Case No. 20-11996

In the United States Court of Appeals
for the Eleventh Circuit

Donald Dobson,

Plaintiff-Appellant,

vs.

Alex M. Azar, II, Secretary of Health and Human Services,

Defendant-Appellee.

Appeal from the United States District Court
For the Southern District of Florida
Case No. 4:18-cv-10038-JB

BRIEF *AMICUS CURIAE* OF AMERICAN MEDICAL ASSOCIATION IN SUPPORT OF APPELLANT AND REVERSAL

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Certificate of Interested Persons and Corporate Disclosure Statement

Amicus certifies that, to the best of their knowledge, the Certificate of Interested Persons in the Brief for Plaintiff-Appellant is complete.

Pursuant to Federal Rule of Appellate Procedure 26.1, *amicus* states that it has no parent corporation and no corporation, publicly held or otherwise, owns 10% or more of any of their stock.

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Statement of Interest

The American Medical Association (AMA) is the largest professional association of physicians, residents and medical students in the United States. Additionally, through state and specialty medical societies and other physician groups seated in its House of Delegates, substantially all US physicians, residents and medical students are represented in the AMA's policy making process. The AMA was founded in 1847 to promote the science and art of medicine and the betterment of public health, and these remain its core purposes. AMA members practice in every state and in every medical specialty. The AMA "strongly supports the autonomous clinical decision-making authority of a physician," which is undermined when patients' access to necessary medication is impeded by unduly restrictive payer policies. AMA Policy H-120.988, *Patient Access to Treatments Prescribed by Their Physicians* (2015)[1].

Statement of the Issues

Part D of the Medicare Act affords qualified seniors and individuals with disabilities prescription drug coverage. The Food and Drug Administration ("FDA") regulates labeling and marketing of prescription drugs and devices by the pharmaceutical and device industries to medical professionals and the public, but does not regulate the practice of medicine. If a physician prescribes a medication to

[1] *Available at* https://bit.ly/3bWvVMg.

a Part D beneficiary that is different from the label's FDA approved use, Part D will cover the use so long as it is "supported by . . . [a] citation" in an approved drug index. An approved drug index lists the drug dronabinol as a treatment for disease-related, treatment-resistant nausea. Appellant suffers from disease-related, treatment-resistant nausea and his physician prescribed dronabinol. However, the Secretary found that his use was not "supported by . . . [a] citation[]" in the compendium because he did not have the same diagnosis as the patient described in the relevant index entry.

The issues presented are:

1. Did the Secretary err in interpreting "supported by . . . [a] citation[]" to mean that Appellant must suffer from the same underlying diagnosis as a patient described in the relevant index entry, when he ignored the treating physician's medical opinion that the index "support[ed]" Appellant's use?

2. Did the District Court err in affording elevated deference to the Secretary's interpretation and application of the statutory phrase "supported by . . . [a] citation[]," when it disregarded the opinion of the treating physician?

Summary of the Argument

Donald Dobson, the plaintiff and Medicare Part D beneficiary in this case, suffers from Central Cord Syndrome and Eagle's Syndrome as the result of an injury to his spinal cord. These conditions cause Mr. Dobson to suffer from persistent nausea, which if left untreated put him at risk for serious medical complications, including stroke, increased blood pressure and seizures, significant

weight loss, increased pain and muscle spasms. After exhausting other options, Mr. Dobson's physician prescribed him the drug dronabinol. Fortunately, this drug has been effective in treating Mr. Dobson's symptoms and has prevented him from suffering these severe medical risks.

Unfortunately for Mr. Dobson, and in contradiction to his examining physician's clinical judgment, Medicare has declined to cover the cost of this treatment. Here, Mr. Dobson is like many patients in the United States who have been examined and treated by a physician or medical team, prescribed a medication or therapy best-suited to alleviate the presenting condition, only then to find that this treatment will not be covered by Medicare and thus interrupting his care and imposing a barrier to necessary medical treatment.

