

January 25, 2019

Via Electronic Submission

Centers for Medicare & Medicaid Services Department of Health and Human Services

P.O. Box 8013

Baltimore, MD 21244–8013

Re: CMS-4180-P: Proposed Rule Allowing Medicare Advantage Plans To Implement Step Therapy

Dear Sir or Madam:

USRetina, one of the largest associations of private retina practices in the United States with 263 member practices representing over 1,000 physicians, respectfully submits

comments in opposition to the proposal of the Centers for Medicare & Medicaid Services (CMS) to allow Medicare Advantage plans (MA plans) to implement step therapy requirements as a way to reduce the costs of prescription drugs. The proposal is contained within “Modernizing Part D and Medicare Advantage to Lower Drug Prices and Reduce Out-of-Pocket Expenses,” the proposed rule published by CMS on November 30, 2018 (83 Fed. Reg. 62152).

Introduction

The physicians who make up USRetina are committed above all to the care and well- being of our patients. We also recognize the critical importance of pursuing opportunities for cost-savings in our health care system. To that end, we work with industry and clinical organizations to create new opportunities for patients to receive timely, affordable, and quality retina care and we support patient-centered innovation in health care delivery that will promote and maintain the fiscal health of the Medicare system without compromising quality of care.

USRetina opposes the step therapy proposal in the proposed rule. The proposed rule specifically targets drugs to treat serious retinal conditions that are prevalent in the Medicare population—age-related macular degeneration (AMD), which affects more than 2 million Americans and is the leading cause of legal blindness in the United States, and diabetic macular edema (DME), which affects about 750,000 people in the U.S. Under the proposed rule, MA plans could restrict Medicare enrollees’ access to the two leading FDA-approved therapies for AMD and DME—aflibercept (brand name Eylea) and ranibizumab (Lucentis)—unless the patients have tried and failed to benefit from bevacizumab (Avastin), which is less expensive but is neither approved for AMD or DME nor manufactured in the appropriate dosage form. The proposed rule is highly problematic for our patients because it promotes short-term cost-savings at the expense of individualized patient care. It would allow MA plans to erect barriers that, in practice, will restrict access to the full range of drugs available under Medicare.

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We urge CMS to develop and implement a patient-centered, value-based model that serves Medicare’s important goal of reducing drug costs, but without compromising a physician’s fundamental right to prescribe, and a Medicare beneficiary’s right to receive, the therapy that is best for that individual patient. In passing the Medicare Access and CHIP Reauthorization Act (MACRA), Congress supported this approach by creating the Quality Payment Program (QPP), which places quality, patient experience and outcomes, as well as cost of care into the equation. The step therapy proposal, particularly in the context of AMD and DME therapy, runs completely counter to these principles.

1. Mandated Step Therapy Is Inappropriate for the Treatment of Leading Retinal Diseases USRetina’s biggest concern with the proposed rule is that step therapy undercuts our

highest priority: ensuring that retina patients get the treatment that is best for them when they

need it. In the context of treatment for AMD and DME, MA plans imposing step therapy will require that enrollees try Avastin before they can receive Eylea or Lucentis.1 USRetina does not dispute that, for the right patient in the right circumstances, Avastin can be a useful treatment for AMD and DME; indeed, the physicians of USRetina currently prescribe about 65,000 doses of Avastin per month.2 Thus, we recognize that Avastin can be an important clinical option for particular patients based on their individual needs. And we similarly recognize that using Avastin, when appropriate, offers the potential for significant cost-saving.

However, the use of Avastin as a first-line treatment for every patient is subject to a critically important caveat: our clinical experience—and the peer-reviewed medical literature— tell us that Avastin is not *always* the right first-line treatment. Forcing a patient to try Avastin before moving to one of the FDA-approved therapies can retard or compromise patient health while exposing them to an elevated risk of serious adverse events and debilitating side effects.3

First, many of our patients should receive Eylea or Lucentis as a first-line treatment. Most particularly, there is compelling evidence that patients with worse visual acuity at baseline fare better on those drugs than on Avastin. Protocol T, an important clinical trial funded by the National Institutes of Health and conducted by the Diabetic Retinopathy Clinical Research Network, showed that patients with 20/50 or worse vision related to DME who were treated with Avastin were significantly more likely to suffer from persistent DME after six months of

1 USRetina is aware that many MA plans have already implemented Avastin-first step therapy, or plan to do so in 2019, under the guidance memorandum that CMS issued in August 2018.

