Abbreviated Prescribing Information

Eylea 40 mg/mL solution for injection in pre-filled syringe & Eylea 114.3 mg/mL solution for injections in a vial (aflibercept).

Please refer to full SmPC before prescribing.

Presentation(s): **Eylea 40mg/mL**: One pre-filled syringe contains an extractable volume of at least 0.09 mL, equivalent to at least 3.6 mg aflibercept. Each vial contains an extractable volume of at least 0.1 mL, equivalent to at least 4 mg aflibercept. This provides a usable amount to deliver a single dose of 0.05 mL containing 2 mg aflibercept to adult patients or a single dose of 0.01 mL containing 0.4 mg aflibercept to preterm infants. *Excipients:* Polysorbate 20, Sodium dihydrogen phosphate, monohydrate, Disodium hydrogen phosphate,heptahydrate, Sodium chloride, Sucrose, Water for injection. This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially 'sodium-free'. **Eylea 114.3mg/mL:** 1 mL solution for injection contains 114.3 mg aflibercept. One vial contains 30.1 mg aflibercept in 0.263 mL solution providing a usable amount to deliver a single dose of 0.07 mL containing 8mg aflibercept. *Excipients:* Sucrose,Arginine hydrochloride, Histidine hydrochloride monohydrate, Histidine, Polysorbate 20, Water for Injection.

Indication: **Eylea 40mg/mL**: Eylea is indicated for adults for treatment of neovascular (wet) age-related macular degeneration (AMD), visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO), visual impairment due to diabetic macular oedema (DME) and visual impairment due to myopic choroidal neovascularisation (myopic CNV). Eylea is indicated in preterm infants for the treatment of retinopathy of prematurity (ROP) with zone I (stage 1+, 2+, 3 or 3+), zone II (stage 2+ or 3+) or AP-ROP (aggressive posterior ROP) disease. **Eylea 114.3mg/mL:** Eylea (8mg) is indicated in adults for the treatment of neovascular (wet) age-related macular degeneration (AMD) and visual impairment due to diabetic macular oedema (DME).

***Administration and Dosage*:** For intravitreal injection only. Each vial or pre-filled syringe should only be used for the treatment of a single eye. Extraction of multiple doses from a single vial or pre-filled syringe may increase the risk of contamination and subsequent infection. Administration only by qualified physician experienced in administering intravitreal injections.

Recommended dose: **Eylea 40mg/mL**: In adults, the recommended dose is 2 mg aflibercept equivalent to 0.05 mL solution. **Eylea 114.3mg/mL:** In adults, the recommended dose is 8 mg aflibercept, equivalent to 0.07 mL solution. **Eylea 40mg/mL**: For wet AMD, treatment is initiated with 1 injection per month for 3 consecutive doses. The treatment interval is then extended to 2 months. Based on the physician's judgement of visual and/or anatomic outcomes, the treatment interval may be maintained at 2 months or further extended using a treat-and-extend dosing regimen, where injection intervals are increased in 2- or 4-weekly increments to maintain stable visual and/or anatomic outcomes. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly. There is no requirement for monitoring between injections. Based on the physician's judgement the schedule of monitoring visits may be more frequent than the injection visits. Treatment intervals greater than four months or shorter than 4 weeks between injections have not been studied. For RVO (branch RVO or central RVO), after initial injection, treatment is given monthly. The interval between the 2 doses should not be shorter than 1 month. If visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment, Eylea should be discontinued. Monthly treatment continues until maximum visual acuity is achieved and/or there are no signs of disease activity. Three or more consecutive, monthly injections may be needed. Treatment may then be continued with a treat-and-extend regimen with gradually increased treatment intervals to maintain stable visual and/or anatomic outcomes, however there are insufficient data to conclude on the length of these intervals. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly. The monitoring and treatment schedule should be determined by the treating physician based on the individual patient's response. Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography). For DME, initiate treatment with 1 injection/month for 5 consecutive doses, followed by 1 injection every 2 months. Based on the physician's judgement of visual and/or anatomic outcomes, the treatment interval may be maintained at 2 months or individualized, such as with a treat-and-extend dosing regimen, where the treatment intervals are usually increased by 2-week increments to maintain stable visual and/or anatomic outcomes. There are limited data for treatment intervals longer than 4 months. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly. Treatment intervals shorter than 4 weeks have not been studied. The schedule for monitoring should be determined by the treating physician. If visual and anatomic outcomes indicate that the patient is not

