HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
20 NOVEMBER 2019

rituximab
MABTHERA concentrate for solution for infusion

New indication

Key points

Favourable opinion for reimbursement in the maintenance treatment of adult patients with severe, active granulomatosis with polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA).

What therapeutic improvement?

No therapeutic improvement compared to IMUREL (azathioprine).

Role in the care pathway?

In the first-line treatment for induction of remission of systemic GPA and MPA, rituximab may be prescribed in the same way as cyclophosphamide. Following the achievement of remission, relapses, which occur in more than half of GPA patients and around 30% of MPA patients at 5 years, require the initiation of maintenance treatment with azathioprine (IMUREL) or methotrexate (used off-label) or even mycophenolate mofetil (used off-label) for a period of 12 to 24 months, with the aim of consolidating remission and limiting the risk of relapse.

Role of MABTHERA (rituximab) in the care pathway:

In treatment for the maintenance of remission of systemic GPA and MPA, MABTHERA (rituximab) is a first-line maintenance treatment option for systemic vasculitis. No relevant data are available enabling its role in the care pathway to be ranked compared to the alternatives currently available.

Experience with the use of rituximab in the MAINRITSAN study is limited to 18 months of treatment, which corresponds to 5 rituximab infusion cycles. However, the SPC for MABTHERA recommends a treatment duration of at least 24 months and schedules the possibility of treating patients at high risk of relapse for up to 5 years. Uncertainties remain concerning the optimal administration regimen for MABTHERA (rituximab) as maintenance treatment and its long-term safety associated with its use in this context.

Special recommendations

Monitoring of the safety of rituximab is essential in the context of its long-term prescription.

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Severe, active granulomatosis with polyangiitis (GPA) (formerly called Wegener's disease) and microscopic polyangiitis (MPA) are serious and incapacitating rare diseases.
◗ This proprietary medicinal product is a curative treatment.
◗ The efficacy/adverse effects ratio of MABTHERA (rituximab) as a treatment for the maintenance of remission is high.
◗ There are therapeutic alternatives.
◗ MABTHERA (rituximab) is a first-line maintenance treatment. No relevant data are available enabling its role in the care pathway to be ranked compared to its clinically relevant comparators defined in section 05.

◗ Public health impact:
Considering:
- the seriousness of the disease,
- its rarity (see section 010.3 Target population),
- the medical need for maintenance treatment that is currently partially covered,
- the absence of robust data in terms of the impact of MABTHERA (rituximab) on quality of life,
- the lack of any demonstrated impact on the organisation of care (hospitalisation, AE, etc.),
- the partial response of MABTHERA (rituximab) to the identified need given the methodology of the MAINRITSAN study (open-label study with assessment of the primary outcome measure by the investigator),

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

Considering all these elements, the Committee deems that the clinical benefit of MABTHERA (rituximab) is substantial in the MA indication extension.

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

Clinical Added Value

Considering:
- **the demonstration of the superiority of MABTHERA (rituximab) in a study versus IMUREL (azathioprine), a clinically relevant comparator, in terms of major relapse rate assessed at 28 months (primary outcome measure) but,**
- **the methodological limitations of the study (open-label study with assessment of the primary outcome measure by the investigator, whereas a double-blind study could have been conducted),**
- **the experience of use of rituximab limited to 18 months, whereas the SPC recommends a treatment duration of at least 24 months and schedules the possibility of treating patients at high risk of relapse for up to 5 years,**
- **uncertainties concerning the optimal administration regimen for MABTHERA (rituximab) as maintenance treatment and its long-term safety associated with its use in this context,**

the Transparency Committee considers that MABTHERA (rituximab) provides no clinical added value (CAV V) compared to IMUREL (azathioprine) in combination with glucocorticoids in the maintenance treatment of adult patients with severe, active granulomatosis with polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA).