June 14, 2021

Dorothy Verbrugge, MD
VP Clinical Quality
Medical Affairs
151 Farmington Avenue
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VIA ELECTRONIC DELIVERY
VerbruggeD@aetna.com

Dear Dr. Verbrugge:

On behalf of members of the American Society of Retina Specialists (ASRS)[i] and American Academy of Ophthalmology (AAO)[ii], we write to express concerns that patients with eye diseases such as macular degeneration and diabetic retinopathy currently do not have adequate access to sight saving drugs. As you may know, there is a supply issue with off-label, repackaged bevacizumab (Avastin), which stems from Optum Specialty Pharmacy's initiation of a stoppage due to a series of out of specification test results. This stoppage has a far-reaching impact on the supply chain given that this outsourcing facility has 45% of the market share and has initiated an indefinite halt on the distribution of all bevacizumab syringes.

We anticipate that other outsourcing facilities will ramp up their production and onboard new customers. However, there will be a lag in the availability of repackaged Avastin. On behalf of our members who treat and their patients for blinding conditions, we strongly urge CVS-Aetna to:

- Ensure patients currently receiving Avastin who require dose(s) of FDA-approved branded drug due to the supply issue will not be required to return to Avastin if the FDA-approved branded drug proves more efficacious; and
- Permanently reverse its step therapy requirement for anti-VEGF drugs. This requirement not only relies on obtaining repackaged Avastin through a fragile supply chain from few suppliers, but also interferes with the physician's clinical judgement and potentially results in permanent vision loss for patients who must wait to be approved for the most appropriate treatment.

Ongoing Repackaged Avastin Supply Issues

There are several issues that have led to the uncertain and inconsistent supply of Avastin: including sterility issues, changes in testing requirements, outsourcing facilities leaving the market, and patient safety concerns related to syringe type. These include,

- In 2013, the FDA alerted consumers, patients and health care providers of sterility assurance with Avella's independent testing laboratory.
- In 2018, Avella issued a voluntary recall due to sterility assurance.

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- In 2019, retina specialists were impacted by difficulties obtaining Avastin due to changes Avella was undertaking to comply with USP testing requirements.
- In 2018 and 2019, AmEx Pharmacy (no longer packaging Avastin) voluntarily recalled one lot of Avastin due to ocular damage that may occur when desiccated Avastin clogged the Monojet syringe and created difficulties expressing the Avastin from the syringe.
- In 2020, in addition to regulatory changes that were still being implemented, there was a spike in demand that led to delays fulfilling orders.

Additionally, our organizations are aware of class action lawsuit activity regarding repackaged Avastin that led to adverse events associated with silicone droplets present in syringes used for Avastin.

Patients Should Continue with the Most Effective Treatment

Our previous letters have highlighted the differences between Avastin, Eylea, Lucentis and Beovu. Clinical studies such as the randomized Diabetic Clinical Research Network (DRCR.net) Protocol T study[iii] and the NIH funded CATT trials[iv] showed that these drugs are not interchangeable and their efficacy, safety and clinical usage must be considered when determining the most appropriate drug for a specific disease presentation given an individual patient's co-morbidities and risks. For patients who are able to benefit from treatment with FDA-approved branded drugs during this time, we ask that they not be required to switch to Avastin once the access issues are resolved.

We understand that FDA-approved brand-name drugs are more costly and that insurers are seeking ways to decrease their costs. However, alternatives such as requiring changes to specialty pharmacy drug delivery, which make ordering and handling unpredictable for the practice, and suggesting the use of biosimilars that have not been tested for use in the eye, are not appropriate options for our patients.

Permanently Suspend Step Therapy for Anti-VEGF Treatments

Given the complexities of the retinal diseases and the drugs needed, we are asking for more flexibility in treating patients during this shortage. Furthermore, we recommend that CVS-Aetna permanently reverse Avastin-first step-therapy policies that limit retina specialists and their patients from tailoring their treatment to the individual patient and each patient’s unique response to therapy. While lower-cost Avastin can be effective for some patients, the ability to individualize treatment and select the most efficacious agent for each patient is the key to recovering and maintaining visual acuity and retinal function in patients with blinding diseases of the retina.

We would like to discuss this with CVS-Aetna further. Please contact Allison Madson, vice-president of health policy at allison.madson@asrs.org. Thank you for your consideration.

Sincerely,

Carl C. Awh, MD
President
American Society of Retina Specialists

Michael X. Repka, MD, MBA
Medical Director for Governmental Affairs
American Academy of Ophthalmology

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i ASRS is the largest retina organization in the world, representing over 3,000 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.

ii The American Academy of Ophthalmology is the world's largest association of eye physicians and surgeons. A global community of 32,000 medical doctors, AAO protects sight and empower lives by setting the standards for ophthalmic education and advocating for patients and the public. The mission of AAO is to advance the ophthalmic profession and to ensure the delivery of the highest-quality eye care.

[iii] The New England Journal of Medicine, The Diabetic Retinopathy Clinical Research Network, "Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema," (also known as Protocol T, Year 1), March 26, 2015. http://www.nejm.org/doi/full/10.1056/NEJMoa1414264#t=article

[iv] Comparison of Age-related Macular Degeneration Treatment Trials (CATT) Research Group, Martin DF, Maguire MG, Fine SL, Ying GS, Jaffe GJ, Grunwald JE, Toth C, Redford M, Ferris FL 3rd. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. Ophthalmology. 2012 Jul;119(7):1388-98