Consider Xofigo®▼ (radium-223 dichloride) in patients with mCRPC, symptomatic bone metastases and no known visceral metastases*

Checklist for initiating treatment with Xofigo

- Adult male with mCRPC with symptomatic bone metastases and no known visceral metastases, in progression after at least two prior lines of systemic therapy for mCRPC (other than LHRH analogues) or ineligible for any available systemic mCRPC treatment†
- Symptomatic bone metastases on bone scan[1–3]
- ≤3 cm lymph node involvement on conventional imaging[2]
- No known visceral metastases on conventional scanning[1–3]
- Clinical indicators (e.g. increase in biomarker levels such as PSA and/or ALP, progression seen on imaging scans and emerging symptoms such as weight loss and fatigue)[2,4,5]

*Xofigo is a targeted alpha therapy, which specifically targets areas of high bone turnover.[4] Most patients with mCRPC and bone metastases will be eligible for Xofigo during their treatment, before the onset of visceral disease.[6,7] Xofigo can be administered with BSC, including external beam radiotherapy and bone supportive agents, but cannot be used in combination with systemic cancer therapy.[1,2,5]

†Full details on Xofigo can be found in the Summary of Product Characteristics, available at: https://www.medicines.org.uk/emc/product/5204/smpc#gref.

Abbreviations: ALP, alkaline phosphatase; BSC, best standard of care; LHRH, luteinising hormone-releasing hormone; mCRPC, metastatic castration-resistant prostate cancer; PSA, prostate-specific antigen.

Prescribing Information can be found on page 8.

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Xofigo® ▼
radium – 223 dichloride

Why treat with Xofigo?

Treatment with Xofigo has a triple benefit in eligible patients with mCRPC: it has been shown to improve OS, time to first SSE and QoL compared with placebo plus BSC.[*,2] Xofigo has also demonstrated an acceptable tolerability profile in these patients.[†]

14.9 months	Significantly improved OS vs placebo + BSC (P<0.001)[‡,2]
15.6 months	Significantly prolonged time to first SSE vs placebo + BSC (P<0.001)[‡,2]
QoL[§]	Slower decline in QoL vs placebo + BSC[‡,2]

*The ALSYMPCA trial showed an increase in OS (HR 0.70, 95% CI 0.58–0.83; P<0.001) and time to first SSE (HR 0.66, 95% CI 0.52–0.83; P<0.001) for Xofigo compared with placebo + BSC.[2] [†]The tolerability profile of Xofigo in ALSYMPCA was similar to placebo (all AEs: 93% vs 96%; Grade 3–4 AEs: 56% vs 62%; serious AEs: 47% vs 60%; discontinuations due to AEs: 16% vs 21%).[2] [‡]The use of Xofigo is not recommended in patients with low levels of osteoblastic bone metastases. [§]The mean changes in the FACT-P total score from baseline to Week 16 were -2.7 vs -6.8 for Xofigo vs placebo + BSC (P=0.006).

Abbreviations: AE, adverse event; BSC, best standard of care; CI, confidence interval; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; OS, overall survival; QoL, quality of life; SSE, symptomatic skeletal event.

In which patients should Xofigo be considered?

Patients ineligible for chemotherapy

Xofigo can be offered in the first-line setting to appropriate patients with mCRPC who are ineligible for all other systemic therapies. It can also be prescribed as a second-line therapy in patients with mCRPC who have received prior ARi treatment and are ineligible for chemotherapy. Factors to consider when determining a patient's eligibility for chemotherapy are outlined below:[*,8]

1. Patients contraindicated for docetaxel
2. Patients with poor performance status
3. Patients with comorbidities
4. Patients whose cognition and/or social support will result in:
   - Non-compliance with the treatment regimen
   - Inadequate toxicity monitoring
   - Inability to understand treatment fully and provide informed consent
5. Patient choice:
   - Patients should be fully briefed (as per the General Medical Council guidelines) on all therapeutic options, including alternative treatments and the option of receiving no treatment, in order to provide their consent

*These recommendations were developed as an output of a Bayer-funded meeting that brought together UK-based prostate cancer experts to discuss eligibility criteria for treatment with chemotherapy.[8]

