UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

JAZZ PHARMACEUTICALS, INC., Plaintiff, v. AVADEL CNS PHARMACEUTICALS, LLC, Defendant.	Civil Action No. 21-691-GBW

FEDERAL TRADE COMMISSION'S BRIEF AS *AMICUS CURIAE*

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Pending before the Court is Defendant Avadel CNS Pharmaceuticals, LLC's renewed motion for an order delisting one of Plaintiff Jazz Pharmaceuticals, Inc.'s patents from the FDA's Orange Book. Under the Hatch-Waxman Act, a brand drug company may only list patents in the Orange Book that claim either a drug or a "method of using" a drug. Other types of patents, such as those on packaging or manufacturing processes, may not be listed, even if they might be infringed by a competing drug product. Congress has created a statutory delisting procedure to remove such patents from the Orange Book.

The strict statutory limits on Orange Book patent listings serve a vital purpose because the listing process has significant implications for consumers and for competition. If a brand company sues a competitor for infringement of an Orange Book listed patent, it triggers an automatic statutorily imposed bar on the FDA's ability to approve the competitor's drug for up to 30 months. When triggered by an appropriately listed patent, this 30-month stay, as it is commonly known, reflects Congress's intent to balance the interests of brand and generic drug manufacturers by facilitating the resolution of certain types of patent disputes before generic or 505(b)(2) products are introduced. But when this stay is triggered by a patent that does not meet the statutory listing criteria, the stay merely blocks consumer access to a competing product that might reduce prices, improve quality, or both. Given the high cost of many drugs, even a short delay in competition can have enormous consequences for the public.

The prospect of an automatic 30-month block on competition (and accompanying higher profits) can incentivize brand companies to wrongfully list non-listable patents in the Orange Book. These companies take advantage of the FDA's long-standing position that it has a purely ministerial role in the listing process. The FDA does not verify that the patents submitted by the brand actually meet the statutory listing criteria nor does the FDA remove improperly listed

patents. Thus, the only available remedy for an improper Orange Book listing is the statutory delisting provision that Avadel has invoked in this case.

The patent at issue—Jazz's '963 patent—involves the implementation of a distribution system that Jazz uses to ensure its Xyrem product is dispensed only to patients with a valid prescription. The FTC takes no position on the scope or claim construction of the '963 patent. As a general matter, however, patents that claim a distribution system do not meet the Orange Book listing criteria; to the extent they claim a method at all, it is a method of *distributing* a drug rather than a method of *using* one. This is an important distinction. A method of using a drug encompasses its selection, prescription, dosing, and administration. A method of distributing a drug, however, involves only the logistical processes used to transfer the drug safely from one entity to another in the supply chain. To the extent that the '963 patent claims only a distribution system, it does not meet the statutory criteria for listing in the Orange Book and should be delisted. A contrary result may cause substantial harm to consumers of sodium oxybate products and encourage other brand companies to improperly list distribution patents to block competition for other drugs.

INTEREST OF THE FTC

The FTC is an independent agency charged by Congress with protecting the interests of consumers by enforcing competition and consumer protection laws.[1] It exercises primary responsibility for federal antitrust enforcement in the pharmaceutical industry.[2] The Commission has substantial experience evaluating pharmaceutical competition under the Hatch-Waxman Act

[1] 15 U.S.C. § 41–58.

[2] For a summary of the FTC's actions in the pharmaceutical industry, see *Overview of FTC Actions in Pharmaceutical Products and Distribution* (July 2022), https://www.ftc.gov/system/files/ftc_gov/pdf/2022.07.12OverviewPharmafinalupdated.pdf.

and has brought numerous enforcement actions challenging anticompetitive abuses of the Hatch-Waxman framework.[3]

The FTC has long been concerned about Orange Book listing abuses. The Commission first examined the effect of Orange Book listings on competition as part of a 2002 study. *See* Generic Drug Entry Prior to Patent Expiration: An FTC Study, at 39-52 (2002) ("FTC Study"). Around the same time, the FTC entered an order against Biovail Corporation for, among other things, wrongfully listing a patent in the Orange Book to block generic competition. Order, *In re Biovail Corp.*, FTC Dkt. No. C-4060 (Oct. 2, 2002). The FTC also filed an amicus brief on improper Orange Book listings in the private Buspirone litigation. *See* Memorandum of Law of *Amicus Curiae* the Federal Trade Commission, *In re: Buspirone Patent Litig.*, No. 1:01-md-1410-JGK (S.D.N.Y. Jan. 8, 2002) (Doc. No. 31). In addition to Orange Book abuse, the FTC has successfully challenged sham patent litigation, a related form of regulatory abuse in which a brand company files an objectively baseless patent suit to obtain an automatic 30-month stay. *See FTC v. AbbVie, Inc.*, 976 F.3d 327, 339 (3d Cir. 2020). Although this case involves a dispute between private parties, it may have much broader implications for the Commission's competition mission and for consumers.

