HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
1 APRIL 2020

lenalidomide
REVLIMID 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg and 25 mg hard capsules

New indication

Key points

Unfavourable opinion for reimbursement as combination therapy with bortezomib and dexamethasone for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.

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).

When patients are not eligible for a transplant (in particular, due to their age, their comorbidities and/or their general condition), the therapeutic strategy is based on a chemotherapy protocol, potentially combined with an anti-CD38 monoclonal antibody:

- chemotherapy with either bortezomib (VELCADE) combined with melphalan and prednisone (MPV protocol) for a fixed period, or lenalidomide (REVLIMID) combined with low doses of dexamethasone (Rd protocol) until disease progression; the Committee had considered that in the absence of data comparing the Rd and MPV protocol, the choice of one or the other could be made on the basis of the patient's safety profile.
- combination of the anti-CD38 monoclonal antibody DARZALEX (daratumumab) with the MPV has demonstrated its superiority until disease progression compared to the MPV protocol alone in patients not eligible for a transplant. In addition, DARZALEX (daratumumab) recently obtained an MA in combination with the Rd protocol in patients ineligible for transplant (lenalidomide-dexamethasone).

Role of the medicinal product in the care pathway

Considering:
- demonstration of the superiority of the VELCADE (bortezomib) plus REVLIMID (lenalidomide) plus dexamethasone combination (VRd protocol) compared to the Rd protocol administered alone in terms of progression-free survival (increase in median of +12.6 months), without, however, any demonstration of a benefit in terms of overall survival (exploratory secondary endpoint);
- the impossibility of quantifying the contribution of REVLIMID (lenalidomide) in terms of efficacy in the VRd triple combination in view of the study design assessing the addition of VELCADE (bortezomib) for a fixed period of 8 cycles to the Rd protocol until progression;
- the higher frequency of certain grade 3 or 4 adverse events (AEs) with the VRd protocol compared with the Rd protocol, in particular peripheral sensory neuropathies (22.9% versus 2.7%), as well as more frequent treatment discontinuations following the occurrence of an AE (37.0% versus 25.0%);
- limitations in terms of the transposability of the study results to the population defined by the MA (patients not eligible for transplant), given the inclusion in the study of patients eligible for transplant (for whom transplant was reserved for a subsequent treatment line) and in the absence of available robust data in patients not eligible for transplant (whose characteristics in terms of age, comorbidities and/or general condition are different);
- the absence of demonstration of the impact on quality of life due to a lack of data;
- the introduction into the therapeutic strategy, since performance of the study, of protocols including DARZALEX (daratumumab) (combined with MPV or Rd) as first-line therapy in patients not eligible for transplant and the impossibility of defining the role of the protocol proposed in the current care pathway in the absence of comparative data;

the Committee deems that REVLIMID (lenalidomide) as combination therapy with bortezomib and dexamethasone has no role in the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.

01 COMMITTEE'S CONCLUSIONS

01.1 Clinical benefit

◗ Multiple myeloma is a serious disease that is life-threatening.
◗ This is curative multiple myeloma treatment.
◗ The efficacy/adverse effects ratio of REVLIMID (lenalidomide) in combination with bortezomib and dexamethasone has not been adequately established, due in particular to:

- the demonstration of the superiority of the VELCADE (bortezomib) plus REVLIMID (lenalidomide) plus dexamethasone combination (VRd protocol) compared to the Rd protocol administered alone in terms of progression-free survival (increase in median of +12.6 months), without, however, any demonstration of a benefit in terms of overall survival (exploratory secondary endpoint);
- the impossibility of quantifying the contribution of REVLIMID (lenalidomide) in terms of efficacy in the VRd triple combination in view of the study design assessing the addition of VELCADE (bortezomib) for a fixed period of 8 cycles to the Rd protocol until progression;
- the higher frequency of certain grade 3 or 4 adverse events (AEs) with the VRd protocol compared with the Rd protocol, in particular peripheral sensory neuropathies (22.9% versus 2.7%), as well as more frequent treatment discontinuations following the occurrence of an AE (37.0% versus 25.0%).

◗ There are medicinal alternatives in adult patients with previously untreated multiple myeloma who are not eligible for transplant.
◗ The Committee deems that REVLIMID (lenalidomide) as combination therapy with bortezomib and dexamethasone has no role in the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant (see 08. Role in the care pathway).

Public health impact

Considering:

- the seriousness of multiple myeloma, a progressive, life-threatening disease,
- the number of incident cases of multiple myeloma, estimated to be around 5,442 patients in France in 2018,
- the partially met medical need in adult patients with previously untreated multiple myeloma who are not eligible for transplant,
- the lack of elements supporting the absence of a deterioration in the care and/or life pathway in the absence of quality of life data collected in the study,
- the absence of any demonstrated impact on the organisation of care, in particular in terms of reduction of hospitalisations or adverse events,
- the lack of additional response to the identified partially met medical need,

REVLIMID is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of REVLIMID is insufficient to justify its reimbursement by public funding in view of the alternatives available in the indication "as combination therapy with bortezomib and dexamethasone for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant".

The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication "as combination therapy with bortezomib and dexamethasone for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant" and at the MA dosages.

01.2 Clinical Added Value

Not applicable.