benefiting from continued treatment, treatment should be discontinued. For myopic CNV, a single injection is to be administered. Additional doses may be administered if visual and/or anatomic outcomes indicate that the disease persists. Recurrences should be treated as a new manifestation of the disease. The schedule for monitoring should be determined by the treating physician. The interval between 2 doses should not be shorter than 1 month. For ROP, the recommended dose for Eylea is a single intravitreal injection of 0.4 mg aflibercept equivalent to 0.01 mL. Treatment of ROP is initiated with a single injection per eye and may be given bilaterally on the same day. In total, up to 2 injections per eye may be administered within 6 months of treatment initiation if there are signs of disease activity. The treatment interval between the 2 doses injected into the same eye should be at least 4 weeks. For treatment of preterm infants, the PICLEO paediatric dosing device in combination with the prefilled syringe must be used for administration of a single dose of 0.4 mg aflibercept (0.01 mL solution for injection). The injection needle should be inserted into the eye 1.0 to 2.0 mm from the limbus with the needle pointing towards the optic nerve. **Eylea 114.3mg/mL:** For wet AMD and DME, treatment is initiated with 1 injection per month for 3 consecutive doses. Injection intervals may then be extended up to every 4 months based on physician's judgement of visual and/or anatomic outcomes. Treatment intervals may be further extended up to 5 months, such as with a treat-an-extend dosing regimen, while maintaining stable visual and/or visual anatomic outcomes. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly based on physician's discretion. The shortest interval between 2 injections is 2 months in the maintenance phase. Eylea at monthly doses of 8mg has not been studies for more than 3 consecutive doses. Frequency of monitoring visits should be based on patient's status and physician's discretion. Posology is the same nAMD and DME indications.

Contraindications: Hypersensitivity to aflibercept or to any of the excipients. Active or suspected ocular or periocular infection. Active severe intraocular inflammation.

Warnings and Precautions: Record name and batch number of administered product for traceability. Intravitreal injections have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear, and iatrogenic traumatic cataract. Proper aseptic injection techniques are essential. Additionally, patients should be monitored during the week following the injection to permit early treatment if an infection occurs. Adult patients must report any symptoms of endophthalmitis or any of the above-mentioned events without delay. Patients with ROP should be observed by healthcare professionals for any signs suggestive of endophthalmitis. Patients and caregivers should also be instructed to observe and report any signs suggestive of endophthalmitis without delay. The pre-filled syringe contains more than the recommended dose of 2 mg aflibercept (equivalent to 0.05 mL) for adult patients. The excess volume must be expelled prior to administration. The pre-filled syringe contains more than the recommended 0.4 mg (equivalent to 0.01 mL) for preterm infants. The pre-filled syringe must be used in combination with the PICLEO paediatric dosing device to avoid a higher than recommended volume that could result in increased intraocular pressure. Increases in intraocular pressure (IOP) have been seen within 60 min of intravitreal injection. Special precaution is needed in poorly controlled glaucoma (no injection while IOP is ≥ 30 mmHg). In all cases, IOP and perfusion of optic nerve head must be monitored and managed appropriately. Potential for immunogenicity. Instruct patients to report any signs or symptoms of intraocular inflammation, e.g. pain, photophobia, or redness, which may be a clinical sign attributable to hypersensitivity. Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of VEGF inhibitors. Safety and efficacy of concurrent use in both eyes have not been systematically studied. No data is available on the concomitant use of Eylea with other anti-VEGF medicinal products (systemic or ocular). Risk factors associated with development of retinal pigment epithelial tear after anti-VEGF therapy for wet AMD, include large and/or high pigment epithelial retinal detachment. When initiating therapy, use caution in patients with these risk factors for retinal pigment epithelial tears. Withhold treatment in patients with rhegmatogenous retinal detachment or stage 3 or 4 macular holes. Withhold dose and treatment should not be resumed in event of a retinal break until break is adequately repaired. Withhold dose and do not resume treatment earlier than next scheduled treatment in event of decrease in best-corrected visual acuity of ≥ 30 letters compared with last assessment; subretinal haemorrhage involving centre of fovea, or, if size of haemorrhage is ≥ 50%, of total lesion area. Withhold dose within previous or next 28 days in event of performed or planned intraocular surgery. Populations with limited data: There is limited

experience with treatment of patients with ischaemic CRVO and BRVO. In patients presenting with clinical signs of irreversible ischaemic visual function loss, the treatment is not recommended. There is limited experience in DME due to type I diabetes (**40 mg/mL only**) or in diabetic patients with an HbA1c over 12% or with proliferative diabetic retinopathy. Eylea has not been studied in patients with active systemic infections, concurrent eye conditions such as retinal detachment or macular hole, or in diabetic patients with uncontrolled hypertension. This lack of information should be considered when treating such patients. In myopic CNV there is no experience with Eylea in the treatment of non-Asian patients, patients who have previously undergone treatment for myopic CNV, and patients with extrafoveal lesions. The warnings and precautions for adults also apply to preterm infants for ROP.

