Aflibercept (Eylea)

New Biosimilar for Macular Degeneration and Retinopathy

Although we hear the word biosimilar commonly now in medication management, the biosimilars coming to market stretch well beyond the new biosimilar for Humira. Disease treatment moved from the use of chemical compounds to biologics years ago, and now with patent expiration, we are seeing a surge of biosimilars; the newest of which is a VEG-F Inhibitor used in the treatment of eye conditions.

VEG-F Inhibitor Drugs are medications that inhibit Vascular Endothelial Growth Factor (VEG-F) in the body and are used to treat a variety of diseases, including several degenerative eye conditions such as wet (neovascular) age-related macular degeneration (wAMD), diabetic macular edema (DME), diabetic retinopathy (DR), and retinopathy of prematurity (ROP). DME and wAMD are two of the leading causes of vision loss in individuals 65 years of age and older. The U.S. VEG-F Inhibitor market is expected to grow substantially in the coming years. This is primarily due to increasing prevalence of these chronic diseases, growing healthcare expenditure, increasing awareness of viable treatment options and advancements in biotechnology.

As the U.S. population ages and diabetes is diagnosed more frequently, both wAMD and DME are projected to increase in prevalence over the next decade. Off-label use of Genentech's Avastin (bevacizumab) as a compound is the most commonly prescribed VEG-F inhibitor therapy for retinal indications due to its substantially lower cost. Compounded bevacizumab typically represents about 40%–50% of utilization, followed by Eylea at around 30%, and Roche's Lucentis (ranibizumab) at around 20%. Payers will typically apply step therapy that encourages compounded bevacizumab before other VEG-F inhibitor products.

Table 1. VEG-F Inhibitor Biologics Used for Degenerative Eye Conditions
*Annual treatment cost is based on administration frequency for the product which will vary by patient and condition.

Generic Name	Brand Name	Manufacturer	Dosing Frequency
Aflibercept	Eylea	Regeneron	Every 8 weeks
Brolucizumab	Beovu		
Faricimab-svoa	Vabysmo	Genentech	Up to every 16 weeks
Ranibizumab	Lucentis 0.3mg 0.5mg	Genentech	Every 4 weeks
Ranibizumab – nuna	Byooviz, (biosimilar to Lucentis) 0.5mg	Biogen	Every 4 weeks
Ranibizumab – eqrn	Cimerli (biosimilar to Lucentis, interchangeable) 0.3mg 0.5mg	Coherus	Every 4 weeks
Ranibizumab	Susvimo - Ocular Implant (Initial) - Fill/Refill	Genentech	 Every 24 weeks

Biosimilar Competition

With patent expiry of these biologics, biosimilars can prove to be less expensive options. Numerous biosimilars have gained or are expected in the near future to gain FDA approval for clinical use.

Both Lucentis and Eylea are market leaders with combined annual sales of over $10 billion. Lucentis was among the first VEG-F inhibitor products to lose its patent and contend with lower cost biosimilar competition from Byooviz and Cimerli (an interchangeable biosimilar for Lucentis).

Eylea is protected from biosimilar competition until May 2024; based on its Biologic Data Exclusivity, which protects Eylea from biosimilar competition until November 2023 plus the additional six months of pediatric exclusivity granted by the FDA. There are at least three additional patents on Eylea and barring any patent litigations, the earliest we could see biosimilars for Eylea is by the summer of 2024; however, if any of these

additional patents prevail, it could be as late as 2040. There are at least 6 manufacturers on track to compete with Eylea as a biosimilar (Alvotech, Amgen, Celltrion, Samsung Bioepsis, Sandoz, and Viatris).

Other Product Competitions on the Horizon

In February 2023, the FDA granted priority review of Regeneron's Biologics License Application (BLA) for aflibercept 8 mg, which is used to treat DME, DR, and wAMD.

- A decision by the FDA is expected in June 2023.
- If approved, aflibercept 8 mg may allow for extended dose intervals of 12 or 16 weeks for DME, DR, and wAMD.

With the approval of Eylea biosimilars expected in 2024, Regeneron will likely attempt to maintain market share by transitioning patients from Eylea to aflibercept 8 mg. However, these conversion efforts and uptake may be dampened by:

- Payers and ophthalmologists who prefer to maintain patients on current therapy in anticipation of cost-savings opportunities with the biosimilars.
- Competition with Genentech's Vabysmo, a VEG-F and angiopoietin-2 inhibitor, which offers an extended dose interval of up to 16 weeks for DME and wAMD.

Despite the potential for extending the dose interval to 16 weeks, ophthalmologists may prefer to maintain patients on Eylea if they are doing well on the medication. Most ophthalmologists use a "treat-and-extend" strategy with ophthalmic VEG-F inhibitors; therefore, some patients on Eylea may already have extended dose intervals to 12 weeks or perhaps longer.

Given similar safety and efficacy between the many products in this space, net cost is likely to drive payer decision-making. The annual cost of agents across this category varies significantly based on the product and dose interval. For example, the wholesale acquisition cost (WAC) per dose of Vabysmo is higher than that of Eylea ($2,190 vs. $1,850); however, Vabysmo is less expensive than Eylea on an annual basis when Vabysmo is administered every 16 weeks ($6,570), versus Eylea if administered every 8 weeks ($11,100).

New utilization management strategies initiated by payers are likely to impact only members new to therapy; patients are generally not required (with some exceptions) to switch ophthalmic VEG-F inhibitors based on preferred product strategies.

If aflibercept 8 mg is approved, we expect Regeneron will attempt to convert utilization from Eylea to aflibercept 8 mg in order to retain market share in the face of competition from additional therapies and Eylea biosimilars, which could enter the market as early as 2024. Eylea has demonstrated consistent efficacy and safety in real-world utilization over the past decade, and we expect Regeneron will be able to retain a substantial portion of the VEG-F inhibitor market.

A forecasted price for aflibercept 8 mg assumes that it will be priced similarly to Eylea on a per-injection basis ($1,850) and that the label for aflibercept 8 mg will recommend the every-12-week to every-16-week

dosing that was tested in clinical trials. As a new product formulation, the prediction is that this product would not face biosimilar competition until 2039.

With the coming of 2024 and beyond, we expect fierce competition in this market across original innovator products, new longer-acting products, and the several biosimilars in development.

About PayerAlly

PayerAlly's mission is to provide cutting-edge support for our clients as they look to better manage their medication costs. We offer best-in-class clinical, financial, and consultative solutions to help better manage costs and improve vendor performance.

