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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ZYKADIA (ceritinib), tyrosine kinase inhibitor

Minor improvement in the treatment of adults with ALK+ advanced non-small cell lung cancer previously treated with crizotinib

Main points

- ZYKADIA has conditional Marketing Authorisation as monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK+) advanced non-small cell lung cancer previously treated with crizotinib.
- Its efficacy in the third-line treatment of ALK+ lung cancer has been demonstrated in a non-comparative study primarily in terms of overall response rate.
- We still await comparative data versus chemotherapy.

Therapeutic use

- The treatment of non-small cell lung cancer differs according to tumour stage. The reference treatment for early-stage non-small cell lung cancer (NSCLC) is surgery. However, a large proportion of patients are diagnosed at an advanced stage of the disease (about 25 to 30% at the locally advanced stage and 40% at the metastatic stage), with the early stage accounting for only about 25 to 30%.
- The treatment of these cancers is based on systemic treatment. The treatment strategy depends on whether EGFR gene mutation is present or absent. Other criteria are also factors in the treatment decision: tumour histology, the patient's performance score and comorbidities.
- As first-line, the reference treatment is dual therapy combining a platinum salt (cisplatin or, if contraindicated, carboplatin) with one of the following: pemetrexed, gemcitabine, a taxane (docetaxel or paclitaxel) or vinorelbine.
- In metastatic ALK+ NSCLC, chemotherapy with a platinum salt and pemetrexed followed by maintenance treatment with pemetrexed is recommended. In the event of progression or toxicity, second-line treatment with crizotinib is recommended. However, in patients in whom platinum salts and pemetrexed have been shown to be contraindicated, treatment with crizotinib may be instituted as first line if approved by an interdisciplinary consultation meeting. Provided progression under treatment with crizotinib is slow, with few symptoms, this treatment can then be maintained.
- **Role of the medicinal product in the therapeutic strategy**
  On the basis of the data from the pivotal study, ZYKADIA is a third-line treatment for ALK + NSCLC that does not respond to crizotinib.

Clinical data

- Efficacy data are based primarily on a non-comparative phase II study of 140 patients with ALK+ NSCLC (median age 51 years). Most patients had an adenocarcinoma (92.1%). Nearly half the patients (43.6%) had failed to respond to two lines of treatment and approximately one third (37.5%) to three lines.
  Median follow-up was 7.4 months and the objective response rate (primary efficacy endpoint) was 37.1% according to the investigators and 34.3% according to the independent panel, with a median duration of response of 9.2 months. Median progression-free survival was 5.7 months and median overall survival was 14 months.
- Safety data are limited. The most commonly reported adverse events in the above study and in the phase I studies were:
  - gastrointestinal (diarrhoea and nausea) and hepatic events (ALT, AST and gamma-GT elevations associated with hepatotoxicity observed in 53.1% of patients),
  - general symptoms such as fever, fatigue and asthenia, observed in approximately one third of patients.

- We still await data on the efficacy of ZYKADIA in the treatment of patients previously treated with crizotinib as well as the final results of the phase III efficacy study comparing ceritinib with chemotherapy (third-line docetaxel or pemetrexed monotherapy).

Special prescribing conditions

- Medicine for hospital prescription
- Prescription restricted to oncologists or doctors with cancer training

Benefit of the medicinal product

- The actual benefit* of ZYKADIA is substantial.
- Pending the results of the comparative study versus third-line chemotherapy, ZYKADIA provides minor clinical added value** (CAV IV) in the treatment strategy for adult patients with ALK+ advanced non-small cell lung cancer previously treated with crizotinib.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 07 October 2015 (CT-14455) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The 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. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.