HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New medicinal product
May 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

KYPROLIS (carfilzomib), antineoplastic

Minor improvement in the treatment of patients with multiple myeloma who have received at least one line of treatment, in combination with lenalidomide and dexamethasone, when compared with the combination of lenalidomide and dexamethasone.

Main points

- KYPROLIS has a Marketing Authorisation in combination with lenalidomide and dexamethasone in the treatment of multiple myeloma in adults who have had at least one previous line of treatment.
- The efficacy of Kyprolis combined with lenalidomide and dexamethasone has been demonstrated on progression free survival when compared to the combination of lenalidomide and dexamethasone alone..
- Cardiac function monitoring is necessary with KYPROLIS treatment, especially in patients who have already suffered a myocardial lesion.

Therapeutic use

- There is no standard treatment for relapsing or progressive multiple myeloma. The therapeutic decision-making depends on the patient's age, previous treatments, the duration of the first remission and the circumstances of the relapse, on the availability of peripheral stem cells if the patient can have intensified treatment, on their general state of health and their comorbidities.
- From the second relapse onwards, the choice depends on the same parameters as before, in particular on the efficacy and tolerability of previous treatments. Combinations including immunomodulators (lenalidomide or thalidomide), corticosteroids, anthracyclines, alkylating agents, are possible in patients who have received 2 or 3 lines of treatment.
- Hereafter, treatment options for refractory patients at a very advanced stage and who have been heavily pre-treated, are limited and these patients are most of the time in a treatment impasse. Pomalidomide is an alternative in patients who have already been treated with bortezomib and lenalidomide.
- **Role of the medicinal product in the therapeutic strategy**
  KYPROLIS in combination with lenalidomide and dexamethasone is a new therapeutic option, and should be preferred over the lenalidomide/dexamethasone combination, in the treatment of multiple myeloma in adults who have received at least one previous line of treatment.

Clinical data

- A phase III study included 792 multiple myeloma patients who had received between 1 and 3 lines of treatment, treated until disease progression either with carfilzomib/lenalidomide/dexamethasone (KRd), or with lenalidomide/dexamethasone (Rd). Progression-free survival (primary endpoint) was superior in the KRd group compared to the Rd group (HR = 0.69; 95% CI [0.57;0.83]; p < 0.0001) with a median progression-free survival of 26.3 months versus 17.6 months, after a median follow-up of about 30 months. There was no statistical difference in overall survival between the two groups.
- A greater toxicity level was reported in the KRd group in terms of cardiac signals (appearance and/or exacerbation of heart failure, myocardial ischaemia and myocardial infarction), blood disorders (including thrombocytopenia), fluid and electrolyte disorders (hypokalemia), and thromboembolic events.

Special prescribing conditions

- Medicinal product reserved for hospital use.
- Prescription restricted to haematology specialists or doctors with blood disorder training.
- Medicinal product requiring special monitoring during treatment.

Benefit of the medicinal product

- The actual benefit* of KYPROLIS is substantial.
- KYPROLIS in combination with lenalidomide and dexamethasone provides minor clinical added value* (CAV IV) in comparison with the combination of lenalidomide and dexamethasone in multiple myeloma patients who have already received at least one line of treatment.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 25 May 2016 (CT-14858) 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”.