HAUTE AUTORITÉ DE SANTÉ

# TRANSPARENCY COMMITTEE
## SUMMARY
## 21 JULY 2021

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

***entrectinib***
**ROZLYTREK 100 mg hard capsules**
**ROZLYTREK 200 mg hard capsules**

**New indication**

### Key points

Unfavourable opinion for reimbursement in the treatment of adult patients with ROS1-positive (ROS1+), advanced non-small cell lung cancer (NSCLC) not previously treated with ROS1 inhibitors.

## ◗ Role in the care pathway?

Currently, crizotinib is the only treatment to have a specific MA in ROS1-positive NSCLC. In its opinion of 13 May 2020, the Transparency Committee estimated that crizotinib had no role in the first-line treatment of ROS1+, advanced NSCLC. Before the arrival of crizotinib, the treatment of ROS1+, advanced NSCLC was based on chemotherapy combining a platinum-based drug with one of the following: taxane, pemetrexed (in non-squamous NSCLC), gemcitabine or vinorelbine. Bevacizumab can also be combined with this chemotherapy, in non-squamous NSCLC, in patients with an ECOG score of 0-1.

As second or later-line therapy, the use of crizotinib, or platinum-based chemotherapy is recommended.

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

**Considering:**

- **the very preliminary nature of the available efficacy data**, based primarily on the results of a phase 2 non-comparative basket study (STARTRK-2) not meeting the Committee's minimum requirements to provide formal evidence of the clinical benefit of ROZLYTREK (entrectinib),
- **the absence of robust comparative data enabling assessment of the contribution of ROZLYTREK (entrectinib) in ROS1+ NSCLC compared to the available alternatives (chemotherapy or crizotinib), even though, notably, a direct comparative study would have been possible,**
- **the toxicity marked by an incidence of serious adverse events (AEs) reported in almost a third of patients (34%) and of grade ≥3 adverse events in more than one in two patients (56%),**

**the Transparency Committee considers that, on the basis of currently available data, ROZLYTREK (entrectinib) has no role in the care pathway.**

**It considers that in a context in which no robust comparative data is available to guarantee the solidity of the conclusion with respect to the effect of treatment with ROZLYTREK (entrectinib), the introduction of this medicinal product into the care pathway is accompanied by a higher risk than for medicinal products for which the efficacy is based on a comparison conducted with control of the risk of wrongly concluding that the treatment is effective (two-tailed alpha risk conventionally accepted to be 5%).**

## COMMITTEE'S CONCLUSIONS

**Considering all of this information and further to debate and voting, the Committee considers:**

### Clinical benefit

◗ Advanced non-small cell lung cancer (NSCLC) is a serious, life-threatening condition.

◗ ROZLYTREK (entrectinib) is a curative medicinal product.

◗ Considering the preliminary data available derived from a cohort of 37 patients that was one of six included in a phase 2, non-comparative basket study, which does not enable the clinical benefit of ROZLYTREK (entrectinib) to be determined given the uncertainties related to the following in particular (see Section 07.4 Summary and Discussion):
- the absence of comparative data, even though there were clinically relevant comparators available,
- the toxicity noted with time-limited follow-up of patients,
its efficacy/adverse effects ratio versus these comparators cannot be determined.

◗ There are therapeutic alternatives.

◗ ROZLYTREK (entrectinib) has no role in the care pathway (see section 08 Role in the care pathway).

**Public health impact**

Considering:
- the seriousness of the disease and its prevalence,
- the partially met medical need,
- the lack of response to the identified need, in the absence of an additional demonstrated impact on morbidity and mortality or quality of life, given the absence of direct comparative data versus clinically relevant comparators, even though this would have been possible,
- the absence of data enabling assessment of the impact on quality of life or the organisation of care,

ROZLYTREK (entrectinib) is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of ROZLYTREK (entrectinib) is insufficient to justify public funding cover in the MA indication in view of the available alternatives.**

**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 the MA indication and at the MA dosages.**