2 Unfortunately, a not-insignificant number of those doses are prescribed to patients who request Avastin on cost grounds because their insurance does not cover the FDA-approved drugs or they lack insurance altogether. In such circumstances, the patient is forced to choose between Avastin and no treatment at all—even if, all things being equal, Eylea or Lucentis would be a preferable clinical option.

3 Step therapy would also put doctors in an untenable position by pressuring them to prescribe drugs for their patients enrolled in MA plans that, but for the step requirement, they would not prescribe. In that respect, the proposed rule potentially exposes prescribing doctors to liability risk that they would not otherwise assume.

treatment than patients treated with Eylea or Lucentis.4 Moreover, those patients treated with Avastin were more likely to have worse visual outcomes and a higher incidence of persistent retina thickening after two years—meaning that patients with Avastin never fully catch up, in regards to visual outcomes, to those treated with the FDA-approved therapies.5 And patients treated with Eylea showed significant improvement in visual acuity after a year compared to those treated with Avastin.6 Patients treated with Lucentis when compared to Avastin also were much more likely to experience improvement at one year: 40.6% compared to 24.1%.7

Similarly, the leading clinical trial comparing Avastin and Lucentis head-to-head for AMD found that Lucentis administered monthly decreased central retinal thickness significantly more than Avastin given monthly or as needed.8

When treating AMD and DME, a top priority is to remove the fluid from within and underneath the retina because the presence or absence of retinal fluid is highly correlated to vision and patients’ quality of life as shown by questionnaires obtained during the FDA approval process. Thus, it is important that the leading comparative studies have shown that Eylea and Lucentis demonstrate significantly better anatomic retinal fluid outcomes as assessed by optical coherence tomography (OCT), regardless of presenting visual acuity, and that Lucentis is significantly better at eliminating retinal fluid within four weeks compared to Avastin.9 Indeed, in DRCR Protocol T, the need for additional macular photocoagulation treatment was greatest for the Avastin-treated subjects through two years, indicating that Avastin had a lesser effect on reducing retinal fluid compared to both Eylea and Lucentis.10

Second, Avastin poses a greater risk of serious adverse events and debilitating side effects compared to Lucentis. The CATT Study showed a higher incidence of serious systemic adverse events after one year for patients treated with Avastin. Moreover, Avastin must be compounded for ophthalmologic use, because the drug must be repackaged in syringes for proper dosing. The composition of Avastin changes when it is compounded, as shown by significant

4 Bressler NM, *et al.*, Persistent Macular Thickening Following Intravitreous Aflibercept, Bevacizumab, or Ranibizumab for Central-Involved Diabetic Macular Edema With Vision Impairment: A Secondary Analysis of a Randomized Clinical Trial, JAMA Ophthalmol. 2018 Mar 1;136(3):257-269.

5 *Id.*

6 *Id.*

7 Bressler, SB, *et al.*, Change in Diabetic Retinopathy Through 2 Years Secondary Analysis of a Randomized Clinical Trial Comparing Aflibercept, Bevacizumab, and Ranibizumab, JAMA Ophthalmol. 2017;135(6):558-568.

8 Comparisons of Age-Related Macular Degeneration Treatments Trials (CATT) study, CATT Research Group, Ranibizumab and Bevacizumab for Neovascular Age-Related Macular Degeneration, N. Engl. J. Med.

2011;364:1897-908 (CATT Study).

9 Diabetic Retinopathy Clinical Research Network, Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema, N. Engl. J. Med. 2015 March 26; 372(13): 1193–1203 (author manuscript available at https://[www.ncbi.nlm.nih.gov/pmc/articles/PMC4422053/pdf/nihms677065.pdf);](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4422053/pdf/nihms677065.pdf%29%3B) CATT Study.

