HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
Investigation
May 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

HERCEPTIN (trastuzumab), monoclonal antibody

GASTRIC CANCER

Minor improvement in combination with chemotherapy in the treatment of metastatic HER2+ gastric or gastro-oesophageal junction cancer

Main points

- HERCEPTIN has Marketing Authorisation in the treatment of metastatic adenocarcinoma of the stomach or gastro-oesophageal junction, with tumour HER2 overexpression, in combination with fluoropyrimidine (5FU or capecitabine) and cisplatin, in patients who have not been previously treated for their metastatic disease.
- In the only available comparative study, its addition to chemotherapy was associated with a modest benefit in terms of median overall survival (gain of 4.2 months) without benefit in quality of life. No new clinical data confirmed these results, resulting from a *post-hoc* subgroup analysis.
- The only targeted therapy available in this indication, it is nevertheless the standard treatment in combination with chemotherapy.

Therapeutic use

- The treatment of HER2+ metastatic adenocarcinoma of the stomach or the gastro-oesophageal junction is based on the administration of chemotherapy (double or triple therapy based on: cisplatin, 5-FU, capecitabine) combined with a targeted anti-HER2 therapy (trastuzumab).
- **Role of the medicinal product in the therapeutic strategy**
  HERCEPTIN is the only targeted therapy to have Marketing Authorisation in combination with chemotherapy for the treatment of HER2+ metastatic adenocarcinoma of the stomach or gastro-oesophageal junction and represents the targeted therapy of choice in this indication.

Clinical data

- The interim results of the pivot study (assessed in 2011) showed that the absolute increase in median overall survival (primary efficacy endpoint) was + 2.7 months with the HERCEPTIN + chemotherapy combination (13.8 months versus 11.1 months; HR=0.74; 95% CI [0.60-0.91]; p=0.0046), with no gain in terms of quality of life. A post-hoc analysis of the results of this study suggested a gain of 4.2 months in median overall survival in favour of the addition of HERCEPTIN to chemotherapy only in the subgroup strongly overexpressing HER2 (population specified in the MA).
- It is unfortunate that no new efficacy data are available to confirm the results suggested by the *post-hoc* analysis of the study above in terms of overall survival in the population of the Marketing Authorisation.
- The HERCEPTIN safety data, regardless of the indication, confirm the known safety profile of this proprietary medicinal product. The main concerns remain cardiac toxicity, hypersensitivity reactions, haemotoxicity (febrile neutropenia in particular), and pulmonary adverse events. An initial assessment of cardiac function is necessary at treatment initiation and then every 3 months during treatment and every 6 months after treatment discontinuation up to 24 months after discontinuation.

Special prescribing conditions

- Medicine for hospital prescription.
- Prescription restricted to cancer treatment and oncology specialists and departments.

Benefit of the medicinal product

- The actual clinical benefit* of HERCEPTIN is substantial in this indication.
- HERCEPTIN retains a minor clinical added value ** (CAV IV) in terms of efficacy (non-optimal level of evidence) in the treatment strategy for metastatic adenocarcinoma of the stomach or the gastro-oesophageal junction with tumour HER2 overexpression defined by IHC3+ or IHC2+ confirmed by a SISH+ or FISH+ result, in combination with capecitabine or 5-fluorouracil and cisplatin in patients who were not previously treated for their metastatic disease.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 11 May 2016 (CT-15036) available at **www.has-sante.fr**

* 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".