HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
16 DECEMBER 2020

The legally binding text is the original French opinion version

belantamab mafodotin
BLENREP 100 mg powder for concentrate for solution for infusion

First assessment

Key points

Favourable opinion for reimbursement as monotherapy for the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

In heavily pretreated patients in the very advanced stages of the disease, in particular those who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody such as daratumumab (DARZALEX), there are no validated treatment options following the failure of an anti-CD38 antibody and patients are usually in a situation where all the treatment options have been exhausted.

Role of the medicinal product in the care pathway

Considering:
- early efficacy data having demonstrated, in around one hundred patients, the benefit of BLENREP for obtaining an overall response in the management of advanced multiple myeloma following the failure of an anti-CD38 antibody (around 32% of the population in the group of patients having received the dose indicated by the MA, i.e., 2.5 mg/kg (CI97.5% [21.7; 43.6]), with a median response duration of 11 months),
- the extremely limited experience (around 13 months) and the resulting uncertainties relative to the efficacy and maintenance of efficacy,
- the safety profile, marked in the short term by eye disorders, in particular keratopathy, requiring appropriate monitoring, and infusion reactions,
- the value of having access to a new mechanism of action targeting the BCMA receptor in salvage situations,
- and pending additional data,

BLENREP (belantamab mafodotin) is a salvage therapy for multiple myeloma when all the other treatment options have been exhausted, following the opinion of a multidisciplinary team (MDT) meeting.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Multiple myeloma is a serious, life-threatening blood disease.
◗ BLENREP (belantamab mafodotin) is a last-line specific curative treatment for multiple myeloma, targeting the CDBCMA receptor.
◗ The efficacy/adverse effects ratio is high only in the short term considering the data available, with median follow-up of around 13 months in the DREAMM 2 study.
◗ In heavily pretreated patients in the very advanced stages of the disease, having received at least four prior therapies and whose disease is refractory to at least one IP, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, there are no validated treatment options following the failure of an anti-CD38 antibody and patients are usually in a situation where all the treatment options have been exhausted. Apart from supportive care, there are no clinically relevant comparators for BLENREP.
◗ BLENREP (belantamab mafodotin) is a salvage therapy when all the other treatment options have been exhausted, following the opinion of a multidisciplinary team (MDT) meeting (see section 08).

Public health impact

Considering:
- the seriousness of the disease, particularly in heavily pretreated patients,
- its incidence,
- the unmet medical need at this stage of the disease,
- the lack of evidence to support an absence of deterioration in the care and/or life pathway,
- the absence of an expected additional impact on the organisation of care compared to supportive care (which may include intravenous treatments) despite the fact that this medicinal product is administered by intravenous infusion over a minimum period of 30 minutes, once every 3 weeks.
- the lack of response to the identified need (no additional impact on morbidity and mortality or on quality of life demonstrated to date),

BLENREP (belantamab mafodotin) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of BLENREP (belantamab mafodotin) is substantial "as monotherapy for the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy".

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication "as monotherapy for the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy" and at the MA dosages.

Clinical Added Value

Considering:

- **the short-term efficacy data obtained relative to the overall response (around 32% of the population in the group of patients having received the dose indicated by the MA, i.e., 2.5 mg/kg (CI97.5% [21.7; 43.6]), with a median response duration of 11 months), in life-threatening clinical situations in which the treatment options are limited,**
- **uncertainties concerning the clinical relevance of the primary endpoint used (overall response rate) and its transposability to overall survival time or improvement of quality of life.**
- **uncertainties with respect to the real effect size of this medicinal product in the absence of comparative data, in a context in which a formalised comparison with a historic patient cohort could theoretically have been envisaged but was not performed,**
- **uncertainties with respect to the clinical efficacy and its longer-term maintenance, in a context of extremely short follow-up (median follow-up of around 13 months),**
- **the significant short-term toxicity, with a specific profile, particularly ocular (with grade 3 or 4 keratopathy reported in 30% of patients in the 2.5 mg/kg group), and the absence of long-term safety data,**
- **and despite the benefit of having access to a medicinal product having been assessed following the failure of an anti-CD38 antibody in a context of an unmet medical need,**

the Transparency Committee considers that, on the basis of currently available data, BLENREP (belantamab mafodotin) provides no clinical added value (CAV V) in the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

anti-CD38 monoclonal antibody that can be used from the first line of treatment. The pharmaceutical company supplied data from an unpublished retrospective observational study, aimed at describing the management in France of patients with multiple myeloma and treated in hospital, from the time of the initial diagnosis, in 70 randomly selected centres who are members of the *Intergroupe Francophone du Myélome* (IFM - French-speaking Myeloma Intergroup) (EMMY study; sponsor IFM). The results are available for 1,929 patients for whom multiple myeloma treatment was initiated in 2017 or 2018. In this study, which is more recent than the previously cited one, 12% (223/1,929) of patients started a fifth line of treatment.

Following extrapolation of these results to the French population and despite the limitations of this observational study (in particular, uncertainty with respect to the representativity of the patients included), and assuming that all the patients on fifth-line therapy would have received an anti-CD38 monoclonal antibody, a proteasome inhibitor and an immunomodulatory agent, a maximum of 600 patients per year would be likely to receive BLENREP (belantamab mafodotin).

Consequently, the target population of BLENREP (belantamab mafodotin) may be estimated to be a maximum of around 600 patients per year.