OPINION ON MEDICINAL PRODUCTS

capmatinib
TABRECTA 200 mg and 50 mg,
film-coated tablet

First assessment

Adopted by the Transparency Committee on 18 January 2023

SUMMARY

The legally binding text is the original French opinion version

Key points

Disapproval of reimbursement for adult patients with advanced non-small cell lung cancer (NSCLC) presenting with mesenchymal-epithelial transition factor gene exon 14 skipping (METex14) mutation, requiring systemic treatment after previous immunotherapy and/or platinum-based chemotherapy.

Role in therapeutic strategy?

The current second-line therapeutic strategy of NSCLC (after a first-line chemotherapy and/or immunotherapy treatment) is identical to that for patients with or without MET exon 14 skipping (METex14 mutation) with in particular:

- **platinum-based chemotherapy,** for patients having received immunotherapy monotherapy as a first-line treatment (pembrolizumab if PD-L1 ≥ 50%),
- **monochemotherapy such as docetaxel (regardless of histology) or pemetrexed (non-epidermoid only),** for patients who have previously received immunotherapy in association with chemotherapy as a first-line treatment;
- **immunotherapy** (pembrolizumab for PD-L1 levels ≥ 1%, nivolumab or atezolizumab) in the absence of contraindication to immunotherapy, for patients who have previously received bichemotherapy without associated immunotherapy as a first-line treatment.

In France, in addition to TABRECTA (capmatinib), one other MET inhibitor has been granted a marketing authorisation since 2022, namely TEPMETKO (tepotinib) not reviewed by the

Transparency Committee to date, for the treatment of adult patients with advanced NSCLC with METex14 mutation, requiring systemic treatment after previous immunotherapy and/or platinum-based chemotherapy. Crizotinib (XALKORI), a multikinase inhibitor not specific for MET, is covered for compassionate access in this context (off-label).

In thoracic oncology, the 2022 United States National Comprehensive Cancer Network (NCCN) guidelines recommend systematic METex14 mutation screening in metastatic NSCLC patients. They recommend, after a first systemic treatment, capmatinib or tepotinib as treatments to be preferred as a second-line approach. Crizotinib is considered as an option under certain circumstances.

The 2022 French Auvergne Rhône Alpes (AURA) guidelines suggest screening for METex14 mutation systematically as a second-line and subsequent approach, in advanced-stage NSCLC patients. These guidelines (AURA) specify that patients affected by this mutation should be directed to a clinical trial or to capmatinib as a second-line approach, on an optional basis.

Role of TABRECTA (capmatinib) in the therapeutic strategy

Considering:

- the low level of evidence in view of the merely descriptive nature of the findings (study design), with efficacy findings primarily obtained from a multi-cohort, non-comparative phase II study;
- the data available from indirect comparison not suitable for quantifying the therapeutic improvement of this product with respect to the alternatives available on account of the major biases observed during its analysis;
- limited data on the prognostic and predictive value on METex14 mutation;
- the different safety profile of the treatments available, particularly marked by a proportion of grade ≥3 adverse events of 70%, and serious adverse events in approximately half of patients (53.1%);
- the early discontinuation of inclusion of the comparative, randomised, multi-centre phase III study versus chemotherapy (docetaxel) with only 20 randomised patients out of the 90 patients envisaged (while a significant number of patients could have been recruited in a temporary authorisation of use cohort in France).

the Committee deems that, based on the data currently available, TABRECTA (capmatinib) has no role in the therapeutic strategy for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) presenting with mesenchymal-epithelial transition factor gene exon 14 skipping (METex14) mutation, requiring systemic treatment after previous immunotherapy and/or platinum-based chemotherapy.

Committee's conclusions

Actual Clinical Benefit

- Non-small cell lung cancer with METex14 mutation is a serious life-threatening disease.
- The proprietary medicinal product TABRECTA (capmatinib) is a curative medicinal product.
- The efficacy/adverse effect ratio of TABRECTA (capmatinib) is poorly defined considering (see Section 07.6 Summary and Discussion):
  - the low level of evidence obtained with limited clinical data, from different cohorts (cohort 4 (n=69) and additional cohort not initially envisaged in the protocol (cohort 6, n=31)) in a non-comparative phase II study, which only allow a conclusion on the absolute effect size of this proprietary medicinal product,
  - the lack of robust comparison with respect to the current treatment,
  - the limited data concerning the prognostic value of the mutation;
  - the significant toxicity observed with time-limited follow-up of the patients of the non-comparative phase study and despite the severity of the clinical contexts in question.
- There are clinically relevant comparators (see Clinically relevant comparators section of this opinion).
- Based on the data currently available, considering the low level of evidence of the data, the Committee deems that TABRECTA (capmatinib) has no role in the therapeutic strategy for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with mesenchymal-epithelial transition factor gene exon 14 skipping (METex14) mutation, requiring systemic treatment after previous immunotherapy and/or platinum-based chemotherapy.

Public health benefit

Considering:

- the severity of the disease and the low incidence,
- the partially met medical need,
- the lack of additional response to the identified need in the absence of evidence of an additional impact in terms of morbidity-mortality (on progression-free survival and overall survival) and quality of life,
- the lack of data making it possible to assess any additional impact on the care pathway with the need to implement, in routine clinical practice, one (or more) diagnostic test(s) with a mesenchymal-epithelial transition factor gene exon 14 skipping (METex14) mutation fusion screening strategy.

TABRECTA (capmatinib) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of TABRECTA (capmatinib) is insufficient to justify public funding in the marketing authorisation indication (adult patients with advanced non-small cell lung cancer (NSCLC) presenting with mesenchymal-epithelial transition factor gene exon 14 skipping (METex14) mutation, requiring systemic treatment after previous immunotherapy and/or platinum-based chemotherapy).

The Committee disapproves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the marketing authorisation indication and at the marketing authorisation dosages.