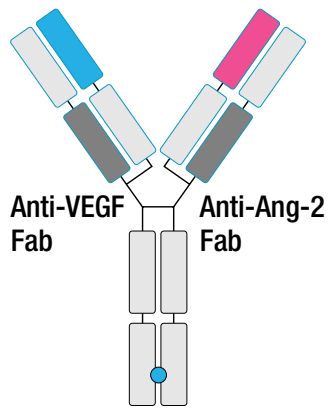
Intravitreal Anti-VEGF & Bispecific Therapies for DME & nAMD

FDA Approved

Faricimab

Bispecific Ab, binds VEGFA & Ang2



DME Dosing

- 6 mg Q4W (≥ 4X) → dosing interval may be extended in ≤ Q4W increments or shortened by ≤ Q8W increments based on CST and VA evaluations

OR

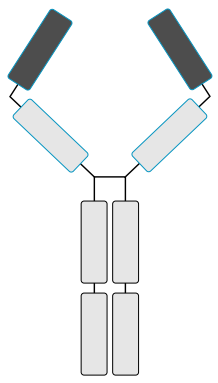
- 6 mg Q4W (X6) → Q8W thereafter

nAMD Dosing

- 6 mg Q4WX4 with OCT and VA assessment at 8 & 12 weeks later to determine whether to administer Q16W, Q12W, or Q8W

Aflibercept

VEGFR1/2-Fc fusion protein, binds VEGFA, VEGFB, PLGF



Standard Formulation

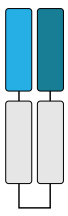
- **DME:** 2 mg Q4WX5 → Q8W (Select patients may require monthly dosing beyond the initial 5 months)
- **nAMD:** 2 mg Q4WX3 → Q8W

High Dose Formulation

- **DME Dosing:** 8 mg Q4WX3 → Q8W-Q16W (±1W)
- **nAMD Dosing:** 8 mg Q4WX3 → Q8W-Q16W (±1W)

Ranibizumab

Humanized, mAb fragment, binds VEGFA



Standard Formulation

- **DME:** 0.3 mg Q4W [or PRN/T+E (≤Q12W) based on ophthalmologic assessment]
- **nAMD:** 0.5 mg Q4W [or PRN/T+E (≤Q12W) based on ophthalmologic assessment]

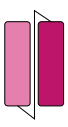
Port Delivery System (PDS)

- **nAMD:** 2 mg delivered continuously via surgical implant w/ refills Q24W
  - Supplemental treatment with standard IVT 0.5 mg ranibizumab may be administered in the affected eye if clinically necessary

In late 2022, the ocular implant, insertion tool assembly, (including the drug vial & initial fill needle) for ranibizumab PDS were voluntarily recalled due to septum dislodgement and paused implantations including ongoing global clinical trials; this did not include the refill vial and needle.

Brolucizumab

Single-chain Ab fragment that binds VEGFA



Dosing:

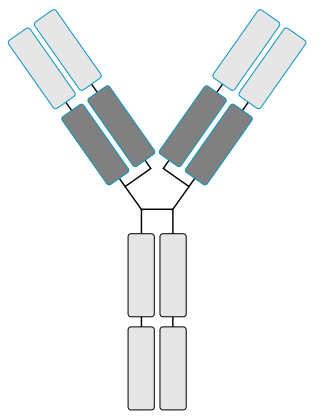
- **DME:** 6 mg Q6W (5X) → Q8W-Q12W
- **nAMD:** 6 mg Q4W (3X) → Q8W-Q12W

The potential risk for intraocular inflammation (IOI), including retinal vasculitis and retinal vascular occlusion has precluded many healthcare providers from using this agent in patients with DME, as well as nAMD.

Off-Label

Bevacizumab

Humanized mAb that binds VEGFA.



Dosing:

- **DME:** 1.25 mg Q4W initially with PRN/T+E/fixed dosing thereafter
- **nAMD:** 1.25 mg Q4W initially with PRN/T+E/fixed dosing thereafter

Ab: antibody; Ang-2: angiopoietin-2; CST: center subfield thickness; DME: diabetic macular edema; mAb: monoclonal antibody; nAMD: neovascular age-related macular edema; OCT: optical coherence tomography; PLGF: placental growth factor; PRN: pro re nata; T+E: treat and extend; VA: visual Acuity; VEGF: vascular endothelial growth factor.

Faricimab. Prescribing Information (fda.gov). Aflibercept. Prescribing Information (FDA.gov). Aflibercept HD. Prescribing Information (fda.gov) Ranibizumab Prescribing Information (fda.gov) *Ranibizumab* PDS. Prescribing Information (fda.gov) Sharma A, et al. *Int J Retina Vitreous.* 2023;9:6. Brolucizumab. Prescribing Information (fda.gov) Khanani AM, et al. *Ophthalmology.* 2022;129:974-985. Fonollosa A, et al. *Arch Soc Oftalmol (Engl Ed).*2022 Jul 23;S2173-5794(22)000846. Khanani AM, et al. *JAMA Ophthalmol.* 2022;140:20-28.