IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AKEBIA THERAPUETICS, INC., Plaintiff, v. ALEX M. AZAR II, in his official capacity as Secretary of Health and Human Services; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; SEEMA VERMA, in her official capacity as Administrator of the CENTERS FOR MEDICARE & MEDICAID SERVICES; Defendants	Civil Action No. 1:19-cv-12132-ADB (Leave to file granted on 12/4/2019)

AMICUS BRIEF OF CENTER FOR MEDICARE ADVOCACY, INC. IN SUPPORT OF PLAINTIFF'S MOTION FOR PRELIMINARY INJUNCTION OR FOR SUMMARY JUDGMENT

STATEMENT OF INTEREST

The Center for Medicare Advocacy, Inc. ("Center") is a national, private, non-profit organization,[1] founded in 1986, that provides education, analysis, advocacy, and legal assistance nationwide to help older adults and people with disabilities access Medicare and necessary health care. The Center responds to over 7,000 calls and e-mails annually, produces educational materials, and provides training and technical assistance to advocates across the country on problems pertaining to Medicare. The Center also pursues Medicare coverage for beneficiaries in

[1] The Internal Revenue Service has determined that the Center is organized and operated exclusively for charitable purposes pursuant to Section 501(c)(3) of the Internal Revenue Code and is exempt from income tax. The Center has no parent corporation, nor has it issued shares or securities.

administrative and legislative forums, and serves as legal counsel in litigation of national significance, especially on issues of import to people with low incomes and long-term conditions.

The Center has a substantial interest in the outcome of this case, as it strives to assist Medicare beneficiaries – and here, specifically, those with chronic kidney disease (CKD) – in securing medically necessary health care for which they are legally entitled to coverage. The Center files this amicus brief because this Court's ruling will have an impact on whether current and future Medicare beneficiaries who live with CKD can readily access a medication that is proven to be effective in managing two serious complications of that disease.

I. INTRODUCTION

Of the estimated 37 million U.S. adults who have CKD, 38 percent (over 14 million) are aged 65 and older. Centers for Disease Control, *Chronic Kidney Disease in the United States, 2019* (Mar. 2019).[2] The prevalence of CKD among beneficiaries in the Medicare Fee-For-Service population was 24 percent (roughly 9 million) in 2017. Centers for Medicare & Medicaid Services (CMS), *Chronic Conditions, Prevalence State/County Level: All Beneficiaries by Age, 2007-2017*.[3] Analyses suggest comparable prevalence of CKD among the one-third of beneficiaries who are enrolled in private Medicare Advantage plans. U.S. Renal Data System, *2018 Annual Data Report, Ch. 7: Healthcare Expenditures for Persons with CKD*.[4]

[2] https://www.cdc.gov/kidneydisease/pdf/2019_National-Chronic-Kidney-Disease-Fact-Sheet.pdf (last visited Nov. 25, 2019).

[3] https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/CC_Main at second download link (last visited Nov. 25, 2019).

[4] https://www.usrds.org/2018/view/v1_07.aspx (last visited Nov. 25, 2019).

CKD refers to five stages of kidney damage, from mild in stage 1 to complete kidney failure in stage 5, necessitating renal replacement therapy with dialysis, or kidney transplant surgery. As kidney function worsens over time, CKD patients become more prone to developing iron deficiency anemia (IDA). The prevalence of anemia increases from 8.4 percent at stage 1 to 53.4 percent at stage 5. IDA is associated with weakness, fatigue, insomnia, cognitive impairment, dyspnea, cardiovascular comorbidities (*i.e.*, angina, heart failure), CKD progression and higher mortality. Melissa E. Stauffer & Tao Fan, *Prevalence of Anemia in Chronic Kidney Disease in the United States*, PLOS ONE, Jan. 2014.[5]

