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Prostate cancer medicine Xofigo must not be used with Zytiga and prednisone/prednisolone

Ongoing clinical study shows an increased risk of death and fractures with the combination

The European Medicines Agency (EMA) has recommended contraindicating the use of the prostate cancer medicine Xofigo (radium-223 dichloride) with Zytiga (abiraterone acetate) and prednisone/prednisolone, due to an increased risk of death and fractures with this combination.

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has reviewed the preliminary data from an ongoing clinical study in metastatic prostate cancer patients. In this study 34.7% of patients treated with Xofigo, Zytiga and prednisone/prednisolone have died so far, compared with 28.2% of patients given placebo, Zytiga and prednisone/prednisolone.

Fractures have also occurred more frequently with the Xofigo combination than the placebo combination (26% versus 8.1%).

In view of the seriousness of the events reported, the PRAC has taken action by introducing a contraindication as a temporary measure to protect patients' safety while an in-depth review of the benefits and risks of Xofigo is ongoing.

Xofigo is currently authorised for use in men whose prostate cancer has spread to the bones and is causing symptoms. The ongoing clinical study includes metastatic prostate cancer patients who have not previously received chemotherapy and who have no symptoms or only mild symptoms, such as pain. Patients have completed the Xofigo part of the study, and the combination is no longer being used; all the patients involved are being monitored closely.

Healthcare professionals in the EU must not use a combination of Xofigo with the anti-androgen Zytiga and prednisone/prednisolone, and should stop this combination in men currently treated with it and review the treatment for these patients. Healthcare professionals are also warned that the safety and efficacy of Xofigo in combination with a class of medicines called second generation androgen receptor antagonists, such as Xtandi (enzalutamide), have not been established.

These are temporary measures until the ongoing in-depth review of the benefits and risks of Xofigo is complete. EMA will communicate further at the conclusion of the review.

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Information for patients

- Doctors are being advised that the medicine for prostate cancer Xofigo must not be used with the prostate cancer medicine Zytiga and prednisone/prednisolone because there is evidence that the combination may be harmful to patients due to a possible increased risk of fractures and death.
- If you are currently being treated with this combination, your doctor will alter your treatment.
- Both medicines can continue to be used separately, in line with the recommendations in their product information.
- If you are being treated with Xofigo and have any questions, you should contact your doctor.

Information for healthcare professionals

- Xofigo must not be used with the anti-androgen Zytiga (abiraterone acetate) and prednisone/prednisolone because of possible increased risk of fractures and mortality.
- The safety and efficacy of Xofigo in combination with second generation androgen receptor antagonists such as Xtandi (enzalutamide) have not been established.
- Both medicines can continue to be used separately, in line with the recommendations in their product information.
- Further information will be made available once an ongoing review of the evidence is complete.

More about the medicine

Xofigo is used to treat adult men with cancer of the prostate (a gland of the male reproductive system). It is authorised for use when medical or surgical castration (stopping the production of male hormones in the body using medicines or surgery) does not work, and when the cancer has spread to the bones and is causing symptoms such as pain but is not known to have spread to other internal organs.

The ongoing study of Xofigo in combination with Zytiga and prednisone/prednisolone included patients with castration-resistant prostate cancer that has spread mainly to the bones, who have no symptoms or only mild symptoms and who have not been treated with chemotherapy.

Xofigo was authorised in the European Union in November 2013. More information on Xofigo is available.

More about the procedure

The review of Xofigo has been initiated at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations.

During the review, the PRAC made provisional recommendations to protect public health. This will be forwarded to the European Commission (EC), which will issue a provisional legally binding decision applicable in all EU Members States.

Once the PRAC review is concluded, any further recommendations will be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for evaluating medicines for human use, which will adopt a final opinion.

The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.