BACKGROUND

The Hatch-Waxman framework and Orange Book patent listings

Congress passed the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act,[4] to "'speed the introduction of low-cost generic

[3] *See, e.g. FTC v. Actavis, Inc.*, 570 U.S. 136 (2013); *Impax Labs., Inc. v. FTC*, 994 F.3d 484 (5th Cir. 2021); *FTC v. AbbVie Inc.*, 976 F.3d 327 (3d Cir. 2020); *FTC v. Shkreli*, 581 F. Supp. 3d 579 (S.D.N.Y. 2022); *King Drug Co. of Florence, Inc. v. Cephalon, Inc.*, 88 F. Supp. 3d 402 (E.D. Pa. 2015).

[4] Pub. L. No. 98-417, 98 Stat. 1585 (1984), 21 U.S.C. § 355 and 31 U.S.C. § 271.

drugs to market' and promote competition." *AbbVie*, 976 F.3d at 339 (quoting *FTC v. Actavis, Inc.*, 570 U.S. 136, 142 (2013)). The first company to seek approval for a novel drug must file a New Drug Application (NDA) and go through the FDA's "full-length" application process, which requires extensive safety and efficacy data. *See AbbVie*, 976 F.3d at 338–39. The Act then allows subsequent companies to seek FDA approval for similar drugs through a streamlined process. This in turn allows them to get to market faster and offer their competing products at a lower cost. The net result is significant health care savings for consumers.

The Hatch-Waxman Act's streamlined application process offers two pathways. A company seeking to market an essentially identical generic version of a brand drug can file an Abbreviated New Drug Application (ANDA) under Section 505(j). *See id.* at 339. An ANDA applicant does not need to do its own safety or efficacy studies. Instead, it can rely on the brand company's data so long as it demonstrates to the FDA that its product is bioequivalent to the brand—meaning that it contains the same active ingredient and is absorbed into the body in the same way. *See* 21 U.S.C. § 355(j)(2)(A)(iv).

Alternately, a company seeking to market a modified version of an existing brand drug—such as one with a "new indication or new dosage form"—can file a so-called hybrid NDA under Section 505(b)(2). *AbbVie*, 976 F.3d at 339. Like an ANDA applicant, a 505(b)(2) applicant "need not produce all safety and efficacy data about the drug." *Id.* It must only "produce some data, including whatever information is needed to support the modifications." *Id.* (cleaned up). Because a 505(b)(2) applicant does not need to re-do all of the brand company's testing, it saves substantial costs, resulting in lower prices for consumers.

The Hatch-Waxman framework also has provisions "that encourage the quick resolution of patent disputes" for certain types of patents. *Id.* During the initial NDA application, "the

Hatch-Waxman Amendments and FDA regulations direct brand manufacturers to file information about their patents." *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405 (2012). A brand NDA applicant must submit "the patent number and the expiration date of any patent which claims the drug for which the [brand] submitted the [application] or which claims a method of using such a drug." *Id.* (discussing 21 U.S.C. § 355(b)(1)).[5] The brand must also provide a description of any method-of-use patent it submits, known as a use code. *Id*. The brand may not submit patents that do not cover the drug or a method of using the drug, even if those patents could potentially be asserted against a competing product.

Once a brand applicant has received NDA approval, the FDA takes the patent information the company submitted—patent numbers, expiration dates, and use codes—and publishes it in "a brightly hued volume known as the Orange Book." *Id*. at 405–06. The FDA's role in this listing process is "purely ministerial." *Organon Inc. v. Mylan Pharms., Inc.*, 293 F. Supp. 2d 453, 458–59 (D.N.J. 2003). Even though the FDA does not scrutinize the accuracy of the information provided by the brand company, any subsequent ANDA or 505(b)(2) applicant must then review the listed patents and make one of several certifications to "assure the FDA that its proposed [] drug will not infringe" them. *Caraco*, 566 U.S. at 406; *see also AbbVie*, 976 F.3d at 339. If the applicant seeks to market its product before the expiration date of a listed patent, it must make a "paragraph IV certification" that the patent is either invalid or the applicant's

