[DO NOT PUBLISH]

In the

United States Court of Appeals

For the Eleventh Circuit

No. 20-11996

DONALD DOBSON,

Plaintiff-Appellant,

versus

SECRETARY OF HEALTH AND HUMAN SERVICES,

Defendant-Appellee.

Appeal from the United States District Court
for the Southern District of Florida
D.C. Docket No. 4:18-cv-10038-JB

Before WILSON, ROSENBAUM, and HULL, Circuit Judges.

PER CURIAM:

Appellant Donald Dobson is a Medicare participant. As a result of disease, he suffers from intractable and severe nausea and vomiting, which interfere with his ability to function and threaten other aspects of his medical condition. Dobson's doctors tried in vain to relieve Dobson's condition by prescribing various medications. None worked. None, that is, until they tried dronabinol.

But dronabinol is not FDA-approved for use in this way, so Medicare Part D would not reimburse Dobson for the drug unless his use qualified as an approved off-label use, known as a "medically accepted indication." This case requires us to determine whether the statutory definition of "medically accepted indication" covers Dobson's off-label use of dronabinol to relieve disease-related stubborn nausea and vomiting.

We conclude that the governing statute's text and structure, as well its purpose, require the conclusion that the term "medically accepted indication" includes those off-label uses for which an approved medical compendium tends to show or helps prove the efficacy and safety of the prescribed off-label use. Because the use of dronabinol to relieve refractory, disease-related nausea and vomiting satisfies that standard, we vacate the district court's entry of summary judgment for Appellee Secretary of Health and Human Services and its denial of summary judgment for Dobson and remand with instructions to enter summary judgment for Dobson.

I.

A. Statutory and Regulatory Framework

To explain some of the factual and procedural background, we must begin with a description of the statutory and regulatory framework that governs this case.

In its current iteration, Medicare is a federal health-insurance program for those who are at least 65 years old and for the disabled, among others. 42 U.S.C. § 1395 *et seq*. Medicare traces its roots to 1965, when Congress, as part of the Social Security Act, originally created the program.

In 2003, Congress added Medicare Part D—a subsidized prescription drug benefit program. Jennifer O'Sullivan, *Medicare Part D Prescription Drug Benefit: A Primer*, Cong. Rsch. Serv. 1 (Aug. 20, 2008). https://www.everycrsreport.com/files/20080820_RL34280_e39d4ec97b3863a3a1184d12f5aa790527fd3174.pdf. To administer Medicare Part D, the Centers for Medicare & Medicaid Services ("CMS"), a part of the U.S. Department of Health and Human Services, contracts with private insurers, called "plan sponsors," to provide prescription drug coverage to Medicare beneficiaries for "covered part D drugs." 42 U.S.C. §§ 1395w-111 to 1395w-112.

Beneficiaries who enroll in Part D select their preferred sponsor and pay out-of-pocket expenses, such as monthly premiums and deductibles. Id. § 1395w-102(b); see also Akebia Therapeutics, Inc. v. Azar, 976 F.3d 86, 89 (1st Cir. 2020) (providing

background on Part D). The sponsors then receive reimbursements from the Medicare program for the cost of the covered drugs. Id. at 89.

A Medicare Part D plan will cover the cost of only those prescription drugs that are considered "covered part D drugs." *Id.* § 1395w-102(e)(1). The statute defines "covered part D drug[s]" as those that are used "for a medically accepted indication." *Id.* In turn, the statute defines "medically accepted indication" as "any use for a covered outpatient drug which is approved under the Federal Food, Drug, and Cosmetic Act or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in subsection (g)(1)(B)(i)." 42 U.S.C. § 1396r-8(k)(6); *see also id.* § 1395w-102(e)(4)(A)(ii) (incorporating definition from § 1396r-8(k)(6)).

Uses approved by the FDA are called "on-label" uses, while those that are not are called "off-label" uses. So Medicare Part D covers (1) "on-label" uses and (2) "off-label" uses that are "supported by one or more citations included or approved for inclusion in" approved drug compendia. 42 U.S.C. § 1396r-8(k)(6).

The governing statute lists three approved compendia that may provide a supporting citation for an off-label use. The compendia are "large reference books that contain a variety of information about the prescription pharmaceuticals currently available on the American market—everything from their chemical makeup to potential side-effects to the age ranges of patients the drugs have

been tested on." *United States v. King-Vassel*, 728 F.3d 707, 715 (7th Cir. 2013). As relevant here, one of the three approved compendia is known as the DRUGDEX Information System ("DRUGDEX"). 42 U.S.C. § 1396r-8(g)(1)(B)(i).

