ONCOLOGY
New indication
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HAUTE AUTORITÉ DE SANTÉ

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

HALAVEN (eribulin), antineoplastic agent

No clinical benefit demonstrated in the second-line treatment of locally advanced or metastatic breast cancer in patients in whom the disease has progressed, compared with the existing therapeutic strategy

Minor improvement in the treatment confirmed in third-line and later line of treatment of locally advanced or metastatic breast cancer that has progressed

Main points

- HALAVEN now has Marketing Authorisation in the treatment of locally advanced or metastatic breast cancer in patients in whom the disease has progressed after at least one chemotherapy protocol for the treatment of the advanced stage. The previous treatment, in the adjuvant or metastatic situation, must have included an anthracycline and a taxane, unless the patient cannot be given these treatments.
- In second-line treatment in a phase III study, no improvement in overall survival or in progression-free survival by comparison with XELODA (capecitabine) was demonstrated.

Pre-existing indication

HALAVEN already has Marketing Authorisation in the treatment in monotherapy of locally advanced or metastatic breast cancer after failure of at least two chemotherapy protocols that included an anthracycline and a taxane, unless the patient cannot be given these treatments.

Therapeutic use

Starting from the second line of treatment (patients who have been given an adjuvant treatment in the locally advanced stage or already given first-line treatment for metastatic disease) and in the absence of overexpression of the HER2 receptor by the tumour (patients with a HER2-negative tumour), the preferred treatment for metastatic HER2-negative breast cancer is monotherapy with capecitabine, vinorelbine or eribulin.

Role of the medicinal product in the therapeutic strategy

HALAVEN in second-line monotherapy is a treatment alternative to the other recommended monotherapies: capecitabine (XELODA) or vinorelbine (NAVELBINE), in the treatment of locally advanced or metastatic breast cancer in patients with an HER2-negative tumour that has progressed.

Clinical data

- *In second-line treatment:* in an open, randomised study carried out in 1102 patients with locally advanced or metastatic breast cancer previously treated with anthracyclines and taxanes, regardless of the HER2 status of their tumours, there was no difference between the eribulin 1.23 mg/m^2 group, with IV infusion, and the capecitabine 2500 mg/m^2 group, with oral administration, in terms of overall survival (co-primary efficacy endpoint) (15.9 months versus 14.5 months, HR = 0.879) nor in terms of progression-free survival (4.1 months versus 4.2 months, HR = 1.079).

- *In third-line treatment and later:* in an open study carried out in 762 patients with locally advanced or metastatic breast cancer following failure of at least two lines of treatment including an anthracycline and a taxane, the median overall survival was higher in the eribulin group than in the "physician's treatment of choice" group, at 13.2 months compared with 10.6 months, i.e. an absolute gain of 2.6 months (HR = 0.815). The analysis of the updated survival data confirms the superiority of eribulin over the "physician's treatment of choice" group in terms of median overall survival, which is of the same order as in the previous analyses.

- The most common adverse effects observed with eribulin versus capecitabine were: neutropenia (54% versus 16%), leukopenia (31% versus 10%), anaemia (20% versus 18%), alopecia (35% versus 4%) and peripheral neuropathies (13% versus 7%). On the other hand, gastrointestinal disorders were more often observed with capecitabine (44% versus 53%, including diarrhoea 14% versus 29%).
  The percentage of grade ≥ 3 adverse events was higher in the eribulin group (65%) than in the capecitabine group (46%), the principal ones were: neutropenia (53% versus 5%) and leukopenia (15% versus 2%); on the other hand, palmoplantar erythrodysesthesia was not observed in the eribulin group (0% versus 14.5%). These proprietary medicinal products do not have the same safety profiles.
- The most commonly reported adverse events (eribulin versus TCM) were asthenia (54.5% versus 40.1%), neutropenia (52.7% versus 30.0%), alopecia (44.7% versus 9.7%), peripheral neuropathy (34.6% versus 16.2%) and nausea (30.5% versus 28.3%).
  The incidence of grade 3-4 adverse events was higher in the eribulin group (grade 3: 62.9% and grade 4: 30.2%) than in the group treated with TCM (grade 3: 46.6% et grade 4: 13.4%).

Prescribing conditions

Medicine for hospital prescription, restricted to oncologists, haematologists or doctors with cancer training and requiring special supervision during treatment.

Benefit of the medicinal product

The actual benefit* of HALAVEN:
- is substantial in locally advanced or metastatic breast cancer in patients with a HER2-negative tumour in whom the disease has progressed after at least one chemotherapy protocol for the treatment of the advanced stage; the previous treatment, in the adjuvant or metastatic situation, must have included an anthracycline and a taxane, unless the patient cannot be given these treatments;
- and remains substantial after at least two chemotherapy protocols for locally advanced or metastatic breast cancer; the previous treatment, in the adjuvant or metastatic situation, must have included an anthracycline and a taxane, unless the patient cannot be given these treatments.

- HALAVEN does not provide clinical added value** (CAV V) relative to the existing therapeutic strategy in second-line treatment of locally advanced or metastatic breast cancer when the disease has progressed.
  HALAVEN continues to provide clinical added value** (CAV IV, minor) in third-line and later line of treatment of locally advanced or metastatic breast cancer in patients in whom the disease has progressed.

- Recommends inclusion on the list of reimbursable products for hospital use in the new indication.

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This document was created on the basis of the Transparency Committee Opinion of 23 September 2015 (CT-14274 & CT-14276) and is available at **www.has-sante.fr**

[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".