HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
16 DECEMBER 2020
The legally binding text is the original French opinion version

brolucizumab
BEOVU 120 mg/ml solution for injection in pre-filled syringe
BEOVU 120 mg/ml solution for injection in vial

First assessment

Key points

Unfavourable opinion for reimbursement for the treatment of neovascular (wet) age-related macular degeneration (AMD) in adults.

Role in the care pathway?

Currently, the treatment of exudative AMD is based on intravitreal (IVT) injections of anti-VEGF, which make it possible to stabilise or improve patients' vision but cannot cure the condition. Two anti-VEGF therapies that already have an MA in this indication are used in France: ranibizumab (LUCENTIS) and aflibercept (EYLEA). Another anti-VEGF therapy is available in this indication: bevacizumab (AVASTIN). It is the subject of a Temporary Recommendation for use (RTU) granted by the ANSM in AMD.

There are different protocols for the treatment of AMD using anti-VEGF therapy, such as, notably, the fixed-interval injection regimen (monthly or two-monthly injections depending on the drug used), or personalised regimens, such as the "Treat and Extend" protocol aimed at reducing the frequency of injections and visits depending on disease activity, or the IOI (injection – observation – individualisation) protocol proposed by the France Macula Federation.

Role of the medicinal product in the care pathway

In the first-line treatment of neovascular (wet) age-related macular degeneration, taking into account the following elements:

- the demonstrated non-inferiority of brolucizumab compared to aflibercept in terms of the mean variation in best corrected visual acuity (non-inferiority margin of -4 letters) and
- its demonstrated superiority on ranked secondary endpoints (central retinal thickness, presence of intraretinal/subretinal fluid and investigator-assessed disease activity),

but also:

- its ocular safety profile, marked by a higher frequency of ocular serious adverse events (AEs) compared to aflibercept (3.4% versus 1.5%), and especially
- an additional risk of retinal vasculitis and/or retinal vascular occlusion, which are serious AEs since they can lead to severe visual acuity loss, not currently characterised with the other available anti-VEGF therapies,

the Transparency Committee considers that BEOVU (brolucizumab) has no role in the first-line treatment of neovascular (wet) age-related macular degeneration.

As second or later-line treatment, despite an identified medical need in the event of failure of the anti-VEGF therapies already available (resistance, intolerance, contraindication), the role of BEOVU (brolucizumab) in this situation cannot be determined due to the lack of available data.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Age-related macular degeneration (AMD) is the leading cause of visual disability in France in patients over the age of 50. Among severe forms of AMD, exudative or neovascular forms are responsible for the largest number of severe visual acuity reductions.
◗ This proprietary medicinal product is a curative treatment for the consequences of the disease.
◗ In first-line treatment, considering:
- the non-inferiority of brolucizumab in terms of the mean variation in best corrected visual acuity compared to aflibercept, for which the administration regimen used in the study, although authorised in its SPC, does not all reflect current clinical practice, and
- its demonstrated superiority on secondary endpoints (central retinal thickness, presence of intraretinal/subretinal fluid and investigator-assessed disease activity), but
- the ocular toxicity of brolucizumab marked by a higher frequency of ocular serious adverse events compared to aflibercept (3.4% versus 1.5%) and by the important identified additional risk of retinal vasculitis and retinal vascular occlusion in comparison with the anti-VEGF therapies already available, constituting serious AEs since they can lead to severe visual acuity loss and occurring with a not insignificant frequency (approximately 1 case for 1,000 units of product used according to current data),

the efficacy/adverse effects ratio of this proprietary medicinal product is not adequately established. As second-line treatment, in the event of failure of the anti-VEGF therapies already available (ranibizumab, aflibercept and bevacizumab) its efficacy/adverse effects ratio has not been established due to the absence of available data.
◗ There are therapeutic alternatives.
◗ BEOVU (brolucizumab) has no role in the first-line treatment of neovascular AMD. In the absence of available data, its value as a salvage therapy (second-line) has not been demonstrated (see section 08. Role in the care pathway).

Public health impact

Considering:
- the seriousness of the disease, progressing to visual disability, and its incidence,
- the partially met medical need,
- the lack of response to the identified need in the absence of any demonstrated additional impact on morbidity as the dossier currently stands (data supporting the efficacy but with ocular toxicity marked by serious cases of retinal vasculitis and retinal vascular occlusion not shared with other anti-VEGF therapies) and the absence of robust data on quality of life,
- the lack of evidence to support an absence of deterioration in the care and/or life pathway,
- the lack of demonstrated impact on the organisation of care (hospitalisation, AEs, etc.),

BEOVU (brolucizumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of BEOVU (brolucizumab) is insufficient to justify its public funding cover in view of the alternatives available in the MA indication.

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 indication and dosages.