BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

HALAVEN (eribulin), antineoplastic agent

Moderate clinical added value relative to dacarbazine as a monotherapy in advanced or metastatic unresectable liposarcoma in patients who have received prior anthracycline containing chemotherapy.

Main points

- HALAVEN now has Marketing Authorisation in the treatment of “patients with unresectable liposarcoma who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease”
- It improves overall survival relative to dacarbazine with an uncertainty in the precise estimation of the extent of the effect in the subgroup of patients covered by the Marketing Authorisation and having liposarcoma.
- No comparison is available with YONDELIS (trabectedin).
- The frequency of grade 3 or 4 adverse events was higher in the eribulin arm (62.8%) than in the dacarbazine arm (54.9%), notably due to a higher proportion of neutropenia, peripheral neuropathies and infections.

Therapeutic use

Soft-tissue sarcomas respond poorly to chemotherapy and there is only a small number of drugs, used alone or in combination, available: anthracyclines, mainly doxorubicin, ifosfamide and dacarbazine. After failure of treatment including doxorubicin and ifosfamide as monotherapy or in combination, trabectedin (YONDELIS) can be used in liposarcoma and leiomyosarcoma. Currently, YONDELIS has not demonstrated improvement in overall survival in these patients.

Dacarbazine can also be used in second line and beyond, possibly combined with gemcitabine; one phase II study assessed the benefit of this combination relative to dacarbazine alone, in terms of overall survival and progression-free survival.

Role of the proprietary medicinal product in the therapeutic strategy

HALAVEN is an additional therapeutic alternative in the treatment of adults with unresectable liposarcoma who have received prior anthracycline-containing chemotherapy (unless unsuitable) for treatment of advanced or metastatic disease. Currently, no comparison is available between YONDELIS (trabectedin) and HALAVEN (eribulin). Note that, due to haematological toxicity, complete blood count monitoring should be done in all patients before administration of each dose of eribulin. This treatment should only be initiated in patients whose neutrophil counts are ≥1.5 x 10⁹/l and platelet counts are > 100 x 10⁹/l.

Clinical data

- A phase III, randomised, open-label study compared eribulin to dacarbazine in 452 adults with locally-recurrent, unresectable and/or metastatic liposarcoma and leiomyosarcoma. Patients previously received at least two chemotherapy protocols including one with an anthracycline (unless contraindicated) Around one third (34%, n=153) of patients had liposarcoma and 66% (n=297) had leiomyosarcoma. Nearly 90% of patients (87.3%, n=395) had already received at least two prior treatment lines and 48.5% (n=219) had already received trabectedin.
- Median overall survival (primary endpoint for the final analysis) was higher in the eribulin arm than in the dacarbazine arm, with an absolute gain of two months (13.5 versus 11.5 months, HR=0.768, 95% CI [0.618;
In the subgroup of patients with liposarcoma, median overall survival was higher in the eribulin arm than in the dacarbazine arm, with an absolute gain of 7.2 months (15.6 months versus 8.4 months, HR=0.511; 95% CI [0.346; 0.753]; p=0.0006).

- No difference in progression-free survival (secondary endpoint) was observed between the eribulin arm and the dacarbazine arm (2.6 months in both arms).
- The frequency of grade 3 or 4 adverse events was higher in the eribulin arm (62.8%) than in the dacarbazine arm (54.9%), notably due to a higher proportion of neutropenia (35.4% versus 15.6%), peripheral neuropathies (1.8% versus 0%) and infections (10.2% versus 4.9%).
- The Committee emphasised that Marketing Authorisation was granted for second line and beyond, while 90% of the patients enrolled were in third line and beyond and 50% of patients had already received trabectedin; second-line data are therefore limited.

**Special prescribing conditions**

- Prescription restricted to oncology or haematology specialists or doctors with cancer training
- Medicinal product requiring special monitoring during treatment.

**Benefit of the medicinal product**

- The actual clinical benefit* of HALAVEN is substantial.
- HALAVEN provides moderate clinical added value** (CAV III) compared to dacarbazine as a monotherapy in adult patients with unresectable liposarcoma who have received prior anthracycline containing chemotherapy (unless unsuitable) for treatment of advanced or metastatic disease.
- Recommends inclusion on the list of reimbursable products 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 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”.

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