Report Eylea® - aflibercept

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: aflibercept **Brand Name:**Eylea® **Originator/licensee:** Bayer AG **Classification:** NI **ATC code:** S01LA05 **Orphan Status:** **EU:** No **US:** No **Mechanism of action:** Aflibercept acts as a soluble decoy receptor that binds VEGF-A and PlGF with higher affinity thantheir natural receptors, thereby inhibiting the binding and activation of VEGFreceptors.Excessive activation of these receptorscan result inpathological neovascularisation and excessive vascular permeability, and the role of upregulation of VEGF in retinopathy of prematurity has been well established [1-2].	**Authorized Indication:** **EMA:** Aflibercept isindicated in preterm infants for the treatment of ROP with zone I (stage 1+, 2+, 3 or 3+), zone II (stage 2+ or 3+) or AP-ROP disease [3]. **FDA:** - **Route of administration:** IVT **Licensing status** **EU CHMP P.O. date:** 10/11/2022 **FDA M.A. date:** - **EU Speed Approval Pathway:**No **FDA Speed Approval Pathway:** - ---------- **ABBREVIATIONS:** AE: adverse event AP-ROP: aggressive posterior retinopathy of prematurity CHMP: Committee for Medicinal Products for Human Use IVT: intravitreal M.A.: marketing authorization PlGF: placental growth factor P.O.: positive opinion Pts: patients ROP: retinopathy of prematurity VEGF-A: vascular endothelial growth factor-A	**Summary of clinical EFFICACY:**NCT04004208 (FIREFLEYE trial) was a noninferiority, phase 3, 24-week, open-label randomizedclinical trial assessing the efficacy and adverse events profile of IVT aflibercept vs laser photocoagulation ininfantswith ROP requiring treatment.Eligible pts were infants born at a gestational age ≤32 weeksor had a birthweight ≤1500 g, weighed ≥800 g at the time of treatment, and had ROPwithin the spectrum of severity requiring treatment (zone Istage 1+, 2+, 3, or 3+, zone IIstage 2+ or 3+, or AP- ROP). Ptswere randomized 2:1 to receive either a single 0.4mg dose of IVTaflibercept or transpupillary conventional laser photocoagulationforeach eye requiring treatment at baseline.The primary outcome was the proportion of pts withoutactive ROP and unfavorable structural outcomes (retinal detachment,macular dragging,macular fold, or retrolental opacity)24 weeks after starting treatment. Overall, 113 pts were included in the primary analysis (75 pts receiving aflibercept vs 38 laser photocoagulation). The bayesian-estimated treatment success ratewith IVT aflibercept was 85.5% (90%CrI: 78.0% - 91.3%) comparedwith 82.1% (90%CrI: 70.5% - 90.8%) with laser photocoagulation. The difference between the two groups was3.4% (1-sided 95%CrI: −8.0% to ∞) in favor of IVT aflibercept. However, because the lower limit of the 95%CrIwas −8.0%, and not greater thanthe prespecified value (−5.0%), noninferiority could not beconcluded [2]. **Summary of clinical SAFETY:**In FIREFLEYE trial, ocular treatment-emergent AEs in the treated eyes were reported among 38.7% of pts in the aflibercept group vs 36.8% in thelaser photocoagulation group, while systemic treatment-emergent AEs occurred in 52.0% of ptsreceiving aflibercept vs 63.2% of pts receiving laser photocoagulation. The serious AE rates were 13.3% (ocular) and24.0% (systemic) in the aflibercept group vs 7.9% and 36.8%, respectively, in the laser photocoagulationgroup. Three deathswere reported overall (2.7%); all occurred ininfants born before 27 weeks' gestational age in the aflibercept group. Among the reported causes of death,there was one each for bronchiolitis and bronchopulmonary dysplasiaand one infant had both bronchopulmonary dysplasia andpneumothorax. Deaths occurred 4 to 9 weeks after aflibercept treatment and were considered by the investigatorsand the sponsor to be unrelated to the study drug[2]. **Ongoing studies:** ● ***For the same indication:***Yes ● ***For other indications:***Yes **Discontinued studies (for the same indication):**No **References:** 1.https://www.ema.europa.eu/en/documents/product-information/eylea-epar-product-information_en.pdf 2. https://pubmed.ncbi.nlm.nih.gov/35881122/ 3. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/eylea 4. https://gallery.farmadati.it/ 5.https://www.osservatoriomalattierare.it/malattie-rare/malattie-rare-della-retina/17656-retinopatia-del-prematuro-nuove-possibilita-diagnostiche-e-un-farmaco-salva-vista 6. https://pubmed.ncbi.nlm.nih.gov/35955664/ 7.https://www.osservatoriomalattierare.it/malattie-rare/malattie-rare-della-retina/17897-retinopatia-del-prematuro-aifa-approva-la-rimborsabilita-di-ranibizumab 8. https://www.ema.europa.eu/en/documents/product-information/lucentis-epar-product-information_en.pdf 9. https://clinicaltrials.gov/	**Cost of therapy:**The ex-factory price for a pre-filled syringe containing a single dose of aflibercept is 667.85€ [4]. **Epidemiology:**In Italy, it is estimated that more than 900 children/year are affected by severe ROP [5]. **POSSIBLE PLACE IN THERAPY:**Laser photocoagulation is the current standard treatment for ROP. The pharmacological therapy for ROP consists in IVT injections of anti-VEGF agents, that can be administered as monotherapy or with laser therapy [2, 6].Ranibizumab (Lucentis®) was the firstauthorized drug for ROP in Italy[7],followed by Eylea®. The authorized indication for ranibizumab is the same of aflibercept, except it does not include ROP zone II stage 2+ [8]. **OTHER INDICATIONS IN DEVELOPMENT:** idiopathic macular telangiectasia type 1 [9]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:-** **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** bevacizumab [9]. *Service reorganization: No *Possible off label use: Yes

Issued on: