HAUTE AUTORITÉ DE SANTÉ

OPHTHALMOLOGY
New indication
March 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

EYLEA (aflibercept), anti-VEGF

Minor improvement, as is the case with LUCENTIS, in the treatment of visual impairment due to diabetic macular oedema

Main points

- EYLEA now has Marketing Authorisation in the treatment of visual impairment due to diabetic macular oedema (DME) in adults.
- Its efficacy versus laser photocoagulation has been demonstrated. The observed differences versus ranibizumab in the change in BCVA, although statistically significant, are not clinically relevant.
- As is the case with LUCENTIS, the therapeutic benefit provided by EYLEA in the treatment of visual impairment due to DME is minor in the diffuse form or in lesions close to the centre of the macula in patients with visual acuity less than or equal to 5/10 in whom management of diabetes has been optimised.

Pre-existing indications

- EYLEA is indicated in adults for the treatment of neovascular (wet) age-related macular degeneration (AMD) and visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO).
- This summary does not cover these indications.

Therapeutic use

- Optimised management of diabetes and other risk factors associated with DME (hypertension, dyslipidaemia and sleep apnoea syndrome) is a prerequisite for the treatment of DME.
- Laser photocoagulation in focal DME and an anti-VEGF in DME cases that cannot be treated by laser (diffuse forms or forms with central macular involvement) are the first-line treatment in patients with visual acuity less than or equal to 5/10. In diffuse oedema unresponsive to an anti-VEGF, grid photocoagulation can be proposed.
- The second-line treatments are intravitreal implants of fluocinolone acetonide (ILUVIEN, not currently reimbursable) and dexamethasone (OZURDEX,not currently reimbursable).

- **Role of the medicinal product in the therapeutic strategy**
  Aflibercept, like ranibizumab, is a first-line treatment for visual impairment due to DME in the diffuse form or in lesions close to the centre of the macula in patients with visual acuity less than or equal to 5/10 in whom management of diabetes has been optimised.

Clinical data

- Two randomised, double-blind studies with similar protocols (VISTA and VIVID) compared aflibercept 2 mg with laser photocoagulation over a 52-week period in adults with visual impairment due to DME, central macular involvement and a best corrected visual acuity (BCVA) of between 24 and 73 letters (ETDRS). At week 24, patients could receive additional treatment (laser in the aflibercept group and aflibercept in the laser group) according to predefined criteria. The percentage of patients in the laser group who received additional treatment was higher than in the aflibercept group (31.8% versus 0.7% in the VISTA study and 24.1% versus 8.1% in the VIVID study).
  After 52 weeks, the adjusted mean change in BCVA versus baseline was greater in the aflibercept group than in the laser group:
  - in the VISTA study: 10.7 versus 0.2 letters, i.e. a difference of 10.45 letters ($p < 0.0001$).

- in the VIVID study: 10.7 versus 1.2 letters, i.e. a difference of 9.1 letters ($p < 0.0001$).

- In an indirect comparison meta-analysis, aflibercept showed superiority over ranibizumab of 4.8 letters in the mean change in BCVA, which was close to the clinical relevance threshold of 5 letters.
- An independent clinical study compared 2 mg aflibercept with 0.3 mg ranibizumab over a 52-week period in adults with visual impairment due to DME, central macular involvement and a BCVA of between 24 and 78 letters. The aflibercept and ranibizumab dosages did not correspond to those of their Marketing Authorisation. After 24 weeks, patients who had not responded could be treated with laser photocoagulation or other treatments. After 52 weeks, the difference between the groups in the change in BCVA versus baseline was significant but not clinically relevant (difference of 2.1 letters, $p < 0.001$).
- The safety profile is consistent with that observed for the earlier indications of aflibercept in AMD and central vein occlusion, except for cases of punctate keratitis.

Special prescribing conditions

- Exception drug status

Benefit of the medicinal product

- The actual benefit* of EYLEA is substantial.
- As is the case with LUCENTIS, EYLEA provides minor clinical added value** (CAV IV) in the treatment of visual impairment due to diabetic macular oedema in the diffuse form or in lesions close to the centre of the macula in patients with visual acuity less than or equal to 5/10 in whom management of diabetes has been optimised.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 18 March 2015 (CT-14030) and is available at **www.has-sante.fr**

[i]* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means "no clinical added value".