SUMMARY

rituximab

MABTHERA 100 mg and 500 mg,

concentrate for solution for infusion

Reassessment at the request of the TC

Adopted by the Transparency Committee on 19 April 2023

The legally binding text is the original French opinion version

Key points

Favourable opinion on the maintenance of reimbursement in the treatment of moderate to severe pemphigus vulgaris (PV) in adults.

What therapeutic improvement?

Therapeutic improvement in relation to management.

Role in the care pathway?

The new data confirm the role of MABTHERA (rituximab) in combination with brief systemic corticosteroid therapy, in the first-line treatment of moderate to severe PV in adults.

Transparency Committee's Conclusions

Clinical Benefit

- Pemphigus vulgaris is a rare, chronic autoimmune disease, that is potentially serious and can be life-threatening.
- MABTHERA 100 mg and 500 mg (rituximab), concentrate for solution for infusion, is a curative treatment.
- The efficacy/adverse effect ratio is significant.
- There are therapeutic alternatives.
- Rituximab, in combination with brief systemic corticosteroid therapy, is the first-line treatment for moderate to severe pemphigus vulgaris in adults.

Public health benefit

In view of:

- the gravity of the disease and its rarity,
- the partially met medical need,
- the partial response to the need identified due to:
  - a significant effect, in association with low-dose, short-term corticosteroid therapy, in terms of complete remission compared with long-term systemic corticosteroid therapy and in terms of durable complete remission (16 weeks) compared with MMF,
  - the reduction in the number of relapses under treatment compared to MMF,
  - the demonstration of the cortisone sparing compared to MMF,
  - the absence of proven impact on the improvement in the patient's care pathway and/or life course particularly due to administration constraints (treatment by infusion in a hospital setting, close monitoring by an experienced health professional, pre-medication and drug-based prophylaxis),

MABTHERA (rituximab) is not liable to have an additional impact on public health.

In view of all of these elements, the Committee considers that the clinical benefit provided by MABTHERA100 mg and 500 mg (rituximab), concentrate for solution for infusion, remains significant in the MA indication.

The Committee gives a favourable opinion on the maintenance of the inclusion of MABTHERA 100 mg and 500 mg (rituximab), concentrate for solution for infusion, on the list of medicinal products approved for the use of communities in the MA indication and at the MA doses.

Clinical Added Value

In view of:

- the results previously provided by the phase III study (ML22196), which demonstrated the superiority of a short course (3-6 months) of the combination rituximab + prednisone at a low dose, compared to prednisone alone at a standard dose for a prolonged course (12-18 months), in terms of complete remission after 24 months, in adults with moderate to severe pemphigus vulgaris (PV) (89.5% vs 27.8%, p < 0.0001), despite the methodological weaknesses of the study (open study, with no control of alpha risk, analysis of a subgroup of patients);
- the results of a new phase III study (PEMPHIX), with good quality methodology, comparative versus mycophenolate mofetil (MMF), in combination with brief corticosteroid therapy in each group, in adults with active moderate to severe PV requiring oral corticosteroid therapy, which demonstrated:
  - the superiority of rituximab compared to MMF after 52 weeks of treatment with regard to the percentage of patients obtaining a complete response (with discontinuation of corticosteroid therapy) maintained for at least 16 weeks with a significant effect: 40.3% vs 9.5% respectively (p <0.0001),
  - the superiority of rituximab compared with MMF after 52 weeks of treatment, with also a significant effect, on the following hierarchical endpoints:
    - cortisone sparing,
    - number of relapses during treatment,
    - time period until the first relapse,
    - time period until complete lasting remission was obtained,
  - the superiority of rituximab compared to MMF with regard to the variation in the DLQI (quality of life) score, although the difference observed is not clinically relevant (-2.87 points);
- the unchanged tolerance profile, marked mainly by the reactions associated with the infusion and infections;

the Committee considers that MABTHERA 100 mg and 500 mg (rituximab) now provides moderate clinical added value (CAV III) in the management of moderate to severe pemphigus vulgaris in adults, which comprises long-term corticosteroid therapy and short-term corticosteroid therapy combined with an immunosuppressant (mycophenolate mofetil, methotrexate or azathioprine).