Studies have shown that the correction of IDA in CKD can improve overall quality of life, help avoid the need for blood transfusions, and slow the progression of renal disease. Susan Krikorian *et al.*, *Managing Iron Deficiency Anemia of CKD with IV Iron*, U.S. Pharmacist (Aug. 2013).[6] Despite its importance, management of IDA in CKD with oral or intravenous iron supplementation can prove difficult. Many CKD patients are unable to tolerate or adequately absorb oral supplemental iron. *Id.* Weekly IV iron therapy is a recommended alternative for such patients and those with severe IDA in stages 3-5. But iron infusions are expensive and burdensome, taking 3-4 hours to administer. Factors like distance from a clinic, weather, health status, physical mobility, and the need for transport and assistance can further hinder compliance. Moreover, attendant to IV infusions is an increased risk for iron toxicity, infection, arterial inflammation, and scarring of the veins – the latter a serious concern for those CKD patients who may later require vascular access for dialysis. *Id. See also* Complaint ¶¶ 47, 48.

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3879360/ (last visited Nov. 25, 2019).

[6] https://www.uspharmacist.com/article/managing-iron-deficiency-anemia-of-ckd-with-iv-iron-42386 (last visited Nov. 25, 2019).

The advent of Plaintiff's drug, Auryxia (ferric citrate), introduced an effective oral therapy for IDA in non-dialysis CKD patients and for hyperphosphatemia in CKD patients on dialysis. Complaint ¶¶ 30, 31. Leading renal organizations and physicians have recognized Auryxia's importance in offering a more conservative approach and convenient alternative to aggressive IV iron administration for these patients. *Id.* ¶ 49. Having gained approval from the federal Food and Drug Administration (FDA) as a new drug for both of these therapeutic uses, Auryxia was added to CMS's list of covered drugs. *Id.* ¶ 34. In September 2018, however, CMS reversed course by excluding Auryxia as a covered drug for the IDA use, stating its decision was "[c]onsistent with other iron products," and imposing prior authorization restrictions on the use of Auryxia for the treatment of hyperphosphatemia. *Id.* ¶¶ 35-36. Defendants' actions are legally improper and thwart the medical care of CKD patients.

II. ARGUMENT

A. Defendants' action contravenes the Medicare Act and the Food, Drug, and Cosmetic Act.

Medicare is a federal program established under Title 18 of the Social Security Act that provides health insurance for the elderly and disabled. 42 U.S.C. §§ 1395 *et seq.* The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), added a prescription drug benefit, known as Medicare Part D, which has provided assistance in paying for prescription drugs since 2006. *Id.* at § 1395w-101 *et seq.* Part D is not part of the traditional Medicare program but rather is offered through private insurance plans. Enrollment in Part D coverage is voluntary. Seventy percent (45 million) of the Medicare population is currently enrolled in plans that provide the Part D drug benefit. Kaiser Family Foundation, *An Overview of*

the Medicare Part D Prescription Drug Benefit (Nov. 2019) ("KFF Overview").[7] In 2020, the Part D base monthly premium is $32.74, but actual premiums paid by enrollees vary widely from this amount. *Id*.

The MMA established a standard drug benefit that Part D plans may offer. 42 U.S.C. § 1395w-102(b). The standard benefit is defined in terms of the financial structure of beneficiaries' cost-sharing amounts and not in terms of the drugs that must be covered. In 2020, this standard benefit requires payment of a $435 deductible. The beneficiary is then responsible for 25 percent of the cost of *covered* Part D prescription drugs, until reaching the catastrophic coverage threshold of $9,719, after which they pay 5 percent of their total *covered* drug costs. KFF Overview. The MMA also established subsidies to provide Part D cost-sharing assistance for beneficiaries with incomes up to 150 percent of the federal poverty level and with limited resources. 42 U.S.C. § 1395w-114. Subsidies vary according to income, Medicaid status, and institutional status. 42 C.F.R. §§ 423.773, 423.782. Significantly, the MMA eliminated all Medicaid pharmacy benefits for beneficiaries who qualify for both Medicare and Medicaid, requiring these "dual eligibles" to receive their drug coverage through Medicare Part D. 42 U.S.C. § 1396u-5(c). The particularly vulnerable population of dual eligibles, affected by both limited incomes and age or disability, is thus generally limited to coverage under Part D for their prescription medication needs.

