Xofigo▼(radium 223 dichloride) pocket treatment guide

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.

Prescribing information and adverse event reporting can be found on the final slide.
This promotional material has been organised and funded by Bayer and is intended for UK Healthcare Professionals (HCPs) only.

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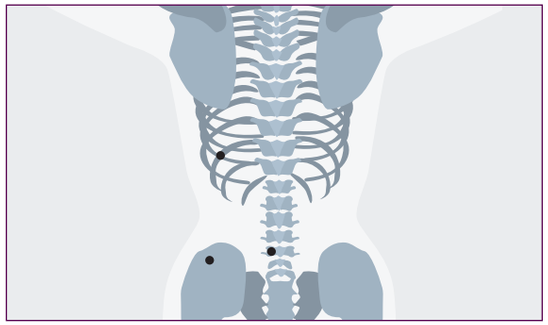
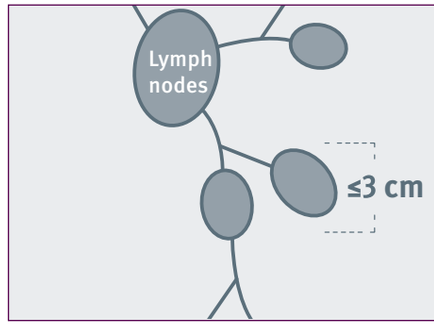
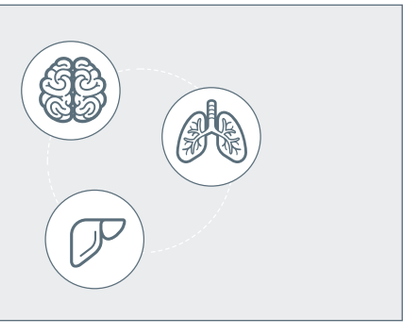
Who can receive Xofigo?

Xofigo is a **targeted alpha therapy**. It is indicated as monotherapy or in combination with luteinising hormone releasing hormone (LHRH) analogue for the treatment of adult patients with 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.[1]

Consider Xofigo[1–8]

≥2 symptomatic bone metastases, including mild symptoms[2*]	≤3cm lymph node involvement (conventional imagery)[2]	Clinical indicators[2–5]
		mCRPC that has progressed on two lines of systemic therapy, or is ineligible for systemic treatment Bone metastases detectable with 99mTc-phosphonate bone scan or 18F-NaF PET/CT scan, or MRI ECOG performance status 0–1 preferred (0–2 allowed)
Biochemical and/or radiographic progression on first-line antihormonal therapy and inelligible for chemotherapy		

Unsuitable for Xofigo[1,2]

Visceral metastases[1,2]

Lymphadenopathy >3cm diameter

Most patients with **metastatic castration-resistant prostate cancer (mCRPC) and bone metastases** will be eligible for **Xofigo** during their treatment, **before** the onset of **visceral disease**.[7,9] Xofigo can be administered with best standard of care, including **external beam radiotherapy** and bone supportive agents , but cannot be used in combination with systemic cancer therapy.[1,2,8,10**]

*Xofigo is not recommended in patients with a low level of osteoblastic bone metastases[1]

**Xofigo is contraindicated in combination with abiraterone acetate and prednisone/prednisolone

CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; F, fluorine; LHRH, luteinising hormone releasing hormone; mCRPC, metastatic castration-resistant prostate cancer; MRI, magnetic resonance imaging; NaF, sodium fluoride; PET, positron emission tomography; Tc, technetium.

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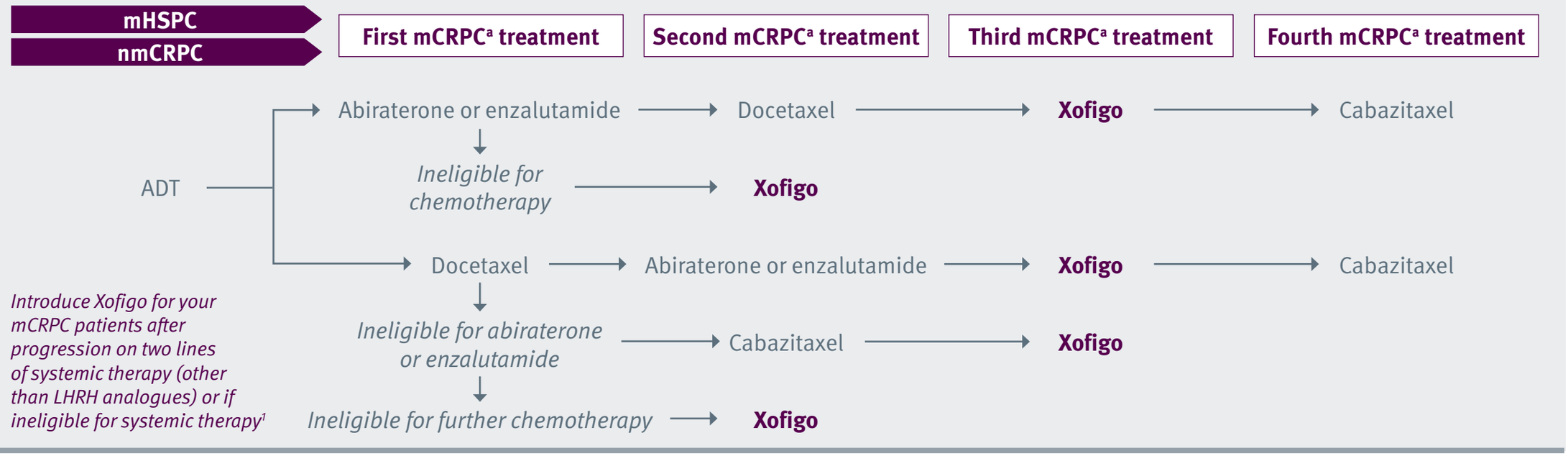
When to start treatment with Xofigo

The aim of treatment is to **extend survival** and provide the best possible **quality of life** for patients with mCRPC.[6]

Sequencing of systemic therapies for mCRPC[1,11]



Sequencing of systemic therapies for mCRPC. Potential sequencing options for approved life-prolonging agents following progression on ADT. These are illustrative algorithms based on the revised EU indication for Xofigo. Not all potential treatment options are shown. Concurrent use of bone health agents to treat osteoporosis or for patients with bone metastases is recommended. Sequential use of abiraterone and enzalutamide (or vice versa) is not considered as an option due to likely futility of treatment. Consider clinical trials or best supportive care after all available systemic therapies have been administered.

Consider Xofigo while there is an opportunity for action before the development of visceral metastases[11]

[a] mCRPC with bone metastases and no visceral metastases.

ADT, androgen deprivation therapy; EU, European Union; LHRH, luteinising hormone releasing hormone; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; nmCRPC, nonmetastatic castration-resistant prostate cancer.

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Defining symptomatic bone metastases

Xofigo treatment in metastatic CRPC patients should be started after progression on at least two prior lines of systemic therapy upon the emergence of signs and symptoms of bone metastases.[1,6] A statistically significant overall survival benefit of treatment could not be demonstrated in the subgroups of patients with fewer than 6 metastases (HR for radium-223 to placebo 0.901; 95% CI [0.553 -1.466], p=0.674). Therefore, efficacy may be diminished in patients with a low level of osteoblastic activity from their bone metastases.[1]

Signs and symptoms of bone metastases
Hypercalcaemia[12]
Pathological fracture[12]
Newly onset or increased fatigue/generalised weakness[13]
Impaired mobility[13]
Anaemia, neutropenia, or thrombocytopenia[13]
Back pain (due to spinal cord compression)[13]
Pain and discomfort[13,14]
Reduced activities of daily living due to pain[14]
Sleep disturbance due to pain[14]

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Potential questions to ask your patients

- Are you experiencing any difficulties with day-to-day activities?
- How are you sleeping?
- Have you noticed any stiffness or numbness?
- How frequently are you taking painkillers?
- Have you experienced loss of appetite?

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Before giving treatment – Initial injections

The Xofigo dose is 55 kBq/kg. Given as a 1 minute injection every 4 weeks for 6 injections.[1]

Before initial injection (cycle 1)[1,8,9,15]	
Requirements	
Prior treatment	Progression on two lines of systemic therapy[a] or ineligible for available systemic therapy
Imaging	Confirmed presence of bone metastases by 99mTc-phosphonate bone scan or ^{18}F-NaF PET/CT scan, or MRI[b] Visceral metastases excluded by imaging techniques such as CT, MRI or plain radiography Lymphadenopathy ≤3 cm diameter allowed
Haematological evaluation	Absolute neutrophil count ≥1.5 x 10^9/L Platelet count ≥100 x 10^9/L Haemoglobin ≥10.0 g/dL
Overall health	ECOG PS 0–1 preferred (0–2 allowed) Life expectancy ≥6 months

[a]Other than luteinising hormone releasing hormone analogues.