The reason the Secretary cites for not covering this important medical treatment is that because the drug is prescribed "off-label" and Mr. Dobson's diagnosis does not match the exact diagnosis of the patient referenced in the relevant drug index, it is not "supported by" a citation in the drug index. Such rationale eliminates the ability of physicians to employ their training and individual experience of the patient's condition. Instead, complex decisions regarding medical treatment are sacrificed for a formula convenient to the payer.

It is the physician, not the Secretary, who must determine and justify whether a particular treatment is "supported by" a citation in the appropriate drug

index, because it is the physician, not the Secretary, who understands the unique combination of factors that contribute to the patient's particular diagnosis or cluster of symptoms. To do otherwise risks absurd results and impacts millions of Americans who rely on their examining physicians, and not the slow-moving monolith of the regulatory system, to determine what is best for their health.

Argument

I. Whether a Drug is "Supported by" a Citation to the Appropriate Drug Index Should Be a Matter of Interpretation for the Treating Physician.

The core issue of this case is whether Mr. Dobson's physician's decision to prescribe dronabinol to treat his patient's severe medical condition was "supported by . . . [a] citation[]" in a drug compendium approved by the Centers for Medicare and Medicaid Services ("CMS") in its Part D prescription drug program. 42 U.S.C. §§ 1395w-102(e)(1), 1396r-8(k)(6) (2009). When the prescription of a drug or use of a device represents safe and effective therapy, third party payers, including Medicare, should consider the intervention as clinically appropriate medical care, irrespective of labeling, and should fulfill their obligation to their beneficiaries by covering such therapy, and be required to cover appropriate 'off-label' uses of drugs on their formulary. AMA Policy H-120.988, *Patient Access to Treatments Prescribed by Their Physicians* (2015).

Physicians have been and continue to be at the forefront of the intersection of providing patients' medical care and advancing medical knowledge to improve upon the current standard of care. Physicians are unique stakeholders who have both an ethical and legal obligation to each individual patient to whom they render medical care. The first directive of physicians is to advance the interest of their patients to whom they provide medical services. Physicians have a direct relationship with patients and an obligation to provide medical services that meet patient specific clinical needs. Physicians should "[p]rescribe drugs, devices, and other treatments based solely on medical considerations, patient need, and reasonable expectations of effectiveness for the particular patient." AMA Code of Medical Ethics Opinion 9.6.6., *Prescribing & Dispensing Drugs & Devices* (2016)[2].

Mr. Dobson's physician submitted evidence stating that Mr. Dobson's use of dronabinol was supported by the relevant drug index. This is the very definition of medicine, i.e., a physician using his or her clinical expertise to appropriately diagnose and treat a patient who may require care that is not "one-size fits all." Competent and quality medical care rests on physicians' discretion and responsibility to treat patients in a manner that meets each patient's individual needs.

[2] *Available at* https://bit.ly/3ki7DPO.

It is, therefore, the physician's role to make the determination of whether the use of dronabinol is "supported by" a citation in the relevant drug index. Physicians possess the training and clinical understanding of the biological pathways of illness that underly one diagnosis versus another. A patient's symptoms cannot always be conveniently sorted into one narrow diagnosis. It is the physician who is able to understand the mechanisms of action within a particular body system that would be affected by a medication or treatment and provide the necessary justification for one course of action over another. To replace this individualized approach to medicine would risk absurd results.

Deference to regulators over physicians interrupts care and frustrates resources physicians and their staff could use elsewhere. Indeed, 90 percent of physician practices report that administrative burdens result in care delays, and 80 percent report they are sometimes, often, or always required to repeat prior authorization for prescription medications when a patient is stabilized on a treatment for a chronic condition, interrupting an effective course of care.[3] These administrative hassles interrupt care and jeopardize patient health. In addition, the very menial, time-consuming processes used for exceptions also burden providers and divert

[3] *See* AMA, *2019 AMA prior authorization physician survey*, https://www.ama-assn.org/system/files/2020-06/prior-authorization-survey-2019.pdf; AMA, *2019 Update Measuring progress in improving prior authorization*, https://www.ama-assn.org/system/files/2020-06/prior-authorization-reform-progress-update-2019.pdf.

valuable resources away from direct patient care. In fact, physicians report that their practices spend over 14 hours on average each week on prior authorizations of prescriptions and medical services, even though the vast majority are ultimately approved. *Id*. Many practices resort to employing a full-time staff member with the sole responsibility of navigating insurer administrative policies.

