11th December 2017

▼ Radium-223-dichloride (Xofigo): Increased risk of death and fractures in a randomized clinical trial with Xofigo used in combination with abiraterone acetate and prednisolone/prednisone

Dear Healthcare Professional,

Bayer AG, in agreement with the European Medicines Agency and the Health Products Regulatory Authority (HPRA), would like to inform you of the following:

Summary

An increased incidence of deaths and fractures has been identified in a randomised clinical trial in patients with chemotherapy-naïve metastatic castration-resistant prostate cancer (CRPC) receiving radium-223 dichloride in combination with abiraterone acetate and prednisone/prednisolone (15396/ERA-223 study).

Until the full analysis of the results is completed, the following is recommended:

- **Do not treat patients with radium-223 dichloride in combination with abiraterone acetate and prednisone/prednisolone with metastatic castration-resistant prostate cancer**

Background on the safety concern

Xofigo is approved for the treatment of men with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastatic disease.

Preliminary data from a randomised, double blind, placebo controlled study, showed that there was an increased incidence of fractures (24% vs 7%) and deaths (27% vs 20%) among patients receiving Xofigo in combination with abiraterone acetate and prednisone/prednisolone (n=401) compared to patients receiving placebo in combination with abiraterone acetate and prednisone/prednisolone (n=405). This study in asymptomatic or mildly symptomatic chemotherapy-naïve patients with bone predominant metastatic CRPC was un-blinded early based on an Independent Data Monitoring Committee recommendation.

The measures outlined above should be followed while there is further investigation of the implications of these findings. Further advice will be communicated as appropriate at the end of the review.

Call for reporting

Reporting of adverse drug reactions will allow for quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions to

via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. Reports of suspected adverse reactions can also be made to Bayer Ltd, contact details below.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Company contact point

If you have any questions, or if you require any further information, please contact the medical information service of contact Bayer Ltd, The Atrium, Blackthorn Road, Dublin 18; Tel: +353 1 2999313; Fax: +353 1 2061456; E-mail: info.ireland@bayerhealthcare.com.

With kind regards,

Dr. Tristan P. Cooper
Medical Director