HAUTE AUTORITÉ DE SANTÉ

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

FEMARA (letrozole), aromatase inhibitor

No clinical benefit over standard care demonstrated in the neoadjuvant treatment of HER-2 negative breast cancer

Main points

- FEMARA now has Marketing Authorisation in the neoadjuvant treatment of postmenopausal women with hormone receptor positive, HER-2 negative breast cancer where chemotherapy is not suitable and immediate surgery is not indicated.
- It has demonstrated an improvement in overall response and an increase in the percentage of patients who can undergo conservative surgery in comparison with tamoxifen, but the population studied in the clinical trial differs from the Marketing Authorisation population; the transferability of the results is therefore uncertain.

Pre-existing indications

- FEMARA already has Marketing Authorisation in the adjuvant treatment of postmenopausal women with hormone-dependent early breast cancer and in the treatment of postmenopausal women with hormone-dependent advanced breast cancer.
- This summary does not cover this indication.

Therapeutic use

- Neoadjuvant treatments (before surgery) are currently widely prescribed in the management of breast cancer. They aim to:
  - shrink the tumour and therefore make less aggressive surgery (conservative surgery) possible or make any surgery possible in the case of an initially unresectable tumour;
  - determine the nature of post-operative treatment.
- Chemotherapy is generally recommended and used as a first-line neoadjuvant treatment for hormone-dependent, HER-2 negative tumours. When chemotherapy is not appropriate, starting hormone therapy is recommended; in postmenopausal women, preferably with an aromatase inhibitor.
- **Role of the medicinal product in the therapeutic strategy**
  In this indication, FEMARA is a first-line neoadjuvant treatment, as are the other aromatase inhibitors.

Clinical data

- FEMARA has primarily been studied in a phase III, randomised, double-blind comparative trial versus tamoxifen, which had the primary objective of determining the anticancer activity of letrozole and tamoxifen in patients with HR+ breast cancer (T2-T4 a, b, c N0-N2, M0) that is not operable or not eligible for conservative surgery.
  Letrozole was found to be superior to tamoxifen on the primary efficacy endpoint: the objective response rate was 55% in the letrozole group versus 36% in the tamoxifen group (OR = 2.23, 95% CI = [1.43; 3.50]). Letrozole was also found to be superior on secondary endpoints, notably the percentage of patients who underwent conservative surgery (45% versus 35%, p = 0.022).
- The HER-2 status of the tumours was not taken into account on inclusion and eligibility for neoadjuvant chemotherapy was not discussed, so the population studied is potentially different from the Marketing Authorisation population and the transferability of the results is uncertain.

Benefit of the medicinal product

- The actual benefit* of FEMARA is substantial.
- FEMARA does not provide clinical added value** (CAV V, absent) in comparison with the current treatment strategy for these patients.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

HAUTE AUTORITÉ DE SANTÉ

This document was created on the basis of the Transparency Committee Opinion of 02 December 2015 (CT-14424) and is available at **www.has-sante.fr**

[i]

[i] * 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".