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BY EDIS

July 6, 2020

The Honorable Lisa R. Barton
Secretary to the Commission
U.S. International Trade Commission
500 E Street, SW, Room 112
Washington, DC 20436

Re: *Certain Pre-filled Syringes for Intravitreal Injection and Components Thereof, DN 3460*

Dear Secretary Barton:

Weil, Gotshal & Manges LLP hereby files the enclosed public interest statement on behalf of Szilárd Kiss, M.D. Weil, Gotshal & Manges LLP is representing Dr. Szilárd Kiss for the purposes of filing this statement.

Thank you for your attention to this matter.

Sincerely,

/s/ Robert T. Vlasis
Robert T. Vlasis

Weil, Gotshal & Manges LLP, Counsel for Respondent Regeneron Pharmaceuticals, Inc.

UNITED STATES INTERNATIONAL TRADE COMMISSION
WASHINGTON, D.C.

In the Matter of CERTAIN PRE-FILLED SYRINGES FOR INTRAVITREAL INJECTION AND COMPONENTS THEREOF	Docket No. 3460

STATEMENT ON THE PUBLIC INTEREST BY SZILÁRD KISS, M.D.

My name is Szilárd Kiss, M.D., and I am an ophthalmologist, retinal specialist, and surgeon, and the Associate Dean for Clinical Compliance and Associate Professor of Ophthalmology at Weill Cornell Medical College. I received my B.A. in Biology from Columbia College in 1997 and my M.D. from Columbia University in 2002. I was certified by the American Board of Ophthalmology in 2007. I have over fifteen years of experience and am an expert in the treatment of ophthalmological diseases. My clinical practice involves outpatient evaluation and management for complex vitreo-retinal pathologies such as age-related macular degeneration, diabetic retinopathy, retinal vascular disorders, inherited retinal degenerations, infectious and non-infectious uveitis, and inherited and acquired maculopathies.

I have been retained by Regeneron as an expert and key opinion leader, but this statement reflects my independent views on the adverse impact of a remedy on my own practice and patients. Any remedy would severely disrupt my practice, eliminate my ability to choose the best treatment for my patients, and potentially force me to administer less effective and less safe treatments.

I. OPHTHALMIC DISEASES THAT CAUSE VISION LOSS AND BLINDNESS

My practice involves the treatment of serious eye diseases involving the overproduction of a naturally occurring protein in the body called vascular endothelial growth factor ("VEGF"). VEGF triggers the formation of new blood vessels, but when cells secrete too much VEGF into the eye, abnormal blood vessels can grow in the eye underneath the macula and retina. These abnormal blood vessels can leak blood and other fluids, which blurs central vision and leads to blindness. VEGF diseases include, among others, wet age-related macular degeneration ("wAMD"), diabetic retinopathy ("DR"), diabetic macular edema ("DME"), and macular edema following retinal vein occlusion ("MEfRVO").

wAMD is the most severe eye disease and is a leading cause of blindness among older Americans. Patients with wAMD see the world as if looking through distorted lenses: straight lines may appear bent, central vision may be reduced, brightness of colors may be dulled, and patients may see haziness. Patients may also experience a well-defined blurry or blind spot in their central field of vision. These patients thus face severe challenges with reading, writing, driving, or recognizing faces. The onset of wAMD symptoms is abrupt—symptoms can develop in as little as one day. If left untreated, wAMD

may cause permanent vision loss within weeks or months. The debilitating effects of wAMD worsen over time and can be irreversible, ultimately leading to permanent blindness.

DR is the most common diabetic eye disease and can lead to vision loss. DR occurs when too much blood sugar damages the blood vessels in the retina. As a result, the retina does not receive enough oxygen and nutrients, and blood vessels can leak blood and fluid into the retina. DME is a complication of DR that can lead to further vision problems. DME occurs if the macula, the area of the retina at the back of the eye responsible for sharp central vision, swells with fluid leaked from those damaged blood vessels. Finally, MEfRVO occurs when fluid leaks into the macula as a result of a blocked blood vessel. This condition leads to vision loss or blurring as the macula swells with the fluid.

II. TREATMENT FOR SERIOUS EYE DISEASE

While there is currently no cure for wAMD, the advent of anti-VEGF therapies has made remarkable strides in improving vision and easing the burden. Until recently, there were two main FDA-approved anti-VEGF treatments for wAMD: LUCENTIS® (ranibizumab), approved in 2006, and EYLEA® (aflibercept), approved in 2011. A third treatment, BEOVU® (brolucizumab) was approved on October 8, 2019. EYLEA and LUCENTIS are also approved for the other eye diseases I described above, and can be administered using a vial and syringe or a prefilled syringe "PFS."

Anti-VEGF treatments are administered directly into the patient's eye via syringe. This administration is called an intravitreal injection, and it must be performed in a physician's office. One safety issue retinal specialists are concerned about with their patients receiving intravitreal injections of anti-VEGF drugs is a very serious adverse effect called intraocular inflammation, or IOI. IOI involves inflammation of the structures in the interior of the eye. IOI is an urgent medical condition, and it ranges in severity, with severe cases capable of leading to blindness. Severe IOIs present a major concern for retinal specialists and are a key consideration in selecting treatment; even small differences in occurrence rates can be a critical factor in the product a physician chooses to prescribe.

An additional concern is that each injection can introduce foreign particles and microbes into the eye. This can cause irritation or infection of the tissues or fluids of the eyeball (termed endophthalmitis

when encompassing the entire eye). Endophthalmitis can lead to blindness and loss of the eye itself.

III. EYLEA PFS IS MY PREFERRED METHOD OF TREATMENT

I currently have approximately 500 patients who require anti-VEGF treatment. The most common diagnosis which requires anti-VEGF is wAMD, followed by DR/DME, then branch and central vein occlusion. Approximately 85% of my anti-VEGF injections are with EYLEA PFS, and the remainder are with LUCENTIS PFS. We do not use BEOVU (as explained further below), and we do not use vial and syringe because PFS requires fewer steps to administer, takes less time, and is more convenient. The vial, for example, requires two needles. Because PFS requires fewer steps and less time than a vial and syringe, using PFS allows me to treat more patients.

Given the number of patients that I and my staff treat on a daily basis, fewer steps with PFS also translates to a clinically meaningful reduction in the rate of endophthalmitis.[1] Endophthalmitis is one of the most feared and devastating complications following an intravitreal injection, oftentimes leading to severe, irreversible blindness in the affected eye. By reducing the number of steps in which the potential for bacterial introduction can occur, PFS is currently the best method for injection of anti-VEGF therapy into patients' eyes. Switching back to older methods of drawing the drug up from a vial could expose patients to additional, unnecessary risks.

As a practicing physician, I am in the best position to choose the method of treatment that is best for my patients. For all of these reasons, I should not be forced to transition my patients from EYLEA PFS back to the vial and syringe.

IV. LUCENTIS IS LESS CONVENIENT AND LESS EFFECTIVE THAN EYLEA PFS

LUCENTIS is another anti-VEGF treatment, but I would be unable to convert all my patients from EYLEA PFS to LUCENTIS PFS because the products are not interchangeable for insurance approval purposes. Indeed, patients require prior authorization for these treatments (which can take weeks), and an approval for one product cannot be transferred to another product.

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[1] Storey et al., *The Impact of Prefilled Syringes on Endophthalmitis Following Intravitreal Injection of Ranibizumab,* Am J Ophthalmol, 199:200-208 (Mar. 2019), https://pubmed.ncbi.nlm.nih.gov/30552891/.

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