Here, Mr. Dobson has lost access to critical medical treatment due to a bureaucracy many steps removed from the exam room because a regulator, not a clinician, determined that his condition did not exactly match the condition of the patient referenced in the relevant drug index. This result undermines the purpose of Part D, which was added to the Medicare program to provide access to previously cost-prohibitive drug treatments and close gaps in medical care for older adults and people with disabilities. *See* Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003). This Court should not allow such a result.

II. Off-label Prescribing is Lawful, Common, and Appropriate When Supported by Sound Medical Judgment.

At the point in which a drug or device is approved for a particular use by the Food and Drug Administration ("FDA"), it has undergone a typically years-long process to determine its safety and efficacy. In order to gain approval, a new drug application, for example, must generally include results of preclinical animal trials and of the human clinical studies, the drug's ingredients and components, detailed

chemical and biological information, a summary of the risks and benefits, the manufacturing, processing and packaging methods, an environmental impact statement and samples of the proposed labeling. *See* 21 C.F.R. §§ 314.5(c)(5)(vi)(b)(viii), 314.5 (2019).

Once a drug has been approved by the FDA for one purpose, a physician can prescribe that drug for any purpose. This practice of prescribing a drug for a purpose other than that for which it is approved is known as "off-label" use. Madlen Gazarian et al., *Off-label use of medicines: consensus recommendations for evaluating appropriateness*, 185 MED. J. AUST. 544, 548 (Nov. 20, 2006). Off-label use is legal and does not necessarily mean that the drug is being used inappropriately, that the drug is investigational, or that the treatment is experimental. *Id.* Physicians may prescribe a drug off label because they believe it is the best treatment for a specific condition given their patients' individual circumstances even though it has not yet been formally tested for use in that condition. WA Meadows & BD Hollowell,*"Off-label" drug use: an FDA regulatory term, not a negative implication of its medical use*, 20 INT J IMPOT Res. 135, 144 (Nov. 15, 2007).

In fact, the FDA does not have the authority to regulate the practice of medicine or restrict a physicians' ability to prescribe treatments in their patients' best interest. The FDA has continually recognized the value and propriety of off-

label use. In 1982, the *FDA Drug Bulletin* informed the medical community that "once a [drug] product has been approved for marketing, a physician may prescribe it for uses or in treatment regimens or patient populations that are not included in approved labeling." FDA, *Use of Approved Drugs for Unlabeled Indications*, 12 FDA Drug Bulletin 4, 5 (1982) (cited in 59 Fed.Reg. 59,820, 59,821 (Nov. 18, 1994)). The agency went on to state:

> "unapproved" or more precisely "unlabeled" uses may be appropriate in certain circumstances, and may, in fact reflect approaches to drug therapy that have been extensively reported in medical literature.[4] Valid new uses for drugs already on the market are often first discovered through serendipitous observations and therapeutic innovations[.]

Id.

And, when it passed the Food and Drug Administration Modernization Act (FDAMA) of 1997,[5] Congress ensured that the FDA would not interfere with a physician's ability to practice medicine:

> Nothing in this chapter shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship.

21 U.S.C. § 396 (2010).

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[4] *Id*., *see also* James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions*, 53 Food & Drug L.J. 71, 77 (1998) [hereinafter Beck, *Off-label*].

[5] Pub. L. No. 105-115, 105 Stat. 1677 (1997).

