

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**ODOMZO (sonidegib), Hedgehog inhibitor**

Minor clinical added value in the treatment of locally-advanced basal cell carcinoma not eligible for curative surgery or radiotherapy.

Main points

- ▶ ODOMZO has marketing authorisation in the treatment of locally-advanced basal cell carcinoma (BCC) not eligible for curative surgery or radiotherapy.
- ▶ The only available data result from a subgroup of a phase II non-comparative study that included two patient profiles: locally-advanced BCC and metastatic BCC. The efficacy results are based on the overall response rate (complete or partial response)
- ▶ ODOMZO is an alternative to ERIVEDGE in this indication. There are no comparative studies.

Therapeutic strategy

- The standard treatment for basal cell carcinoma is surgical excision or radiotherapy. Metastatic forms are the exception; multiple or locally-advanced forms are much more common. The case of Gorlin syndromes is a specific case secondary to germ-line patched gene mutations induced in patients who have multiple carcinomas and early onset. These patients undergo multiple, ultimately debilitating surgical procedures and seek therapeutic alternatives.
- When surgery or radiotherapy are no longer effective, the treatment for locally-advanced or metastatic basal cell carcinoma focuses on local or general chemotherapies (platinum salts, 5 FU) often poorly tolerated in elderly patients and not completely effective. Vismodegib (ERIVEDGE) is a selective Hedgehog signalling pathway inhibitor. Activation of this pathway, present in over 90% of cases of basal cell carcinoma, causes cell proliferation. It represents a next-line treatment for patients with locally-advanced or metastatic BCC where treatment by surgery or radiotherapy is inappropriate. Implementing this treatment should be decided in a multidisciplinary meeting.
- The main benefit of drug therapy at the locally-advanced stage of BCC is to reduce the tumour volume so as to allow the patient access to surgery as that alone can have a curative objective.
- **Role of the proprietary medicinal product in the therapeutic strategy**
ODOMZO is an alternative to ERIVEDGE in the first-line treatment of locally-advanced basal cell carcinoma not eligible for curative surgery or radiotherapy.

Clinical data

- A phase II study evaluated two dosages of ODOMZO (200 or 800 mg/day) in patients with a locally-advanced basal cell carcinoma (laBCC) or a metastatic basal cell carcinoma (mBCC) for whom surgery and radiotherapy were not appropriate.
A total of 230 patients were included (locally-advanced n = 194; metastatic n = 36). The intent-to-treat population (ITT) included 79 patients in the sonidegib 200 mg arm and 151 patients in the sonidegib 800 mg arm. The majority of patients (laBCC 74%, mBCC 92%) already had had other treatments, including surgery, radiotherapy and antineoplastic treatments.
During an interim analysis after a median followup of 14 months, the overall response rate (primary endpoint criteria) was 36.4% (95% CI: [23.8 - 50.4]) in patients treated with the dosage of 200 mg and 33.6% (95% CI: [25.1 - 43.0]) in patients treated with the dosage of 800 mg. The required limit in the protocol to conclude efficacy was set at 30%. In the per-protocol analysis, a minimal difference was observed between the two dosages (-2.7%; 95% CI: [-18.73 - 12.45]); the marketing authorisation retained the lowest dosage.

At the 200-mg dosage, the overall response rate was 47% in patients with laBCC and 15.4% in patients with mBCC (ITT analysis).

After a follow-up of 26.3 months (third interim analysis), the objective response rate was 56.1% in the subgroup of patients with laBCC and 7% in the subgroup of patients with mBCC, a value that is far from the predefined limit (30%) to conclude treatment efficacy in this subpopulation. After this result, the manufacturer withdrew its marketing authorisation application for metastatic basal cell carcinoma.

In all, the marketing authorisation for sonidegib at the dosage of 200 mg/day was granted only to patients with locally-advanced basal cell carcinoma.

ODOMZO has not been compared with an active treatment.

- The grade 3-4 adverse events most frequently reported with sonidegib 200 mg treatment were: increased serum CPK, increased lipase (6.3% each), asthenia (3.8%), weight loss, muscle spasms, hypertension and hypotension (2.5% each).

Special prescribing conditions

- Medicinal product requiring special monitoring during treatment.
- Hospital prescription restricted to cancer treatment and clinical oncology specialists and departments.

Benefit of the medicinal product

- The actual clinical benefit* of ODOMZO is substantial.
- Like ERIVEDGE, ODOMZO provides minor clinical added value** (CAV IV) in the treatment of locally-advanced basal cell carcinoma not eligible for curative surgery or radiotherapy.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.



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* The actual clinical benefit (ACB) of a 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 ACB, which can be substantial, moderate, low or insufficient for reimbursement of the medicinal product 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 (equivalent to "no CAV") means "no clinical added value".