B. Factual Background

In August 2009, Dobson sustained serious injuries to his neck and spinal cord. To address these problems, he underwent surgery in September 2009. At that time, doctors implanted an artificial disk in his spinal cord. A couple months later, in December 2009, Dobson underwent a second surgery to fix some of the "hardware" that doctors had implanted in September.

Based on his injury and related surgeries, Dobson was diagnosed with Central Cord Syndrome and Eagle Syndrome. Central Cord Syndrome "is the most common form of incomplete spinal cord injury characterized by impairment in the arms and hands and to a lesser extent in the legs." *Central Cord Syndrome Information Page*, National Institute of Health (March 27, 2019), https://www.ninds.nih.gov/Disorders/All-Disorders/Central-Cord-Syndrome-Information-Page (last visited Feb. 11, 2022). The syndrome is "associated with damage to the large nerve fibers that carry information directly from the cerebral cortex to the spinal cord." *Id.* As for Eagle Syndrome, that "is characterized by recurrent pain in the middle part of the throat . . . and face." *Eagle Syndrome*, National Institute of Health (Apr. 18, 2017),

https://rarediseases.info.nih.gov/diseases/9401/eagle-syndrome (last visited Feb. 11, 2022).

Following his surgeries, Dobson developed symptoms of vomiting, frequent headaches, severe neck pain, torso pain, and weight loss. He also often experienced convulsive movements or spasms when he tried to fall asleep, and he had difficulty sleeping. Though he has received treatment for these conditions, Dobson continues to suffer from episodes of severe nausea and vomiting multiple times each day. Based on these circumstances, Dobson has also been diagnosed with autonomic dysreflexia (also known as "dysautonomia"), a syndrome common in people with spinal-cord injuries. Dysreflexia is characterized by the sudden onset of dangerously high blood pressure, excessive sweating, nausea, and cyclic vomiting.

Dobson worries that the constant vomiting will dislodge the disc in his neck. His constant nausea and vomiting also put him at risk for serious medical complications, including stroke, high blood pressure, seizures, increased muscle pain, and muscle spasms.

At first, Dobson's doctors had trouble treating Dobson's persistent nausea and vomiting because the usual drugs used to treat those symptoms would not work. Dobson even had a severe allergic reaction to one of the medications—Reglan (metoclopramide). Eventually, his doctors prescribed Marinol (a brand name of dronabinol).

The medication worked almost immediately, and Dobson's symptoms subsided. Dobson's doctor, Dr. Shaun C. Corbett, described dronabinol as a "palliative treatment for [Dobson's] disease-related symptoms of nausea and vomiting" and characterized the results of using the medication as "excellent." Indeed, Dr. Corbett explained that dronabinol was the optimal treatment for Dobson. He also opined that the DRUGDEX compendium supported Dobson's use of dronabinol.

For dronabinol, DRUGDEX lists two FDA-approved (on-label) uses and six non-FDA-approved (off-label) uses. For each cited use of dronabinol, DRUGDEX provides an overview on the particular use, its efficacy, grade of recommendation, and strength-of-evidence ratings. DRUGDEX also includes a summary that explains the evidentiary basis for each use recommended. According to the DRUGDEX listing for dronabinol, the FDA has approved dronabinol for on-label uses for "AIDS-loss of appetite" and "[c]hemotherapy-induced nausea and vomiting, in patients with inadequate response to conventional antiemetic treatments."

The DRUGDEX compendium also lists six non-FDA approved (off-label) uses. As relevant here, one of those listed uses is for "[n]ausea and vomiting, [d]isease-related, treatment refractory."

That citation has three main components: the title (noted above), the "Overview" section, and the "Summary" section.

The "Overview" section provides (1) information on efficacy, (2) a grade of recommendation, and (3) a rating on the strength of evidence. For this citation, the "Overview" says that the "[e]vidence favors efficacy," and it lists the strength of evidence as Category C, which means that the evidence for the citation is "derived from: Expert opinion or consensus, case reports or case series." This citation also has a class IIb use recommendation. A class IIb recommendation means that the "given . . . treatment may be useful, and is indicated in some, but not most, cases." Put simply, a class IIb rating, means the medication is "recommended, in some cases." (capitalization altered).

