Eylea® HD (aflibercept) – New formulation approval

- On August 18, 2023, Regeneron announced the FDA approval of Eylea HD (aflibercept), for the treatment of:
    - Neovascular (Wet) age-related macular degeneration (nAMD)
    - Diabetic macular edema (DME)
    - Diabetic retinopathy (DR).
- Eylea HD is a high-dose formulation (8 mg) of aflibercept. Aflibercept is also approved under the brand name Eylea as a 2 mg injection.
    - In addition to nAMD, DME, and DR, Eylea 2 mg is also approved for macular edema following retinal vein occlusion and retinopathy of prematurity.
- The efficacy of Eylea HD was established in PULSAR, a randomized, double-masked, active-controlled study in 1,009 treatment-naïve patients with nAMD. Patients were randomly assigned to 1 of 3 treatment groups: 1) Eylea HD every 12 weeks following 3 initial monthly doses; 2) Eylea HD every 16 weeks following 3 initial monthly doses; or 3) Eylea 2 mg every 8 weeks following 3 initial monthly doses. The primary endpoint was the change from baseline in Best Corrected Visual Acuity (BCVA) at week 48 as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) letter score.
    - Both Eylea HD treatment arms were shown to be non-inferior and clinically equivalent to Eylea treatment with respect to the change in BCVA score at week 48 using the pre-specified non-inferiority margin of 4 letters.
- In addition, the efficacy of Eylea HD was established in PHOTON, a randomized, double-masked, active-controlled study in 658 patients with DME involving the center of the macula. Patients were randomly assigned to 1 of 3 treatment groups: 1) Eylea HD every 12 weeks following 3 initial monthly doses; 2) Eylea HD every 16 weeks following 3 initial monthly doses; or 3) Eylea 2 mg every 8 weeks following 5 initial monthly doses. The primary endpoint was the change from baseline in BCVA at week 48 as measured by the ETDRS letter score.
    - Both Eylea HD treatment arms were shown to be non-inferior and clinically equivalent to Eylea treatment with respect to the change in BCVA score at week 48 using the pre-specified non-inferiority margin of 4 letters.
- Efficacy and safety data of Eylea HD in DR are derived from the PHOTON study. In the PHOTON study, a key efficacy outcome was the change in the ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS).
    - The proportion of patients achieving ≥ 2-step improvement on ETDRS-DRSS was similar between the Eylea HD every 12 weeks and Eylea every 8 weeks.
    - The Eylea HD every 16-week treatment arm did not meet the non-inferiority criteria for the proportion of patients with a ≥ 2-step improvement on ETDRS-DRSS and is not considered clinically equivalent to Eylea administered every 8 weeks.
- Eylea HD is contraindicated in patients with:
    - Ocular or periocular infections

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  - Active intraocular inflammation
  - Hypersensitivity.

- Warnings and precautions for Eylea HD include endophthalmitis and retinal detachments; increase in intraocular pressure (IOP); and thromboembolic events.

- The most common adverse reactions (≥ 3%) with Eylea HD use were cataract, conjunctival hemorrhage, increased IOP, ocular discomfort/eye pain/eye irritation, blurred vision, vitreous floaters, vitreous detachment, corneal epithelium defect, and retinal hemorrhage.

- Eylea is an intravitreal injection that must be administered by a qualified physician. The recommended dosing is as follows:

  - nAMD and DME: 8 mg administered every 4 weeks (approximately every 28 days +/- 7 days) for the first three doses, followed by 8 mg once *every* **8 to 16 weeks**, +/- 1 week.
  - DR: 8 mg administered every 4 weeks (approximately every 28 days +/- 7 days) for the first three doses, followed by 8 mg once *every* **8 to 12 weeks**, +/- 1 week.

- Regeneron's launch plans for Eylea HD are pending. Eylea HD will be available as an 8 mg (0.07 mL of 114.3 mg/mL solution) single-dose vial.

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