HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
23 SEPTEMBER 2020
The legally binding text is the original French opinion version

vemurafenib
ZELBORAF 240 mg film-coated tablets

Reevaluation

Key points

Favourable opinion for maintenance of reimbursement as monotherapy for the treatment of adult patients with BRAF mutation-positive unresectable or metastatic melanoma

What therapeutic improvement ?

No clinical added value in the therapeutic strategy.

Role in the care pathway ?

In the presence of BRAF V600 mutation in metastatic melanoma, the strategy is based on targeted dual therapy including the combination of a BRAF inhibitor and a MEK inhibitor: dabrafenib + trametinib, vemurafenib + cobimetinib or encorafenib + binimetinib. The latter combination has demonstrated an increase in progression-free survival compared to vemurafenib but has not demonstrated an increase in overall survival compared to vemurafenib or dabrafenib as monotherapy, in contrast with other BRAF/MEK inhibitors.
The role of nivolumab and pembrolizumab as an alternative to these targeted therapies is currently the subject of debate, as is the profile of patients suitable for receiving either of these two therapies as a first-line treatment.
The use of a BRAF inhibitor as monotherapy in BRAF V600 mutation-positive patients is only recommended in the event of contraindication or intolerance to MEK inhibitors.

Role of the medicinal product in the care pathway

ZELBORAF as monotherapy now has a limited role as first-line therapy only in the event of contraindication or intolerance to MEK inhibitors.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Melanoma is a skin cancer with a high metastatic potential, which may be complicated by metastases in advanced forms and be life-threatening in the short or medium term.
◗ ZELBORAF (vemurafenib) as monotherapy is a specific curative treatment for melanoma.
◗ The efficacy/adverse effects ratio is high.
◗ There are therapeutic alternatives (see Clinically relevant comparators).
◗ This treatment now has a role only in the event of contraindication or intolerance to MEK inhibitors.

On the basis of currently available data, the PHI is not modified: ZELBORAF as monotherapy is unlikely to have any impact on public health in this indication.

Considering all these elements, the Committee deems that the clinical benefit of ZELBORAF (vemurafenib) as monotherapy remains substantial in the MA indication.

Clinical Added Value

Considering :

- **the evolution of the care pathway with, in particular, demonstration of a superiority of BRAF inhibitor plus MEK inhibitor combinations compared to BRAF inhibitor monotherapy in terms of progression-free survival and overall survival,**
- **the limited role of BRAF inhibitor monotherapy in the care pathway : situation where the MEK inhibitor cannot be used due to a contraindication or intolerance,**

the Committee considers that ZELBORAF as monotherapy provides no clinical added value (CAV V) in the care pathway for BRAF V600 mutation-positive unresectable or metastatic melanoma.