Original French opinion adopted by the Transparency Committee

The legally binding text is the original French opinion version

**SUMMARY**

pembrolizumab

# KEYTRUDA 25 mg/ml

**concentrate for solution for infusion**

Indication extension

**Adopted by the Transparency Committee on 29 January 2025**

## Summary of opinion

**Favourable opinion for reimbursement in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment, for the treatment of resectable non-small cell lung cancer at high risk of recurrence in adults.**

# Transparency Committee's Conclusions

## Clinical Benefit

- 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 modest.
- KEYTRUDA (pembrolizumab) in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment, can be used for the treatment of NSCLC at high risk of recurrence in adults.
- There are other medicinal products that can be used in neoadjuvant or adjuvant situations, but there are no treatments recommended as part of a perioperative strategy.

### Public health benefit

Considering:

- the seriousness of non-small cell lung cancer;
- the prevalence of the NSCLC;
- the inadequately met medical need;
- evidence of an impact on morbidity and mortality and a lack of evidence of an impact on quality of life;
- the lack of an expected impact on the organisation of care;

KEYTRUDA (pembrolizumab) is unlikely to have an additional impact on public health.

**Considering all of these elements, the Committee deems that the clinical benefit of KEYTRUDA (pembrolizumab) is moderate in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment, for the treatment of resectable non-small cell lung cancer at high risk of recurrence in adults.**

**The Committee issues a favourable opinion for inclusion of KEYTRUDA (pembrolizumab) in the list of covered drugs for inpatients approved for use in the above indication.**

## Clinical Added Value

Considering:

- the quality of the evidence for the efficacy of pembrolizumab in the KEYNOTE-671 study, with:
  - a double-blind methodology in two parallel groups, in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment (pembrolizumab + chemotherapy/pembrolizumab) compared to placebo + platinum-containing chemotherapy as neoadjuvant treatment, then placebo alone as adjuvant treatment (placebo + chemotherapy/placebo);
  - the appropriateness of the population included for the MA indication;
- the clinical relevance of the two primary endpoints (overall survival and event-free survival) and two secondary endpoints with management of the alpha risk (major pathological response and complete pathological response);
- the results demonstrating a statistically significant difference for these 4 endpoints in favour of pembrolizumab + chemotherapy/pembrolizumab compared to placebo + chemotherapy/placebo:
  - the overall survival with an estimated difference in mean 5-year survival demonstrating an increase of 4.15 months (95% CI [1.05-7.26]);
  - event-free survival with a reduction in the risk of events (progression/recurrence, tumour resection impossible, or death) of 42% (HR = 0.58, 95% CI [0.46; 0.72], p<0.00001);
  - the major pathological response, with a difference of 19.2 points between the 2 groups (95% CI [13.9; 24.7], p<0.00001);
  - the complete pathological response, with a difference of 14.2 points between the 2 groups (95% CI [10.1; 18.7], p<0.00001);

However, the scope of these findings is limited by the following points:

- the beneficial effect on event-free survival primarily appears to be related to a decrease in the occurrence of progressions/recurrences, whereas deaths without progression/recurrence are increased in the first 6 months; no details are available concerning the effect on each component of the endpoint (in particular cumulative incidences), nor any details for the causes of early censoring;
- the beneficial effect on overall survival was quantified by an HR of 0.72, of the same magnitude as the expected value of 0.70, with a median survival in the control group longer than the expected value (52.4 months versus 34 months);
- the effect on overall survival appears to be delayed (p=0.004), observed after 12 months;
- the benefit of perioperative treatment compared to neoadjuvant treatment alone is not known, whereas KEYTRUDA (pembrolizumab) has an MA as monotherapy for the adjuvant treatment of adults with NSCLC who are at high risk of recurrence following complete resection and

platinum-based chemotherapy (indication not assessed by the Committee) and has not demonstrated an increase in overall survival in this context;

- a change in the definition of the primary endpoint during the study (local review of event-free survival), 3 months after the end of inclusions and 4 months before the first interim analysis;
- the safety of the product and, in particular, the proportion of patients with a treatment discontinuation, with serious and grade ≥ 3 events was higher in the group treated with pembrolizumab;
- the long-term efficacy in this indication is not known;

**the Committee deems that KEYTRUDA (pembrolizumab) provides a minor clinical added value (CAV IV) compared to platinum-containing chemotherapy as neoadjuvant treatment.**