Courts across the country have likewise acknowledged the appropriateness of off-label prescribing.[6]

Off-label uses of drugs can perform an important therapeutic role in many areas of medical practice. When the Government Accountability Office ("GAO") surveyed in 1991, it found that prescriptions for off-label uses of drug products "account[ed] for more than 25% of the approximately 1.6 billion prescriptions written each year, with some …estimates running as high as 60%." GAO, *Off-Label Drugs: Initial Results of a National Survey*.[7] In 1995, the AMA reported "that approximately half of all prescriptions were written for off-label uses." Am. Med. Ass'n, *Drug Evaluations Annual* (1995).

Examples of medical conditions whose standard treatments involve or have involved extensive off-label use include cancer, heart and circulatory disease, AIDS, kidney diseases requiring dialysis, osteoporosis, and spinal fusion surgery, in addition to other, less common diseases. Beck, *Off-Label* at 80

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[6] *See, e.g., Sorrell v. IMS Health Inc.,* 564 U.S. 552 (2011); *Rhone-Poulenc Rorer Pharm., Inc. v. Marion Merrell Dow, Inc*., 93 F.3d 511, 514 n. 33 (8th Cir. 1996); *Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1496 (D.C.Cir. 1996); *Ortho Pharm. Corp. v. Cosprophar, Inc*., 32 F.3d 690, 692 (2d Cir. 1994); *Weaver v. Reagen*, 886 F.2d 194, 198 (8th Cir. 1989); *United States v. An Article of Device ... Diapulse*, 768 F.2d 826, 832 (7th Cir. 1985); *Washington Legal Found. v. Kessler*, 880 F. Supp. 26, 37 n. 1 (D.D.C. 1995); *United States v. Evers*, 453 F.Supp. 1141, 1149-50 (M.D.Ala. 1978), *aff'd*, 643 F.2d 1043, 1052-53 (5th Cir. 1981); *Jones v. Petland Orlando Store*, 622 So.2d 1114, 1115 (Fla.Dist.Ct.App. 1993).

[7] *Available at* https://www.gao.gov/assets/80/78042.pdf.

(1998). Pediatric care also relies on off-label use.[8] As a former editor of the Journal of the American Medical Association testified,

> "[p]rescribing FDA-approved drugs for off-label (unlabeled) uses often is necessary for optimal patient care. For a product to have the most effective potential benefits, law and regulation should and must follow, not precede, science. There are too many variations in clinical circumstances and too much time delay in regulations to allow the government to impede the physician's ability to practice in these regards when it is medically appropriate."

Promotion of Drugs and Medical Devices for Unapproved Uses: Hearing Before the Human Resources and Intergovernmental Relations Subcomm. of the House Comm. on Gov't Operations, 102d Cong. 1 (1991) (statement of George Lundberg, M.D.).

Off-label use is thus commonplace and should not be automatically considered experimental, investigational, or subject to heightened review, if its use is based upon sound clinical judgment. "[A] treatment found to be in accordance with generally accepted standards of medical practice would hardly be experimental." *Pirozzi v. Blue Cross-Blue Shield*, 741 F.Supp. 586, 590

[8] "[O]ver 80% of all drugs prescribed for children carry ... orphaning clauses in their package labels." Rober Levine, *Ethics and Regulation of Clinical Research 241* (Yale Univ. Press, 2d ed. 1986). "Orphaning clauses" are disclaimers with respect to pediatric use that FDA requires because of the paucity of clinical studies involving children. *Id.* at 239.

(E.D.Va.1990) (quotation marks omitted).[9] Finally, as one medical ethicist explained,

> "[m]any drugs and devices approved for use by the FDA are prescribed for uses that are not listed on the FDA-approved package label. This does not mean that all such uses must be made the object of a formal study designed to establish safety and efficacy."

Robert Levine, *Ethics and Regulation of Clinical Research* 241 (Yale Univ. Press, 2d ed. 1988).

