HAUTE AUTORITÉ DE SANTÉ

ASSESSING HEALTH TECHNOLOGIES

OPINION ON MEDICINAL PRODUCTS

lorlatinib

LORVIQUA 25 mg and 100 mg,

tablets

New indication

Adopted by the Transparency Committee on 5 October 2022

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SUMMARY

The legally binding text is the original French opinion version

Key points

Approval for reimbursement in the treatment of adult patients with ALK (anaplastic lymphoma kinase) positive advanced non-small cell lung cancer (NSCLC) not previously treated with an ALK inhibitor, as monotherapy

Therapeutic improvement?

LORVIQUA (lorlatinib) provides a therapeutic advance over crizotinib, along with alectinib and brigatinib, in the first-line treatment of advanced non-small cell lung cancer (NSCLC) with an ALK rearrangement (ALK positive)

Role in therapeutic strategy?

In NSCLC with an ALK mutation, management has been transformed by the arrival of anti-ALK targeted therapy, the first example of which was crizotinib, which has shown superiority over systemic chemotherapy. Other anti-ALK TKIs were subsequently developed (ceritinib, alectinib, brigatinib). According to the latest AURA guidelines of 2022, given the demonstrated superiority over crizotinib in terms of progression-free survival, alectinib (ALECENSA), brigatinib (ALUNBRIG) and lorlatinib (LORVIQUA) are preferred options in the first-line treatment of ALK+ lung cancer

Role of LORVIQUA (lorlatinib) in the therapeutic strategy:

Lorlatinib is an additional therapeutic option for the first-line treatment of ALK+ advanced NSCLC.

Like alectinib and brigatinib, its superiority over crizotinib has been demonstrated only in terms of progression-free survival. In view of the available data, its role compared to these molecules still needs to be specified. However, the choice of an anti-ALK drug as the first-line treatment should take into account the level of evidence for each molecule and its tolerance profile. In this context, alectinib has a demonstrated effect on brain metastases.

Furthermore, the conditions of use may be discussed in case of sensitivity of the mutation to the molecule (as determined by phenotyping of resistance mechanisms by "liquid biopsy" or in situ sampling), and following consideration of the benefit/tolerance ratio of each molecule.

Committee's conclusions

Clinical Benefit

- Non-small cell lung cancer (NSCLC) is a serious life-threatening condition.
- This is a specific treatment for ALK+ NSCLC with curative intent.
- The efficacy/adverse effect ratio is significant.
- There are alternatives - see paragraph on clinically relevant comparators.
- First-line treatment.

- **Public health benefit**

Considering:

- the severity of the disease and the incidence of locally advanced or metastatic non-small cell lung cancer,
- the partially covered medical need considering the existing alternatives,
- clinical data from a comparative study versus crizotinib that showed a gain in progression-free survival but no evidence concerning overall survival,
- the lack of formal conclusions on the improvement of quality of life,
- the lack of data providing evidence of an additional impact on the delivery of care,

LORVIQUA (lorlatinib) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the actual clinical benefit of LORVIQUA (lorlatinib) is substantial in this new marketing authorisation indication.

The Committee approves the inclusion of LORVIQUA (lorlatinib) in the list of proprietary medicinal products qualifying for reimbursement under social security (retail formulary list) and in the list of proprietary products approved for community use (hospital formulary list) for the marketing authorisation indication and at the marketing authorisation dosages.

Commenté [GM1]: Alignement aux traductions des listes de remboursement utilisés dans la synthèse ALUNBRIG
"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

Considering:

- **the evidence of the superiority of lorlatinib over crizotinib in terms of progression-free survival (primary outcome measure) in the phase III, open-label CROWN study: median not reached in the lorlatinib group versus 9.3 months in the crizotinib group (HR =0.28 CI 95% [0.19; 0.41], p<0.0001);**
- **the failure to demonstrate an improvement in overall survival (immature data);**
- **the lack of evidence of an improvement in quality of life;**
- **the safety profile of lorlatinib, marked in particular by the occurrence of effects on the central nervous system (in particular, cognitive effects and mood disorders, mainly grades 1-2);**
- **an indirect comparison that does not enable a judgement to be made about the clinical benefit of lorlatinib compared to other available anti-ALK TKIs,**

the Transparency Committee deems that LORVIQUA (lorlatinib) provides a minor improvement in clinical added value (CAV IV) compared to crizotinib, in the same manner as alectinib and brigatinib for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with ALK gene rearrangement (ALK+), not previously treated with an ALK inhibitor.