Package leaflet: Information for the patient

Xofigo 1100 kBq/mL solution for injection

radium Ra 223 dichloride

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor who will supervise the procedure.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Xofigo is and what it is used for

This medicine contains the active substance radium Ra 223 dichloride (radium-223 dichloride).

Xofigo is used to treat adults with advanced castration-resistant prostate cancer in progression after at least two other cancer treatments apart from treatments to maintain reduced levels of male hormone (hormone therapy), or who cannot take any other cancer treatment. Castration-resistant prostate cancer is a cancer of the prostate (a gland of the male reproductive system) that does not respond to treatment that reduces male hormones. Xofigo is only used when the disease has spread to the bone but is not known to have spread to other internal organs, and is causing symptoms (e.g., pain).

Xofigo contains the radioactive substance radium-223 which mimics the calcium found in bones. When injected into the patient, radium-223 reaches the bone where the cancer has spread to and emits short-range radiation (alpha particles) which kills the surrounding tumour cells.

2. What you need to know before Xofigo is used

Xofigo must not be given
- in combination with abiraterone and prednisone/prednisolone (which are used together to treat prostate cancer).

Warnings and precautions
Talk to your doctor before you are given Xofigo

- Xofigo must not be given in combination with abiraterone and prednisone/prednisolone due to a possible increase in the risk of bone fracture or death. Additionally, there are uncertainties about the effects of Xofigo in combination with other medicines used to treat metastatic prostate cancer. If you are already taking one of those medicines, please tell your doctor.
- If you plan to take Xofigo following treatment with abiraterone and prednisone/prednisolone, you must wait 5 days before starting treatment with Xofigo.
- If you plan to take other cancer therapy following treatment with Xofigo, you must wait at least 30 days before starting treatment.
- Xofigo is not recommended if cancer in your bones is not causing symptoms, such as pain.
- Xofigo can lead to a decrease in the number of your blood cells and blood platelets. **Before starting treatment and before each subsequent dose your doctor will perform blood tests.** Depending on the results of these tests your doctor will decide if treatment can be started, can be continued, or needs to be postponed or discontinued.
- If you suffer from **decreased blood cell production in the bone marrow,** e.g., if you have received prior chemotherapy (other medicines used to kill cancer cells) and/or radiation therapy, you may be at higher risk and your doctor will give you Xofigo with caution**.**
- If your tumour has spread to the bone extensively, you may also be more likely to have decreases in your blood cells and platelets, so your doctor will give you Xofigo with caution.
- The limited data available do not suggest any major differences in the blood cell production of patients receiving chemotherapy after treatment with Xofigo compared with those who did not receive Xofigo.
- There are no data on the use of Xofigo in patients with **Crohn's disease** (a long-term inflammatory disease of the intestines) and with **ulcerative colitis** (a long-term inflammation of the colon). As Xofigo is excreted in the faeces, it may make acute inflammation of your bowels worse. Therefore, if you suffer from these conditions your doctor will carefully consider if you can be treated with Xofigo.
- If you suffer from untreated **spinal cord compression** or if it is thought likely that you are developing spinal cord compression (pressure on the spinal cord nerves which can be caused by a tumour or other lesion), your doctor will first treat this disease with standard treatment before starting or continuing treatment with Xofigo.
- If you have **osteoporosis** or a known increased risk for fractures (e.g., **recent bone fracture**, **fragility**), or take or have been taking **steroids** (e.g., prednisone/prednisolone), please tell your doctor. You might be at a higher risk of bone fractures. Your doctor might prescribe you a medicine to prevent bone fractures before starting or continuing treatment with Xofigo.
- If you experience any **new or unusual pain** or **swelling in bone region** prior, during or after your treatment with Xofigo, you should consult your doctor.
- If you experience a **bone fracture**, your doctor will first stabilise the fractured bone before starting or continuing treatment with Xofigo.
- If you take or have taken **bisphosphonates** or have received chemotherapy prior to treatment with Xofigo, please tell your doctor. A risk of *osteonecrosis of the jaw* (dead tissue in the jawbone which is mainly seen in patients who have been treated with bisphosphonates) cannot be excluded (see section 4).
- Xofigo contributes to your overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure may increase your risk for developing cancer (in particular of bone cancer and leukaemia) and hereditary abnormalities. No cases of cancer caused by Xofigo have been reported in clinical studies with a follow-up of up to three years.

Your doctor will test your bone health before deciding whether you can be given Xofigo. During treatment and for 2 years after starting treatment with Xofigo, your doctor will continuously monitor your bone health.

Children and adolescents
This medicine is not for use in children and adolescents.

Other medicines and Xofigo
No interaction studies with other medicines have been done.

Xofigo must not be given in combination with abiraterone and prednisone/prednisolone due to a possible increase in the risk of bone fracture or death. Additionally, there are uncertainties about the effects of Xofigo in combination with other systemic medicines used to treat metastatic prostate cancer. If you are already taking one of those medicines, please tell your doctor.

If you take or have taken bisphosphonates or other medicines to protect your bone health or steroids (e.g., prednisone/prednisolone) prior to treatment with Xofigo, please tell your doctor. You might be at a higher risk for bone fractures.

If you are taking calcium, phosphate and/or Vitamin D, your doctor will carefully consider if you need to temporarily stop taking these substances before you start treatment with Xofigo.

There are no data on the **use of Xofigo at the same time as chemotherapy** (other medicines used to kill cancer cells). Xofigo and chemotherapy used together may further decrease the number of your blood cells and blood platelets.

Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding
Xofigo is not for use in women and must not be given to women who are, or may be, pregnant or who are breast-feeding.

Contraception in males and females
If you are engaged in sexual activity with a woman who could become pregnant you are advised to use effective birth control methods during and up to 6 months after treatment with Xofigo.

Fertility
There is a potential risk that radiation from Xofigo could affect your fertility. Please ask your doctor how this may affect you, especially if you are planning to have children in the future. You may wish to seek advice on conservation of sperm before treatment starts.

Driving and using machines
It is considered unlikely that Xofigo will affect your ability to drive or to use machines.

Xofigo contains sodium
Depending on the volume administered, this medicine can contain up to 54 mg sodium (main component of cooking/table salt) per dose. This is equivalent to 2.7% of the recommended maximum daily dietary intake of sodium for an adult.

3. How Xofigo is used

There are strict laws on the use, handling and disposal of medicines like Xofigo. It will only be used in special controlled areas. This radiopharmaceutical will only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this radiopharmaceutical and will keep you informed of their actions.

The dose you receive depends on your body weight. The doctor supervising the procedure will calculate the quantity of Xofigo to be used in your case.
The recommended dose of Xofigo is 55 kBq (Becquerel, the unit used to express radioactivity) per kilogram body weight.
No dose adjustment is necessary if you are 65 years of age or older or if you have reduced kidney or liver function.

Administration of Xofigo and conduct of the procedure
Xofigo will be injected slowly via a needle into one of your veins (intravenously). The healthcare professional will flush the intravenous access line or cannula before and after injection with a sodium chloride solution.

Duration of the procedure
- Xofigo is given once every 4 weeks for a total of 6 injections.
- There are no data available on the safety and efficacy of treatment with more than 6 injections of Xofigo.

After administration of Xofigo
- Care should be taken when handling materials, such as bed linen, that come into contact with body fluids (such as spill of urine, faeces, vomiting etc.). Xofigo is excreted mainly via the faeces. The doctor will tell you if you need to take any special precautions after receiving this medicine. Contact your doctor if you have any questions.

If you have been given more Xofigo than you should
An overdose is unlikely.
However, in the case of an accidental overdose, your doctor will start appropriate supportive treatment and will check you for changes in the number of blood cells, and for gastrointestinal symptoms (e.g. diarrhoea, nausea [feeling sick], vomiting).