Patients who progress on treatment with ARis

Treatment with abiraterone acetate/enzalutamide is common in patients with mCRPC; as such, it is important for physicians to recognise when these treatments should be discontinued to increase the potential benefit of subsequent therapies, such as Xofigo. The PCWG3 consensus proposes discontinuation criteria for abiraterone acetate/enzalutamide treatment based on disease sites (Table 1).[9]

Table 1. PCWG3 consensus on discontinuation criteria for abiraterone acetate/enzalutamide.*[,9]

Area	Details
Nodes	• Nodal progression is sufficient independent of PSA • Measurable lesions are not required • Use modified RECIST v1.1 criteria; separate pelvic and extrapelvic disease; up to five nodal lesions recorded • Previously normal (<1.0 cm) lymph nodes are considered to have progressed if they have grown by ≥5 mm in the short axis • If the node progresses to ≥1.5 cm in the short axis, it is measurable; nodes that have progressed to <1.5 cm are pathological, subject to clinical discretion and non measurable • For existing pathological adenopathy, progression is defined per RECIST v1.1 • Record presence of nodal and/or visceral disease separately
Viscera	• Visceral progression is sufficient independent of PSA and recorded separately by site of spread (lung, liver, adrenal, CNS); up to five lesions per site of spread • Measurable lesions are not required • Use RECIST to record visceral lesions as target or non target • Record presence of nodal and/or visceral disease (visceral sites: lung, liver, adrenal, CNS) separately
Bone	• Two new lesions • Confirm ambiguous results using other imaging modalities (e.g. CT or MRI) but only positive bone scan identifies metastatic disease to bone

*Taken together, biochemical progression (PSA dynamics/kinetics, haemoglobin levels, ALP levels and lactate dehydrogenase levels), radiological progression (on conventional imaging), site-specific progression, AEs and patient choice can be used to help guide clinicians on if/when to discontinue abiraterone acetate/enzalutamide treatment.

Abbreviations: AE, adverse event; ALP, alkaline phosphatase; ARi, androgen receptor inhibitor; CNS, central nervous system; CT, computed tomography; mCRPC, metastatic castration-resistant prostate cancer; MRI, magnetic resonance imaging; PCWG3, Prostate Cancer Working Group 3; PSA, prostate-specific antigen; RECIST (v1.1), Response Evaluation Criteria in Solid Tumors (Version 1.1).

What does a patient suitable for Xofigo look like?

Patient perspectives: Luka's story

'I want more time, but not if side effects take over my life.'

Luka, aged 80 years

Background

- Retired law enforcement officer who walks daily for fitness and enjoys painting
- He lives alone with limited support, although his daughter and granddaughter live close by
- Luka strongly refused chemotherapy after watching his wife experience AEs associated with chemotherapy; he wants to live longer without compromising his QoL

Treatment goals

- Maintain independence without having to rely on others for care

Treatment history

	Clinical characteristics	Treatment
5 years ago	• Locally advanced prostate cancer diagnosis • Gleason score = 9	• Radiation + ADT (24 months)
2.5 years ago	• PSA increased from a nadir of 0.5 ng/mL to 8 ng/mL with a doubling time of 9 months	• ADT reintroduced
2 years ago	• Progression to nmCRPC	
12 months ago	• Bone scan revealed progression to mCRPC with one asymptomatic bone metastasis • PSA slowly rose	• Enzalutamide
Current status	• After rising PSA and pelvic pain, bone scan showed >6 bone metastases • No visceral metastases • ECOG PS = 1 • G8 score = 14	• Bone health agent • Chemotherapy declined

Abbreviations: ADT, androgen deprivation therapy; AE, adverse event; ECOG, Eastern Cooperative Oncology Group; G8, geriatric 8; mCRPC, metastatic castration-resistant prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; PS, performance status; PSA, prostate-specific antigen; QoL, quality of life.

Xofigo can help patients live longer without impacting their QoL.[2]

Xofigo + BSC has a comparable tolerability profile with placebo + BSC. The most frequently observed AEs (≥10%) in patients who received Xofigo were diarrhoea, nausea, vomiting, thrombocytopenia and bone fracture.[10] For full safety information, please refer to the Summary of Product Characteristics.[10]

Continuity of Xofigo treatment services following the COVID-19 pandemic

The COVID-19 pandemic has impacted the delivery of cancer services across the UK, including the administration of Xofigo. Changes to models of care have been implemented by some UK centres to ensure the continuation of Xofigo treatment services and now serve as best practice examples for maintaining delivery of Xofigo post pandemic.

