**SUMMARY**

# selpercatinib
# RETSEVMO 40 mg and 80 mg,
## hard capsules
## New indication

**Adopted by the Transparency Committee on 1 February 2023**

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

## Key points

**Unfavourable opinion for reimbursement, in first-line therapy**, as monotherapy for the treatment of adult patients with rearranged during transfection (RET) fusion-positive advanced non-small cell lung cancer (NSCLC).

**Maintenance of the favourable opinion for reimbursement, in second and later-line therapy only**, as monotherapy for the treatment of adult patients with rearranged during transfection (RET) fusion-positive advanced non-small cell lung cancer (NSCLC). (See Transparency Committee opinion of 2 June 2021). This opinion of June 2021 had been **conditional** on the reassessment of this medicinal product within a maximum period of three years on the basis of the results of the phase 3 study in first-line treatment (LIBRETTO-431, primary analysis for end 2023) in RET fusion-positive NSCLC, in this indication.

## What therapeutic improvement?

No clinical added value, on the basis of currently available data.

## Role in the care pathway?

At the advanced stage of non-small cell lung cancer (NSCLC), patients are not eligible for surgery and their treatment is based on systemic therapy.

The first-line treatment of advanced NSCLC, in the absence of molecular abnormalities (EGFR mutations, or ALK or ROS-1 rearrangements) or in the presence of a molecular alteration for which

no targeted therapy is currently available), is based on immunotherapy or immuno-chemotherapy, for eligible patients.

The second-line treatment of NSCLC is based on:

- the administration of a PD-1/ PD-L1 inhibitor if pembrolizumab has not been used as monotherapy or in combination (platinum and pemetrexed for non-squamous NSCLC; carboplatin and paclitaxel for squamous NSCLC) as metastatic first-line treatment in the event of PD-L1 ≥ 50%: OPDIVO (nivolumab), TECENTRIQ (atezolizumab) or KEYTRUDA (pembrolizumab) only in the event of tumours with PD-L1 over-expression ≥ 1%;
- chemotherapy with, in particular, pemetrexed-based protocols if this has not previously been used, or docetaxel-based protocols.

In France, the AURA 2022 guidelines recommend RET inhibitors (selpercatinib or pralsetinib) as second-line therapy following platinum-based chemotherapy in patients with RET-positive advanced NSCLC, with optional referral to a clinical trial to enable them to benefit from a specific treatment targeting RET alterations. These two medicinal products, selpercatinib (RETSVEMO) and pralsetinib (GAVRETO), received a favourable opinion for reimbursement in 2021 (low clinical benefit and CAV V) as second-line therapy in patients with RET-positive advanced NSCLC.

In its 2022 American guidelines, the NCCN recommends the preferential use of selpercatinib or pralsetinib as first-line treatment when RET fusion has been detected before the initiation of treatment and following progression with first-line systemic treatment.

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

Considering:

- the lack of robustness of the data available in a small number of patients included in the phase 1/2 multi-cohort study and from a subgroup of patients naive to prior systemic treatment (n = 69);
- the impossibility of assessing the contribution of RETSEVMO (selpercatinib) compared to chemotherapies in the absence of a direct comparison (single-arm trial) despite this comparison being possible;
- the existence of a phase 3 study, in first-line therapy, assessing RETSEVMO (selpercatinib) compared to pemetrexed combined with platinum-based chemotherapy and combined or otherwise with pembrolizumab, for which the results of the final analysis are expected by the end of 2023;

**The Committee considers that, on the basis of currently available data, RETSEVMO (selpercatinib) has no role in the care pathway as first-line treatment in previously untreated patients.**

**In second and later-line treatment, the Committee considers that the role in the care pathway of RETSEVMO (selpercatinib) remains unchanged relative to the assessment conducted on 2 June 2021.**

