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PRAC recommends restricting use of prostate cancer medicine Xofigo

Medicine should only be used after two previous treatments or when other treatments cannot be taken

EMA's safety committee PRAC has recommended restricting the use of the cancer medicine Xofigo (radium-223 dichloride) to patients who have had two previous treatments for metastatic prostate cancer (prostate cancer that has spread to the bone) or who cannot receive other treatments.

These restrictions follow a review of data from a study suggesting that patients given Xofigo seemed to be at risk of dying earlier and had more fractures than patients given placebo (a dummy treatment). The study included patients with no or only mild symptoms, whereas Xofigo is only authorised in patients with symptoms. In the study, patients given Xofigo with Zytiga (abiraterone acetate) and prednisone/prednisolone died on average 2.6 months earlier than those given placebo with Zytiga and prednisone/prednisolone. In addition, 29% of patients who received the Xofigo combination had fractures, compared with 11% of patients given placebo.

It is thought that Xofigo, which is taken up by the bone, accumulates at sites where the bone is already damaged, for example by osteoporosis or micro-fractures, increasing the risk of fracture. However, the reasons for a possible earlier death in this study are not fully understood.

The PRAC also confirmed its previous interim recommendation that the medicine must not be used with Zytiga and prednisone/prednisolone.

Xofigo should not be used with other systemic cancer therapies, except for treatments to maintain reduced levels of male hormone (hormone therapy). The medicine should not be used in patients who have no symptoms, in line with the current indication, nor in those with a low number of bone metastases called osteoblastic bone metastases.

Patients should be carefully assessed for their risk of fractures before, during and after treatment. Preventive measures such as the use of bisphosphonates or denosumab as agents to increase bone strength should be considered before starting or resuming treatment with Xofigo.

The company marketing Xofigo is requested to conduct studies to investigate, in particular, the mechanisms responsible for the possible risk of earlier death and the increased risk of fractures reported in the study. The benefits and risks of Xofigo in the restricted indication should also be further characterised.

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The PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's opinion.

More about the medicine

Xofigo is currently 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.

Xofigo was authorised in the European Union in November 2013. More information on Xofigo is available on the EMA website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

More about the procedure

The review of Xofigo was initiated on 1 December 2017 at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review was carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations.

In March 2018, the PRAC recommended contraindicating the use of Xofigo with Zytiga and prednisone/prednisolone, as an interim measure, while the review was ongoing.

The PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's 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.