SUMMARY

aflibercept

EYLEA 114.3 mg/mL

solution for injection in vials

First listing

Original French opinion adopted by the Transparency Committee on 3 July 2024

The legally binding text is the original French opinion version

Summary of opinion

Favourable opinion for reimbursement only in the treatment of visual impairment due to diabetic macular oedema (DMO) in adults, in the event of diffuse forms or leakages close to the centre of the macula, in patients with a visual acuity of less than or equal to 7/10 and in whom diabetes management has been optimised.

Unfavourable opinion for reimbursement in the other situations covered by the MA indication.

Transparency Committee's conclusions

Clinical Benefit

- Diabetic macular oedema (DMO) is a complication of diabetic retinopathy. It is asymptomatic but progresses gradually to visual impairment and blindness, resulting in disability and a marked deterioration in quality of life.
- EYLEA 114.3 mg/mL (aflibercept), solution for injection in vials is a curative medicinal product.
- The efficacy/adverse effects ratio is high.
- This proprietary medicinal product is a first-line treatment in patients unable to undergo laser therapy, i.e. in the event of diffuse forms of macular oedema or leakages close to the centre of the macula. Treatment with aflibercept can be initiated when visual acuity is less than or equal to 7/10 and diabetes management has been optimised.

Public health benefit

Considering:

- the seriousness of the disease and its prevalence (3% of diabetic patients),
- the identified partially met medical need,
- the partial response to the identified partially met medical need, given:

- the lack of evidence of an additional impact compared to EYLEA 40 mg/mL (aflibercept) in terms of visual acuity (functional clinical endpoint) after 48 and 60 weeks of treatment,
- the lack of robust evidence of an additional impact on quality of life (exploratory endpoint),
- the lack of evidence of an additional impact on the patient's care or life pathway compared to other VEGF inhibitors despite a dosing regimen enabling the injections to be given at intervals of up to 5 months and the number of injections during the induction phase to be reduced compared to EYLEA 40 mg/mL (aflibercept) (3 injections instead of 5),

EYLEA 114.3 mg/mL (aflibercept) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of EYLEA 114.3 mg/mL (aflibercept) solution for injection in vials is:

- **substantial only for the treatment of visual impairment due to diabetic macular oedema in adults, in the case of diffuse forms or leakages near the centre of the macula in patients with visual acuity of less than or equal to 7/10 and for whom the management of diabetes has been optimised;**
- **insufficient to justify public funding cover in the other MA situations.**

The Committee issues the following opinions:

- **a favourable opinion for inclusion of EYLEA 114.3 mg/mL (aflibercept) solution for injection in vials in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the indications only within the scope retained and at the MA dosages;**
- **an unfavourable opinion for inclusion of EYLEA 114.3 mg/mL (aflibercept) solution for injection in vials in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the other situations covered by the MA indication.**

➔ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%**

Clinical Added Value

Considering:

- the phase 2/3, randomised, double-blind, multicentre PHOTON trial having compared aflibercept 8 mg every 12 weeks (Q12W) or every 16 weeks (Q16W) with a variable dosing regimen (after 3 initial monthly injections) with aflibercept 2 mg every 8 weeks (Q8W) with a fixed dosing regimen (after 5 initial monthly injections) in adults with visual impairment due to DMO (BCVA of between 24 and 78 ETDRS letters inclusive) involving the centre of the fovea, in whom the management of diabetes has been optimised, and the results of which demonstrated:
  - the non-inferiority, without demonstration of a superiority, of the aflibercept 8 mg Q12W and 8 mg Q16W groups compared to the aflibercept 2 mg Q8W group in terms of change in best corrected visual acuity (BCVA, ETDRS) compared to baseline after 48 (primary endpoint) and 60 weeks (ranked secondary endpoint) of treatment;

- the non-inferiority of aflibercept 8 mg Q12W compared to aflibercept 2 mg Q8W on the proportion of patients who achieved an at least 2-step improvement in diabetic retinopathy severity on the ETDRS-DRSS scale compared to baseline at week 48 (ranked secondary endpoint);

– a comparable tolerance between aflibercept 8 mg Q12W or Q16W and aflibercept 2 mg Q8W;
– the lack of evidence of a superiority of aflibercept 8 mg Q12W or Q16W compared to aflibercept 2 mg Q8W in terms of quality of life;
– a dosing regimen for EYLEA 114.3 mg/mL enabling a reduction in the number of injections compared to EYLEA 40 mg/mL during the induction phase of treatment (3 monthly intravitreal injections instead of 5) and an interval of up to 5 months between injections, but with no evidence of an additional impact on the organisation of care or the care or life pathway of patients compared to the other VEGF inhibitors used with a Treat & Extend regimen;

the Committee deems that EYLEA 114.3 mg/mL (aflibercept) solution for injection in vials provides no clinical added value (CAV V) compared to EYLEA 40 mg/mL (aflibercept) solution for injection in vials and pre-filled syringe.