University Hospital Southampton NHS Foundation Trust

1 day per week is dedicated to Xofigo administration to minimise the number of patients attending hospital and reduce the risk of infection transmission in patients with weakened immune responses

Each patient sees the same specialist on their treatment day (i.e. an oncologist or clinical nurse specialist); this helps to mitigate infection transmission and improve the relationship between the patient and specialist, which is important through numerous treatment cycles

The Christie NHS Foundation Trust

The Clatterbridge Cancer Centre NHS Foundation Trust and Leeds Teaching Hospitals

A number of 'patient-friendly' services have been implemented, including electronic consent forms and remote clinics to reduce unnecessary travel

Coadministration of zoledronic acid or alendronic acid throughout treatment with Xofigo to minimise fracture risk in patients with mCRPC

Concomitant use of bone health agents with Xofigo

Abbreviation: mCRPC, metastatic castration-resistant prostate cancer.

References

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Abbreviations: AE, adverse event; ARi, androgen receptor inhibitor; BSC, best standard of care; mCRPC, metastatic castration-resistant prostate cancer; OS, overall survival; PCWG3, Prostate Cancer Working Group 3; QoL, quality of life; SSE, symptomatic skeletal event.

▼ **Xofigo® 1100 kBq/mL solution for injection (radium-223 dichloride) Prescribing Information** (Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: Each vial contains 6 mL of solution (6.6 MBq radium223 dichloride at the reference date). Each mL of solution contains 1100 kBq radium Ra 223 dichloride (radium-223 dichloride), corresponding to 0.58 ng radium-223 at the reference date. **Indication(s):** Xofigo monotherapy or in combination with luteinising hormone releasing hormone (LHRH) analogue is indicated for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC), symptomatic bone metastases and no known visceral metastases, in progression after at least two prior lines of systemic therapy for mCRPC (other than LHRH analogues), or ineligible for any available systemic mCRPC treatment. **Posology & method of administration:** Xofigo should be administered only by persons authorised to handle radiopharmaceuticals in designated clinical settings, and after evaluation of the patient by a qualified physician. Xofigo is for intravenous use and must be administered by slow injection (generally up to 1 minute). The intravenous access line or cannula must be flushed with isotonic sodium chloride 9 mg/mL (0.9%) solution for injection before and after injection of Xofigo. ***Adults:*** The dose regimen of Xofigo is an activity of 55 kBq per kg body weight, given at 4 week intervals for 6 injections. ***Hepatic impairment:*** No dose adjustment is considered necessary in patients with hepatic impairment. ***Renal impairment:*** No dose adjustment is considered necessary in patients with renal impairment. ***Elderly patients:*** No dose adjustment is considered necessary in elderly patients. ***Children & adolescents:*** There is no relevant use of this medicinal product in the paediatric population for prostate cancer. ***Contra-indications:*** Xofigo is contraindicated in combination with abiraterone acetate and prednisone/prednisolone. **Warnings & precautions:** The safety and efficacy of Xofigo in combination with cancer therapies other than LHRH analogues have not been established; an increased risk of mortality and fractures is possible. The combination of radium-223 with other systemic cancer therapies other than LHRH analogues is not recommended. The use of Xofigo is not recommended for treatment of adults with CRPC and only asymptomatic bone metastases. In adults with CRPC and mildly symptomatic bone metastases the benefit of treatment should be carefully assessed to outweigh the risks considering that high osteoblastic activity is likely to be required for treatment benefit. In clinical studies, patients with fewer than 6 bone metastases had an increased risk of fractures and did not have a statistically significant survival benefit. A pre-specified subgroup analysis also showed that overall survival was not significantly improved in patients with a total ALP < 220 U/L. Therefore, in patients with a low level of osteoblastic bone metastases treatment with radium-223 is not recommended. Bone marrow suppression, notably thrombocytopenia, neutropenia, leukopenia and pancytopenia, have been reported in patients treated with Xofigo. Haematological evaluation of patients must be performed at baseline and prior to every dose of Xofigo. In case there is no recovery in values for absolute neutrophil count (ANC), platelets and