Moving to the "Summary" section, that contains information about the scientific study or evidence that provides the basis for the citation. It states that "[i]ntractable nausea and vomiting related to metastatic cancer of the gastrointestinal mucosa resolved only after addition of [dronabinol]." The remainder of the citation then summarizes a single case study of a 50-year-old patient with a metastatic malignant tumor in the mucosa of his stomach. The patient was admitted to the hospital with a variety of symptoms including "severe nausea and vomiting." The authors of the study believed the nausea and vomiting were "principally" attributed to his gastrointestinal cancer. Though the doctors prescribed various medications to alleviate the study patient's nausea and vomiting, nothing worked. Eventually, after several days in the hospital, doctors administered dronabinol, which successfully alleviated the study patient's nausea and vomiting.

The study cited in the compendium was published in the Journal of Pain and Symptom Management. See Francisco Gonzalez-Rosales & Declan Walsh, Intractable Nausea and Vomiting Due to Gastrointestinal Mucosal Metastases Relieved by Tetrahydrocannabinol (Dronabinol), 14 J. of Pain & Symptom Manag. 311 (1997), https://www.jpsmjournal.com/article/S0885-3924(97)00229-7/pdf. The study explained that after the study patient was administered dronabinol, his nausea and vomiting completely abated. Though the authors did not know with certainty how dronabinol worked to alleviate the patient's nausea and vomiting, they posited that it might work by "indirect inhibition of the vomiting center in the medulla as a result of binding to opiate receptors in the forebrain." Id. at 313.

C. Procedural Background

With this information in mind, we discuss how this case got to us. The procedural background here involves Medicare administrative proceedings as well as proceedings in the district court.

1. The Administrative Proceedings

After his injury, Dobson became a Medicare beneficiary and enrolled in a Part D prescription drug plan with UnitedHealthCare. In December 2015, Dobson's physician submitted a request to his Part D prescription drug plan for prior authorization of coverage for his dronabinol prescription. After UnitedHealthCare denied coverage, Dobson's doctor filed an appeal with the

UnitedHealthCare Medicare Part D Appeals and Grievance Department in December 2016. The Grievance Department denied the claim because it concluded that "[d]ronabinol is not FDA approved for nausea and vomiting not associated with cancer, chemotherapy, or following breast surgery. This condition is not one of the uses for the drug listed in . . . DRUGDEX. Therefore, this drug is not a Medicare Part D drug."

Dobson filed another appeal in February of 2017. Again, the Grievance Department denied the appeal. It concluded that "[d]ronabinol is not FDA approved for nausea and vomiting related to Eagle Syndrome and central cord syndrome. This condition is not one of the uses for the drug listed in . . . DrugDex. Therefore, this drug is not a Medicare Part D drug."

Dobson then appealed that decision through three levels of Medicare administrative review. Primarily, Dobson argued that the DRUGDEX entry titled, "Nausea vomiting, Disease-related, treatment refractory," supported his use of dronabinol. On April 4, 2017, Dobson filed a Reconsideration Request with Medicare Part D's Independent Review Entity ("IRE"), MAXIMUS Federal Services. The IRE ruled against Dobson, concluding that the Part D Plan is not required to cover dronabinol to "treat an enrollee with nausea and vomiting related to Eagle syndrome and central cord syndrome." It also opined that the approved compendia "do not contain any citations to support the use of [dronabinol] for these conditions." As a result, the IRE concluded, the drug "is not

being prescribed for a medically accepted indication as defined by Medicare law."

Next, on June 30, 2017, Dobson appealed the IRE's decision to an administrative law judge ("ALJ") and requested a hearing. The ALJ held a telephonic hearing on August 14, 2017. Dobson testified at the hearing and was represented by counsel. The ALJ later issued a decision affirming the IRE's denial of coverage for Dobson's use of Dronabinol. In reaching this decision, the ALJ concluded that "[d]ronabinol is not approved by the FDA for the Enrollee's medical condition or indicated by the appropriate compendia as accepted for treatment of the Enrollee's medical condition."

Finally, Dobson timely appealed the ALJ's decision to the Medicare Appeals Council. The Council upheld the ALJ's denial of Part D coverage for Dobson's off-label use of dronabinol. According to the Council, the citation in the DRUGDEX compendium supported "the use of dronabinol to treat nausea and vomiting related to [only] metastatic cancer of the gastronintestinal mucosa that is treatment refractory." For that reason, the Council concluded, the citation could not be used to support the use of dronabinol to treat Central Cord Syndrome and Eagle Syndrome. The Council also opined that the medically accepted indications standard could not "turn on an enrollee's symptoms, alone." Rather, in the Council's opinion, the determination must be based on the diagnosis or condition for which the drug is being prescribed.

