BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ALIMTA (pemetrexed), antimetabolite

No clinical added value demonstrated in 1st and 2nd lines of locally advanced or metastatic non-squamous non-small cell lung cancer.
Minor improvement of clinical added value in maintenance therapy in patients whose the disease has not progressed after first-line treatment.

Main points

- ALIMTA has Marketing Authorisation in the following indications:
  - In combination with cisplatin, in the first-line treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC), in other than predominantly squamous cell histology,
  - In monotherapy for the maintenance treatment therapy of locally advanced or metastatic NSCLC other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum-based chemotherapy,
  - In monotherapy for the second-line treatment of patients with locally advanced or metastatic NSCLC other than predominantly squamous cell histology.
- It is part of the first-line and second-line options in treatment of NSCLC. In maintenance therapy, ALIMTA is the standard treatment option, if this molecule is administered at the onset (“continued maintenance”) or in stable or responders patients after 4 to 6 cycles of a platinum-based doublet without pemetrexed (“switch maintenance”).

Therapeutic use

- **First-line treatment of NSCLC:**
  In the absence of activating EGFR or ALK mutation, or if the mutational status of the tumour is not available or is uncertain, the standard first-line treatment of advanced stage, inoperable or metastatic patients is based on platinum-based combination therapy. In the case of a non-squamous cell NSCLC, chemotherapy with two components is recommended, combining cisplatin or, in case of contraindication, carboplatin with gemcitabine, vinorelbine, paclitaxel, docetaxel or pemetrexed.
  AVASTIN (bevacizumab) can be combined with platinum-based doublet chemotherapy, in the absence of contraindication, in patients with a performance status of 0-1 and aged less than 70 years.

- **Maintenance treatment**
  Patients whose disease has not progressed after first-line treatment should continue with either one of the medicines used in first-line – this option should be implemented for patients with a performance status of 0 or 1, responders or stable after 4 to 6 cycles of platinum-based doublet chemotherapy - or a chemotherapy molecule other than those used during induction.

- **Second-line treatment**
  In the absence of activating EGFR mutation or ALK rearrangement, eligible patients should be offered second-line chemotherapy, the nature of which will depend on the molecules previously used.

- **Role of the medicinal product in the therapeutic strategy**
  **First-line treatment**
  According to experts, the two main first-line strategies used in France are cisplatin/pemetrexed in combination or not with AVASTIN and the combination of AVASTIN/carboplatin/paclitaxel.
  ALIMTA is a therapeutic option in the first-line treatment of non-squamous NSCLC.
  **Maintenance treatment**
ALIMTA in monotherapy is the standard treatment option, if this molecule is administered at the onset ("continued maintenance") or in stable or responders patients after 4 to 6 cycles of a chemotherapy with two medicines, including a platinum salt without pemetrexed in first-line ("switch maintenance").

Second-line treatment
ALIMTA in monotherapy is a therapeutic option in the second-line treatment of non-squamous NSCLC.

Clinical data
- According to experts, pemetrexed has provided several factors:
  - Organisational: pemetrexed and docetaxel have the same D1/D21 dosage regimen. Gemcitabine and vinorelbine require a supplemental injection (generally at the day hospital) on D+8. Moreover, pemetrexed is not contraindicated in case of radiotherapy, unlike gemcitabine. This is sometimes a determining factor in the treatment of patients, especially for analgesic or symptomatic treatment of metastases.
  - Safety profile: pemetrexed is responsible for less haematological toxicity than gemcitabine and docetaxel. Therefore, the use of growth factors, EPO, transfusion support and hospitalisation for febrile neutropenia is less common. Docetaxel is usually responsible for alopecia, unlike pemetrexed (occasional), which contributes to an improvement in the quality of life.
  - Pemetrexed is the only maintenance treatment possible in patients with non-squamous NSCLC not eligible for bevacizumab (and/or who have not received induction chemotherapy) either after induction by pemetrexed (continuation) or another medicine (switch).

Special prescribing conditions
- Medicine for hospital prescription.
- Prescription restricted to certain specialists.

Benefit of the medicinal product
- The actual clinical benefit* of ALIMTA is substantial.
- ALIMTA does not provide clinical added value** (CAV V) in the first-line and second-line treatment of non-squamous non-small cell lung cancer.
- ALIMTA provides a minor clinical added value** (CAV IV), in maintenance treatment of non-squamous non-small cell lung cancer in patients whose disease has not progressed after a first-line treatment.

* The actual benefit (AB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV (equivalent of "no CAV") means "no clinical added value".