III. The Secretary's Unduly Restrictive Approach May Jeopardize Future Medical Advances.

There are many examples of drugs having successful off-label use before the FDA approves that particular use for marketing purposes. In the 1960s, British pharmacologist John Vane made a breakthrough in his laboratory at the University of London.[10] Zain Mithani, *Informed Consent for Off-Label Use of Prescription Medications*, AMA J. Ethics (2012) (*citing* Diarmuid Jeffreys, *Aspirin*, *The Remarkable Story of a Wonder Drug*, Bloomsbury (2004)). Vane found that aspirin, a drug that for many years was used primarily to relieve minor pain and fevers, could disrupt a pathway needed for platelet aggregation. *Id*. Further studies

[9] *See also Weaver*, 886 F.2d at 198 (experimental treatment is "not generally accepted by the professional medical community as an effective and proven treatment for the condition" or is "rarely used, novel or relatively unknown").
[10] *Available at* https://journalofethics.ama-assn.org/article/informed-consent-label-use-prescription-medications/2012-07.

in the 1980s showed that this effect could be used for the prevention of heart attacks and stroke. *Id.* The FDA, however, prevented manufacturers from advertising this information until more convincing clinical trials of aspirin's anticoagulant action had been completed. *Id*. Doctors, in the meantime, relying on this evidence, prescribed aspirin for this use in the normal practice of medicine. In fact, it was not until 1998 that the FDA finally approved aspirin for the prevention of cardiovascular events. *Id*.

Thus, "[t]he pace of medical discovery invariably runs far ahead of FDA's regulatory machinery, and off-label use is frequently state-of-the-art treatment." Beck, *Off-label* at 79 (1998). As the United States Court of Appeals for the Third Circuit noted,

> [n]ew uses for drugs are often discovered after FDA approves the package inserts that explain a drug's approved uses. Congress would have created havoc in the practice of medicine had it required physicians to follow the expensive and time-consuming procedure of obtaining FDA approval before putting drugs to new uses. Thus Congress exempted the practice of medicine from the [FDCA] so as not to limit a physician's ability to treat his patients.

United States v. Algon Chem. Inc., 879 F.2d 1154, 1163 (3d Cir. 1989).

Narrowing physicians' ability to prescribe treatments that their patients can access could have the effect of slowing the pace of medical advancement, and to limit patients covered by Medicare Part D to care below current standards. For

example, one study found that the indexes Part D relies upon only included only 31-45% of current, evidence-based treatments for dermatological disorders.[11] This is especially true of "orphan diseases," or diseases that have patient populations too small or that are too rare for a manufacturer to invest resources and time to obtain FDA approval for a drug treatment. Beck,*Off-label* at 83. Off-label prescribing may be the standard, if not the only method for treating a patient who has an orphan disease. *Id*. This Court should not allow a narrow reading of regulatory guidance to impede access to critical care.

Conclusion

For the foregoing reasons, *amicus* respectfully urges the Court to reverse the District Court's decision and rule that Mr. Dobson's use of dronabinol is covered by Medicare Part D.

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[11]John S. Barbieri et al., *Evaluation of Clinical Compendia Used for Medicare Part D Coverage Determinations for Off-label Prescribing in Dermatology*, JAMA Dermatol, Vol. 155, No. 3, 315, 316 (Jan. 23, 2019) https://jamanetwork.com/journals/jamadermatology/fullarticle/2720747?resultClick=1.

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1. This brief complies with the Federal Rule of Appellate Procedure 32(a)(7)(B)‘s type-volume requirement. As determined by Microsoft Word’s word-count function, excluding parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii) and 11th Circuit Rule 32-4, this brief contains, this brief contains 3,148 words.

2. This brief further complies with Federal Rule of Appellate Procedure 32(a)(5)‘s typeface requirements and with Federal Rule of Appellate Procedure 32(a)(6)‘s type-style requirements. Its text has been prepared in a proportionally spaced serif typeface using Microsoft Word’s 14-point Times New Roman font.

September 15, 2020

/s/ Erin G. Sutton
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Certificate of Service

I hereby certify that on September 15, 2020, I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the Eleventh Circuit by using the CM/ECF system. I certify that all participants in this case are registered CM/ECF users and that service will be accomplished by the CM/ECF system.

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