HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New medicinal product
March 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

COTELLIC (cobimetinib), anti-MEK, protein kinase inhibitor

Moderate improvement in the first-line treatment of unresectable or metastatic melanoma, in patients with a BRAF V600 mutation

Main points

- COTELLIC now has Marketing Authorisation in combination with vemurafenib, in the treatment of adults with unresectable or metastatic melanoma with a BRAF V600 mutation.
- Its combination with vemurafenib (ZELBORAF) improves progression-free survival (+3.7 months) and overall survival (+4.9 months) in comparison with vemurafenib alone.
- Like the trametinib/dabrafenib (MEKINIST/TAFINLAR) combination, the cobimetinib/vemurafenib combination is a first-line treatment in this indication.

Therapeutic use

- The current management of advanced (unresectable or metastatic) melanoma involves screening patients as soon as they are diagnosed for a BRAF mutation in the tumour:
  In case of a BRAF mutation, dual therapy combining a BRAF inhibitor and a MEK inhibitor is started as first-line treatment: vemurafenib (ZELBORAF) / cobimetinib (COTELLIC) or dabrafenib (TAFINLAR) / trametinib (MEKINIST).
  The role of nivolumab and pembrolizumab as alternatives to these targeted therapies is currently debated, and particularly the profile of patients who are likely to receive one of these two treatments as first-line therapy.
- Nivolumab and pembrolizumab are recommended as second-line therapy. The combination of a BRAF inhibitor and a MEK inhibitor is not recommended as second-line therapy in patients who have already received a BRAF inhibitor as monotherapy in first-line treatment.
- **Role of the medicinal product in the therapeutic strategy**
  COTELLIC, in combination with vemurafenib (ZELBORAF), is a first-line therapy in the management of unresectable or metastatic melanoma with a BRAF mutation, like trametinib/dabrafenib combination.

Clinical data

- Cobimetinib was primarily evaluated in a phase III, randomised, double-blind study comparing the cobimetinib/vemurafenib combination with vemurafenib alone in 495 previously untreated patients with unresectable or metastatic locally advanced melanoma with the BRAF V600 mutation. The cobimetinib/vemurafenib combination demonstrated its superiority versus vemurafenib alone on:
  - median progression-free survival (primary endpoint): 9.9 months versus 6.2 months, i.e. a gain in absolute terms of 3.7 months: HR=0.51 95% CI = [0.39; 0.68];
  - percentage of objective response: 67.6% versus 44.8%, i.e. a difference of 22.8% 95% CI = [14.1; 31.6];
  - median overall survival: 22.3 months versus 17.4 months, i.e. a gain in absolute terms of 4.9 months (HR = 0.70; 95% CI = [0.55; 0.90]).
- More patients from the cobimetinib/vemurafenib than in the vemurafenib group had at least one serious adverse event (AE) (37.2% versus 28.0%) and at least one grade 3 or higher AE (75.3% versus 61.4%). In the study, the rate of skin toxicity (squamous cell carcinoma and keratoacanthoma) was lower under the cobimetinib/vemurafenib combination than that known for vemurafenib monotherapy.

Special prescribing conditions

- Medicine for hospital prescription.
- Prescription restricted to oncology specialists or doctors with cancer training.

Benefit of the medicinal product

- The actual benefit* of COTELLIC is substantial.
- Like trametinib/dabrafenib combination, COTELLIC in combination with vemurafenib provides moderate clinical added value** (CAV III) in the therapeutic strategy of unresectable or metastatic melanoma with a BRAF V600 mutation.
- 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 18 March 2016 (CT-14929) 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".