[5] In 2021, the Orange Book Transparency Act of 2020, Pub. L. No. 116-290, 134 Stat. 4889, amended the language of 21 U.S.C. § 355(b)(1) and 355(c)(2). The two categories of patents requiring submission remain the same, although the "claims the drug" patent category has been clarified to cover only "a drug substance (active ingredient) patent or a drug product (formulation or composition) patent."

product will not infringe it. 21 U.S.C. § 355(b)(2)(A)(iv), 355(j)(2)(A)(vii)(IV); *AbbVie*, 975 F.3d at 339.[6]

A paragraph IV certification constitutes an act of statutory infringement of the relevant patent. *Caraco*, 566 U.S. at 407; *AbbVie*, 976 F.3d at 339–40. If the brand company files a patent suit within 45 days, it receives an automatic 30-month stay during which the FDA cannot approve the competitor's application. 21 U.S.C § 355(c)(3)(C), 355(j)(5)(B)(iii); *see also AbbVie*, 976 F.3d at 340. This 30-month stay is not a "stay" in the traditional sense. It is not ordered or enforced by a court, but instead is a hold on the FDA's regulatory approval process that triggers automatically if paragraph IV patent litigation is initiated within the specified timeframe.

Originally, the Hatch-Waxman Act did not provide any way to remove improperly listed patents from the Orange Book. In the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2452 (the "MMA"), however, Congress created a "delisting" mechanism to address improper listings. *See Caraco*, 566 U.S. at 408. An ANDA or 505(b)(2) applicant that is sued for infringement of an Orange Book listed patent can file a counterclaim "seeking an order requiring the [brand] to correct or delete" the listing if the patent does not claim either (a) the brand drug, or (b) "an approved method of using the drug." 21 U.S.C. § 355(c)(3)(D)(ii)(I), 355(j)(5)(C)(ii)(I). This delisting counterclaim is the

[6] There is one exception to this rule: if the applicant does not intend to market its product for the use described in the brand's use code (for example, if a drug has multiple indications and an applicant seeks approval only for unpatented ones), the applicant can file a "method of use carveout" statement to this effect and avoid making any certification. This in turn avoids the automatic 30-month stay. *See* 21 U.S.C. § 355(b)(2)(B).

only effective way to remove an inappropriately listed patent.[7] Delisting a patent from the Orange Book negates a paragraph IV certification and nullifies any 30-month stay based on that patent.

Xyrem, its REMS, and the '963 patent

Jazz Pharmaceuticals, Inc. ("Jazz") holds an approved NDA for Xyrem, a sodium oxybate oral solution used to treat narcolepsy. Sodium oxybate has been a treatment for narcolepsy since the 1960s, and the compound itself is no longer covered by any patents. *See In re Xyrem (Sodium Oxybate) Antitrust Litig.*, 555 F. Supp. 3d 829, 838 (N.D. Cal. 2021). Xyrem was approved in 2002. Jazz did not develop Xyrem but rather acquired it in 2005 when it purchased another drug company. *See In re Xyrem*, 555 F. Supp. 3d at 838. Since then, Jazz has obtained multiple patents relating to Xyrem's use and distribution. Xyrem remains an expensive and highly profitable brand drug product even 20 years after introduction. Xyrem's most recent annual sales were $1.3 billion,[8] and in 2020 Medicare Part D alone spent an average of $14,360 per prescription and $138,116 per beneficiary on Xyrem, totaling $287.1 million.[9]

[7] In addition to the delisting counterclaim, 21 U.S.C. § 355(j)(5)(B)(iii) provides a mechanism for a court in which the infringement suit is pending to lengthen or shorten the stay if "either party to the action fail[s] to reasonably cooperate in expediting the litigation." This rarely used provision has been generally limited to situations where "a party obstructed discovery, sought a stay of the underlying action, or otherwise interfered with the expeditious resolution of the infringement action." *Bayer Schera Pharma AG v. Sandoz, Inc.*, No. 08 Civ. 03710(PGG), 2010 WL 3447906, at *4 (S.D.N.Y. Sept. 2, 2010); *see also Dey, L.P. v. Ivax Pharms., Inc.*, 233 F.R.D. 567 (C.D. Cal. 2005).

[8] Jazz Pharmaceuticals, Inc., Annual Report (Form 10-K) (Mar 1, 2022), at 7.

