HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
30 MARCH 2022

The legally binding text is the original French opinion version

ixazomib
NINLARO 2.3 mg hard capsules
NINLARO 3 mg hard capsules
NINLARO 4 mg hard capsules

Re-evaluation

Key points

Favourable opinion for maintenance of reimbursement in combination with lenalidomide and dexamethasone in the treatment of adult patients with multiple myeloma who have received at least one prior treatment.

What therapeutic improvement?

No clinical added value compared to the lenalidomide/dexamethasone combination.

Role in the care pathway?

In symptomatic patients, the first treatment is dependent on whether the subject is eligible or not for intensive chemotherapy combined with autologous peripheral blood stem cell transplantation (PBSCT). DARZALEX (daratumumab) has also been added to the care pathway as a first treatment, irrespective of PBSCT status, in combination with protocols including an immunomodulatory agent (thalidomide or REVLIMID (lenalidomide)) and/or a proteasome inhibitor (VELCADE (bortezomib)) and/or melphalan.

In the event of relapse or progression following a first treatment, 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. Treatments 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 at an earlier stage, the role of IMNOVID (pomalidomide) in combination with dexamethasone has become limited. In addition, earlier use of IMNOVID (pomalidomide) in the context of combination with bortezomib and dexamethasone is likely to substantially reduce the benefit of pomalidomide/dexamethasone dual therapy in subsequent treatments. 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 (IMiD). DARZALEX (daratumumab) is also an option in patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor (PI) and an IMiD; however, its earlier use (currently possible as first treatment) in the context of combination with a PI or an IMiD, substantially reduces the benefit of this monotherapy in subsequent treatments. 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.

Recently, ABECMA (idecabtagene vicleucel) was also granted an MA for 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. The Transparency Committee considered that it was fourth or later-line treatment, and that, considering the absence of methodologically robust comparative data, its role compared to BLENREP (belantamab mafodotin) could not be specified.

Role of the medicinal product in the care pathway

NINLARO (ixazomib) in combination with lenalidomide and dexamethasone remains a therapeutic option in patients with multiple myeloma who have received at least one prior treatment.

Considering the absence of comparative data, it is not possible to determine the role of the ixazomib + lenalidomide + dexamethasone combination compared to the alternatives that can be used following at least one prior treatment. The choice should be made based on the clinical efficacy and safety data available for each medicinal product, as well the patient's profile and preferences.

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 NINLARO (ixazomib) is a curative medicinal product.

◗ The efficacy/adverse effects ratio is moderate given the not very robust demonstration with respect to progression-free survival, and the absence of a demonstrated effect on overall survival.

◗ There are therapeutic alternatives (see chapter 5).

◗ NINLARO (ixazomib) in combination with lenalidomide and dexamethasone remains a treatment option in patients with multiple myeloma who have received at least one prior treatment (see section 9).

Public health impact
On the basis of currently available data, the previous assessment of the PHI is not modified: NINLARO (ixazomib) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of NINLARO (ixazomib) remains substantial in the MA indication.

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

Clinical Added Value

Considering:
- previously examined data from a randomised, double-blind study having enabled only a not very robust demonstration of a difference in progression-free survival in favour of NINLARO (ixazomib) in combination with lenalidomide and dexamethasone compared to this same combination administered alone, this difference having been observed on assessment by the independent review committee but not found in the assessment conducted by the investigators,
- the lack of evidence of an increase in overall survival (final analysis),
- new medium and long-term safety data that have not revealed any new signals,

the Committee considers that NINLARO (ixazomib), in combination with lenalidomide and dexamethasone, provides no clinical added value (CAV V) compared to the lenalidomide and dexamethasone combination, in patients with multiple myeloma having already received at least one prior treatment.