HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

23 SEPTEMBER 2020

The legally binding text is the original French opinion version

lenalidomide

REVLIMID 2.5 mg / 5 mg / 7.5 mg / 10 mg / 15 mg / 20 mg hard capsules

New indication

Key points

Favourable opinion for reimbursement in the treatment of previously treated follicular lymphoma (Grade 1, 2 or 3a) in adult patients not refractory to rituximab (patients not previously treated with rituximab or who have not relapsed under treatment including rituximab or within 6 months following its discontinuation)[1].

What therapeutic improvement ?

No clinical added value in the therapeutic strategy.

Role in the care pathway ?

In the event of relapsed follicular lymphoma in patients not refractory to rituximab, the treatments depend on the previous treatment lines, the type and duration of the remission previously obtained and the spread of the disease. They are based on :

[1] This indication corresponds to the pharmaceutical company's application for public funding and the scope of the reimbursable indication retained by the Committee following its assessment. It is more limited than the MA indication ("REVLIMID in combination with rituximab (anti-CD20 antibody) is indicated for the treatment of adult patients with previously treated follicular lymphoma (Grade 1 - 3a)").

- immunochemotherapy (R-CHOP, R-CVP, R-bendamustine) that is different from that previously initiated in order to reduce the risk of resistance (bendamustine after CHOP or vice versa) or,
- radio-immunotherapy if the degree of bone marrow involvement allows or,
- stem cell transplantation if the patient's age allows and, in particular, in the event of early relapse.

As third and later-line therapy, treatment with ZYDELIG (idelalisib) may be proposed in patients refractory to two previous treatment lines.

Role of the medicinal product in the care pathway

In the event of relapsed follicular lymphoma in patients not refractory to rituximab, a second-line regimen is proposed. The treatment depends on the first-line therapy received, the type and duration of the remission previously obtained and the spread of the disease. The second-line treatment of patients not refractory to rituximab is based on a new chemotherapy (such as CHOP, bendamustine or CVP) in combination with rituximab. In the absence of comparative data for REVLIMID (lenalidomide) in combination with rituximab versus standard chemotherapy regimens in combination with rituximab, its use should therefore be reserved for situations in which CHOP, bendamustine or CVP-type chemotherapy is not possible. In patients refractory to two previous treatment lines, its role compared to ZYDELIG (idelalisib) as monotherapy is not known in the absence of comparative data. The Committee highlights the fact that no data supporting the benefit of treatment with REVLIMID (lenalidomide) in combination with rituximab for more than twelve 28-day cycles is available.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Follicular lymphomas are slow-progressing indolent non-Hodgkin lymphomas, which are life-threatening.
◗ REVLIMID (lenalidomide), in combination with rituximab, is a curative treatment.
◗ Its efficacy/adverse effects ratio is low, given :

- demonstration of a benefit in terms of progression-free survival (primary endpoint) with REVLIMID (lenalidomide) plus rituximab compared to rituximab as monotherapy, with an increase of +25.3 months, without any demonstrated benefit in terms of overall survival, an exploratory secondary endpoint of the study considered to be more clinically relevant than progression-free survival in relapsed follicular lymphoma and,
- reservations with respect to the validity of the choice of comparator (rituximab as monotherapy), which does not guarantee the transposability of the results of this study to French practices, particularly for patients for whom CHOP, bendamustine or CVP-type chemotherapy can be administered as second or later-line treatment.

◗ There are medicinal and non-medicinal (stem cell transplantation) alternatives.

◗ Role in the care pathway : see chapter 08.

Public health impact

Considering :

- the seriousness of the disease,
- its incidence,
- the medical need partially met by the available alternatives,
- the lack of demonstrated impact on the care and/or life pathway,
- the lack of demonstrated impact on the organisation of care (hospitalisation, AEs, etc.),
- the lack of response to the identified need,

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

Considering all these elements, the Committee deems that the clinical benefit of REVLIMID (lenalidomide) in combination with rituximab is low in the treatment of previously treated follicular lymphoma (Grade 1, 2 or 3a) in adult patients not refractory to rituximab (patients not previously treated with rituximab or who have not relapsed under treatment including rituximab or within 6 months following its discontinuation).

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication "in combination with rituximab for the treatment of previously treated follicular lymphoma (Grade 1, 2 or 3a) in adult patients not refractory to rituximab (patients not previously treated with rituximab or who have not relapsed under treatment including rituximab or within 6 months following its discontinuation)" and at the MA dosages.

Clinical Added Value

Considering :

- **demonstration of the superiority of addition of lenalidomide to rituximab compared to rituximab administered alone, for a maximum duration of twelve 28-day cycles, in terms of progression-free survival (primary endpoint), with a median increase of +25.3 months (HR = 0.46; 95% CI [0.34- 0.62]),**
- **the absence of demonstration of a benefit in terms of overall survival, an exploratory secondary endpoint of the study considered to be more clinically relevant than progression-free survival in relapsed follicular lymphoma,**
- **reservations with respect to the validity of the choice of comparator (rituximab as monotherapy), which does not guarantee the transposability of the results of this study to French practices, particularly for patients for whom CHOP, bendamustine or CVP-type chemotherapy can be administered (who represented 71 % of patients in the study),**
- **the lack of demonstrated impact on quality of life,**

the Committee deems that REVLIMID in combination with rituximab provides no clinical added value (CAV V) in the care pathway for previously treated follicular lymphoma (Grade 1, 2 or 3a) in adult patients not refractory to rituximab (patients not previously treated with rituximab or who have not relapsed under treatment including rituximab or within 6 months following its discontinuation).