HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
3 MARCH 2021
The legally binding text is the original French opinion version

ceritinib
ZYKADIA 150 mg hard capsules

Reevaluation

Key points

Favourable opinion for maintenance of reimbursement in the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

In the case of ALK-positive NSCLC, treatment has been significantly modified by the arrival of anti-ALK targeted therapies, the first of which was crizotinib, which has demonstrated its superiority compared to systemic chemotherapy. Other anti-ALK tyrosine kinase inhibitors (TKIs) have been developed subsequently (ceritinib and alectinib). Given its demonstrated superiority versus crizotinib in terms of progression-free survival and risk of intracranial disease progression, alectinib (ALECENSA) is the option to be favoured in the first-line treatment of ALK+ lung cancer. Depending on the choice of first-line treatment and the type of progression (slow and symptomatic, development

of brain metastases, isolated or multiple systemic lesions) of the disease, a switch to another anti-ALK TKI may be considered.

Role of the medicinal product in the care pathway:

ZYKADIA (ceritinib) could be proposed in the event of resistance linked to an ALK-dependent mutation as a possible option after first-line treatment with a TKI (preferentially alectinib) and as second-line treatment if not previously used, in the event of an ALK mutation sensitive to this drug (as determined by resistance phenotyping mechanisms by "liquid biopsy" or in situ sampling).

Considering the evolution of the care pathway, with the integration of second-generation anti-ALK drugs (alectinib, ceritinib, brigatinib, lorlatinib) as first and/or second-line therapy, and the lack of any specific data in patients in whom treatment with these anti-ALKs has failed, the role of ZYKADIA (ceritinib) remains to be specified in this situation.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Non-small cell lung cancer (NSCLC) is a serious, life-threatening condition.

◗ The proprietary medicinal product ZYKADIA (ceritinib) is a curative treatment specific to NSCLC with ALK rearrangement.

◗ Its efficacy/adverse effects ratio is high.

◗ There are medicinal alternatives (see: 05 Clinically relevant comparators).

◗ It is a second or later-line therapy (see section 9 of the opinion).

Public health impact

Considering:

- the seriousness of the disease and its low incidence (ALK+ alteration),
- the medical need, which is considered to be partially met,
- the lack of additional response to the identified medical need, due to:
    - the absence of randomised data versus TKIs indicated from the second line of treatment of ALK+ NSCLC;
    - the lack of transposability to clinical practice of the data from the ASCEND-5 study provided given the evolution of the care pathway. Consequently, it is impossible to quantify any impact on morbidity and mortality and on quality of life compared to the available alternatives.
- an impact on the organisation of the healthcare system (hospitalisations avoided, transfer of care to consultations), which is not documented,

ZYKADIA (ceritinib) is unlikely to have an additional impact on public health.

Given all these elements, the Committee deems that the clinical benefit of ZYKDIA (ceritinib) remains substantial in the MA indication.

The Committee issues a favourable opinion for maintenance of inclusion in the hospital formulary list and/or the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication "ZYKADIA (ceritinib) as monotherapy is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib" and at the MA dosages.

- **Recommended reimbursement rate: 100%**

Clinical Added Value

Taking into account both:

- **demonstration of an improvement in progression-free survival versus chemotherapy (absolute increase of 3.8 months (HR = 0.49, CI 95% [0.36; 0.67], p<0.001, following a median follow-up of 16.5 months) with no demonstrated impact on overall survival or quality of life,**
- **the profile of the patients included in the pivotal study, that complied with care pathway at the time the study was conducted but that no longer corresponds to the profile of patients currently treated at this treatment line,**

the Committee considers that ZYKADIA (ceritinib) does not provide any clinical added value (CAV V) in the care pathway of patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib.