HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
June 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ARZERRA (ofatumumab), monoclonal antibody

No clinical benefit demonstrated in the treatment of patients with chronic lymphocytic leukaemia who have not received prior therapy and who are not eligible for fludarabine-based therapy

Main points

- ARZERRA has Marketing Authorisation in the treatment of chronic lymphocytic leukaemia (CLL) in combination with chlorambucil or bendamustine in patients who have not received prior therapy and who are not eligible for fludarabine-based therapy.
- In one study, progression-free survival was 9 months longer in the ofatumumab+chlorambucil group than in the group treated with chlorambucil alone, which is a comparator of low relevance. No difference in overall survival was observed.
- Its efficacy in combination with bendamustine has been evaluated only in a non-comparative study.

Pre-existing indication

ARZERRA already has Marketing Authorisation for the treatment of CLL in patients who are refractory to fludarabine and alemtuzumab.
This summary does not cover this indication.

Therapeutic use

- The patients considered not eligible for treatment with fludarabine are patients with severe renal failure and frail individuals with comorbidities that would impact on their ability to withstand a severe infection. One of the first-line treatment options in such patients is the combination of rituximab and chlorambucil (R-Clb protocol). Chlorambucil and bendamustine have Marketing Authorisation in the event of an associated morbidity. R-Clb or R-bendamustine combinations are being used in practice without them having been approved by Marketing Authorisation in this situation. Moreover, obinutuzumab in combination with chlorambucil is now one of the first-line treatment options in patients with CLL who are not eligible for treatment with high doses of fludarabine.
- The 2011 European guidelines recommend the use of chlorambucil or bendamustine in patients with comorbidities. In such cases, the 2014 US guidelines recommend one of the following options: obinutuzumab+chlorambucil, ofatumumab+chlorambucil, rituximab+chlorambucil, bendamustine+/-rituximab.
- **Role of the medicinal product in the therapeutic strategy**

  ARZERRA, in combination with chlorambucil or bendamustine, is one of the first-line treatment options in patients with CLL who are not eligible for fludarabine-based therapy.

Clinical data

- The efficacy of ofatumumab in combination with chlorambucil (OCHL group) has been evaluated in a randomised open study versus chlorambucil (CHL group) in 447 patients. After a median follow-up period of 28.9 months, the median progression-free survival (primary efficacy endpoint) was 22.4 months in the OCHL group and 13.1 months in the CHL group, i.e. an absolute increase of 9 months in favour of the ofatumumab+chlorambucil combination (HR = 0.57; 95% CI: [0.45; 0.72]). No difference in overall survival was observed between the two groups.
- The efficacy of ofatumumab in combination with bendamustine has been evaluated in a phase II non-comparative study in 44 patients of whom the majority had received six cycles of the combination. After a median follow-up period of 8.5 months, the overall response rate for the ofatumumab+bendamustine combination was 95% (42/44

patients; 95% CI: [84.53; 99.44]) and the complete response rate was 43% (19/44 patients). No deaths were reported during the median follow-up period and one patient progressed.

- The principal adverse events of grade 3 or higher were neutropenia, which in the phase III study was more common in the OCHL group (26% versus 15%), thrombocytopenia, which was more common in the CHL group (5% versus 10%), and anaemia (5% in each group). In the phase II study, this percentage was 57%, primarily neutropenia (36%) and rash (5%).

Special prescribing conditions

- Orphan medicinal product
- Prescription restricted to certain specialists
- Medicinal product requiring special monitoring during treatment.

Benefit of the medicinal product

- The actual benefit* of ARZERRA is substantial.
- In view of the absence of evidence of the superior efficacy of ofatumumab over relevant comparators in current use, ARZERRA, in combination with chlorambucil or bendamustine, does not provide clinical added value (CAV V) in the treatment of patients with CLL who have not received prior therapy and who are not eligible for fludarabine-based therapy.
- 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 03 June 2015 (CT-13934) 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".