Nevertheless, the Council did agree with the parties that dronabinol was medically necessary in Dobson's case.

2. District Court Proceedings

After the Council's decision, Dobson filed suit in the district court. The parties filed cross-motions for summary judgment. After consideration, the district court entered an order denying Dobson's motion and granting the Secretary's.[1]

In its order, the district court first addressed whether the Council's decision should be afforded deference under either *Chevron USA v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984) or *Skidmore v. Swift & Co.*, 323 U.S. 134 (1944). The district court determined that *Chevron* does not apply because Congress did not "delegate authority to the Secretary [of the Department of Health and Human Resources] 'to make rules carrying the force of law' with respect to Part D coverage of an off-label drug, nor did it explicitly leave a gap for the Secretary to fill with rules that carry the force of law." But the district court did apply *Skidmore* deference to the Council's decision. In so doing, the district court reasoned that Medicare law is "complex," which puts the Council "in a better position to evaluate questions involving subject matter[s] that are technical, complex, and dynamic."

[1] The parties consented to adjudication by a magistrate judge.

As for the merits, the district court was persuaded by the Council's reading of the relevant citation in the DRUGDEX compendium. The court noted that, upon "[r]eading the entire citation," the Council found that the citation applied "to [only] cases where patients are suffering from metastatic cancer of the gastrointestinal mucosa." In other words, the district court, opined, the citation did not apply to "*any* case where a patient has nausea and vomiting related to *any* disease." In the district court's view, only that reading avoided rendering "the remainder of the citation superfluous." The district court also found that the Council's interpretation was supported by the Medicare Prescription Drug Benefit Manual and previous Council decisions.

Dobson filed a timely notice of appeal.

II.

We review de novo the district court's grant of summary judgment to the Secretary, "viewing the facts and drawing all reasonable inferences in favor of the nonmoving party." *Moore ex re. Moore v. Reese*, 637 F.3d 1220, 1231 (11th Cir. 2011). "Summary judgment is appropriate when 'there is no genuine dispute as to any material fact' and the moving party is entitled to judgment as a matter of law." *Id.* (quoting Fed. R. Civ. P. 56(a)).

We review the Secretary's decision regarding a claim for Medicare benefits under the standards set forth in 42 U.S.C. § 405(g), which has been incorporated into the Medicare statute at

42 U.S.C. § 1395w-22(g)(5) and 42 U.S.C. § 1395ff(b)(1)(A). *See Gulfcoast Med. Supply, Inc. v. Sec'y, Dep't of Health & Human Servs.*, 468 F.3d 1347, 1350 n.3 (11th Cir. 2006) ("*Gulfcoast*"). Under § 405(g), we review the Secretary's findings of fact for substantial evidence. 42 U.S.C. § 405(g) ("The findings of [the Secretary] as to any fact, if supported by substantial evidence, shall be conclusive"); *Gulfcoast*, 468 F.3d at 1350 n.3. "Substantial evidence is more than a scintilla and is such relevant evidence as a reasonable person would accept as adequate to support a conclusion." *Fla. Med. Ctr. of Clearwater, Inc. v. Sebelius*, 614 F.3d 1276, 1280 (11th Cir. 2010). With respect to the Secretary's legal conclusions, we engage in de novo review. *See Martin v. Soc. Sec. Admin., Comm'r*, 903 F.3d 1154, 1159 (11th Cir. 2018).

III.

A. The initial question here—the meaning of "supported by" in 42 U.S.C. § 1396r-8(k)(6)—presents a question of law

Here, the Secretary argues that Dobson challenges a factual finding, so we should review for substantial evidence. On this record, we disagree. The parties agree on the key facts related to Dobson's medical history. For example, they agree that he had two surgeries to his back and neck, that he was diagnosed with Central Cord Syndrome and Eagle Syndrome, that he suffers from persistent nausea and vomiting as a result of his back and neck injuries,

and that dronabinol has helped alleviate Dobson's nausea and vomiting.

The only question at issue is whether Dobson's use of the drug dronabinol to alleviate his constant nausea and vomiting meets the standard Congress set for coverage under Medicare Part D—that is, whether it is "supported by [at least one] citation[] included . . . in [DRUGDEX]." 42 U.S.C. § 1396r-8(k)(6).

In the first instance, that requires us to construe the term "supported by" in the governing statute. And statutory construction presents a question of law. *United States v. Endotec, Inc.*, 563 F.3d 1187, 1194 (11th Cir. 2009). Indeed, "[t]he judiciary is the final authority on issues of statutory construction and must reject administrative constructions which are contrary to clear congressional intent." *Chevron,* 467 U.S. at 843 n.9.