haemoglobin within 6 weeks after the last administration of Xofigo despite receiving standard of care, further treatment with Xofigo should only be continued after a careful benefit/risk evaluation. Patients with evidence of compromised bone marrow should be treated with caution. Safety and efficacy of Xofigo have not been studied in patients with Crohn's disease and ulcerative colitis. Due to faecal excretion of Xofigo, radiation may lead to aggravation of acute inflammatory bowel disease. Therefore, Xofigo should only be administered after a careful benefit-risk assessment in patients with acute inflammatory bowel disease. In patients with untreated imminent or established spinal cord compression, treatment with standard of care, as clinically indicated, should be completed before starting or resuming treatment with Xofigo. Xofigo increases the risk of bone fractures, especially in patients with medical history of osteoporosis and in patients with <6 bone metastases. Prior to starting radium-223 bone status and baseline risk of fractures of patients (e.g. osteoporosis, less than 6 bone metastases, medication increasing fracture risk, low body mass index) should be carefully assessed, and closely monitored for at least 24 months. Preventive measures should be considered before starting or resuming treatment with Xofigo. In patients with a high baseline risk of fracture, the benefit of treatment should be carefully assessed to outweigh the risk. In patients with bone fractures, orthopaedic stabilisation of fractures should be performed before starting or resuming treatment with Xofigo. In patients treated with bisphosphonates and Xofigo, an increased risk of development of osteonecrosis of the jaw (ONJ) cannot be excluded. Xofigo contributes to a patient's overall long-term cumulative radiation exposure which may be associated with an increased risk of cancer and hereditary defects. In particular, the risk for osteosarcoma, myelodysplastic syndrome and leukaemias may be increased. Xofigo increases the incidence of diarrhoea, nausea, and vomiting which may result in dehydration. Oral intake and fluid status of patients should be carefully monitored. Patients should be advised to seek medical advice if they experience severe or persistent diarrhoea, nausea, vomiting. Patients who display signs or symptoms of dehydration or hypovolemia should be promptly treated. This medicinal product can contain up to 2.35 mmol (54 mg) sodium per dose, depending on the required volume, and must be taken into consideration by patients on a controlled sodium diet. **Interactions:** No clinical interaction studies have been performed. Interactions with calcium and phosphate cannot be excluded. Safety and efficacy of concomitant chemotherapy with Xofigo have not been established. **Fertility, pregnancy & lactation:** Xofigo is not indicated in women. Results from animal studies, indicate there is a potential risk that radiation from Xofigo could cause adverse effects on fertility. Male patients should seek advice on conservation of sperm prior to treatment. Due to potential effects on spermatogenesis associated with radiation, men should be advised to use effective contraceptive methods during and up to 6 months after treatment with Xofigo. **Effects on ability to drive and use machines:** There is no evidence, nor is it expected, that Xofigo will affect the ability to drive or use machines. **Undesirable effects:** Very common: Thrombocytopenia, diarrhoea, vomiting, nausea, bone fracture. Common: Neutropenia, pancytopenia, leukopenia and injection site reactions. Uncommon: Lymphopenia, osteoporosis. Serious: Thrombocytopenia and neutropenia. Prescribers should consult the SmPC in relation to other side effects. **Overdose:** No specific antidote. In the event of an inadvertent overdose, general supportive measures, including monitoring for potential haematological and gastrointestinal toxicity should be undertaken. **Incompatibilities:** Do not mix with other medicinal products. **Special Precautions for Storage:** Store in accordance with national regulation on radioactive materials. **Legal Category:** POM. **Package Quantities & Basic NHS Costs:** Single vial pack £4040. **MA Number(s):** EU/1/13/873/001 and PLGB 00010/0710. **Further information available from:** Bayer plc, 400 South Oak Way, Reading, Berkshire, RG2 6AD United Kingdom. Telephone: 0118 206 3000. **Date of preparation: November 2022**

Xofigo® is a trademark of the Bayer Group

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in Google Play or Apple App Store.

Adverse events should also be reported to Bayer plc. Tel.: 0118 206 3500; Fax: 0118 206 3703; Email: pvuk@bayer.com

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