X-clusive preview of a consensus document by an interactive MDT session

Appropriateness of treatment options in mCRPC patients:

Outcomes of a Belgian multidisciplinary consensus meeting*

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*Publication following soon

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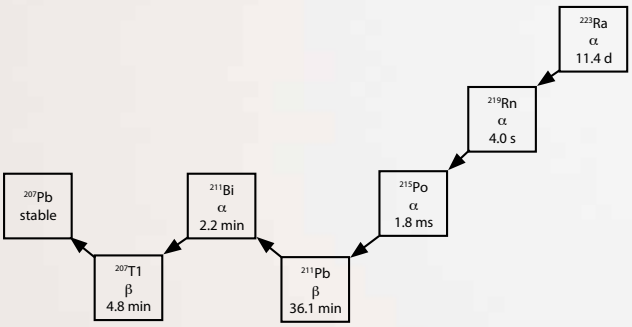
▼ This medicinal product is subject to additional monitoring. **NAME OF THE MEDICINAL PRODUCT:** Xofigo 1100 kBq/mL solution for injection. **QUALITATIVE AND QUANTITATIVE COMPOSITION:** Each mL of solution contains 1100 kBq radium Ra 223 dichloride (radium-223 dichloride), corresponding to 0.58 ng radium-223 at the reference date. Radium is present in the solution as a free ion. Each vial contains 6 mL of solution (6.6 MBq radium-223 dichloride at the reference date). Radium-223 is an alpha particle-emitter with a half-life of 11.4 days. The specific activity of radium-223 is 1.9 MBq/ng. The six-stage-decay of radium-223 to lead-207 occurs via short-lived daughters, and is accompanied by a number of alpha, beta and gamma emissions with different energies and emission probabilities. The fraction of energy emitted from radium-223 and its daughters as alpha-particles is 95.3% (energy range of 5.0 – 7.5 MeV). The fraction emitted as beta-particles is 3.6% (average energies are 0.445 MeV and 0.492 MeV), and the fraction emitted as gamma-radiation is 1.1% (energy range of 0.01 - 1.27 MeV). **Figure 1: Radium-223 decay chain with physical half-lives and mode of decay:**



Excipients with known effect: Each mL of solution contains 0.194 mmol (equivalent to 4.5 mg) of sodium. **PHARMACEUTICAL FORM:** Solution for injection. Clear, colourless isotonic solution with pH between 6.0 and 8.0. **CLINICAL PARTICULARS: Therapeutic indications:** Xofigo is indicated for the treatment of adults with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastases. **Posology and 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. Posology: The dose regimen of Xofigo is an activity of 55 kBq per kg body weight, given at 4 week intervals for 6 injections. Safety and efficacy beyond 6 injections with Xofigo have not been studied. **Elderly:** No overall differences in safety or efficacy were observed between elderly (aged ≥ 65 years) and younger patients (aged < 65 years) in the phase III study. No dose adjustment is considered necessary in elderly patients. **Hepatic impairment:** Safety and efficacy of Xofigo have not been studied in patients with hepatic impairment. Since radium-223 is neither metabolised by the liver nor eliminated via the bile, hepatic impairment is not expected to affect the pharmacokinetics of radium-223 dichloride. No dose adjustment is considered necessary in patients with hepatic impairment. **Renal impairment:** In the phase III clinical study, no relevant differences in safety or efficacy were observed between patients with mild renal impairment (creatinine clearance [CLCR]: 50 to 80 mL/min) and normal renal function. Limited data are available for patients with moderate (CLCR: 30 to 50 mL/min) renal impairment. No data are available for patients with severe (CLCR < 30 mL/min) renal impairment or end-stage renal disease. However, since excretion in urine is minimal and the major route of elimination is via the faeces, renal impairment is not expected to affect the pharmacokinetics of radium-223 dichloride. No dose adjustment is considered necessary in patients with renal impairment. **Paediatric population:** The safety and efficacy of Xofigo in children and adolescents below 18 years of age have not been studied. There is no relevant use of this medicinal product in the paediatric population in the indication of prostate cancer. Method of administration: Xofigo is for intravenous use. It 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. **Contraindications:** There are no known contraindications to the use of Xofigo. **Undesirable effects:** Summary of the safety profile: The overall safety profile of Xofigo is based on data from 600 patients treated with Xofigo in the phase III study. **The most frequently** observed adverse reactions (≥ 10%) in patients receiving Xofigo were diarrhoea, nausea, vomiting and thrombocytopenia. **The most serious** adverse reactions were thrombocytopenia and neutropenia (see 'Description of selected adverse reactions' below). Tabulated list of adverse reactions: The adverse reactions observed with Xofigo are represented in the table below (see Table 1). They are classified according to System Organ Class. The most appropriate MedDRA term is used to describe a certain reaction and its synonyms and related conditions. Adverse reactions from clinical trials are classified according to their frequencies. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. **Table 1: Adverse reactions reported in clinical trials in patients treated with Xofigo:**

System Organ Class (MedDRA)	Very common	Common	Uncommon
Blood and lymphatic system disorders	Thrombocytopenia	Neutropenia, Pancytopenia, Leukopenia	Lymphopenia
Gastrointestinal disorders	Diarrhoea, Vomiting, Nausea		
General disorders and administration site conditions		Injection site reactions	