10 Wells, JA, *et al.*, Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema: Two-year Results from a Comparative Effectiveness Randomized Clinical Trial, Ophthalmology, 2016 June; 123(6):1351–1359 (author manuscript available at https://[www.ncbi.nlm.nih.gov/pmc/articles/PMC4877252/pdf/nihms-760345.pdf).](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4877252/pdf/nihms-760345.pdf%29)

reductions in protein concentration compared to the drug as manufactured.11 Given the numerous instances in recent years where the compounding of drugs—including ophthalmologic drugs— has caused sterility and purity problems,12 using Avastin introduces risks that simply do not exist for Eylea and Lucentis. As but one example, some compounding pharmacies have improperly transferred Avastin into syringes coated with silicone oil, causing patients injected with Avastin from those syringes to suffer from silicone oil bubbles (“floaters”) in their field of vision.13

Physicians need to be free to weigh these known risks of Avastin and the relative efficacy of the three therapies on a patient-by-patient basis. It is the physician who is responsible for ensuring that patients are receiving the appropriate care, and it is the physician who is generally at risk when a patient does not think they have received that care. Thus, in the absence of a legally enforceable hold harmless provision, physicians should not be forced to use a certain drug based on cost. An Avastin-first step requirement is particularly problematic here, when there is no drug manufacturer for the patient to hold liable because the use is off-label and the drug is compounded.

1. The Proposed Rule Is Legally Infirm

The proposed rule is also inconsistent with the Medicare law and existing regulations, and CMS fails to justify its about-face in policy. In 2012, CMS concluded that MA plans could not utilize step therapy under existing regulations which require MA plans to “provide coverage of, by furnishing, arranging for or making payments for, all services that are covered by Part A and B of Medicare . . . and that are available to beneficiaries residing in the plan’s service area.”14 That memorandum further noted that the regulation also requires MA plans to comply with National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs) and that while plans may create coverage policies in the absence of NCDs or LCDs, these policies may not be more restrictive than what original Medicare allows and may not impose

11 Yannuzzi, NA, *et al.*, Evaluation of Compounded Bevacizumab Prepared for Intravitreal Injection, JAMA Ophthalmol. 2015 Jan;133(1):32-9.

12 *E.g.*, FDA, “Compounded Products Containing Triamcinolone-Moxifloxacin by Guardian Pharmacy Services (Dallas, Texas): Alert to Health Professionals - Adverse Events Reported After Receiving Eye Injections” (June 14, 2018) (43 patients reporting adverse events after receiving injection of compounded eye drug), available at https://[www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm610835.htm;](http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm610835.htm%3B) FDA, “Sterile Injectable Products by Premier Pharmacy Labs: Recall - Lack of Sterility Assurance” (Apr. 12, 2018), available at https://[www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/](http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/) ucm604466.htm; “Ranier’s Rx Laboratory Issues Voluntary Recall of All Sterile Compounded Products Within Expiry Due to Lack of Sterility Concerns (July 28, 2018) (recall of drugs for ocular administration), available at https://[www.fda.gov/Safety/Recalls/ucm](http://www.fda.gov/Safety/Recalls/ucm) 615054.htm.

13 Avery RL, *et al.*, Large Silicone Droplets After Intravitreal Bevacizumab (Avastin), Retin Cases Brief Rep. 2017 Mar 15.

14 Mem. from D. Moon, *Prohibition on Imposing Mandatory Step Therapy for Access to Part B Drugs and Services*

(Sept. 17, 2012) ((citing 21 C.F.R. § 422.101(a) and (b)), available at https://[www.asrs.org/content/documents](http://www.asrs.org/content/documents)

/cms\_step\_therapy\_memo\_091712-2.pdf.

barriers to Part A and B services, including the imposition of step therapy requirement for Part B drugs.15

Though neither the statute nor the regulations have changed, in August 2018 CMS reversed its position, and with minimal discussion opened the door for MA plans to require step therapy.16 The proposed rule seeks to promulgate this new policy as a regulation. CMS does not explain why a policy it found had violated its regulations in 2012 no longer does so. CMS instead merely cites to section 1852 of the Social Security Act as support for allowing step therapy as an appropriate utilization tool. 83 Fed. Reg. at 62169.

CMS’s new policy, however, is inconsistent with the statutory requirement that MA plans “provide to members enrolled under [MA] . . . benefits under the original Medicare fee-for service option,” and which define these benefits as “items and services . . . for which benefits are available under parts A and B.”17 The existence of an appeals process does not remedy this problem because an appeal does not guarantee a beneficiary access to the same services that are covered under Medicare Parts A and B. In the absence of an adequate explanation as to why step therapy does not violate the Medicare statute and regulations, CMS’s new policy also may violate Section 706 of the Administrative Procedures Act.18

CMS’s step therapy policy is also inconsistent with section 1801 of the Social Security Act, which prohibits CMS from interfering with the practice of medicine. 42 U.S.C. § 1395.

