HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
May 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ADCETRIS (brentuximab vedotin), monoclonal antibody

Substantial clinical benefit in the treatment of CD30+ Hodgkin's lymphoma with increased risk of relapse or progression following autologous stem cell transplant and minor clinical added value in the management of this disease

Main points

- ADCETRIS has Marketing Authorisation in the treatment of adult patients with CD30+ HL at increased risk of relapse or progression following autologous stem cell transplant (ASCT).
- Its efficacy has been demonstrated compared with placebo in terms of progression-free survival.
- A gain in overall survival has not been demonstrated to date, and so the benefit of this preventive strategy for post-ASCT recurrence cannot be determined compared with the treatment of the relapse with brentuximab vedotin.
- Serious adverse events may occur during treatment with brentuximab vedotin.

Pre-existing indications*

ADCETRIS already has Marketing Authorisation in the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL):

- following autologous stem cell transplant (ASCT) or
- following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option, and for the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL).

Therapeutic use

- The first-line treatment of choice for CD30+ HL relies on intensive chemotherapy like ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) or BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone), possibly followed by radiotherapy of the initially involved lymph node regions. The choice of protocol and number of cycles must depend on the prognostic factors for the disease and potential long-term treatment complications.
- In case of relapse of HL, salvage chemotherapy (DHAP, MINE, ICE or IVA) followed by ASCT leads to complete response in approximately 50% of patients. If disease progression or relapse after the second-line treatment is observed, treatment with brentuximab vedotin is recommended. A next-line treatment with nivolumab can be offered in case of progression after brentuximab vedotin.
- **Role of the proprietary medicinal product in the therapeutic strategy**
  ADCETRIS is a first-line treatment in adults with increased risk of recurrence or progression following ASCT, defined as having:
  - a history of disease refractory to chemotherapy, or
  - a relapse or disease progression during the 12 months following the first-line treatment, or
  - extranodal involvement at the time of the pre-ASCT relapse.

* This summary does not cover these indications.

Clinical data

- The assessment of brentuximab vedotin in this extension of indication is based primarily on one randomised, double-blind, placebo-controlled +/- supportive care study. This study was conducted in 329 patients who received ASCT for their second-line treatment of HL within the 30 to 45 days prior to inclusion and were considered at high risk of relapse, defined as:
  - having a history of disease refractory to chemotherapy, or
  - having had a relapse or disease progression during the 12 months following the first-line treatment, or
  - having extranodal involvement at the time of the pre-ASCT relapse.
- Brentuximab vedotin demonstrated its superiority versus placebo on median progression-free survival (primary endpoint): 42.9 months versus 24.1 months, HR=0.57, 95% CI [0.4; 0.8], p<0.0001. The gain in progression-free survival seems to have been obtained in the first months of treatment; therefore, the optimal duration of this maintenance therapy (16 cycles in the study) is not clearly established. No difference in terms of overall survival was found at the time of the interim analysis (HR=1.12, 95% CI = [0.69; 1.82]).
- More grade ≥3 adverse events (56% versus 32%), serious adverse events (25% versus 13%) and adverse events leading to treatment discontinuation (32% versus 6%) occurred in the brentuximab vedotin group than in the placebo group. Overall, the safety profile observed in this study is consistent with the profile known for this product. The primary risks are progressive multifocal leukoencephalopathy (PML), peripheral neuropathies (sensory and motor), neutropenia, opportunistic infections and Stevens-Johnson and Lyell's syndromes.

Special prescribing conditions

- Medicinal product reserved for hospital use
- Medicine restricted to haematologists or doctors trained in blood diseases.

Benefit of the medicinal product

- The actual benefit* of ADCETRIS is substantial.
- ADCETRIS provides clinical added value** (CAV IV) in the therapeutic strategy for the management of patients with increased risk of recurrence or progression following ASCT, defined as having:
  - a history of disease refractory to chemotherapy, or
  - a relapse or disease progression during the 12 months following the first-line treatment, or
  - extranodal involvement at the time of the pre-ASCT relapse.
- Recommends inclusion on the list of reimbursable products for hospital use.

HAUTE AUTORITÉ DE SANTÉ
This document was created on the basis of the Transparency Committee Opinion of 03 May 2017 (CT-15701) and is available at **www.has-sante.fr**

* 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".