B. The text, structure, purpose, and legislative history of 42 U.S.C. § 1396r-8(k)(6) require the conclusion that "supported by" means that the compendium citation relied upon must tend to show or help prove the efficacy and safety of the prescribed off-label use

When we review an agency's construction of a statute it administers, the first step always requires us to ascertain whether the meaning of the provision is "genuinely ambiguous" on the question at issue. *See Kisor v. Wilkie*, 139 S. Ct. 2400, 2414 (2019); *see also Chevron*, 467 U.S. at 842-43. For "the possibility of deference

can arise only if a [provision] is genuinely ambiguous." *Kisor*, 139 S. Ct. at 2414; *see also Chevron*, 467 U.S. at 842-43. And as the Supreme Court has recently emphasized, when [the Supreme Court] use[s] that term, [it] mean[s] it—genuinely ambiguous, even after a court has resorted to all the standard tools of interpretation." *Kisor*, 139 S. Ct. at 2414. Indeed, "a court cannot wave the ambiguity flag just because it found the [provision] impenetrable on first read." *Id.* at 2415.

"If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron*, 467 U.S. at 842-43. In that case, "there is no plausible reason for deference." *Kisor*, 139 S. Ct. at 2415. As the Court has explained in the context of considering whether deference is due an agency's interpretation of its own regulation, "if there is only one reasonable construction of a [provision]—then a court has no business deferring to any other reading, no matter how much the agency insists it would make more sense." *Id.* "Deference in that circumstance would permit the agency, under the guise of interpreting a [provision], to create *de facto* a new [provision]." *Id.* (cleaned up).

Therefore, we begin our inquiry with a hard and deep look at the governing statutory provision. As we explain below, our review yields fruit: the intent of Congress here is clear and 42 U.S.C. § 1396r-8(k)(6) is not genuinely ambiguous. For that reason, we do not defer to the Medicare Appeals Council's interpretation of the

term "supported by," and instead must give effect to the unambiguously expressed intent of Congress.

Here, we must determine the meaning of "supported by [at least one] citation[] included . . . in [DRUGDEX]" in 42 U.S.C. § 1396r-8(k)(6). We ascertain whether Congress had an intention on that question by "employing traditional tools of statutory construction." *Id.* at 843 n.9. Those tools include reviewing the text of the statute and the statute's structure (which we examine using the rules of statutory construction as appropriate), the statute's stated purpose, and the statute's legislative history. *See In re Gateway Radiology Consultants, P.A.*, 983 F.3d 1239, 1256, 1261 n.9 (11th Cir. 2020).

The Supreme Court has explained that "our inquiry begins with the statutory text," and if that is "unambiguous," it "ends there as well." *Nat'l Ass'n of Mfrs. v. Dep't of Def.*, 138 S. Ct. 617, 631 (2018) (citation and quotation marks omitted). Here, the statutory scheme does not define the material term "supported by." So we must consider the "common usage of words for their meaning." *In re Walter Energy, Inc.*, 911 F.3d 1121, 1143 (11th Cir. 2018) (citation and quotation marks omitted). To do that, "we often look to dictionary definitions for guidance." *Id.* Nevertheless, we must then consider the term as used in its statutory context. *Id.* Along the way, the canons of construction can provide helpful assistance in understanding the broader statutory context. *Id.*

The *Oxford English Dictionary* defines the verb "support" to mean "[t]o provide evidence or authority for, or corroboration of, (a statement, etc.); to bear out, substantiate." *Support*, *v.*, Oxford English Dictionary, https://www.oed.com/view/Entry/194674?rskey=MoK3yx&result=2#eid (last visited Feb. 11, 2022) (definition 6.b). Similarly, *Webster's New World College Dictionary* defines "support" as "to show or tend to show to be true; help prove; vindicate, or corroborate." *See Support*, Webster's New World College Dictionary (3d ed. 1997).

Using these definitions to construe the phrase "supported by" as used in § 1396r-8(k)(6) therefore requires the conclusion that the compendium citation must tend to show or help prove the efficacy and safety of the prescribed off-label use. Nothing about the common meaning of "support" means that a compendium citation must hyperspecifically identify a prescribed off-label use to tend to show or help prove its efficacy and safety.

And while the compendia themselves are obviously not a part of the statute, any reading of the statute must make sense in terms of how it applies to the compendia. So it is appropriate to examine the compendia entries for additional clues they may provide in helping us to understand what Congress meant when it required a compendium entry to "support" the prescribed off-label use.