Part D plan sponsors must provide beneficiaries access to "covered part D drugs," which the MMA defines by direct reference to the definition of "covered outpatient drug" in the Medicaid program. 42 U.S.C. §§ 1395w-102(e)(1), 1396r-8(k)(2). Accordingly, a covered Part D

[7] https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/ (last visited Nov. 19, 2019).

drug is one that may be dispensed only upon a prescription, and that is "approved for safety and effectiveness as a prescription drug under section 505…of the Federal Food, Drug, and Cosmetic Act" for a medically accepted indication. *Id.* § 1396r-8(k)(2)(A)(i). The term "medically accepted indication" is defined in part as "any use for a covered outpatient drug which is approved under the Federal Food, Drug, and Cosmetic Act…." *Id.* § 1396r-8(k)(6). Congress's plain intent here was to cover drugs that meet the FDA's stringent criteria for development and approval. New drug products undergo a lengthy and extensive process in order to be approved by FDA for general marketing. 21 U.S.C. § 355. The FDA is charged with approving new drug applications only upon direct determination that the legal and scientific standards for establishing clinical safety and efficacy as set forth in relevant laws and regulations have been met. Complaint ¶¶ 16, 17.

There can be little doubt that Auryxia meets the statutory definition of a covered Part D drug. 42 U.S.C. § 1395w-102(e)(1). This is established by the fact that (1) Auryxia can only be dispensed upon prescription, and (2) based on relevant data, including from multiple randomized clinical trials, the FDA approved Auryxia as a medically safe and effective drug for the indication of hyperphosphatemia in CKD patients on dialysis, and subsequently, for IDA in non-dialysis CKD patients. Complaint ¶¶ 30-33.

Defendants offer no justification for abruptly revoking their recognition of Auryxia as a covered Part D drug for IDA. They make only the vague assertion that their decision here is "[c]onsistent with other iron products." *Id.* ¶ 35. One may assume that by "other iron products" Defendants are not referring to *intravenous* iron therapies (*e.g.*, iron sucrose), which are not covered Part D drugs by virtue of being administered in a physician's office or clinic, but *are covered as FDA-approved drugs* under Medicare Part B. 42 U.S.C. §§ 1395k(a)(2)(B),

1395x(s)(2)(A). Presumably, Defendants are referring to oral iron supplements, which are excluded from Part D coverage as "[p]rescription vitamins and mineral products." *Id.* § 1396r-8(d)(2)(E).

Defendants can claim no basis, though, for excluding Auryxia as an ordinary mineral when it has been recognized as a drug by the FDA for treatment of a specific medical condition. Under the FDCA, minerals are dietary ingredients contained in products classified as "dietary supplements," which the FDA regulates under a different set of regulations than those applying to drug products. 21 U.S.C. §§ 321(ff), 350. Unlike with drug products, manufacturers do not have to secure FDA approval for safety and effectiveness prior to marketing and selling dietary supplements to consumers. Significantly, in contrast to drug products, which are legally defined as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease," it would be illegal for a dietary supplement to "claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases." *Id.* §§ 321(g)(1); 343(r)(6)(C).

The FDA approved Auryxia as a drug specifically targeted and demonstrated to treat IDA and hyperphosphatemia in the setting of CKD. In doing so, the agency expressly noted that the active ingredient in Auryxia differs from the mineral-based iron that the agency recognizes as a dietary supplement. Complaint ¶¶ 26, 27. This ingredient is a novel, chemically-synthesized metal-ion compound that is structurally and functionally distinct from naturally occurring iron. *Id.* Auryxia's unique active ingredient acts both to reduce serum phosphorus levels, and to facilitate systemic absorption of iron by raising hemoglobin levels, which conventional iron does not do. *Id.* ¶¶ 30, 32, 33. That Auryxia, in clinical testing, successfully treated IDA in CKD patients "who were intolerant of or have had an inadequate therapeutic response to oral iron

supplements" is further evidence that it is not a mineral product like those dietary supplements. *See* Auryxia® Prescribing Information at 9 (Nov. 2017).[8]