# Committee's conclusions

## Clinical Benefit

### First-line treatment of RET-positive advanced NSCLC

- Non-small cell lung cancer (NSCLC) is a serious and life-threatening disease.
- RETSEVMO (selpercatinib) is a curative medicinal product.
- The efficacy/adverse effects ratio has not been adequately established due to:
  - the weakness of demonstration of its efficacy (preliminary data from a phase 1/2 non-comparative study, in which the primary endpoint - the objective response rate - is not the most appropriate for measuring a clinical benefit) and the absence of comparative data, at least with external control scheduled in advance, and
  - the toxicity profile: occurrence of grade ≥ 3 adverse events in 73.9% of patients with NSCLC and serious adverse events recorded in 48.6% of patients with NSCLC;
- There are therapeutic alternatives not specific to RET fusion in the management of NSCLC (see 05 Clinically relevant comparators) based on immuno-chemotherapies.
- On the basis of currently available data, the Committee considers that RETSEVMO (selpercatinib) is a second and later-line treatment.

### Public health benefit

Considering:

- the seriousness of the condition,
- the low prevalence or incidence of RET fusion-positive NSCLC,
- the medical need partially met by non-specific treatments (without specific data in RET fusion-positive NSCLC),
- the lack of an additional response to the identified need in first-line therapy, in the absence of any demonstrated impact on morbidity and mortality, and on quality of life,
- the absence of any demonstrated impact on the organisation of care,

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

**Considering all these elements, the Committee deems that the clinical benefit of RESTEVMO (selpercatinib) is insufficient to justify public funding, in first-line therapy, as monotherapy for the treatment of adult patients with rearranged during transfection (RET) fusion-positive advanced non-small cell lung cancer (NSCLC).**

**The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in this part of the indication.**

### Second and later-line treatment of RET fusion-positive advanced NSCLC not previously treated with a RET inhibitor

- Non-small cell lung cancer (NSCLC) is a serious and life-threatening disease.
- RETSEVMO (selpercatinib) is a curative medicinal product.
- The efficacy/adverse effects ratio has not been adequately established due to:

- the weakness of demonstration of its efficacy (preliminary data from a phase 1/2 non-comparative study, in which the primary endpoint - the objective response rate - is not the most appropriate for measuring a clinical benefit) and the absence of comparative data, at least with external control scheduled in advance;
- the medical need in second-line therapy, where the treatment options are more limited;
- and pending new efficacy and safety data.

➔ There are therapeutic alternatives not specific to RET fusion in the management of NSCLC (see 05 Clinically relevant comparators) based on immuno-chemotherapies as well as a therapeutic alternative specific to RET fusion in the management of NSCLC as second-line therapy with GRAVETO (pralsetinib).

➔ On the basis of currently available data, the Committee considers that RETSEVMO (selpercatinib) is a second and later-line treatment.

### ➔ Public health benefit

Considering:

- the seriousness of the condition,
- the low prevalence or incidence of RET fusion-positive NSCLC,
- the medical need partially met by non-specific treatments (without specific data in RET fusion-positive NSCLC),
- the partial response to the identified need that RETSEVMO (selpercatinib) may provide in view of the available preliminary data, and pending additional data.
- the absence of any demonstrated impact on the organisation of care,

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

**Considering all these elements, the Committee deems that the clinical benefit of RETSEVMO (selpercatinib) remains low in second and later-line therapy, as monotherapy for the treatment of adult patients with rearranged during transfection (RET) fusion-positive advanced non-small cell lung cancer (NSCLC), pending new efficacy and safety data.**

**The Committee had made maintenance of this opinion conditional on the reassessment of RETSEVMO (selpercatinib) within a maximum period of three years based on the results of the phase 3 study in first-line treatment (LIBRETTO-431, results of the primary analysis expected for end 2023).**

**The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in this part of the indication.**

## Recommended reimbursement rate: 100%

## Clinical Added Value

### Second and later-line treatment of RET fusion-positive advanced NSCLC not previously treated with a RET inhibitor

**The Transparency Committee maintains its opinion of 2 June 2021 and considers that RETSEVMO (selpercatinib) provides no clinical added value (CAV V) in the care pathway for the treatment of adult patients with RET fusion-positive advanced non-small cell lung cancer (NSCLC), in second and later-line treatment.**