Fertility, pregnancy & lactation: Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk to the foetus. Limited data in pregnant women. Animal studies have shown reproductive toxicity. Women of childbearing potential should use effective contraception during treatment and for at least 3 months (**Eylea 40mg/mL)** or 4 months (**Eylea 114.3mg/mL)** after the last intravitreal injection of aflibercept. Not recommended during breastfeeding, aflibercept may be excreted in human milk at low levels, effect on infant unknown. No fertility data in humans. Animal studies with high systemic exposure indicate aflibercept can impair male and female fertility.

Undesirable effects: Common/Very common**: Eylea 40 mg/mL & Eylea 114.3 mg/mL:** cataract, intraocular pressure increased, vitreous floaters, vitreous detachment, vitreous hemorrhage, retinal haemorrhage, visual acuity reduced, eye pain, conjunctival haemorrhage, punctate keratitis. **Eylea 40 mg/mL:** retinal pigment epithelial tear (observed in wet AMD studies only), detachment of the retinal pigment epithelium, Retinal degeneration, corneal abrasion, corneal erosion, vision blurred, injection site pain, foreign body sensation in eyes, injection site haemorrhage, lacrimation increased, eyelid oedema, conjunctival hyperaemia, ocular hyperaemia. Uncommon: **Eylea 40 mg/mL:** Hypersensitivity - reports of hypersensitivity included rash, pruritus, urticaria and isolated cases of severe anaphylactic/anaphylactoid reactions, culture positive and culture negative endophthalmitis, retinal detachment, retinal tear, iritis, uveitis, iridocyclitis, lenticular opacities, corneal epithelium defect, injection site irritation, abnormal sensation in eye, eyelid irritation, anterior chamber flare, corneal oedema. **Eylea 114.3 mg/mL:** Hypersensitivity – reports of hypersensitivity included rash, pruritus, urticaria, retinal detachment, retinal tear, retinal pigment epithelial tear, detachment of the retinal pigment epithelium, iritis, iridocyclitis, vitritis, cataract cortical, cataract nuclear, cataract subcapsular, corneal erosion, corneal abrasion, vision blurred, injection site pain, foreign body sensation in eyes, lacrimation increased, injection site haemorrhage, conjunctival hyperaemia. Rare: **Eylea 40 mg/mL:** Blindness, Cataract traumatic, Vitritis, Hypopyon. **Eylea 114.3 mg/mL:** Blindness, uveitis, eyelid oedema, injection site irritation, corneal oedema. Description of selected adverse reactions: **Eylea 40 mg/mL**: In the wet AMD phase III studies, there was an increased incidence of conjunctival haemorrhage in patients receiving anti-thrombotic agents. Arterial thromboembolic events (ATEs) are adverse events potentially related to systemic VEGF inhibition. There is a theoretical risk of arterial thromboembolic events, including stroke and myocardial infarction, following intravitreal use of VEGF inhibitors. As with all therapeutic proteins, there is a potential for immunogenicity. For ROP, adverse reactions reported in more than one patient treated with aflibercept 0.4 mg were retinal detachment, retinal haemorrhage, conjunctival haemorrhage, injection site haemorrhage, intraocular pressure increased and eyelid oedema. Adverse reactions established for adult indications are considered applicable to preterm infants with ROP, though not all were observed. **Eylea 40 mg/mL & Eylea 114.3 mg/mL:** The following adverse reactions of Eylea 40 mg/ml are also considered expected with Eylea 114.3 mg/ml but have not been reported in the clinical studies with Eylea 114.3 mg/ml: ocular hyperaemia, retinal degeneration, abnormal sensation in eye, lenticular opacities, corneal epithelium defect, anterior chamber flare, eyelid irritation, endophthalmitis, traumatic cataract, hypopyon, severe anaphylactic/anaphylactoid reactions. **Overdose**: Overdosing with increased injection volume may increase intraocular pressure. Patients should be monitored, and adequate treatment initiated if deemed necessary by the treating physician. **Classification of sale or supply**: **Prescription-only. Marketing Authorisation Holder:** Bayer AG, 51368 Leverkusen, Germany. **MA number:** EU/1/12/797/001. **Further information available from:** Bayer Ltd., 1st Floor, The Grange Offices, The Grange, Brewery Road, Stillorgan, Dublin 18, A94 H2K7. Tel: 01 2163300. **Date of Preparation:** 14/03/24.