[b]A statistically significant overall survival benefit of treatment could not be demonstrated in the subgroups of patients with fewer than 6 metastases (HR for radium-223 to placebo 0.901; 95% CI [0.553 -1.466], p=0.674) or a baseline total alkaline phosphatase (ALP) ‹ 220 U/L (HR 0.823; 95% CI [0.633 -1.068], p=0.142) in the phase III ALSYMPCA study. Therefore, efficacy may be diminished in patients with a low level of osteoblastic activity from their bone metastases.[1]

CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; F, fluorine; MRI, magnetic resonance imaging; NaF, sodium fluoride; PET, positron emission tomography; Tc, technetium.

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Before giving treatment – Subsequent injections

The Xofigo dose is 55 kBq/kg. Given as a 1 minute injection every 4 weeks for 6 injections.[1]

Before subsequent injections (cycles 2–6)[1]	
Requirements	
Haematological evaluation	Absolute neutrophil count ≥1.0 x 10^9/L
	Platelet count ≥50 x 10^9/L
	Haemoglobin ≥8.0 g/dL[a]

Additional considerations before starting or resuming treatment with Xofigo[1]

Spinal cord compression and bone fractures should be treated with standard of care, as clinically indicated.

Benefit–risk assessment should be completed for patients with:

- Advanced diffuse infiltration of bone (superscan)
- Ulcerative colitis
- Crohn's disease

[a]Threshold according to ALSYMPCA study protocol.[15]
ALSYMPCA, ALpharadin in SYMptomatic Prostate CAncer.

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Monitoring treatment

Suggested regimen for monitoring treatment based on a European consensus.[7]

		Baseline	1	2	3	4	5	6	Follow-up
Biomarkers	✔ Total ALP		(✔)	(✔)	✔	(✔)	(✔)	✔	✔
	✔ PSA[a]		–	–	(✔)	–	–	✔	✔
	✔ LDH		✔	✔	✔	✔	✔	✔	✔
Imaging	✔ Bone scintigraphy[b]		–	–	–	–	–	✔	–
	✔ CT		–	–	(✔)	–	–	✔	✔
	✔ Axial MRI[c]		–	–	(✔)	–	–	(✔)	(✔)
Other assessments	✔ Clinical symptoms	✔	✔	✔	✔	✔	✔	✔	✔
	✔ Haematological parameters	✔	✔	✔	✔	✔	✔	✔	✔

✔ Indicates recommended

(✔) indicates 'if clinically indicated'

– indicates 'not routinely recommended'

Treating for all 6 cycles of Xofigo could maximise the overall survival benefit[1,16]

[a]PSA levels do not correlate with survival in patients receiving Xofigo.[17]

[b]Progression of bone metastases is uncommon during Xofigo treatment. Bone flare (pain and/or radiological) may be noted during the first 3 months of treatment and should not be confused with progression.[18]

[c]Next-generation imaging techniques (e.g. MRI and PET/CT) may have better accuracy than bone scintigraphy when monitoring treatment response in bone.[19]

ALP, alkaline phosphatase; CT, computed tomography; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; PET, positron emission tomography; PSA, prostate-specific antigen.

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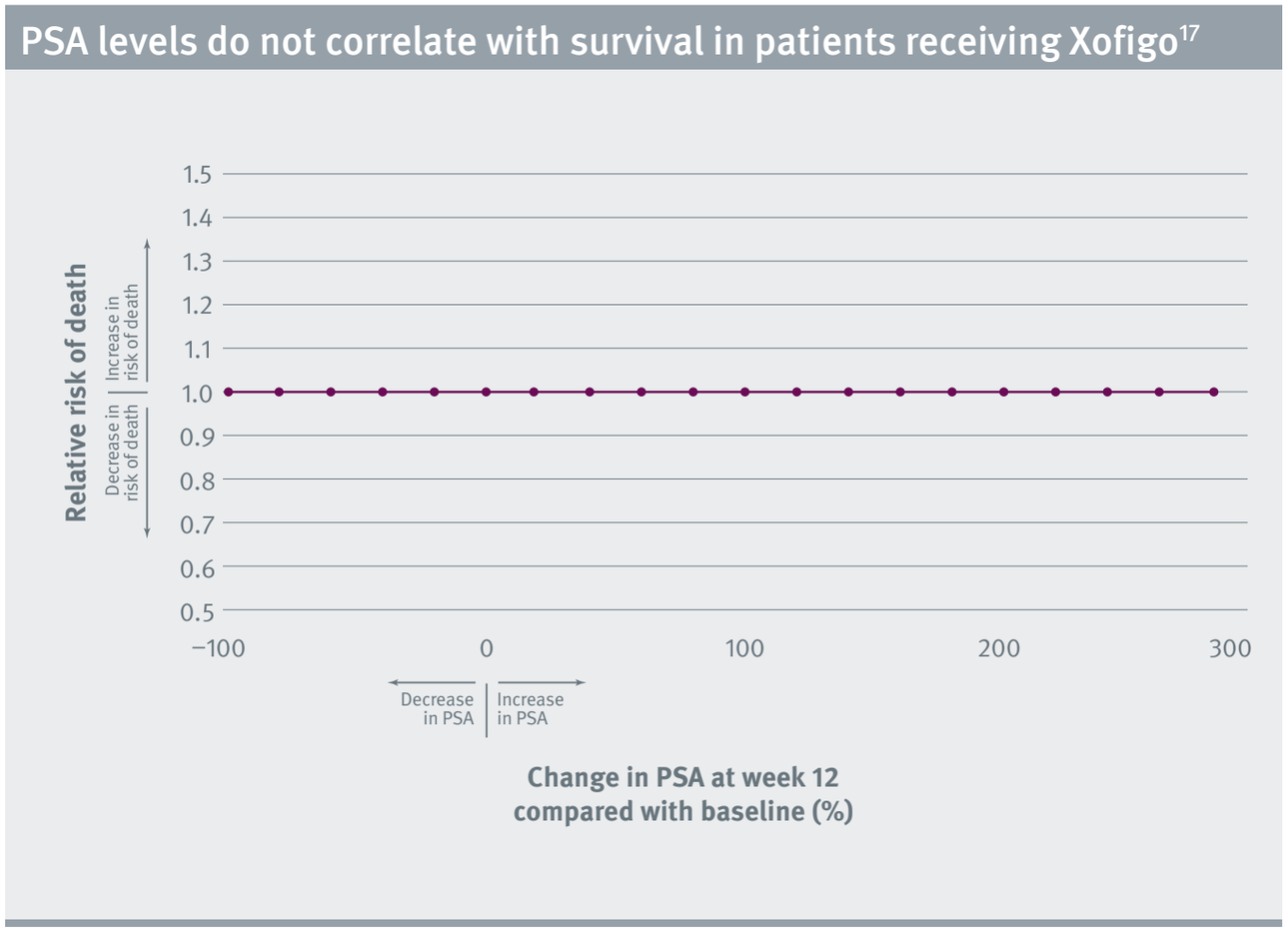
Biomarker changes with Xofigo – PSA

Xofigo targets tumours in the bone, not in the prostate; therefore, its effectiveness cannot be measured using prostate-specific antigen (PSA) levels.[2,17]



Adapted from Sartor et al 2017

Patients should understand that even though their PSA levels may change, this does not reflect the effectiveness of Xofigo treatment[2,17]

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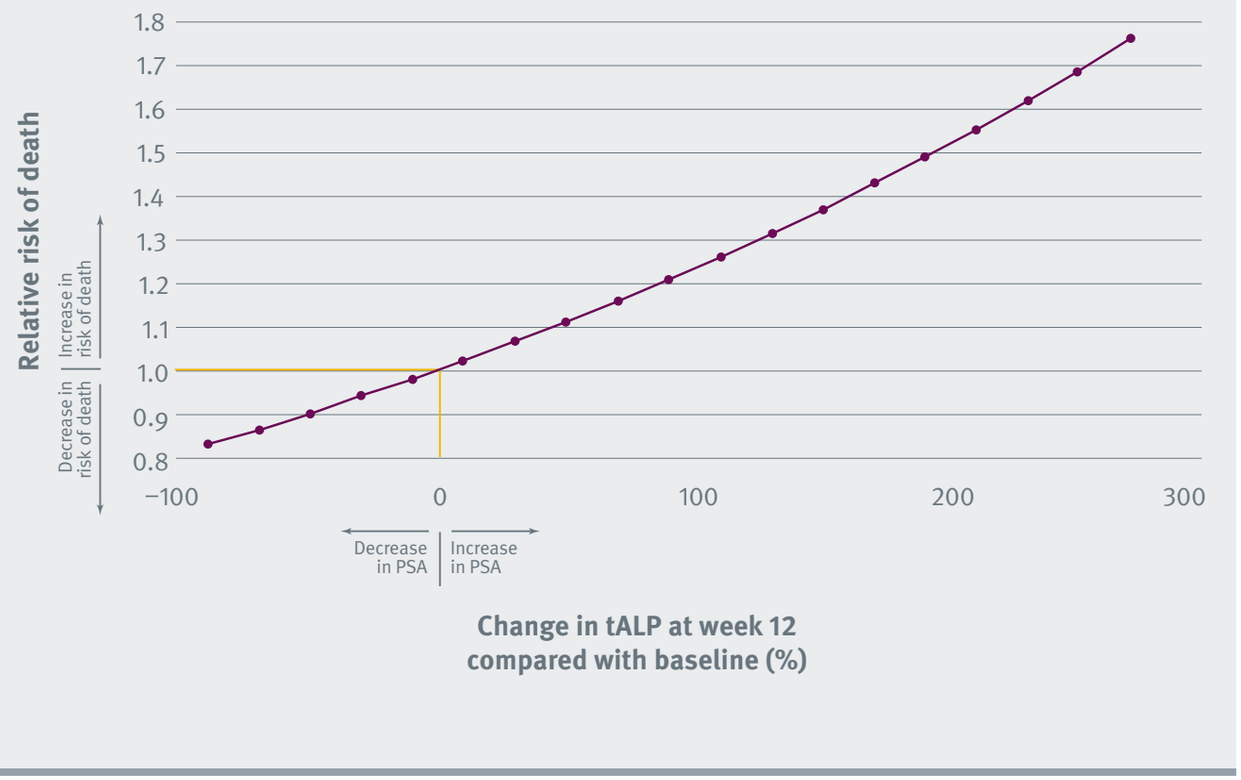
PSA, prostate-specific antigen.

