HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
11 DECEMBER 2019

rituximab
MABTHERA 100 mg/ml and 500 mg/50 ml concentrate for solution for infusion

New indication

Key points

Favourable opinion for reimbursement in the treatment of patients with moderate to severe pemphigus vulgaris.

What therapeutic improvement?

Slight therapeutic improvement compared to systemic corticosteroid therapy.

Role in the care pathway?

The primary objective of treatment is to achieve and maintain remission. This implies the suppression of blister formation, the healing of skin and/or mucous membrane erosions and the reduction of treatment. The secondary objectives are to control the disease, prevent relapses, limit cumulative corticosteroid doses, reduce circulating antibody levels, limit adverse effects and maintain quality of life.

Rituximab is the first-line induction treatment for moderate to severe pemphigus vulgaris, in combination with short-term (3 to 6 months) low-dose systemic corticosteroid therapy. Rituximab will be used alone (or with topical corticosteroids) in the event of absolute or relative contraindications to systemic corticosteroid therapy.

The use of standard-dose systemic corticosteroid therapy alone or combined from the outset with a conventional immunosuppressant treatment (particularly in the event of increased risk of corticosteroid therapy-related complications and in order to enable rapid withdrawal) may be an alternative in the event of contraindication to rituximab or if this treatment cannot be administered.

The conventional immunosuppressive agents recommended are mycophenolate mofetil (off-label, professional agreement), methotrexate (off-label, professional agreement) or azathioprine. Cyclophosphamide as an intravenous bolus or orally is not recommended as a first-line treatment due to the numerous adverse effects.

Following a first course of rituximab, maintenance treatment may be administered depending on the patient's response to treatment (see SPC).

Role of the medicinal product in the care pathway

Rituximab, in combination with systemic corticosteroid therapy, is the first-line treatment in moderate to severe pemphigus vulgaris in adults.

01 COMMITTEE'S CONCLUSIONS

01.1 Clinical Benefit

◗ Pemphigus vulgaris is a potentially serious, rare chronic autoimmune disease that can be life-threatening.
◗ MABTHERA is a curative treatment.
◗ The efficacy/adverse effects ratio is high.
◗ There are therapeutic alternatives.
◗ Rituximab, in combination with systemic corticosteroid therapy, is the first-line treatment in moderate to severe pemphigus vulgaris in adults.

Public health impact

Considering:

- the seriousness of the disease and its rarity,
- the partially met medical need,
- the partial response to the identified medical need due to a high effect size, in combination with short-term low-dose corticosteroid therapy, in terms of complete remission compared to long-term systemic corticosteroid therapy, and results suggesting cortisone-sparing but a lack of demonstrated impact in terms of quality of life and in the absence of long-term efficacy and safety data,
- the lack of a demonstrated impact on improvement of the patient's care and/or life pathway, due, in particular, to the therapeutic constraints (treatment by infusion in a hospital setting, close monitoring by an experienced healthcare professional, premedication and medicinal prophylaxis),

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

Considering all these elements, the Committee deems that the clinical benefit of MABTHERA is substantial in the treatment of patients with moderate to severe pemphigus vulgaris (PV).

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the treatment of patients with moderate to severe pemphigus vulgaris (PV) and at the MA dosages.

01.2 Clinical Added Value

Considering:

- **the demonstrated superiority of rituximab in combination of short-term low-dose oral prednisone, compared to long-term standard-dose oral prednisone, in terms of complete remission at 24 months, having demonstrated a high size effect (89.5% with the rituximab+oral prednisone combination versus 27.8% with oral prednisone alone, RR = 3.221, $CI_{95\%}$ = [1.881; 5.516], p < 0.0001);**
- **the methodological limitations of this research evidence and, in particular, the open-label nature of the study,**
- **results suggesting cortisone-sparing (unranked secondary outcome measure) with the rituximab+oral prednisone combination,**
- **experience limited to 24 months of available data and the absence of long-term efficacy and safety data,**

the Transparency Committee considers that MABTHERA provides a minor clinical added value (CAV IV) in the treatment of moderate to severe pemphigus vulgaris.