HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
15 DECEMBER 2021

The legally binding text is the original French opinion version

Idecabtagene vicleucel
ABECMA 260-500 x 10^6 cells dispersion for infusion

First assessment

Key points

Favourable opinion for reimbursement in the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and 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 symptomatic patients, first-line treatment is dependent on whether the subject is eligible or not for intensive chemotherapy combined with autologous peripheral blood stem cell transplantation (PBSCT). Recently, DARZALEX (daratumumab) was added to the care pathway as a first-line treatment, irrespective of PBSCT status, in combination with protocols including an immunomodulatory agent (thalidomide or REVLIMID (lenalidomide)) and/or proteasome inhibitor (VELCADE (bortezomib)) and/or melphalan.

In the event of relapse or progression following first-line therapy, the therapeutic decision depends on age, previous treatments, the duration of the first remission, the circumstances of the relapse, the availability of PBSC, the general health status of patients and their comorbidities. Second-line therapies are based on dual or triple therapy combining pomalidomide (IMNOVID), daratumumab (DARZALEX), ixazomib (NINLARO) or carfilzomib (KYPROLIS), with bortezomib (VELCADE) or lenalidomide (REVLIMID) and/or dexamethasone.

From the second relapse, in patients who have already been treated with VELCADE (bortezomib) and REVLIMID (lenalidomide), IMNOVID (pomalidomide) has an MA in combination with dexamethasone. However, given the evolution of the care pathway in multiple myeloma, with new medicinal products having been added to the therapeutic arsenal in earlier treatment lines, the role of IMNOVID (pomalidomide) in combination with dexamethasone has become more limited. In addition, earlier use of IMNOVID (pomalidomide) from the second line of treatment in combination with bortezomib and dexamethasone is likely to substantially reduce the benefit of pomalidomide/dexamethasone dual therapy in subsequent treatment lines. FARYDAK (panobinostat) combined with bortezomib and dexamethasone, represents a last-resort treatment option for patients with recurrent and/or refractory myeloma, having previously received two lines of treatment, including bortezomib and an immunomodulator. DARZALEX (daratumumab) is also an option in patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD); however, its earlier use (currently possible from first-line therapy) in the context of combination with a PI or an IMiD, substantially reduces the benefit of this monotherapy in subsequent treatment lines. Recently, SARCLISA (isatuximab) has been added to the care pathway, in combination with pomalidomide and dexamethasone in patients having received at least two prior treatments including lenalidomide and a PI.

Otherwise, in heavily pretreated patients in the very advanced stages, BLENREP (belantamab mafodotin) has been granted an MA 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 antiCD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. The Transparency Committee considered that it was a salvage therapy when all the other treatment options have been exhausted, following the opinion of a multidisciplinary team (MDT) meeting.

Role of the medicinal product in the care pathway

ABECMA (idecabtagene vicleucel) is a fourth or later-line treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

Considering the absence of methodologically robust comparative data, the role of ABECMA (idecabtagene vicleucel) compared to BLENREP (belantamab mafodotin) cannot be specified.

Due to the timeframes for product availability (including the time required for determination of patient eligibility for CAR-T cell treatment, leukapheresis, the production of the genetically modified cells and lymphodepleting chemotherapy through to transportation to the patient for reinjection) and the significant short-term toxicity, the general condition and life expectancy of patients eligible for ABECMA (Idecabtagene vicleucel) must be compatible with these timeframes.

The Committee also highlights that:

- **considering the high frequency of grade ≥ 3 adverse events (99% of patients), with, in particular, cytokine release syndromes, neurological adverse effects and possible hospitalisation in the ICU, as well as the constraints related to the need for a lengthy hospital stay and the potential distance from the patient's home of a qualified centre, it is essential to inform patients about these constraints and the risks, ABECMA (idecabtagene vicleucel) must be administered in a healthcare facility specifically qualified in the use of CAR-T cells,**
- **the summary of product characteristics (SPC) and the risk management plan (RMP) must be complied with and special monitoring during and after treatment is required.**

Special recommendations

The use of ABECMA (idecabtagene vicleucel) is limited to a small number of centres specifically qualified in the use of CAR-T cells given the complexity of the procedure, as stipulated in the order of 19 May 2021. In this context, the Committee highlights the importance of overall care (in particular including travel and local accommodation near healthcare facilities, where required), as reported by patient and user associations.

The Committee highlights the importance of ensuring patients, and their carers if applicable, have access to appropriate information on the complexity of the CAR-T procedure, the constraints related to prolonged hospitalisation and the risks to patients.

The Committee would like to see all stakeholders mobilised to provide responses to the uncertainties of this dossier at the next re-evaluation. To this end, the Committee calls for the participation of all qualified centres in the requested registry in order to obtain exhaustive, high-quality observational data.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Multiple myeloma is a serious blood disease that is life-threatening.

◗ The proprietary medicinal product ABECMA (idecabtagene vicleucel) is a curative medicinal product.

◗ The efficacy/adverse effects ratio is high.

◗ There are therapeutic alternatives (see section 05 of this opinion).

◗ ABECMA (idecabtagene vicleucel) is a fourth or later-line treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

Public health impact

Considering:

- the seriousness of the disease and its incidence,
- the partially met medical need,
- the lack of response to the identified need (additional impact on morbidity and mortality and/or on quality of life not demonstrated),
- the lack of evidence to support an absence of deterioration in the care and/or life pathway, considering, in particular, systematic hospitalisation for the first ten days following infusion and the need for patients to remain near the qualified healthcare facility for at least four weeks after infusion,
- the absence of data enabling assessment of the impact on the organisation of care, considering, in particular, the obligation for accreditation of hospitals based on precise criteria and the close coordination between the various departments of centres authorised to treat patients with CAR-T cells (laboratories, internal pharmacy, clinical departments, etc.),

ABECMA (idecabtagene vicleucel) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ABECMA (idecabtagene vicleucel) is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and at the MA dosages.

Clinical Added Value

Considering:
- efficacy data from a phase 2 non-comparative study, with an overall response rate of 67% [95% CI: 59-75] and a complete response rate of 29% [95% CI: 21-36] in the ITT population, in a life-threatening clinical situation,
- 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 concerning the specific effect size of this treatment, in view of the methodological weaknesses of indirect comparisons, in a context in which a prior formalised comparison, with a robust methodology, with a historic patient cohort could have been envisaged,
- the safety profile marked by significant short and medium-term toxicity,
- uncertainties with respect to the clinical efficacy and safety in the longer term,
- the existence of alternatives in patients having received at least four prior treatments, albeit considered to be concomitant developments,
- and despite the benefit of having access to a medicinal product having been assessed following the failure of prior therapy including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody,

the Transparency Committee considers that, on the basis of currently available data, and pending the results of the randomised phase 3 KarMMa-3 study, ABECMA (idecabtagene vicleucel) provides no clinical added value (CAV V) in the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.