HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
30 MARCH 2022

The legally binding text is the original French opinion version

teriflunomide
AUBAGIO 14 mg film-coated tablets
New indication

AUBAGIO 7 mg film-coated tablets
First assessment

Key points

Unfavourable opinion for reimbursement in the treatment of paediatric patients aged 10 years and older with relapsing remitting multiple sclerosis (MS), in view of the available alternatives.

Role in the care pathway?

The early initiation of disease-modifying therapy is recommended following validation of the diagnosis of MS in children. Several therapeutic options are proposed as first-line treatments and have a paediatric MA: beta 1-a interferons (AVONEX and REBIF), beta 1-b interferons (EXTAVIA and BETAFERON) and glatiramer acetate (COPAXONE). REBIF (interferon beta 1-a) is the only one of these medicinal products to have an MA in children aged 2 years and older, with the others only having an MA for patients aged 12 years and older.

In 2019, the Committee examined the indication extension for GILENYA (fingolimod) as a disease-modifying therapy in highly active relapsing remitting multiple sclerosis in patients aged 10 years and older. It considered that GILENYA (fingolimod) was a first or second-line treatment for highly active relapsing remitting multiple sclerosis in the groups of paediatric patients aged 10 years and older defined by the MA, as follows:

- Patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy, or
- Patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more Gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI.

The Committee also highlighted that monitoring of patients was required in accordance with the SPC and the risk management plan, due to the safety profile of GILENYA (fingolimod), marked in particular by cardiac rhythm disorders (bradyarrhythmia) after the first dose, infections, seizures and skin cancer.

The proprietary medicinal product TYSABRI (natalizumab) does not have a paediatric MA but is nonetheless cited by the 2019 French national diagnostic and care protocol (PNDS) as a therapeutic option in second-line situations following the failure of immunomodulatory therapies in the event of severe or rapidly evolving disease. It is necessary to contact a reference centre specialising in rare inflammatory brain and spinal cord diseases for the use of this proprietary medicinal product in the paediatric population.

Role of AUBAGIO (teriflunomide) in the care pathway for the treatment of paediatric patients aged 10 years and older with relapsing remitting MS:

Considering:
- the non-statistically significant result for the primary endpoint (time to first clinical relapse) in the TERIKIDS comparative study versus placebo, which cannot eliminate the possibility of a loss of opportunity for patients in view of the available clinically relevant comparators,
- the absence of study conducted versus an active comparator, despite this being feasible, in a context in which immunomodulatory substances have been available for several years,
- limited long-term safety data in the paediatric population, particularly in patients beginning this treatment at a very young age,

the Committee considers that AUBAGIO (teriflunomide) has no role in the treatment of paediatric patients aged 10 years and older with relapsing remitting forms of multiple sclerosis (MS).

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Multiple sclerosis is a serious and disabling, progressive chronic neurological disease. It corresponds to inflammation and selective, chronic demyelinisation of the central nervous system. The manifestations are multiple: motor and sensory disorders, sensory deficit, bladder-sphincter and sexual disturbances, cognitive function and mood disorders. They can considerably reduce patients' autonomy and impair their quality of life. The severity of the disease is very variable, ranging from forms causing low incapacity to forms leading to significant disabilities within few years.
◗ The proprietary medicinal product AUBAGIO (teriflunomide) is a preventive treatment for relapses.
◗ Considering:

- the non-statistically significant result for the primary endpoint in the TERIKIDS comparative study versus placebo, which cannot eliminate the possibility of a loss of opportunity for patients in view of the available clinically relevant comparators,
- limited long-term safety data in the paediatric population, particularly in patients beginning this treatment at a very young age,

consequently its efficacy/adverse effects ratio has not been adequately established in the indication extension concerned.
◗ There are medicinal alternatives.
◗ AUBAGIO (teriflunomide) has no role in the care pathway for paediatric patients aged 10 years and older with relapsing remitting forms of multiple sclerosis (MS).

Public health impact

Considering:

- the seriousness of the disease and its prevalence,
- the partially met medical need,
- the lack of additional response to the identified need with:
  - the absence of a demonstrated additional impact on morbidity given the statistically non-significant result for the time to first clinical relapse (primary endpoint) versus placebo,
  - the lack of a demonstrated additional impact on quality of life,
- the lack of a demonstrated additional impact on the organisation of care in the absence of data,

AUBAGIO (teriflunomide) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of AUBAGIO (teriflunomide) is insufficient to justify public funding cover in paediatric patients aged 10 years and older with RRMS, in view of the available alternatives.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA paediatric indication extension and at the MA dosages.