RETINA
CENTER
OF MINNESOTA

April 14, 2015

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2014-D-1525; Draft Guidance on Mixing, Diluting or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application

To Whom It May Concern:

As a practicing retina specialist and board certified ophthalmologist with a doctorate in cellular and molecular physiology, who has served as a sub-investigator in the DRCR trial, I am deeply concerned about proposals included in the Food and Drug Administration's Draft Guidance for repackaging biological products as it relates to repackaging Avastin. The proposed Beyond Use Date (BUD) of 1 and 5 days for traditional compounding and outsourcing facilities, respectively, is too short. The current BUD for repackaged Avastin is typically 90 to 180 days, and numerous published clinical trials over the past 8 years support the safety and efficacy of repackaged Avastin under these circumstances.[1-3]

The restricted BUD would jeopardize patient care in two main ways. First, shortening the interval between opening a vial of Avastin at the compounding pharmacy or outsourcing facility and delivering the dose to a patient in clinic would make using the drug prohibitively difficult. The proposed BUDs are too short to accommodate repackaging, labeling, shipping, handling, and scheduling of patients. Furthermore, it is extremely difficult to predict accurately the need of patients at a given clinic to determine who will need treatment within a 1- or 5-day period.

Second, the restricted BUD puts patients in jeopardy because it is impossible to do sterility testing on repackaged Avastin during the shortened time period. Currently our Avastin is under quarantine for 14 days after repackaging until sterility testing is complete.

Our clinic of 4 retina specialists administered 11,000 doses of Avastin during 2014. During this time period, there was one instance of endophthalmitis (one eye of one patient). Our infection rate is significantly lower than the published infection rate for the alternative treatments (Lucentis and Eylea). This difference is likely because Avastin is repackaged into syringes within a compounding isolator,

instead of loading medication into a syringe at the patient's side, where the environment is less controlled, as is the case with alternative treatments that are not repackaged by a compounding facility. Furthermore, we believe that sterility testing each lot of repackaged Avastin is well worth the extra 14 days.

Avastin is my first-line anti-VEGF treatment for most of my patients, excluding a small subset of diabetic retinopathy patients based on the DRCR Protocol T results. I prefer Avastin because I've used it for many years as neither Lucentis nor Eylea were available when I began my practice. In addition, there is overwhelming evidence to support its efficacy and safety, as well as cost benefits.

Please know that many of my macular degeneration patients cannot afford the more expensive alternatives (Eylea and Lucentis) and will go blind without access to Avastin. Further, from a provider standpoint, caring for retina patients is already very costly due to the high cost of drugs, (primarily Eylea, and Lucentis). If FDA guidelines now restrict my ability to use Avastin and force me to substitute Eylea or Lucentis, the total cost of caring for patients in my clinic will increase by 300% -- just by substituting a more expensive medication for a less expensive one. In my view, this amounts to poor stewardship of healthcare dollars, given that NIH-funded, large, prospective, randomized, double blinded clinical trials (including CATT and DRCR Protocol T) show similar safety among the treatments, and similar efficacy (except in a small subset of patients identified above).

While I believe cost is an appropriate consideration once efficacy and safety are established, I am also concerned that limiting access to Avastin will adversely impact retina specialists' ability to tailor treatment for each patient. In my experience, a small subset of patients do not respond very well to the first medication (Avastin, Lucentis or Eylea) and may respond better after switching to an alternative. I have a few patients who had inflammatory reactions to Eylea and now are doing better on Avastin. I have a patient who had pain after Lucentis, but does not after Avastin. An additional patient of mine suffers corneal edema after Eylea, but is doing better on Lucentis.

Please reconsider the overly restrictive BUD proposed in your draft guidance. For many of our patients, Avastin is the first choice (and for some it is the only choice) and they deserve to have it remain available.

Sincerely,

Geoff Emerson, MD, PhD

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