If you have any further questions on the use of Xofigo, please ask the doctor who supervises the procedure.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The most serious side effects in patients receiving Xofigo are
- **decrease in the number of blood platelets** (thrombocytopenia),
- **decrease in the number of neutrophils, a type of white blood cells** (neutropenia, which may lead to an increased risk of infection).

Contact your doctor immediately if you notice the following symptoms as they may be signs of thrombocytopenia or neutropenia (see above):
- any **unusual bruising**,
- more **bleeding** than usual after injury,
- **fever**,
- or if you seem to be catching a lot of **infections.**

Your doctor will perform blood tests before starting treatment and before each injection to check your number of blood cells and platelets (see also section 2).

The most frequent side effects in patients receiving Xofigo (very common [may affect more than 1 in 10 people]) are:
- **diarrhoea, nausea (feeling sick), vomiting, thrombocytopenia (decrease in the number of blood platelets) and bone fracture**.

Risk of dehydration: tell your doctor if you have any of the following symptoms: dizziness, increased thirst, decreased urination or dry skin as these can all be symptoms of dehydration. It is important to avoid dehydration by drinking plenty of fluids.

Other possible side effects are listed below by how likely they are:

Common (may affect up to 1 in 10 people)
- decrease in the number of white blood cells (leukopenia)
- decrease in the number of neutrophils, a type of white blood cells (neutropenia, which may lead to an increased risk of infection)
- decrease in the number of red and white blood cells and blood platelets (pancytopenia)
- injection site reactions (e.g. redness of the skin [erythema], pain and swelling)

Uncommon (may affect up to 1 in 100 people)
- decrease in the number of lymphocytes, a type of white blood cells (lymphopenia)
- weakened bones (osteoporosis)

Xofigo contributes to your overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure may increase your risk of developing cancer (in particular of bone cancer and leukaemia) and hereditary abnormalities. No cases of cancer caused by Xofigo have been reported in clinical studies with a follow-up of up to three years.

If you have symptoms of pain, swelling or numbness of the jaw, a "heavy jaw feeling" or loosening of a tooth, please contact your doctor. Cases of *osteonecrosis of the jaw* (dead tissue in the jawbone which is mainly seen in patients who have been treated with bisphosphonates) have occurred in patients treated with Xofigo. All these cases were only seen in patients receiving bisphosphonates prior to or at the same time of treatment with Xofigo and chemotherapy prior to treatment with Xofigo.

Reporting of side effects
If you get any side effects talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How Xofigo is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulations on radioactive materials.

The following information is intended for the specialist only:
Xofigo must not be used after the expiry date which is stated on the vial and the lead pot.
This medicine does not require any special temperature storage conditions.
Xofigo must not be used if discolouration, the occurrence of particulate matter or a defective container is noticed.

6. Contents of the pack and other information

What Xofigo contains

- The **active substance** is: radium Ra 223 dichloride (radium-223 dichloride).

  Each mL of solution contains 1100 kBq radium-223 dichloride, corresponding to 0.58 ng radium-223 at the reference date.

  Each vial contains 6 mL of solution (6600 kBq radium-223 dichloride at the reference date).

- The **other ingredients** are: water for injections, sodium citrate, sodium chloride and diluted hydrochloric acid (see end of Section 2 for further information on sodium).

What Xofigo looks like and contents of the pack

Xofigo is a clear and colourless solution for injection. It is supplied in a colourless glass vial closed with a grey rubber stopper and aluminium seal. The vial contains 6 mL of solution. It is stored in a lead pot.

Marketing Authorisation Holder
Bayer plc
400 South Oak Way
Reading
RG2 6AD

Manufacturer
Bayer AS
Drammensveien 288
NO-0283 Oslo
Norway

For any information about this medicine, please contact Bayer plc, Tel: 0118 206 3000.

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The following information is intended for healthcare professionals only

The complete SmPC of Xofigo is provided as a tear-off section at the end of the printed leaflet in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.