SUMMARY

selpercatinib

RETSEVMO 40 mg and 80 mg,

hard capsules

Indication extension and Reassessment at Transparency Committee's request

Original French opinion adopted by the Transparency Committee on 27 March 2024

The legally binding text is the original French opinion version

Summary of opinion

Approval of reimbursement "as monotherapy for the treatment of adults with advanced RET (REarranged during Transfection) fusion-positive non-small cell lung cancer (NSCLC) not previously treated with a RET inhibitor and as a first-line treatment"

Approval of retention of reimbursement "as monotherapy for the treatment of adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC), not previously treated with a RET inhibitor and as a second-line and subsequent treatment."

Transparency Committee's Conclusions

Clinical Benefit

As first-line treatment

- Non-small cell lung cancer (NSCLC) is a serious and life-threatening disease.
- This is a curative medicinal product.
- The efficacy/adverse effects ratio is high.
- This is a first-line treatment of advanced RET fusion-positive NSCLC in view of the therapies available.

Public health benefit

In view of:

- the seriousness of the disease and its rarity,

- the low prevalence or incidence of RET fusion-positive NSCLC,
- the partially met medical need,
- the evidence of superiority in terms of progression-free survival in relation to immunotherapy and chemotherapy treatment in a randomised open-label phase III study, with no evidence of an additional impact on mortality or quality of life,
- the lack of data allowing an assessment of an additional impact on the care and/or life pathway,

RETSEVMO (selpercatinib) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of RETSEVMO (selpercatinib) 40 mg and 80 mg, hard capsules, is substantial for the indication "as monotherapy for the treatment of adults with advanced RET (REarranged during Transfection) fusion-positive non-small cell lung cancer (NSCLC) not previously treated with a RET inhibitor and as a first-line treatment".

The Committee approves inclusion of RETSEVMO (selpercatinib) 40 mg and 80 mg, hard capsules, in the list of covered drugs for outpatients and in the list of covered drugs for inpatients as monotherapy for the treatment of adults with advanced RET (REarranged during Transfection) fusion-positive non-small cell lung cancer (NSCLC) not previously treated with a RET inhibitor and as a first-line treatment and at the dosages of the marketing authorisation.

➔ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 100%**

As second-line and subsequent treatment

➔ Non-small cell lung cancer (NSCLC) is a serious and life-threatening disease.

➔ This is a curative medicinal product.

➔ The efficacy/adverse effects ratio is low, considering:

- the weakness of the evidence of its efficacy (data from a non-comparative phase I/II study, in which the primary outcome measure - the objective response rate - is not the most appropriate for measuring a clinical benefit) and the lack of comparative data, at least with external control scheduled in advance,
- the medical need as a second-line treatment, where the treatment options are more limited.

➔ There are therapeutic alternatives not specific to RET fusion in the management of NSCLC based on immuno-chemotherapies,

➔ This is a second-line and subsequent treatment of advanced RET fusion-positive NSCLC in view of the therapies available.

➔ Public health benefit

In view of:

- the seriousness of the disease,
- the low prevalence or incidence of RET fusion-positive NSCLC,
- the medical need partially met by the non-specific treatments,
- the insufficiently met medical need, in the absence of available data supporting its therapeutic improvement and its role in relation to the alternatives available,
- the lack of data allowing an assessment of an additional impact on the care and/or life pathway,

RETSEVMO (selpercatinib) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of RETSEVMO (selpercatinib) 40 mg and 80 mg, hard capsules, remains low for the indication "as monotherapy for the treatment of adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC), not previously treated with a RET inhibitor and as a second-line and subsequent treatment".

The Committee approves continued inclusion of RETSEVMO (selpercatinib) 40 mg and 80 mg, hard capsules, in the list of covered drugs for outpatients and in the list of covered drugs for inpatients "as monotherapy for the treatment of adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC), not previously treated with a RET inhibitor and as a second-line and subsequent treatment" and at the dosages of the marketing authorisation.

Clinical Added Value

As first-line treatment

In view of:

- the statistically significant superiority of RETSEVMO (selpercatinib) in terms of progression-free survival assessed by an independent review committee, in a randomised, open-label phase III study in relation to chemotherapy and immunotherapy (LIBRETTO-431),

despite:

- the lack of evidence of an effect on overall survival in the interim analysis, in a context of advanced-stage disease with an unfavourable prognosis;
- the lack of formal conclusion that can be drawn from the quality-of-life findings;
- the safety profile of RETSEVMO (selpercatinib) particularly marked by a greater number in the selpercatinib group than in the control group of grade ≥ 3 AEs (70.3% *versus* 57.1%), SAEs (34.8% *versus* 23.5%) and AE-related deaths (4.4% *versus* 0.0%), as well as cardiotoxicity (in particular grade ≥ 3 arterial hypertension (20.3% *versus* 3.1%)) observed in the LIBRETTO-431 study and grade ≥ 3 QT prolongation (8.9% *versus* 0.0%), AEs mentioned in the SPC and the subject of an RMP;

the Committee deems that RETSEVMO (selpercatinib) provides minor clinical added value (CAV IV) in relation to immunochemotherapy treatment as a first-line treatment.

As second-line and subsequent treatment

Considering the update data available from a “basket” type multi-cohort phase I/II study (LIBRETTO-001) of poor methodological quality and not allowing quantification of the effect size in the absence of a comparator,

the Committee deems that RETSEVMO (selpercatinib) provides no clinical added value (CAV V) in the therapeutic strategy as a second-line and subsequent treatment.