Description of selected adverse reactions: **Thrombocytopenia and Neutropenia:** Thrombocytopenia (all grades) occurred in 11.5% of patients treated with Xofigo and 5.6% of patients receiving placebo. Grade 3 and 4 thrombocytopenia was observed in 6.3% of patients treated with Xofigo and in 2% of patients receiving placebo. Overall, the frequency of grade 3 and 4 thrombocytopenia was lower in patients that did not previously receive docetaxel (2.8% in patients treated with Xofigo versus 0.8% in patients receiving placebo) compared to patients that previously received docetaxel (8.9% in patients treated with Xofigo versus 2.9% in patients receiving placebo). In EOD4 ("superscan") patients, thrombocytopenia (all grades) was reported in 19.6% of patients treated with Xofigo and in 6.7% of patients receiving placebo. Grade 3 and 4 thrombocytopenia was observed in 5.9% of patients treated with Xofigo and in 6.7% of patients receiving placebo. Neutropenia (all grades) was reported in 5% of patients treated with Xofigo and in 1% of patients receiving placebo. Grade 3 and 4 neutropenia was observed in 2.2% of patients treated with Xofigo and in 0.7% of patients receiving placebo. Overall, the frequency of grade 3 and 4 neutropenia was lower in patients that did not previously receive docetaxel (0.8% in patients treated with Xofigo versus 0.8% in patients receiving placebo) compared to patients that previously received docetaxel (3.2% in patients treated with Xofigo versus 0.6% in patients receiving placebo). In a phase I study, neutrophil and platelet count nadirs occurred at 2 to 3 weeks after intravenous administration of a single dose of Xofigo. **Injection site reactions:** Grade 1 and 2 injection site reactions, such as erythema, pain and swelling, were reported in 1.2% of patients treated with Xofigo and in 0% of patients receiving placebo. **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. In particular, the risk for osteosarcoma, myelodysplastic syndrome and leukaemias may be increased. No cases of Xofigo-induced cancer have been reported in clinical trials in follow-up of up to three years. Reporting of suspected adverse reactions: Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system. **Belgium,** Federaal agentschap voor geneesmiddelen en gezondheidsproducten, Afdeling Vigilantie, EUROSTATION II, Victor Hortaplein, 40/ 40, B-1060 Brussel, Website: www.fagg.be, e-mail: adversedrugreactions@fagg-afmps.be. **Luxembourg,** Direction de la Santé – Division de la Pharmacie et des Médicaments, Villa Louvigny – Allée Marconi, L-2120 Luxembourg, Site internet: http://www.ms.public.lu/fr/activites/pharmaciemedicament/index.html. **DELIVERY METHOD:** On medical prescription. **MARKETING AUTHORISATION HOLDER:** Bayer AG, 51368 Leverkusen, Germany. **MARKETING AUTHORISATION NUMBER(S):** EU/1/13/873/001. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:** Date of first authorisation: 13 November 2013. **DATE OF REVISION OF THE TEXT:** 08/2017.

Program including “Latest insights in Theranostics”

19:00 Welcome

19:30 Topic 1: Latest insights in Theranostics

20:00 Topic 2: Preview of the Consensus publication

- Intro, objective & methodology consensus
- Patient cases with life voting
- Interactive discussion
- Summary consensus statements

21:30 Q&A followed by walking dinner

You want to be present @ this Preview?
Please send a mail to
michele.vanhove@bayer.com

What do the experts say?

Monday 16th of April

3Square Village
Rijvisschestraat, 124
9052 Zwijnaarde

Speakers

Topic 1:
- **Olivier de Winter,** nuclear medicine physician, OLV Aalst

Topic 2:
- **Piet Ost,** radiation oncologist, UZ Gent
- **Philip Debruyne,** medical oncologist, AZ Groeninge

Tuesday 17th of April

Le Bois d’Arpes
Chaussée de Mons, 30
1400 Nivelles

Speakers

Topic 1:
- **Carlos Artigas,** nuclear medicine physician, Institut Bordet

Topic 2:
- **Thierry Roumeguere,** urologist, CHU Erasme
- **Emmanuel Seront,** medical oncologist, CH Jolimont

Wednesday 18th of April

Park Inn by Radisson Leuven
Martelarenlaan, 36
3010 Leuven

Speakers

Topic 1:
- **Karolien Goffin,** nuclear medicine physician, UZ Leuven

Topic 2:
- **Steven Joniau,** urologist, UZ Leuven
- **Dirk Schrijvers,** medical oncologist, ZNA Middelheim
- **Karolien Goffin,** nuclear medicine physician, UZ Leuven

Thursday 26th of April

Naxhelet
Chaussée de Wavre, 224
4520 Wanze (adresse GPS)

Speakers

Topic 1:
- **Nadia Withofs,** nuclear medicine, CHU Liège

Topic 2:
- **Marco Gizzi,** medical oncologist, GHDC Charleroi
- **Lionel Duck,** medical oncologist, CSP Ottignies
- **Nadia Withofs,** nuclear medicine physician, CHU Liège