HAUTE AUTORITÉ DE SANTÉ

# TRANSPARENCY COMMITTEE
# SUMMARY
# 09 SEPTEMBER 2020

*The legally binding text is the original French opinion version*

***brentuximab vedotin***

**ADCETRIS 50 mg powder for concentrate for solution for infusion**

**New indication**

## Key points

Favourable opinion for reimbursement only in the treatment of previously untreated systemic anaplastic large cell lymphoma (sALCL), in combination with cyclophosphamide, doxorubicin and prednisone, in the absence of an ALK mutation or in the presence of an ALK mutation (ALK+) in patients with an IPI score of ≥2.

Unfavourable opinion for reimbursement in ALK+ patients with an IPI score <2, due to a lack of available data.

## What therapeutic improvement?

Therapeutic improvement compared to the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, prednisone).

## Role in the care pathway?

The first-line treatment of sALCL is based on multi-agent chemotherapy using the CHOP regimen (cyclophosphamide, doxorubicin, vincristine and prednisone) +/- combined with etoposide, which may be followed by an autologous stem cell transplant (ASCT) in certain cases.

**Role of the medicinal product in the care pathway**

**ADCETRIS (brentuximab vedotin) in combination with cyclophosphamide, doxorubicin and prednisone (A-CHP regimen) has demonstrated its superiority compared to the CHOP regimen in terms of progression-free survival and overall survival, with uncertainty with respect to the absolute increase in overall survival in the absence of its quantification. Consequently, ADCETRIS (brentuximab vedotin) in combination with cyclophosphamide, doxorubicin and prednisone is the recommended first-line treatment option in adults with previously untreated systemic anaplastic large cell lymphoma (sALCL), with the exception of ALK+ patients with an IPI score<2, who were excluded from the study and for whom there are no clinical data for brentuximab vedotin as first-line therapy.**

## COMMITTEE'S CONCLUSIONS

### Clinical benefit

◗ Systemic anaplastic large cell lymphoma (sALCL) is a serious, life-threatening condition.
◗ ADCETRIS (brentuximab vedotin) in combination with cyclophosphamide, doxorubicin and prednisone (A-CHP) is a curative treatment for adult patients with previously untreated sALCL.
◗ The efficacy/adverse effects ratio of ADCETRIS (brentuximab vedotin) is high in ALK- patients and ALK+ patients with an IPI score ≥2 and has not been determined in ALK+ patients with an IPI score<2, due to a lack of available data.
◗ There are therapeutic alternatives (see 05. Clinically relevant comparators).
◗ ADCETRIS (brentuximab vedotin) in combination with cyclophosphamide, doxorubicin and prednisone (A-CHP) is a first-line treatment for sALCL, with the exception of ALK+ patients with an IPI score<2, who were excluded from the study and for whom there are no clinical data for brentuximab vedotin as first-line therapy.

**Public health impact**

Considering:
- the seriousness of the disease,
- its incidence,
- the partially met medical need,
- the absence of data concerning the care and/or life pathway,
- the absence of any demonstrated impact on the organisation of care,
- the partial response to the identified need, given the demonstrated benefit in terms of overall survival, with uncertainty with respect to the absolute increase in the absence of quantification, and without any demonstrated additional impact on quality of life,

ADCETRIS (brentuximab vedotin) is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of ADCETRIS (brentuximab vedotin) is:**

- **Substantial in the treatment of previously untreated systemic anaplastic large cell lymphoma (sALCL), in combination with cyclophosphamide, doxorubicin and prednisone (CHP), only in the absence of an ALK mutation (ALK-) or in the presence of an ALK mutation (ALK+) in patients with an IPI score of ≥2.**

- **Insufficient in the treatment of previously untreated sALCL in combination with CHP, in ALK+ patients with an IPI score<2, due to a lack of available data.**

**The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the treatment of previously untreated systemic anaplastic large cell lymphoma (sALCL), in combination with cyclophosphamide, doxorubicin and prednisone (CHP), only in the absence of an ALK mutation (ALK-) or in the presence of an ALK mutation (ALK+) in patients with an IPI score of ≥2 and at the MA dosages.**

**The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the treatment of previously untreated sALCL in combination with CHP, in ALK+ patients with an IPI score<2, due to a lack of available data.**

## Clinical Added Value

**Considering:**

- **demonstration of the superiority of ADCETRIS (brentuximab vedotin) in combination with cyclophosphamide, doxorubicin and prednisone compared to the CHOP regimen, a clinically relevant comparator, in terms of progression-free survival and overall survival, in patients with previously untreated systemic anaplastic large cell lymphoma (subgroup corresponding to the MA), only in the absence of an ALK mutation (ALK-) or in the presence of an ALK mutation (ALK+) in patients with an IPI score of ≥2, with uncertainty, however, with respect to the absolute increase in terms of overall survival in the absence of its quantification,**

**but:**

- **the absence of a demonstrated improvement on quality of life and**
- **the safety profile of ADCETRIS (brentuximab vedotin), primarily marked by neurological and gastrointestinal toxicity,**

**the Transparency Committee considers that ADCETRIS (brentuximab vedotin) in combination with cyclophosphamide, doxorubicin and prednisone provides a moderate clinical added value (CAV III) compared to the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, prednisone) in the treatment of adults with previously untreated systemic anaplastic large cell lymphoma, only in the absence of an ALK mutation (ALK-) or in the presence of an ALK mutation (ALK+) in patients with an IPI score of ≥2.**