ASRS American Society of Retina Specialists

American Society of Retina Specialists' Comments
FDA Drug Compounding Listening Session 4/30/15

Good afternoon. I would like to start by thanking the FDA for hosting this listening session. My name is Dr. Geoff Emerson, representing the American Society of Retina Specialists. ASRS has 2,700 members from 54 countries, including 90% of retina specialists in the US. As a practicing retina specialist and clinical investigator, my remarks will focus primarily on how the draft guidance on repackaging biological products impacts access to Avastin, a sight-saving treatment for macular degeneration and other serious eye conditions.

Before discussing our proposal, I would like to support the remarks from my colleague, Dr. John Thompson, who clearly established the need for access to Avastin and shared the body of literature that supports its efficacy, safety and stability. Since the ASRS is specifically concerned with the excessively-restrictive Beyond Use Dates (BUDs), I would like to emphasize that the medical literature is filled with articles[1-6] documenting the use of various methods to assess the potency, purity, and quality of repackaged Avastin and confirming that Avastin maintains both function and stability for 3 to 6 months.

Avastin is the drug of choice for the majority of US retina specialists and their patients. According to the ASRS 2015 Preferences and Trends survey, 64% use Avastin as first line treatment for age-related macular degeneration (AMD) and >80% percent of US members treat choroidal neovascularization from histoplasmosis and other non-AMD causes with Avastin. Many ASRS members started using Avastin in 2005 when it first became an option for treating AMD. Even now, with Lucentis and Eylea on the market, it remains our first choice because of our extensive hands-on experience with Avastin in our practices, backed by clinical evidence supporting its efficacy, stability, and safety – not to say anything about the cost differential between it and the branded FDA-approved drugs.

By way of example, I would like to share 2014 data from my clinic of 4 retina specialists. We administered 16,115 doses of anti-VEGF intravitreal injections, 90% of which were Avastin. We had only one instance of endophthalmitis after Avastin, an infection rate significantly lower than the published infection rate for either Lucentis or Eylea. Of the 2,803 individual patients treated with Avastin, 2,500 maintained vision, despite their blinding eye disease.

My colleagues at VitreoRetinal Surgery in Minnesota administered 46,431 anti-VEGF injections in 2014, 56% of which were Avastin. They report an infection rate of 0.01% for Avastin, compared to 0.02% for Lucentis and Eylea. My colleagues at Bascom Palmer Institute In Miami administered 119,000 anti-VEGF injections, 56% of which were Avastin. Their publication (in press) reports an infection rate of 0.01% for Avastin, compared to 0.02% and 0.03% for Lucentis and Eylea, respectively. In addition, Kaiser Permanente[7] and the Mayo Clinic are also preparing comment letters to the FDA in support of the safety of repackaged Avastin.

A potential reason that Avastin may have a lower infection rate is because it is repackaged into syringes within a compounding sterile isolator, rather than being drawn into a syringe at the patient's side where the environment is less controlled, as is the case for Lucentis and Eylea. An unintended consequence of an overly restrictive BUD for Avastin may be to discourage repackaging in a sterile environment.

Another unintended consequence of the short BUD is that it will be impossible to follow USP 71 sterility testing guidelines. Presently, the only USP approved method of sterility testing takes 14 days. From our perspective, this is a step in the wrong direction.

ASRS would like to offer the FDA an alternative approach. ASRS believes the FDA should allow outsourcing facilities the option to extend the BUD of a finished biologic based on the results of stability testing. This approach was used by the FDA when it established the shelf life for the Avastin used in the CATT Trial.[8] For that trial, the FDA used stability testing to establish an initial 6-month shelf life that was gradually extended to 2 years.

This approach also is consistent with draft Interim Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act, which provides for the establishment of a stability program to determine appropriate storage conditions and expiration dates, and requires outsourcing facilities to conduct stability testing to ensure that compounded products remain stable and sterile through the expiry period. Also, extending the BUD of a biologic, is consistent with the 2008 United States Pharmacopeial Convention statement that "beyond-use dating periods established from product-specific data acquired from the appropriate instrumental analysis are clearly more reliable than those predicted theoretically." We believe this more scientific approach will work equally well for all biologics and mitigate the problem of trying to find a default number for the whole class of biologics.

In summary, Avastin is an extremely important medication for our patients. For a chronic disease such as macular degeneration, it is important to have all three options, as some patients respond better to one medication than another, or develop tachyphylaxis, or switch therapy due to an adverse reaction. It would be a shame to lose one of three available therapies, let alone the most common first choice. We urge the FDA to consider a longer minimum BUD based on published scientific evidence. For Avastin, existing evidence supports at least a 3 month BUD. We also urge FDA to allow outsourcing facilities to further extend the BUD based on stability testing.

Thank you for the opportunity to present our concerns and suggestions, which also will be detailed in our Society comment letter on the draft guidance.

Geoffrey Emerson, MD, PhD, is a member of the Board of Directors and Chair of the Federal Affairs Committee for the American Society of Retina Specialists. He received his doctorate in cellular and molecular physiology. He is a practicing retina specialists in Minneapolis, and a board certified ophthalmologist.

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