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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

EYLEA (aflibercept), anti-VEGF

Minor improvement in the management of visual impairment secondary to branch retinal vein occlusion.

Main points

- EYLEA now has Marketing Authorisation in the treatment of visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO).
- Its efficacy has been demonstrated versus laser photocoagulation but it has not been compared with LUCENTIS or OZURDEX.
- Like LUCENTIS, it is a first-line treatment that provides minor clinical added value in the management of visual impairment secondary to BRVO.

Pre-existing indications

- EYLEA already had Marketing Authorisation for adults in the treatment of:
  - neovascular (wet) age-related macular degeneration (AMD)
  - visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)
  - visual impairment due to diabetic macular oedema (DME).
- This summary does not cover these indications.

Therapeutic use

- In the treatment of visual impairment due to BRVO, macular photocoagulation may be used for forms that have been present for more than 3 months. The other first-line treatments are OZURDEX (dexamethasone intravitreal implant) and LUCENTIS (ranibizumab intravitreal injection). Patients do not always respond to these treatments, or their response is sometimes insufficient.
  Fluorescein angiography is recommended before starting treatment, in order to rule out ischaemic forms that are not indications for anti-VEGF treatment, and during follow-up. It is actually possible for the oedematous form to progress to the ischaemic form during treatment; therefore, patients should be monitored. Performing optical coherence tomography (OCT) is also recommended for diagnosis and treatment follow-up.

- **Role of the medicinal product in the therapeutic strategy**
  Like OZURDEX (dexamethasone intravitreal implant) and LUCENTIS (ranibizumab intravitreal injection), EYLEA is a first-line treatment for visual impairment due to BRVO. In the absence of any direct comparison between EYLEA, LUCENTIS and OZURDEX, the choice of one of these three medicines should take into account their individual efficacy, the patient's characteristics, contraindications, potential adverse effects and constraints to follow-up. Consequently, when starting one of these treatments, clinicians must take into account:
  - the patient's age
  - the patient's capacity to attend for monthly injections in the case of EYLEA and LUCENTIS
  - whether the lens is present and whether glaucoma is present due to the risk of increased intraocular pressure and cataracts with OZURDEX.

  No data are available that evaluate the benefit of using a second anti-VEGF if the first anti-VEGF fails.

Clinical data

- The efficacy and safety of aflibercept in the treatment of visual impairment due to BRVO were evaluated in a randomised, double-blind study versus laser photocoagulation (n = 183) with a duration of 52 weeks. On

inclusion, patients had to have been diagnosed with BRVO within the previous 12 months, and have a best corrected visual acuity score (BCVA) of between 20/320 and 20/40 in the eye being studied, i.e. 24 to 73 letters read (ETDRS). They had to be naive to treatment for macular oedema, such as laser therapy, anti-VEGFs or intravitreal corticosteroid treatment.

The patients on aflibercept received one monthly injection of 2 mg until week 24, then one injection every 8 weeks from week 32 to week 48. From week 12, patients could receive rescue therapy in accordance with predefined eligibility criteria: patients in the laser group could have laser therapy again from week 12 to week 20; patients in the laser group could be treated with aflibercept from week 24 onwards; and patients in the aflibercept group could have laser therapy only in week 36.

In week 24, the percentage of patients with an improvement in BCVA ≥ 15 letters from baseline (the primary efficacy endpoint) was higher in the aflibercept group (52.7%) than in the laser group (26.7%), i.e. a difference of 26.1% (p = 0.0003).

Aflibercept was superior to laser treatment in terms of:

- adjusted mean change in best corrected visual acuity in week 24: +13.7 letters with aflibercept versus +3.2 letters with laser treatment, i.e. a difference of 10.5 letters (p < 0.0001)
- adjusted mean reduction in central retinal thickness in week 24: -247.5 µm versus -98.9 µm, i.e. a difference of -148.6 µm (p < 0.0001).

No significant difference was observed in NEI VFQ-25 quality of life score in week 24.

- The safety profile was consistent with that observed in the other indications of aflibercept. Because aflibercept has anti-VEGF activity, there is a risk of the adverse event systemic arterial thromboembolism. No cases of endophthalmitis were reported during the study
- Aflibercept has not been compared with ranibizumab (LUCENTIS) or to dexamethasone intravitreal injection (OZURDEX).

Special prescribing conditions

- Prescription-only medicine restricted to ophthalmologists
- Exception drug status.

Benefit of the medicinal product

- The actual benefit* of EYLEA is substantial.
- Like LUCENTIS, EYLEA provides clinical added value** (CAV IV, minor) in the management of visual impairment secondary to BRVO.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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[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".