HAUTE AUTORITÉ DE SANTÉ

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

TAFINLAR (dabrafenib), tyrosine kinase inhibitor

No clinical benefit demonstrated by comparison with dacarbazine in the current management of unresectable or metastatic melanoma with a BRAF V600 mutation

Main points

- TAFINLAR has Marketing Authorisation as monotherapy in the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.
- Its efficacy has been demonstrated in terms of the improvement in progression-free survival by comparison with dacarbazine but with no increase in overall survival.
- No direct comparison with ZELBORAF (vemurafenib) is available.

Therapeutic use

- Current treatment for melanomas is, from diagnosis, directed towards selecting patients based on whether or not they have a BRAF mutation (this mutation is found in 40 to 60% of cases); if they do, the choice of treatment then involves targeted therapy (vemurafenib, ZELBORAF) as monotherapy.
- **Role of the medicinal product in the therapeutic strategy**
  In this setting, TAFINLAR is a first-line treatment as an alternative to ZELBORAF.

Clinical data

- An open randomised study compared dabrafenib (monotherapy of 150 mg 2x/day) with dacarbazine (1000 mg/m^2 every 3 weeks) in 250 patients with stage IIIc unresectable or metastatic (stage IV) melanoma with a BRAF V600 mutation who had not previously been treated.
  At the time of the primary analysis, median progression-free survival (the primary endpoint) in the dabrafenib group was 5.1 months versus 2.7 months in the dacarbazine group, i.e. an absolute increase of 2.4 months (HR = 0.30 (95% CI: [0.18-0.51] ; p<0.0001). At that time, median follow-up was 5.1 months in the dabrafenib group and 4.8 months in the dacarbazine group and overall survival did not differ between the two groups: overall survival at 6 months of 87% in the dabrafenib group versus 79% in the dacarbazine group, HR = 0.61, (95% CI: [0.25-1.48]).
  A post-hoc analysis carried out after the primary analysis concluded that there was no difference between the two groups in terms of overall survival (HR = 0.76; 95% CI: [0.48-1.21]).The percentage overall response evaluated by the investigators was 53% (95% CI: [45.5%-60.3%]) in the dabrafenib group and 19% (95% CI [10.2%-30.9%]) in the dacarbazine group. The quality-of-life analysis did not show any difference between the two treatment groups.
  Safety data are limited because of the short follow-up period. The most commonly reported (> 10% of patients) adverse events in patients who received dabrafenib were hyperkeratosis, headache, hyperthermia, joint pain, cutaneous papilloma and palmar-plantar erythrodysaesthesia syndrome. Cutaneous squamous cell carcinomas were reported in 7 patients (4%) in the dabrafenib group, whereas there were no cases in the dacarbazine group.
  The most commonly reported (> 10% of patients) adverse events in patients who received dacarbazine were gastrointestinal (nausea 51%, vomiting 25% and abdominal pain 14%) and haematological (anaemia 12% and neutropenia 17%).

Prescribing conditions

Medicine for hospital prescription

Prescription medicine restricted to certain healthcare professionals: cancer treatment and clinical oncology specialists and departments.

Benefit of the medicinal product

- The actual benefit* of TAFINLAR is substantial.
- TAFINLAR does not provide any clinical added value** (CAV V, non-existent) in the current treatment 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 22 October 2014 (CT-13127) and is available at **www.has-sante.fr**

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[i] * 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 added clinical value".