Diagnostics
Sector: Hospital

HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
AND
NATIONAL COMMITTEE FOR THE EVALUATION OF MEDICAL DEVICES AND HEALTH TECHNOLOGIES

having met in application of article L. 161-41 of the French Social Security Code

OPINION

18 FEBRUARY 2020

fluoroestradiol (18F)
ESTROTEP 500 MBq/mL solution for injection

Reevaluation

Key points

Favourable opinion for reimbursement only in patients with metastatic, initially oestrogen receptor-positive (ER+) breast cancer in early relapse following treatment with hormone therapy, when biopsy is deemed to be impossible and a hormone therapy line can be envisaged.

Unfavourable opinion for reimbursement in the other MA situations.

Clinical benefit now low (previously it was insufficient) in the restricted perimeter defined above.

What therapeutic improvement?

No clinical added value in the current diagnostic strategy in patients with metastatic, initially oestrogen receptor-positive (ER+) breast cancer in early relapse following treatment with hormone therapy, when biopsy is deemed to be impossible and an hormone therapy line can be envisaged.

Role in the care pathway?

In primary breast cancer, standard imaging assessment is based on mammograms, potentially supplemented by ultrasound. The breast cancer diagnosis is confirmed by anatomical pathology testing of a biopsy specimen.

Staging is used to assess local, lymph node and remote infiltration. It is not routinely performed and should be reserved for patients presenting clinical warning signs. It is performed by a specialised care team and may include laboratory tests (tumour markers) or imaging exams (breast MRI, FDG-PET in the event of suspected recurrence).

The care pathway for metastatic breast cancer mainly depends on the histological characteristics of the tumour, prior treatments received and their tolerability, the site of the metastases, the time until relapse and predictive factors for treatment response (expression of hormone receptors, especially oestrogen (ER), and/or HER2 receptors).

Currently, evaluation of the expression of oestrogen receptors is carried out by anatomical pathology testing after biopsy of the primary tumour and of a secondary lesion for tumours at the metastatic stage. It should be noted that in some situations, biopsy is judged to be impossible or not relevant.

Role of the medicinal product in the care pathway

ESTROTEP (18F-Fluoroestradiol) is a radiopharmaceutical medicinal product with a role in the diagnostic strategy for patients with metastatic, initially oestrogen receptor-positive (ER+) breast cancer in early relapse following treatment with hormone therapy, when biopsy is deemed to be impossible and an hormone therapy line can be envisaged.

ESTROTEP (18F-Fluoroestradiol) has no role in the other clinical situations of the MA.

JOINT COMMITTEE CONCLUSIONS

Clinical Benefit

◗ Hormone-dependent breast cancer is a serious, life-threatening disease. Characterisation of oestrogen receptor status can help optimise patient management.
◗ ESTROTEP (18F-fluoroestradiol) is a diagnostic radiopharmaceutical product.
◗ On the basis of currently available data, the efficacy/adverse effects ratio has not been adequately established given the diagnostic performance suggested in studies that are not highly robust, the absence of data concerning the impact on patient care and the nonetheless satisfactory safety data for this medicinal product.
◗ When biopsy is deemed impossible, there is no therapeutic alternative to identify the presence of oestrogen receptors; in other cases, histopathological analysis of a biopsy specimen is the reference diagnostic method.
◗ The Joint Committee considers that:

- ESTROTEP (18F-Fluoroestradiol) is a radiopharmaceutical medicinal product with a role in the diagnostic strategy for patients with metastatic, initially oestrogen receptor-positive breast cancer in early relapse following treatment with hormone therapy, when biopsy is deemed to be impossible and an hormone therapy line can be envisaged.
- ESTROTEP (18F-Fluoroestradiol) has no role in other clinical situations.

Public health impact

Considering:

- the seriousness of metastatic breast cancer,
- the incidence of breast cancer, with 58,459 new cases in 2018, the partially met identified need to characterise metastases, particularly in the event of early relapse following hormone therapy and when biopsy is deemed to be impossible,
- the absence of data concerning the care and life pathway,
- the absence of any demonstrated impact on the organisation of care,
- the lack of response to the identified need,

ESTROTEP (18F-Fluoroestradiol) is not likely to have an additional impact on public health.

Considering all these elements, the Joint Committee deems that the clinical benefit of ESTROTEP (18F-Fluoroestradiol) is:

- **low in patients with metastatic, initially oestrogen receptor-positive breast cancer in early relapse following treatment with hormone therapy, when biopsy is deemed to be impossible and an hormone therapy line can be envisaged,**
- **insufficient in the other clinical situations to justify public funding cover.**

The Joint Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in patients with metastatic, initially oestrogen receptor-positive breast cancer in early relapse following treatment with hormone therapy, when biopsy is deemed to be impossible and an hormone therapy line can be envisaged, and at the MA dosages.

The Joint Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the other clinical situations of the MA.

Clinical Added Value

Patients with metastatic, initially oestrogen receptor-positive breast cancer in early relapse following treatment with hormone therapy, when biopsy is deemed to be impossible and an hormone therapy line can be envisaged

Considering:

- **the data obtained from a meta-analysis and a grouped analysis versus immunohistochemistry, which, although not very robust, suggest an acceptable diagnostic performance (sensitivity, between 76 and 86%, and specificity between 80 and 100%);**
- **heterogeneous and uncertain results concerning response prediction, with a PPV of between 52 and 95% and an NPV of between 73 et 77.6%, in a phase 2 study that has already been evaluated and in a newly submitted cohort study,**
- **the absence of any data to date documenting the clinical consequences of management of patients following diagnosis with ESTROTEP (18F-Fluoroestradiol),**

the Joint Committee considers that PET with ESTROTEP (18F-Fluoroestradiol) provides no clinical added value (CAV V) in the current diagnostic strategy.

In the other clinical situations of the MA.

Not applicable.