**BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**

**XOFIGO** (radium), radioisotope

**Minor clinical added value relative to placebo in the treatment of castration-resistant prostate cancer, with symptomatic bone metastases**

**Main points**
- XOFIGO has had Marketing Authorisation since 2013 as a monotherapy in the treatment of castration-resistant prostate cancer, with symptomatic bone metastases and no known visceral metastases.
- The benefit of radium dichloride treatment was established relative to placebo in patients with castration-resistant prostate cancer with symptomatic bone metastases. No new optimal-level study is available since the previous assessment.
- In the absence of data, its role in the chronological sequence compared with abiraterone acetate or enzalutamide in patients presenting only bone metastases is unclear.

**Therapeutic use**
- In patients with visceral involvement, chemotherapy with docetaxel is offered as a first-line treatment. For patients not able to receive docetaxel, mainly due to their age or general state of health not enabling them to tolerate the cytotoxic adverse effects (in particular neutropaenia), the mitoxantrone and corticosteroid combination can be offered.
- In asymptomatic patients, there is no evidence justifying the early initiation of chemotherapy, which must be discussed individually and balanced against simple monitoring (treatment abstention).
- In mildly symptomatic patients, abiraterone acetate (ZYTIGA) or enzalutamide (XTANDI) is a first-line treatment after failure of androgen deprivation therapy and for whom chemotherapy is not yet clinically indicated.
- Two radioisotopes (strontium 89Sr chloride and samarium 153Sm linked to a bisphosphonate) are also indicated in the treatment of bone metastases from prostate cancer. They target bone metastases and their indication is limited to the analgesic effect because the impact of these two medicinal products on overall survival has not been studied.
- **Role of the medicinal product in the therapeutic strategy**
  - In the current state of the data, XOFIGO represents a therapeutic option in patients with castration-resistant prostate cancer, with symptomatic bone metastases and no visceral or lymphatic involvement (malignant lymphadenopathy exceeding 3 cm).

**Clinical data**
- A new post-hoc subgroup analysis from the pivotal study was performed after patient selection based on whether or not there was a past history of treatment with docetaxel, with an additional 9 months of follow-up relative to the main analysis. Due to the particularly exploratory nature of this analysis, no conclusion can be drawn. Note that during the main analysis, the result from the subgroup previously treated with docetaxel did not show any difference between XOFIGO and the placebo on overall survival.
- The results from data collection are available for 2 non-comparative studies as part of product early access programmes, with Marketing Authorisation granted for XOFIGO. Due to the particularly concomitant administration of an anti-tumour treatment with abiraterone acetate, which involved almost 20% of patients and by enzalutamide in 13.6% of patients, it is not possible to draw conclusions on the specific effect of XOFIGO, either in terms of safety or efficacy in these two studies.
In all, these new data do not allow new conclusions to be drawn regarding the therapeutic contribution of XOFIGO in its indication.

Special prescribing conditions
- Medicinal product reserved for hospital use.
- Medicinal product requiring special monitoring during treatment.

Benefit of the medicinal product
- The actual clinical benefit* of XOFIGO remains substantial. The new data are not likely to change the previous assessment of the Committee, namely that XOFIGO provides a minor clinical added value (CAV IV) compared with the placebo in the treatment of patients with castration-resistant prostate cancer, with symptomatic bone metastases and no known visceral metastases.
- Recommends continued inclusion on the list of reimbursable products for hospital use.

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.

This document was created on the basis of the Transparency Committee Opinion of 22 June 2016 (CT-14706) and is available at www.has-sante.fr