We use the DRUGDEX entry at issue here as an example. As relevant here, under "Dronabinol," the DRUGDEX entry

identifies six "[n]on-FDA [u]ses": (1) "Gilles de la Tourette's syndrome"; (2) "Loss of appetite, Cancer-related"; (3) "Multiple sclerosis – Spasticity"; (4) "Nausea and vomiting, Disease-related, treatment refractory"; (5) "Postoperative nausea and vomiting; Treatment and Prophylaxis"; and (6) "Pruritus, Cholestasis-associated, treatment refractory." Notably, these titles range from the very specific—"Pruritus, Cholestasis-associated, treatment refractory"—to the more general—"Nausea and vomiting, Disease-related, treatment refractory." The pruritus[2] entry, for example, specifies an off-label use of dronabinol for itchy skin, but only as the itchiness is associated with cholestasis[3]—a very specific condition—and then, only when the itching is stubborn and otherwise unmanageable. Meanwhile, the nausea-and-vomiting entry, at least by its title, encompasses nausea and vomiting that are related to any kind of disease, as long as the nausea and vomiting are stubborn and otherwise unmanageable.

In other words, some citation titles appear to convey very specific disease-focused off-label uses, while others suggest broader off-label uses geared towards particular symptoms but arising from disease more generally. That the titles to the drug-compendium

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[2] Pruritus is itching of the skin. https://www.mayoclinic.org/diseases-conditions/itchy-skin/symptoms-causes/syc-20355006 (last visited Feb. 11, 2022).

[3] Cholestasis is the "reduction or stoppage of bile flow." https://www.merckmanuals.com/home/liver-and-gallbladder-disorders/manifestations-of-liver-disease/cholestasis (last visited Feb. 22, 2022).

citations identify both very specific and more general off-label uses suggests the difference between the two types of entries has meaning—namely, that some citations support only limited, precise applications, while others support broader applications.

Of course, we don't hold drug-compendium entries to the canons we apply to statutory construction. But we do presume Congress was aware of the differences among entries when it defined "[m]edically accepted indication" to be one "which is supported by one or more citations included or approved for inclusion in" approved medical compendia and it authorized the Secretary to add compendia such as DRUGDEX to the list. *See* 42 U.S.C. § 1396r-8(g)(B)(i)(III).

Thus, considering only the title of the citation on which Dobson relies—"Nausea and vomiting, Disease-related, treatment refractory"—we would have to conclude that the citation supports Dobson's use: nausea and vomiting—check; disease-related—check (Central Cord Syndrome and Eagle Syndrome); treatment refractory—check (the usual drugs used to treat nausea and vomiting did not work, and Dobson had a severe allergic reaction to one of them (metoclopramide)).

But of course, the title of a citation alone does not support an off-label application if the citation's overview and summary are inconsistent with that application. So we must also consider those.

Beginning with the overview section, nothing from this part of the citation contraindicates use of dronabinol under Dobson's circumstances. As we have mentioned, the overview indicates that (1) the "[e]vidence favors efficacy" for adults; (2) the strength of evidence falls within "Category C," meaning the evidence for the citation is "derived from: Expert opinion or consensus, case reports or case series"; and (3) the recommendation is class IIb, meaning that "given . . . treatment may be useful, and is indicated in some, but not most, cases." Using dronabinol for refractory, disease-related nausea and vomiting falls within the parameters the overview identifies. Nausea and vomiting are common conditions associated with a variety of circumstances, many of which are not disease-related, such as seasickness, pregnancy, vertigo, surgery, and more. And Dobson's doctors' attempts to use the "usual" antinausea and vomiting drugs on Dobson before turning to dronabinol suggests that even disease-related nausea and vomiting are not generally untreatable with other drugs' labeled uses. So Dobson's understanding of the citation to support refractory, disease-related nausea and vomiting is consistent with the notion indicated in the overview that "treatment [with dronabinol] may be useful, and is indicated in some, but not most, cases" of nausea and vomiting.

As for the summary section, that states, "Intractable nausea and vomiting related to metastatic cancer of the gastrointestinal

mucosa resolved only after addition of tetrahydrocannabinol."[4] It then goes on to explain, in relevant part,

> Adding tetrahydrocannabinol (THC) to therapy produced resolution of refractory nausea and vomiting in a 50-year-old man with metastatic malignant melanoma. . . . On day 8 after admission, oral THC (Dronabinol(R)) 5 mg after meals and at bedtime was initiated. Four days later he was tolerating a soft diet. By the next day, he was reporting no pain, nausea, or vomiting. He was discharged 6 days after the start of THC, with no recurrence of nausea or vomiting. The authors attributed the patient's [nausea and vomiting] ***principally*** to the diffuse gastrointestinal mucosal metastases.

