OPINION ON MEDICINAL PRODUCTS

pembrolizumab
KEYTRUDA 25 mg/mL,

solution for dilution for infusion

New indication(s)

Adopted by the Transparency Committee on 14 December 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement of KEYTRUDA (pembrolizumab) in combination with chemotherapy as neoadjuvant treatment, then continued as monotherapy as adjuvant treatment after surgery, for the treatment of adult patients with locally advanced, or early-stage triple-negative breast cancer at high risk of recurrence.

Therapeutic improvement?

Therapeutic improvement in the care pathway.

Role in therapeutic strategy?

Due to the aggressive nature of the triple-negative breast cancer subtype, administration of a neo-adjuvant chemotherapy regimen has been recommended for over 10 years for patients with a large tumour (≥ 2 cm in the current ESMO European guidelines) and/or with lymph node involvement. The objective of treatment at the operable stage is to limit disease progression as early as possible, even before surgery, by reducing tumour size before the procedure and improving the complete histological response rate, in order to maximize chances of recovery and prevent recurrence or metastatic onset. Chemotherapy regimens combine a taxane (generally paclitaxel), and an anthracycline (doxorubicin or epirubicin + cyclophosphamide) used sequentially. Chemotherapy combinations without anthracycline appear to be inferior for triple-negative type tumours. Adding carboplatin to chemotherapy regimens with anthracycline and taxanes has shown an improvement in the probability of complete response for triple-negative type tumours.

Role of KEYTRUDA (pembrolizumab) in the therapeutic strategy:

KEYTRUDA (pembrolizumab), in combination with chemotherapy as neoadjuvant, and then continued as monotherapy as adjuvant treatment after surgery is the preferred treatment for locally advanced or early-stage triple-negative cancer with a high risk of recurrence.

Committee's conclusions

Clinical Benefit

- Triple-negative breast cancer is a serious life-threatening disease.
- The proprietary medicinal product KEYTRUDA (pembrolizumab) is a curative medicinal product.
- The efficacy/adverse effect ratio is significant.
- Therapeutic alternatives are available (see clinically relevant comparators).
- KEYTRUDA (pembrolizumab) is a first-line treatment for this extension of indication.

Public health benefit

Considering:

- the severity of the disease and its prevalence,
- the partially met medical need,
- the additional partial response to the identified need due to an effect on complete histological response and event-free survival,
- the lack of evidence to date of a gain in overall survival (immature data) or in quality of life (exploratory assessment),
- the lack of expected additional impact on the care and/or life pathway;

KEYTRUDA (pembrolizumab) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the actual clinical benefit of KEYTRUDA (pembrolizumab) is significant in the new marketing authorisation indication.

The Committee approves inclusion in the list of proprietary medicinal products approved for community use for this new marketing authorisation indication and at the marketing authorisation dosages.

Clinical Added Value

Considering evidence in a randomised double-blind study:

- of a superiority of pembrolizumab on the primary outcome measures: complete histological response (64.8% in the pembrolizumab group versus 51.2% in the placebo group) and event-free survival with an HR of 0.63 (95%CI: [0.48; 0.82]),
- the inability to draw a conclusion on an effect on overall survival due to the immaturity of the data available (ranked secondary outcome measure) or on quality of life (exploratory outcome measure),
- the higher incidence of serious adverse events (SAEs) in the pembrolizumab + chemotherapy / pembrolizumab group compared to the placebo + chemotherapy / placebo group (43.6% and 28.5% respectively),

the Committee deems that, based on the data currently available, KEYTRUDA (pembrolizumab) provides minor clinical added value (CAV IV) for the neoadjuvant and subsequently adjuvant treatment of adult patients with locally advanced or early-stage triple-negative breast cancer at high risk of recurrence.