ASRS American Society of Retina Specialists

ASRS Recommendations Regarding the Use of Biosimilar Anti-VEGF Products
June 2022

The American Society of Retina Specialists (ASRS) is the largest retina organization in the world, representing over 3,500 board certified ophthalmologists who have completed fellowship training in the medical and surgical treatment of retinal diseases. The mission of the ASRS is to provide a collegial open forum for education, to advance the understanding and treatment of vitreoretinal diseases, and to enhance the ability of its members to provide the highest quality of patient care.

Retina specialists treat a variety of potentially-blinding, chronic diseases, such as age-related macular degeneration (AMD) and diabetic retinopathy. Care for these patients typically involves regular intravitreal injections with anti-vascular endothelial growth factor (anti-VEGF) products. Currently, there are several FDA-approved branded originator products and one repackaged, off-label product, Avastin (bevacizumab), available. The two most frequently used originator products, Eylea (aflibercept) and Lucentis (ranibizumab), are expected to have and have, approved biosimilar versions respectively. An Avastin biosimilar approved for ocular use also may come to market if approved. Anti-VEGF treatments for retinal diseases account for some of the highest spending in the Medicare Part B program (with significant Quality Adjusted Life Year (QALY) benefits), and biosimilars have the potential to reduce some of that cost.

The FDA defines a biosimilar as, “a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product.” Biosimilar manufacturers must demonstrate that their products are similar in structure and function to the reference product by providing evidence of comparable purity, chemical identity, and bioactivity. To demonstrate that the biosimilar product has no clinically meaningful differences, the FDA requires manufacturers to conduct multiple pre-clinical analyses, and a limited clinical study. Generally, a biosimilar’s clinical trial program is much less extensive than for originator/reference products, which typically involved multiple clinical studies including two phase 3 trials.

While biosimilars are carefully evaluated by the FDA, the more limited clinical trial requirements and allowances for minor differences from the reference product, such as in stabilizers or buffers, necessitate a cautious and likely gradual approach to integrating these products into regular clinical use. Experience with post-approval adverse events and safety concerns associated with new originator products demonstrates that even the most extensive and robust preclinical and clinical trial programs cannot totally duplicate the real-world clinical environment. Clinical trials are conducted on a limited number of carefully evaluated subjects, and therefore some issues with a product may not be readily identified until after the product is in widespread general use. ASRS is aware that the limited number of subjects in biosimilar clinical trials may not be sufficient to adequately identify potential issues, such as post-injection inflammation, that could lead to vision-threatening complications, and patients may experience adverse events once these products are available.

The ASRS recommends that before administering biosimilars to patients, retina specialists should explain the differences between originator and biosimilar products, and any associated risks to patients. Retina specialists should also explain that biosimilars have been used in other specialties, such as oncology, for several years and may provide a lower-cost alternative to originator products. At the same time, retina specialists should continue to monitor clinical literature on biosimilars as they become integrated into clinical practice to be aware of any unexpected adverse effects that may influence usage

of these products. If a retina specialist has a patient who experiences an adverse event following administration of any agent, including an anti-VEGF biosimilar, they should contact the ASRS and a member of the Research and Safety in Therapeutics (ReST) Committee will respond shortly.

The ASRS continues to support the availability of repackaged Avastin, which has been effectively used off-label for over 15 years to treat various retinal diseases that have not been specifically evaluated in clinical trials but are known to benefit from anti-VEGF treatment. While Avastin is off-label for all ocular use, it can be used to treat a wider variety of retinal conditions than many of the FDA-approved branded drugs. For example, some insurers will not cover branded agents for off-label uses such as sickle cell retinopathy, uveal melanoma, vasoproliferative tumor, choroidal neovascularization associated with central serous retinopathy, or for use in retinopathy of prematurity and other diseases in the pediatric population. In these cases, retina specialists commonly use repackaged Avastin to treat these blinding diseases when no other options are practically available. With the advent of an approved Avastin biosimilar for ocular use, the ASRS is concerned that the availability of repackaged Avastin may be threatened, thereby putting patients with less common retinal disorders at risk of losing access to therapies that are not covered by insurers, resulting in more blindness in the population, especially in the pediatric population. We strongly advocate that repackaged Avastin remain available for patients. The ASRS remains opposed to the ocular use of currently available Avastin biosimilars that have not been tested in the eye.

If you have questions or need additional information, please contact Allison Madson, ASRS vice president of health policy, at allison.madson@asrs.org or 312-578-8760.