Biomarker changes with Xofigo - tALP

Although there are currently **no validated biomarkers** for Xofigo efficacy,[2] changes in total alkaline phosphatase (tALP) may prove to be useful.[17a]

Changes in tALP levels may be useful for monitoring response to Xofigo[12]



Adapted from Sartor et al 2017

Treatment decisions about continuing Xofigo should not be made on the basis of biomarker changes, particularly rising PSA levels, owing to the risk that a large fraction of patients who may benefit could be denied effective treatment.[17]

There is insufficient evidence to support using tALP as a surrogate for overall survival.[17]

[a]OS is not significantly improved in patients with a total ALP <220 U/L, therefore Xofigo is not recommended in patients with a low level of osteoblastic bone metastases.[1]

PSA, prostate-specific antigen; tALP, total alkaline phosphatase.

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When to stop Xofigo

It is important to distinguish flare phenomena (new sites of apparent bone disease) from true radiographic progression. The **Prostate Cancer Clinical Trials Working Group 3 (PCWG3)** proposes using the **"2+2" rule**.[20] This rule defines progression as the appearance of ≥2 new lesions on the first on-treatment scan, with ≥2 additional lesions on the next scan. A new baseline bone scan is established once treatment has started.[20]

"2+2" rule			
Week 1	First on treatment bone scan	Next bone scan	Outcome
Start treatment	≥2 new lesions (new baseline bone scan)	No progression	Continue treatment
		≥2 additional new lesions relative to previous bone scan	Stop treatment

The PCWG3 recommends that treatment decisions should be made based on **overall clinical benefit**, and the **primary therapeutic objective**. In cases where there are nonresponding or worsening disease sites, treatment should be continued until the patient is deemed to be **no longer clinically benefiting**.[20]

The **Advanced Prostate Cancer Consensus Conference Panel** recommends that at least two of three criteria should be fulfilled to stop treatment:[21]

- PSA progression
- Radiographic progression
- Clinical deterioration

PSA, prostate-specific antigen.

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Optimising patient experience

Stay on schedule

The full course of Xofigo treatment is six injections, with each treatment cycle lasting for 4 weeks.[1] To get the most benefit from Xofigo, patients must keep to their appointments for haematological assessment and Xofigo injections

Monitoring disease status

Ask patients for feedback on their current health status, and any changes they have experienced in day-to-day activities. Reassure patients that changes in PSA levels do not correlate with the effectiveness of Xofigo[2,17]

Possible adverse events

In general, Xofigo is well-tolerated, but some adverse events have been very commonly reported, including: diarrhoea, nausea, vomiting, bone fracture, thrombocytopenia, neutropenia, pancytopenia, leukopenia, and injection site reaction[1]

Patients should be encouraged to report any adverse events to their healthcare team. Optimal management of adverse events will support patients on treatment, and ensure that six treatment cycles are completed

For a full list of AEs please consult the Xofigo SmPC[1]

PSA, prostate-specific antigen.

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Prescribing Information

Prescribing information and adverse event reporting information for Xofigo®▼(radium-223 dichloride) is available via the QR code on the right.

Either click here or scan the QR code for prescribing information and adverse event reporting information.

For direct access to this prescribing information, please ensure your device's browser settings have automatic PDF download enabled.Adverse events should also be reported to Bayer plc.
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