information.
- An Access Counselor sends a prepopulated Xofigo Order Form for review, signature, and submission back to Xofigo Access Services.
- Upon receipt of the Xofigo Order Form, the Access Counselor conducts the patient benefit verification (or the facility may conduct its own verification)
- Two days prior to the scheduled treatment, the Access Counselor will connect UWHC Nuclear Pharmacist with a nuclear pharmacist at the Cardinal Health central distribution pharmacy to complete the order.
- 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 and 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-133 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.
- 6) Measure dose syringe and ancillary IV items used (e.g. stopcock, flushing syringe etc.) upon completion if administration and prior to removal of peripheral IV.
NOTE: The same dose calibration unit **must** be used for both pre-administration measurement and post-administration measurement.
- 7) If the administered dose meets the prescribed dose + 10% the peripheral IV may be removed

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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**Radiopharmaceutical Therapy Dose Documentation Form
Ra-223 Radium Dichloride (Xofigo®)**

A. WRITTEN DIRECTIVE:		
1. Pt Name:	2. MR#:	3. Birth Date:
4. Radiopharmaceutical (Including Isotope): Ra-223 Radium Dichloride (Xofigo®)		5. Weight (kg):
6. Date of Administration:	7. Time of Administration:	8. Dose (uCi): (1.35 uCi/kg)
9. Referring physician:		
10. Indication: Castration Resistant Prostate Metastases	11. <input type="checkbox"/> Initial Dose <or> <input type="checkbox"/> Subsequent Dose	
12. <input type="checkbox"/> Prior to first administration of Xofigo®, -Absolute neutrophil count (ANC) should be $\geq 1.5 \times 10^9/L$ -Platelet count $\geq 100 \times 10^9/L$ -Hemoglobin ≥ 10 g/dL.	13. <input type="checkbox"/> Prior to subsequent administrations: - Absolute neutrophil count (ANC) should be $\geq 1 \times 10^9/L$ - Platelet count $\geq 50 \times 10^9/L$.	
14. Signature of Authorized MD	15. Date _____ & Time _____ Signed	

B. EXPOSURE CALCULATIONS:
Alpha Radiation Administered. Release criteria assessed and met, calculations not required

Verified by (initial): _____	NOTE: Must NOT be the individual who signed the written directive Must be Authorized ANP, AU, or AMP
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C. PHARMACY COMPUTER ORDER ENTRY DOCUMENTATION:	
Completed by (initial): _____	
Verified by (initial): _____	NOTE: Must NOT be the individual who did the pharmacy computer order entry

D. DOSE PREPARATION DOCUMENTATION:		
Dose Assay: Provided on Cardinal Label	NOTE: Must NOT be the individual administering the product	
Dose Assay (uCi) = _____	Assay Date _____ & Time _____	UWHC RX# _____
Verified by (initial): _____	NOTE: Must NOT be the individual who did the preparation, NOR the one administering	
Dose Assay (uCi) = _____	Assay Date _____ & Time _____	UWHC RX# _____

E. PATIENT INFORMATION/EDUCATION VERIFICATION: (NOTE: To be completed by the Authorized User)	
Completed by (initial): _____	Pt ID Verification (2 methods used; Name must be 1 of the 2) Verified: Name <u>AND</u> Birthdate <OR> MR#
Completed by (initial): _____	Prescribing physician explained dose and treatment to administering clinician.
Completed by (initial): _____	Negative pregnancy test or excluding clinical condition confirmed with reasonable assurance
Completed by (initial): _____	Patient is not currently breast feeding.
Completed by (initial): _____	Informed consent obtained or verified
Completed by (initial): _____	<p>Patient Education provided by Authorized User or Authorized Medical Physicist</p> <ul style="list-style-type: none"> -Compliance with blood cell count monitoring appointments is necessary. -Stay well hydrated and monitor oral fluid intake and urine output. -Report signs of dehydration, hypovolemia, urinary retention, or renal failure/insufficiency to your physician. -There are no restrictions regarding contact with other people after receiving therapy. -Follow good hygiene practices while receiving Xofigo and for at least 1 week after the last injection. -Caregivers should use universal precautions for patient care. -Use an effective method of birth control during treatment and for 6 months following completion of treatment.

F. ADMINISTRATION VERIFICATION: (NOTE: To be completed at the time of treatment)		
Clinician #1 ↓	Clinician #2 ↓	<p>Clinician #1 is the Administering Clinician who is giving the dose. Clinician #2 is NOT administering the dose and did not compound/fill dose</p>
Initial _____	Initial _____	<p>Clinician #1 reads aloud the patient name, radiopharmaceutical and dose from the product label. Clinician #2 reviews the written directive and verifies that the following match: Patient Name <and> Radiopharmaceutical <and> Dose</p>
Initial _____	Initial _____	<p>Assay of dose in the dose calibrator Dose Assay (uCi) = _____ Date _____ Time _____</p>
Initial _____	Pt ID Verification (2 methods used; Name must be 1 of the 2) Check: Name <u>AND</u> Birthdate <OR> MR#	
Initial _____	Negative pregnancy test or excluding clinical condition confirmed with reasonable assurance.	
Initial _____	Patient is not currently breast feeding.	
Initial _____	Ra-223 dose administered via peripheral IV placed by Nuclear Medicine or Radiation Oncology slowly over 1 minute	
Initial _____	At least 10 mL sodium chloride 0.9% administered via peripheral IV before and after dose administered to check patency and flush IV system	
Initial _____	<p>Assay of syringe/ Total Dose Administered:(same dose calibrator to be used for both measurements) _____ (pre-administered syringe) - _____ (post-administered syringe) = _____ If total dose administered is not within 10% of prescribed dose, notify Authorized User</p>	
Initial _____	Patient released at the time of administration	

Clinician #1 Signature _____ **Date** _____ **Time** _____