Although courts have found that an absolute limitation on coverage is permissible, placing a condition on coverage is not.19 Step therapy places a condition on coverage: the MA plan will cover Lucentis or Eylea only if Avastin therapy is tried and fails. Courts do not look favorably on regulations that direct or prohibit treatment.20 Step therapy also directs and prohibits treatment, because it effectively requires that a patient use Avastin first, while prohibiting treatment with Lucentis or Eylea unless and until Avastin fails.

While the proposed rule contains some language suggesting that MA plans that implement step therapy would have to provide a process by which a provider can request a different therapy based on the medical necessity for an individual patient, USRetina’s physicians’ experience with both commercial health plans and MA plans shows that insurers are incentivized to make the pre-authorization request and appeal process an onerous and time- consuming one. USRetina practices and physicians see many patients every day for whom Eylea

15 *Id.*

16 Mem. from S. Verma (Aug. 7, 2018), available at https://[www.cms.gov/Medicare/HealthPlans/HealthPlans](http://www.cms.gov/Medicare/HealthPlans/HealthPlans) GenInfo/Downloads/MA\_Step\_Therapy\_HPMS\_Memo\_8\_7\_2018.pdf.

17 42 U.S.C. § 1852(a)(1)(A) and (a)(B)(1).

18 *See e.g., Motor Vehicle Mfrs. Ass’n of U.S. v. State Farm Mut. Auto Ins. Co.*, 463 U.S. 29 (1983); *United Techs. Corp. v. Dep’t of Def.*, 601 F.3d 557, 562 (D.C. Cir. 2010) (courts do not defer to an agency’s conclusory or unsupported suppositions).

19 *See Virginia Hosp. Ass’n v. Kenley*, 427 F. Supp. 781 (E.D. Va. 1977); *AMA v. Weinberger*, 395 F. Supp. 515 (N.D. Ill.1975), aff’d 522 F.2d 921 (7th Cir. 1975).

20 *Goodman v. Sullivan*, 712 F. Supp. 334 (S.D.N.Y. 1989), aff’d, 891 F.2d 449 (2d Cir.).

or Lucentis is the right first clinical option; thus, step therapy threatens to saddle retina doctors with substantial administrative and bureaucratic burdens, as they will be forced to navigate the appeals process for all of the patients who should be treated with a drug other than Avastin. The practical result is that the step therapy requirement threatens to infringe upon the practice of medicine and to create unlawful barriers to the full range of treatments available under original Medicare.

The experience of our retina specialists indicates that MA plans will enforce step therapy requirements aggressively. We are aware that health plans, including MA plans, closely track how frequently doctors within their networks prescribe Avastin compared to Lucentis or Eylea, and have terminated a doctor’s in-network contract if the plan thinks the doctor prescribes Lucentis or Eylea too often. Thus, we are concerned that strict enforcement of step therapy by MA plans will ultimately deprive Medicare patients of access not only to the right therapy for them when they need it, but also to the retina specialists most qualified to help them determine what that right drug should be.

1. CMS Should Consider a Value-Based, Patient-Centered Model for Care Delivery In light of the foregoing, USRetina urges CMS to develop a value-based model for

delivery of high-quality care by MA plans. In the example of a Medicare patient with AMD

under such a model, coverage for a particular drug would be driven by the patient’s individual circumstances, allowing a patient who should start on Eylea to receive coverage for it, while achieving cost savings through the use of Avastin when it is an acceptable option for the patient. These savings could be used to offset patients’ out-of-pocket costs and to neutralize potential differential revenues to practitioners who participate in value-based pathways.

CMS should take advantage of existing and emerging tools to create a care model that applies evidence-based medicine at an individual level. The availability of large data sets to create real-time feedback tools that assist physicians in efficiently mapping peer-reviewed and accepted clinically pathways while measuring and optimizing objective and quality of life outcomes which create the ideal drug therapy choices while maximizing savings where possible.

Conclusion

For the reasons explained above, USRetina urges CMS to eliminate the provisions in the proposed rule that would authorize MA plans to implement step therapy. We stand ready to work collaboratively with CMS to develop a value-based model, focused on quality and expenditures, that ensures that beneficiaries who choose to enroll in an MA plan receive all of the benefits under original Medicare and have access to high-quality care and receive the drug that their retina specialist determines will give them the best chance to achieve the best possible healthcare outcome and quality of life.

Thank for your consideration of USRetina’s comments on the proposed rule.

Sincerely,

/s/ Sunil Gupta Sunil Gupta, M.D.

Founder & Chief Medical Officer, USRetina