HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
21 JULY 2021

The legally binding text is the original French opinion version

enzalutamide
XTANDI 40 mg film-coated tablets

New indication

Key points

Favourable opinion for reimbursement in the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT).

What therapeutic improvement?

XTANDI (enzalutamide), in combination with ADT, provides a therapeutic improvement compared to ADT alone, in the treatment of metastatic hormone-sensitive prostate cancer (mHSPC).

Role in the care pathway?

The first-line treatment of metastatic hormone-sensitive prostate cancer is based on androgen deprivation therapy (ADT), in combination with either apalutamide or abiraterone acetate plus prednisone or prednisolone, or docetaxel in patients eligible for chemotherapy. These strategies had demonstrated an improvement in overall survival compared to ADT alone.

Role of XTANDI (enzalutamide) in the care pathway:

XTANDI (enzalutamide) in combination with ADT is a first-line option in the treatment of patients with metastatic hormone-sensitive prostate cancer.

In the absence of comparative data, the role of XTANDI (enzalutamide) versus the other available first-line treatment options, i.e., apalutamide, docetaxel or abiraterone acetate (in combination with prednisone or prednisolone) remains to be determined.

According to the experts, the choice of treatment should take into account the patient's age and comorbidities, the patient's informed choice and the level of evidence and the safety profile of each medicinal product.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Metastatic hormone-sensitive prostate cancer is a life-threatening disease.

◗ The proprietary medicinal product XTANDI (enzalutamide) in combination with androgen deprivation therapy (ADT) is a curative treatment.

◗ Its efficacy/adverse effects ratio is high.

◗ There are medicinal alternatives.

◗ This proprietary medicinal product is a first-line treatment. Its role compared to the other alternatives remains to be determined in the absence of comparative data.

Public health impact

Considering:

- the seriousness of metastatic prostate cancer and its incidence,
- the medical need partially met by available drugs,
- the partial response to the identified need, due to the demonstrated additional impact on morbidity of XTANDI (enzalutamide) in combination with ADT compared to ADT alone, but uncertainty with respect to its impact on mortality on the basis of currently available data (demonstration in a single study), pending the final results of the ARCHES study,
- the absence of a demonstrated improvement in terms of patients' quality of life,
- the lack of demonstrated impact on the organisation of care and the care pathway due to its use in combination with ADT,

XTANDI (enzalutamide) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of XTANDI (enzalutamide) is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and at the MA dosage.

◗ **Recommended reimbursement rate: 100%**

Clinical Added Value

Considering, on the one hand:

- **demonstration of an improvement in overall survival with the enzalutamide + ADT combination versus ADT alone in only one of the two studies submitted (the ENZAMET open-label study, HR = 0.67; $CI_{95\%}$ = [0.52; 0.86]) but not confirmed at this stage in the second phase 3, randomised double-blind study (the ARCHES study),**
- **the superiority in terms of radiologic progression-free survival (15.5% versus 34.4%; HR = 0.39, $CI_{95\%}$ = [0.30; 0.50]) demonstrated in the ARCHES study,**
- **the safety profile of XTANDI (enzalutamide) in combination with ADT, deemed to be acceptable compared to the placebo + ADT combination with, respectively, 23.6% and 24.7% grade ≥ 3 adverse events,**

but considering, on the other hand:

- **uncertainties related to the non-availability of the results of the final analysis of the ARCHES study, in a context in which the interim analysis dates from October 2018, and**
- **the absence of demonstration of an improvement in quality of life,**

the Transparency Committee considers that XTANDI (enzalutamide) in combination with androgen deprivation therapy (ADT) provides a minor clinical added value (CAV IV) compared to ADT alone, in the treatment of metastatic hormone-sensitive prostate cancer (mHSPC).