No statutory authority exists for Defendants to disregard the FDA's approval of Auryxia as a drug when used to treat IDA in non-dialysis CKD patients. Defendants' baseless re-classification of Auryxia as a "mineral" should be regarded for what it is – an act that deprives Medicare beneficiaries of coverage for a drug that is legally required to be covered by Part D. Defendants make no effort to explain their inconsistency in recognizing Auryxia as a drug (and not a mineral) when used to treat hyperphosphatemia. To that end, they also present no valid justification for imposing a prior authorization requirement when Auryxia is prescribed for that indication. In sum, Defendants' actions to exclude and constrain Auryxia's coverage under Part D are arbitrary and capricious and inconsistent with Congress's intent as expressed through both the Medicare Act and the Federal Food, Drug and Cosmetic Act.

B. Defendants' actions are inconsistent with the Administration's stated goal of reducing the burden of CKD.

Defendants' actions with respect to Auryxia also conflict with their stated policy goal of reducing the burden of CKD on patients, the Medicare program, and the broader healthcare system. Health care costs increase dramatically as CKD advances to end-stage renal disease (ESRD). ESRD patients make up less than one percent of the Medicare population, but account for roughly seven percent of the Medicare fee-for-service budget. U.S. Renal Data System, *2018 Annual Report, Ch. 9: Healthcare Expenditures for Persons with ESRD*.[9] Treatment with hemodialysis, which has a low five-year survival rate, costs Medicare over $90,000 per patient

[8] https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/205874s013lbl.pdf (last visited Nov. 25, 2019).

[9] https://www.usrds.org/2018/view/v2_09.aspx (last visited Nov. 30, 2019).

annually, for a total of $28 billion. *Id.* Kidney transplantation has better outcomes and is also more cost-effective, but there is an acute shortage of donor organs for ESRD patients. U.S. Dep't of Health & Human Servs., *Advancing American Kidney Health* at 8.[10]

Earlier this year, pursuant to an Executive Order, Defendant Secretary Azar launched a broad-scale kidney health initiative to "improve the lives of Americans suffering from kidney disease, expand options for American patients, and reduce healthcare costs." U.S. Dept. of Health & Human Servs., *HHS Launches President Trump's 'Advancing American Kidney Health' Initiative* (Jul. 2019).[11] Two of the three goals articulated by the Defendant are "[r]educing the number of Americans developing end-stage renal disease by 25 percent by 2030" and "[h]aving 80 percent of new ESRD patients in 2025 either receiving dialysis at home or receiving a transplant." *Id.*

Defendants undermine these goals by preventing full coverage of Auryxia under Part D. Employed as prescribed, Auryxia has been shown to correct IDA in CKD, which in turn can slow the progression of CKD to ESRD. Management of IDA can also help avoid the need for emergent and costly blood transfusions and other CKD-related hospital admissions. Because Auryxia is far less burdensome, risky, and expensive than treatment with IV iron infusions, allowing Medicare beneficiaries access to Auryxia could significantly increase the management of IDA in CKD nationally.

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[10] https://aspe.hhs.gov/system/files/pdf/262046/AdvancingAmericanKidneyHealth.pdf (last visited Nov. 30, 2019); *see also,* Suzanne M. Kirchoff, Congressional Research Service, *Medicare Coverage of End-Stage Renal Disease (ESRD)* at 4 (Aug. 2018), https://fas.org/sgp/crs/misc/R45290.pdf (last visited Nov. 30, 2019).

[11] https://www.hhs.gov/about/news/2019/07/10/hhs-launches-president-trump-advancing-american-kidney-health-initiative.html (last visited Nov. 25, 2019).

