HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

09 SEPTEMBER 2020

The legally binding text is the original French opinion version

brigatinib

ALUNBRIG 30 mg, 90 mg, 180 mg tablets

New indication

Key points

Favourable opinion for reimbursement in the indication “as monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with a tyrosine kinase inhibitor that targets the ALK+ mutation”.

What therapeutic improvement?

ALUNBRIG (brigatinib) provides a therapeutic improvement compared to crizotinib in the first-line treatment of advanced non-small cell lung cancer (NSCLC) with ALK gene rearrangement (ALK positive).

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 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.

Role of the medicinal product in the care pathway:

ALUNBRIG (brigatinib) as monotherapy is a first-line treatment for advanced non-small cell lung cancer (NSCLC) with ALK gene rearrangement (ALK positive). Its superiority compared to crizotinib has only been demonstrated in terms of progression-free survival. In the absence of any comparative data, its role compared to alectinib remains to be specified. However, the level of demonstration of each drug and its safety profile must be taken into account when choosing a first-line anti-ALK therapy. In this context, alectinib has demonstrated an effect on brain metastases.
Furthermore, the conditions of use can be discussed in the event of sensitivity of the mutation to the drug (as determined by resistance phenotyping mechanisms by "liquid biopsy" or in situ sampling), and as an option following consideration of the benefit/safety ratio in other cases.

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.
- This is a specific curative treatment for ALK+ NSCLC.
- The efficacy/adverse effects ratio is high.
- There are medicinal alternatives.
- It is a first-line treatment.

- Public health impact:

Considering:
- the incidence of locally advanced or metastatic non-small cell lung cancer,
- its seriousness,
- the available clinical data from a comparative study having demonstrated an increase in progression-free survival, without it being possible to draw any conclusions with respect to overall survival given the follow-up methodology (and discontinuation of the hierarchical sequence),
- the absence of demonstration of an improvement in quality of life (exploratory data),
- the transposability of the results of the trials to clinical practice, which is considered to be acceptable,

the Committee considers that ALUNBRIG is unlikely to have any impact on public health in this indication.

Considering all these elements, the Committee deems that the clinical benefit of ALUNBRIG (brigatinib) is substantial in this new MA indication.

The Committee issues a favourable opinion for inclusion of ALUNBRIG (brigatinib) in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in this new indication and at the MA dosages.

- **Recommended reimbursement rate: 100%**

Clinical Added Value

Taking into account both:

- **the demonstration in a phase III open-label study of a superiority compared to crizotinib in terms of progression-free survival (primary endpoint: median not reached in the brigatinib group versus 9.8 months in the crizotinib group (HR = 0.492 (95% CI: [0.33; 0.74]),**
- **the absence of any possible conclusion with respect to an increase in overall survival given discontinuation of the analysis sequence for the second ranked endpoint,**
- **the absence of demonstration of an improvement in quality of life,**
- **the safety profile of brigatinib, which is acceptable but with an important identified risk of pulmonary toxicity according to the RMP, in particular pneumonitis,**

the Committee considers that ALUNBRIG (brigatinib) provides a minor clinical added value (CAV IV) compared to crizotinib in the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with a tyrosine kinase inhibitor that targets the ALK+ mutation.