HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
January 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

VELCADE (bortezomib), antineoplastic

Minor improvement in the treatment of mantle cell lymphoma

Main points

- VELCADE now has Marketing Authorisation in combination with rituximab, cyclophosphamide, doxorubicin and prednisone in the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation.
- VELCADE in combination with rituximab, cyclophosphamide, doxorubicin and prednisone (VcR-CAP) has shown an improvement in progression-free survival (a gain in absolute terms of 10.3 months) by comparison with vincristine in combination with these same medicines (R-CHOP) to the detriment of the safety profile, which is less favourable.
- No benefit in terms of overall survival has been demonstrated to date.

Pre-existing indications

- VELCADE already has Marketing Authorisation in the treatment of multiple myeloma.
- This summary does not cover these indications.

Therapeutic use

- The management of mantle cell lymphoma depends on how aggressive it is:
  - in the rare early stages, chemotherapy followed by radiotherapy is usually indicated to achieve long-term remission;
  - in the advanced stages of the disease, there is no curative treatment except haematopoietic stem cell transplantation. When this is not appropriate, polychemotherapy protocols are usually used but offer no prospect of a cure.
- **Role of the medicinal product in the therapeutic strategy**

  In patients with mantle cell lymphoma who are not eligible for haematopoietic stem cell transplantation, the combination of VELCADE, rituximab, cyclophosphamide, doxorubicin and prednisone is a first-line protocol.

Clinical data

- The efficacy and safety of bortezomib in this indication have mainly been evaluated in an open, randomised, phase III study.
  Bortezomib in combination with rituximab, cyclophosphamide, doxorubicin and prednisone (VcR-CAP) has demonstrated its superiority versus R-CHOP (rituximab, cyclophosphamide, hydroxydoxorubicin, vincristine [Oncovin®], prednisone) on the primary efficacy endpoint. After a median follow-up of about 40 months, progression-free survival (assessed blind by an independent review committee) was 24.7 months in the VcR-CAP group compared with 14.4 months in the R-CHOP group (HR = 0.63 95% CI = [0.50; 0.79]), a gain in absolute terms of 10.3 months.
  The superiority of the VcR-CAP protocol versus R-CHOP was also shown on ranked secondary endpoints such as the median time to progression or relapse of the disease (30.5 months versus 16.1 months, HR = 0.58 [0.45; 0.74]), the median time until another treatment was used (44.5 months versus 24.8 months HR = 0.50 [0.38; 0.65]) and the percentage complete response (53.3% versus 41.7% OR = 1.69 [1.15; 2.48]).
  No difference in terms of overall survival has been demonstrated to date. For information purposes, 71 deaths in the VcR-CAP group and 87 in the R-CHOP group had occurred during the study by the date of the final analysis.

More serious adverse effects were observed in the VcR-CAP group than in the R-CHOP group (37.5% versus 29.8%). Grade 3 or higher adverse effects were also more common (92.9% versus 85.1%). This toxicity was mostly haematological.

Special prescribing conditions

- Medicine for hospital prescription only, restricted to cancer treatment, haematology and clinical oncology specialists and departments.
- Medicine requiring special monitoring during treatment

Benefit of the medicinal product

- The actual benefit* of VELCADE is substantial.
- VELCADE provides clinical added value** (CAV IV, minor) in the strategy for the management of patients with mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation.
- 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 06 January 2016 (CT-14667) and is available at **www.has-sante.fr**

[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 clinical added value".