Restricting coverage of Auryxia undercuts Defendants' goal of promoting kidney transplantation in ESRD patients. Studies recommend addressing IDA in the pre-transplant setting to further recovery of anemia post-transplant, thereby minimizing the risk of poor graft outcomes and increased mortality. C. Truax *et al.*, *The Incidence of Iron Deficiency in Kidney Transplant Candidates Based on the Updated KDIGO Guideline for Anemia* (abstract), Am. J. Transplantation (2013).[12] Similarly, it has been shown that elevated pre-transplant phosphorous levels were associated with increased risk of functional graft failure, and all-cause and cardiovascular deaths, suggesting that better control of pre-transplant serum phosphorous may improve post-transplant outcomes. Marcelo S. Sampaio *et al.*, *Association of Pretransplant Serum Phosphorus with Posttransplant Outcomes*, 6 Clinical J. Am. Soc. Nephrology 2712 (2011).[13]

Defendants' restrictions on coverage of Auryxia are thus incongruous with their intent to slow deterioration, and improve quality of life and medical outcomes for Medicare beneficiaries with CKD and ESRD.

C. Defendants' actions harm Medicare beneficiaries with CKD – particularly, those most vulnerable.

Defendants' actions concerning Auryxia have created and will result in even greater health disparities and inequities among CKD patients. For example, CKD is more prevalent among dual eligibles (30.7 percent) than among non-dually eligible beneficiaries (22.3 percent). CMS, *Chronic Conditions, Prevalence State Level: All Beneficiaries by Medicare-Medicaid*

[12] https://atcmeetingabstracts.com/abstract/incidence-of-iron-deficiency-in-kidney-transplant-candidates-based-on-the-updated-kdigo-guideline-for-anemia-the/ (last visited Nov. 25, 2019).

[13] https://cjasn.asnjournals.org/content/clinjasn/6/11/2712.full.pdf (last visited Dec. 1, 2019).

Enrollment and Age, 2007-2017.[14] Defendants' treatment of Auryxia as a mineral may also provide a precedent for state Medicaid programs to revoke coverage of Auryxia on that basis as well. This would harm an even greater number of CKD patients of limited means. In general, restricting coverage of Auryxia will negatively impact treatment for socially and economically disadvantaged CKD patients more than others. The absence of Auryxia as an available treatment for IDA leaves intravenous iron as the most effective therapy. As mentioned, IV infusions entail significant cost, burden, and risk. Because the infusions can pose too much of a hardship for patients with physical, mental, or financial limitations, many go untreated. The inability to access the one effective oral alternative, Auryxia, may also reduce the chances for low-income CKD patients to become candidates for kidney transplant. "Economic circumstances may make medications practically unaffordable and lead to morbidity such as hypertensive urgency and hyperphosphatemia." U.S. Dep't of Health & Human Servs., *Educational Guidance on Patient Referral to Kidney Transplantation* (2015).[15]

Ultimately, it is the CKD patients who are already vulnerable—particularly with respect to financial status, multiple chronic conditions, or social or geographic isolation—who stand to suffer the most from Defendants' unwarranted actions in this case.

III. CONCLUSION

For these reasons, amicus respectfully urges the Court to grant Akebia's pending motion.

Dated: December 4, 2019 Respectfully submitted,

On brief: Wey-Wey Kwok */s/Alice Bers*

[14] https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/CC_Main at fifth download link (last visited Nov. 25, 2019).

[15] https://optn.transplant.hrsa.gov/resources/guidance/educational-guidance-on-patient-referral-to-kidney-transplantation/ (last visited 11/25/19).

ALICE BERS (BBO #650608)
Center for Medicare Advocacy, Inc.
P.O. Box 350
Willimantic, CT 06226*
*admitted only in Massachusetts
Phone: (860) 456-7790
Fax: (860) 456-2614
abers@medicareadvocacy.org

Attorney for *Amicus Curiae*

CERTIFICATE OF SERVICE

I hereby certify that on December 4, 2019, I filed the foregoing Amicus Brief of Center for Medicare Advocacy, Inc. in Support of Plaintiff's Motion for Preliminary Injunction or for Summary Judgment through the CM/ECF system, causing it to be served electronically to all counsel of record as identified on the Notice of Electronic Filing (NEF).

/s/Alice Bers
Alice Bers
Center for Medicare Advocacy, Inc.