Original French opinion adopted by the Transparency Committee

The legally binding text is the original French opinion version.

SUMMARY

larotrectinib

VITRAKVI 25 mg, 100 mg and 20 mg/ml

hard capsules and oral solution

Inclusion on list

Adopted by the Transparency Committee on 12 February 2025

Summary of opinion

Favourable opinion for reimbursement only in "VITRAKVI as monotherapy is indicated for the treatment of adult patients with:

- **soft tissue sarcoma,**
- **salivary gland cancer,**
- **non-medullary thyroid cancer,**

that displays a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory treatment options.

Unfavourable opinion for reimbursement in the other situations covered by the MA indication in adults.

This opinion does not modify the Transparency Committee's conclusions concerning the indications in children, cf. Transparency Committee opinion of 8 March 2023 without any new data supplied.

Transparency Committee's Conclusions

Clinical Benefit

- Locally advanced or metastatic solid tumours in the three locations concerned (soft tissue sarcoma, salivary gland cancer, non-medullary thyroid cancer) are life-threatening, with a variability depending on location and histology, in particular. The natural course of solid cancers with NTRK gene fusion has not been adequately characterised and the prognostic value of NTRK gene fusion in solid cancers is not known in clinical practice.
- This is a specific curative cancer treatment.
- The efficacy/adverse effects ratio has not been adequately established and needs to be confirmed by long-term follow-up data, including safety data, in particular (conditional MA).

➔ This is a last-line treatment in the absence of satisfactory available therapies.

➔ **Public health benefit**

Considering:

- the seriousness of the disease and the low prevalence of these solid tumours with NTRK gene fusion, with a variable frequency depending on the location;
- the medical need considered to be unmet in the situations where no treatment options are available apart from supportive care, following the failure of all standard treatments appropriate to the tumour location or when surgery is likely to result in severe morbidity;
- the partial response to the identified need, due to the expected additional impact on morbidity in view of data suggesting an objective response rate (complete or partial response) of more than 50% in a salvage situation, but considering the methodological limitations of these data;
- the lack of quality of life data supporting an improvement in quality of life;
- the lack of evidence of an additional impact on the organisation of care;

VITRAKVI (larotrectinib) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of VITRAKVI (larotrectinib) is:

- **low only for the treatment of adult patients with:**
  - **soft tissue sarcoma,**
  - **salivary gland cancer,**
  - **non-medullary thyroid cancer,**

  that displays a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory treatment options (see sections 4.4 and 5.1 of the SmPC);
- **insufficient to justify public funding in the other MA situations in adults.**

The Committee issues the following opinions:

- **favourable opinion for inclusion of VITRAKVI (larotrectinib) in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the treatment of adult patients with:**
  - **soft tissue sarcoma,**
  - **salivary gland cancer,**
  - **non-medullary thyroid cancer,**

  that displays a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory treatment options (see sections 4.4 and 5.1 of the SmPC);
- **unfavourable opinion for inclusion of VITRAKVI (larotrectinib)in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the other situations covered by the MA indication in adults.**

This opinion does not modify the Transparency Committee's conclusions concerning the indications in children, cf. Transparency Committee opinion of 8 March 2023 without any new data supplied.

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

Clinical Added Value

Considering:

- data suggesting an objective response rate of more than 50% (variable depending on tumour location) in patients treated with VITRAKVI (larotrectinib) in the non-comparative phase 2 NAVIGATE study;
- the medical need considered to be unmet in the situations where no treatment options are available apart from supportive care, following the failure of standard treatments appropriate to the tumour location or when surgery is likely to result in severe morbidity;

and despite:

- the heterogeneity of the clinical situations covered by the indication, in particular in terms of prognosis, treatment strategy and histology;
- the results for an interim endpoint (partial or complete objective response rate) with no evidence of a correlation with a clinical benefit in terms of overall survival;
- the absence of robust comparative data enabling a formal conclusion to be reached with respect to the clinical benefit of VITRAKVI (larotrectinib) compared to supportive care;
- the lack of evidence of an additional benefit in terms of quality of life;

the Committee deems that VITRAKVI (larotrectinib) 25 mg, 100 mg and 20 mg/mL provides no clinical added value (CAV V) compared to the current care pathway for soft tissue sarcoma, salivary gland cancer and non-medullary thyroid cancer, with NTRK gene fusion.