(emphasis added). We think there are two ways to view this summary: (1) as simply a description of the evidence on which the more general off-label use identified in the citation title is based (in which case the off-label use is limited by the citation title's

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[4] Dronabinol is an isomer of tetrahydrocannabinol. https://pubchem.ncbi.nlm.nih.gov/compound/Dronabinol (last visited Feb. 11, 2022). Isomers are "[m]olecules that share the same chemical formula but have their atoms connected differently, or arranged differently in space." *United States v. Phifer*, 909 F.3d 372, 376 (11th Cir. 2018) (quoting *Hydrocarbon structures and isomers*, Khan Academy, https://www.khanacademy.org/science/biology/properties-of-carbon/hydrocarbonstructures-and-functional-groups/a/hydrocarbon-structures-and-isomers).

specifications), or (2) as a limitation on the citation title, to only the precise off-label use described in the study that appears in the summary. It cannot be viewed as something in between because the citation provides no limiting principle for such a construction. For three reasons, we think the first view is the better one in this case.

First, as the summary notes, the study's authors were careful to qualify their attribution of the patient's nausea and vomiting "principally" to his gastrointestinal mucosal metastases. That—and that the study on which the citation is based notes that the patient suffered from numerous ailments—suggests that the authors did not attribute the patient's nausea and vomiting entirely to his gastrointestinal mucosal metastases. *See* Gonzalez-Rosales & Walsh, *supra*, *J. of Pain & Symptom Mgmt.*, at 311 ("[W]e believe that the main cause [of the patient's nausea and vomiting] was diffuse metastatic disease in the gastrointestinal tract mucosa."). In other words, they attributed the nausea and vomiting at least in part to other diseases. That suggests the citation is not intended to be limited to addressing only that nausea and vomiting in patients suffering from diffuse gastrointestinal mucosal metastases.

Second, viewing the study on which the citation is based as limiting so narrowly what the citation supports to only those cases where nausea and vomiting were attributable to gastrointestinal mucosal metastases would render the title of the citation irrelevant and superfluous. But the same cannot be said of the summary if we read the title to mean what it says. In that case, the summary

has meaning as providing the evidence that warrants the citation's title.

Third, the study's authors theorized that dronabinol resolves nausea and vomiting through a "central action . . . , perhaps by indirect inhibition of the vomiting center in the medulla as a result of binding to opiate receptors in the forebrain." Nothing about that process is described in a way peculiar to cases of diffuse gastrointestinal mucosa metastases (as opposed to being applicable to nausea and vomiting caused by disease in general).

Overall, we think the common understanding of "support," especially in conjunction with a review of the types of entries contained in DRUGDEX and the particular citation involved here, requires the conclusion that the DRUGDEX citation must tend to show or help prove the efficacy and safety of the prescribed off-label use. It does not, as the Medicare Appeals Council concluded, demand that every aspect of the DRUGDEX citation must match the prescribed off-label use precisely. Had that been Congress's desire, Congress easily could have used those terms in its definition of "medically accepted indication." But it didn't.

Of course, we need look no further than the clear terms of the statute. *See CBS Inc. v. PrimeTime 24 Joint Venture*, 245 F.3d 1217, 1222 (11th Cir. 2001). We note, however, that the legislative history of Congress's expansion of Medicare Part D to include off-label uses also supports this plain-text reading of § 1396r-8(k)(6). *See Id.* at 1229 n.7 (recognizing the "bedrock principle" that there

is no need to resort to legislative history where statutory text is clear, but nonetheless reviewing legislative history that "supports and complements the plain meaning of statutory language").

