BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

HERCEPTIN (trastuzumab), monoclonal antibody

Treatment of HER2+ early breast cancer:
Substantial improvement as ADJUVANT
Minor improvement as NEOADJUVANT

Main points

- HERCEPTIN has Marketing Authorisation in the treatment of adult patients with HER2+ early breast cancer:
  - following surgery, chemotherapy (neoadjuvant or adjuvant) and radiation therapy (if applicable);
  - following adjuvant chemotherapy with doxorubicin and cyclophosphamide, in combination with paclitaxel or docetaxel,
  - in combination with adjuvant chemotherapy combining docetaxel and carboplatin,
  - in combination with neoadjuvant chemotherapy followed by adjuvant HERCEPTIN therapy, in patients with locally advanced (including inflammatory) disease or tumours measuring more than 2 cm in diameter.
- In adjuvant treatment of HER2+ breast cancer, new data confirm the benefit of adding trastuzumab to chemotherapy in terms of disease-free survival and overall survival.
- In neoadjuvant treatment of HER2+ breast cancer, trastuzumab, in combination with chemotherapy, has not always demonstrated gain in overall survival. However, its use may improve access to breast-conserving surgery.

Pre-existing indications

HERCEPTIN also has Marketing Authorisation in the treatment of HER2+ metastatic breast cancer and HER2+ metastatic stomach or gastro-oesophageal junction adenocarcinoma.

Therapeutic use

- The strategy for early breast cancer management relies primarily on surgery. When the tumour overexpresses HER2, an adjuvant treatment is generally initiated after the procedure. If the patient is not eligible for breast-conserving surgery from the outset, a neoadjuvant treatment may be set up with the main objective of allowing breast-conserving surgery or making a surgical procedure possible faced with a tumour that was initially not resectable.
- Adjuvant and neoadjuvant treatment of HER2+ early breast cancer relies generally on anthracycline-based chemotherapy followed by taxane-based chemotherapy, combined with trastuzumab. Other chemotherapy protocols are sometimes initiated, but are routinely combined with trastuzumab concomitantly or sequentially. At the end of the last cycle of chemotherapy, trastuzumab treatment must be maintained as a maintenance monotherapy for 1 year.

Role of the medicinal product in the therapeutic strategy

HERCEPTIN, in combination with chemotherapy, is a first-line treatment, as an adjuvant or neoadjuvant, for HER2+ breast cancer.

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1 This summary does not cover these indications.

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Clinical data

- **In adjuvant treatment of HER2+ early cancer:** the results of four clinical studies show a benefit of adding trastuzumab to chemotherapy in terms of disease-free survival (primary efficacy endpoint) relative to chemotherapy alone after a median follow-up of at least one year. This gain in efficacy was found whether trastuzumab was administered:
  - sequentially to chemotherapy: 92.5% versus 87.1%, HR 0.54, 95% CI = [0.44; 0.67];
  - concomitantly with chemotherapy: 92% versus 84.5%, HR 0.48, 95% CI = [0.39; 0.59];
  - concomitantly with chemotherapy with no anthracyclines: 81% versus 75%, HR = 0.75, p=0.04;
- These four studies are also in favour of an improvement in overall survival (secondary efficacy endpoint). The updated data from some studies suggest that efficacy is maintained after a median of 8 years of follow-up.
- **In the neoadjuvant treatment of HER2+ early breast cancer:** The evaluation of trastuzumab in this indication is based mainly on the results of a clinical study demonstrating, after a median follow-up of 3.2 years, a benefit of the addition of trastuzumab to chemotherapy followed by adjuvant monotherapy relative to neoadjuvant chemotherapy alone, in terms of disease-free survival (primary efficacy endpoint): 40% versus 51%, HR = 0.65, 95% CI = [0.44; 0.96]. No benefit in terms of overall survival nor access to breast-conserving surgery has been demonstrated. However, this study has limitations for transposability to current practice: concomitant use of trastuzumab with anthracyclines is not recommended and the patients of the comparator group did not receive adjuvant therapy.

Special prescribing conditions

- Medicine for hospital prescription only, restricted to cancer treatment and clinical oncology specialists.

Benefit of the medicinal product

- The actual clinical benefit* of HERPCETIN is substantial.
- HERCEPTIN provides a substantial clinical added value ** (CAV II) in the adjuvant therapeutic strategy for management of HER2+ early breast cancer.
- HERCEPTIN provides a minor clinical added value ** (CAV IV) in the neoadjuvant therapeutic strategy for management of HER2+ early breast cancer.
- Recommends inclusion on the list of reimbursable products for hospital use.

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* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. HAS Transparency Committee assesses the ACB, 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".

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