Congress's decision to amend Medicare Part D to reimburse for previously uncovered off-label uses of outpatient drugs that are supported by a citation in the compendia obviously represented an enlargement of Medicare drug coverage. Though added in 2008, *see* Pub. L. 110-275, 122 Stat. 2583, § 182(a) (July 15, 2008), this provision echoes a similar provision added to the Medicare statute by the Omnibus Budget Reconciliation Act of 1993, Pub. L. 103-66, 107 Stat. 312–695 Stat. 1025, § 13553(b)(3) (Aug. 10, 1993), codified at 42 U.S.C. § 1395x(t)(2)(B). As relevant here, the 1993 provision expanded coverage for the "medically accepted indication[s]" for which anticancer drugs could be used. *Id.* It defined "medically accepted indication," in part, as "such use [that] is supported by one or more citations which are included (or approved for inclusion) in one or more of the following compendia . . . ." *Id.* The 1993 amendment was enacted following the General Accounting Office's ("GAO") 1991 Report to the Chairman, Committee on Labor and Human Resources, U.S. Senate (written in response to a request by that Senator), entitled, "Off-Label Drugs: Reimbursement Policies Constrain Physicians in Their Choice of Cancer Therapies" ("GAO Report").

That report found, among other things, that Medicare "reimbursement policies can influence how cancer patients are

treated." GAO Report at 5. Indeed, roughly 23 percent of responding oncologists stated that they altered their preferred treatments because certain off-label uses were not covered by Medicare and they had cost concerns. *Id.* at 35. So GAO recommended the adoption of "a policy for Medicare reimbursement for off-label drug use." *Id.* at 5. It noted that although off-label use can be beneficial even when it is not supported by a compendium citation, *id.* at 40, use of the drug compendia can be helpful in determining what drug applications are safe, effective, and not investigational, *id.* at 41.[5]

There appears to be no legislative history expressing any reason for the addition of the 2008 amendment to the definition of "medically accepted indication" in § 1396r-8 of Part D. But as we

[5] During a 1996 hearing before the Subcommittee on Human Resources and Intergovernmental Relations of the Committee on Government Reform and Oversight of the House of Representatives, Sarah Jaggar, Director of Health Services Quality and Public Health Issues for the General Accounting Office, confirmed that the concerns documented in the 1991 GAO report motivated the 1993 amendments, as she testified to Congress about the need for laws regulating promotion and advertisement of off-label drug uses. *See* Off-Label Drug Use and FDA Review of Supplemental Drug Applications Report of Hearing before the Subcommittee on Human Resources and Intergovernmental Relations of the Committee on Government Reform and Oversight of the House of Representatives, 104th Cong., 2d Sess. (Sept. 12, 1996), at 4. During her testimony, she noted that "reimbursement concerns were the primary ones associated with the drug label in the earlier part of this decade [but that] this issue seems to have declined significantly since that time [because of] legislation in 1993 that required Medicare carriers to rely on sources in addition to the FDA-approved label in making reimbursement decisions for cancer therapy." *Id.* at 13.

have mentioned, the language of that amendment is very similar to that of the 1993 amendment to the meaning of "medically accepted indication" under Part B of Medicare. We think that suggests the same or very similar concerns motivated the 2008 amendment to Part D—namely, that Medicare participants receive coverage for off-label uses but that those off-label uses be objectively demonstrated to be efficacious and safe, as demonstrated by their inclusion in one of the drug compendia. Plus, the statutory definition of "medically accepted indication" logically indicates as much.

For these reasons, we conclude that the language and structure of § 1396r-8(k)(6) and the Medicare statute as a whole require the conclusion that "supported by one or more citations included or approved for inclusion" in DRUGDEX means that the DRUGDEX citation relied upon must tend to show or help prove the efficacy and safety of the prescribed off-label use.

We think the DRUGDEX citation for dronabinol titled "Nausea and vomiting, Disease-related, treatment refractory" satisfies that requirement as it pertains to Dobson's use of the drug to treat his Central-Cord-Syndrome and Eagle-Syndrome-related refractory nausea and vomiting. As we have noted, Dobson's nausea and vomiting are disease-related and treatment-refractory, and the hypothesized mechanism by which dronabinol works to relieve nausea and vomiting is believed to be "perhaps by indirect inhibition of the vomiting center in the medulla as a result of binding to opiate receptors in the forebrain"—a process that reasonably and

fairly would be assumed to occur in disease-related cases of nausea and vomiting generally.

We therefore vacate the entry of summary judgment for the Secretary and remand with instructions to enter summary judgment for Dobson because Dobson's use of dronabinol to treat his Central-Cord-Syndrome and Eagle-Syndrome-related refractory nausea and vomiting is "supported by one or more citations included or approved for inclusion" in DRUGDEX. 42 U.S.C. § 1396r-8(k)(6).

IV.

For these reasons, we **VACATE** the entry of summary judgment for the Secretary and the denial of summary judgment for Dobson and **REMAND WITH INSTRUCTIONS** to enter summary judgment for Dobson.

VACATED AND REMANDED.