[9] Medicare Part D Drug Spending, https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-d-spending-by-drug.

Sodium oxybate is a controlled substance. *See* Feb. 27, 2015 Letter from Billy Dunn, FDA to Jazz Pharms. ("Dunn Ltr").[10] Because of the potential for misuse and abuse, including as a dangerous "date rape" drug, the FDA requires that sodium oxybate products have an appropriate Risk Evaluation and Mitigation Strategy (REMS). A REMS is a set of FDA-mandated requirements to mitigate the safety risks of certain dangerous drugs. The 2007 Food and Drug Administration Amendments Act (FDAAA)[11] authorizes the FDA to require a REMS when necessary to ensure that a drug's benefits outweigh its risks. The specific program can take a variety of forms. For example, a REMS might be as simple as a labeling requirement to highlight the drug's risks and safe handling. At the other end of the spectrum, a REMS might strictly restrict distribution such that pharmacies must verify that the prescriber and patient are enrolled in the REMS before dispensing the drug.[12]

The Xyrem REMS falls on the stricter side of the spectrum. To avoid misuse, Xyrem can only be distributed to patients with a valid prescription, and the REMS contains procedures to ensure that it is not dispensed to others.[13] Jazz's Xyrem REMS technically requires the distribution of Xyrem through a single-pharmacy system. Because the FDA views the single

[10] Available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/021196Orig1s015ltr.pdf.

[11] 21 U.S.C. § 355-1.

[12] *See generally What's in a REMS?*, FDA, https://www.fda.gov/drugs/risk-evaluation-and-mitigation-strategies-rems/whats-rems.

[13] To see the REMS for Xyway and Xyrem, see *Approved Risk Evaluation and Mitigation Strategies (REMS)*, FDA, https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=345.

pharmacy limitation as unnecessary and potentially detrimental,[14] it has allowed generic versions of Xyrem (which must have a "comparable" REMS to the brand) to use a REMS that distributes their generic sodium oxybate products through multiple pharmacies with appropriate restrictions. *See In re Xyrem*, 555 F. Supp. 3d at 843; FDA Memorandum, Decision to waive the requirement for a single, shared system REMS for sodium oxybate oral solution at 26 (Jan. 17, 2017) available at https://www.fda.gov/media/102913/download.[15]

Jazz has patents claiming its single-pharmacy REMS distribution system. One of these is U.S. Patent No. 8,731,963 (the "'963 patent"), titled "Sensitive Drug Distribution System and Method." According to Jazz, the claims of the '963 patent "cover methods of using a computer-implemented system to safely distribute GHB [sodium oxybate] for treatment of a narcoleptic patient." (D.I. 43 at 4–5, Aug. 20, 2021.) The '963 patent is listed in the Orange Book as covering a method of using Xyrem. The use code provided by Jazz describes it as a "method of treating a patient with a prescription drug using a computer database in a computer system for distribution."[16]

Avadel and Lumryz

In December 2020, Avadel submitted a Section 505(b)(2) NDA for a sodium oxybate product to treat narcolepsy, referred to as FT218 or Lumryz. Unlike Xyrem, which requires two

[14] See Dunn Ltr. at 3 (explaining that a single-pharmacy requirement "place[s] an unjustified burden on patient access and on the healthcare delivery system" and "could have the effect of blocking or delaying approval of generic versions of Xyrem").

[15] No generic Xyrem ANDA is currently on the market as a result of settlement agreements with Jazz. *See In re Xyrem*, 555 F. Supp. 3d at 837.

[16] *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, Patent and Exclusivity for: N021196, patent use code U-1110, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=021196&Appl_type=N#

doses per night, Lumryz is dosed once nightly. With its NDA, Avadel also submitted a proposed Lumryz REMS, which uses multiple pharmacies and four separate databases to ensure the drug is dispensed only to patients with a valid prescription. Because the Lumryz REMS does not use a single, centralized database, Avadel took the position that Jazz's '963 patent (which covers a single-pharmacy system) was inapplicable. It filed a patent statement to this effect under 21 U.S.C. § 355(b)(2)(B) rather than a paragraph IV certification. *See* Motion for Preliminary Injunction Exhibit 15 at 8, *Avadel CNS Pharms., LLC v. Becerra*, No. 1:22-cv-02159 (APM) (D.D.C. July 21, 2022), Dkt. No. 2-21 ("FDA Patent Decision").

Without assessing infringement, the propriety of the '963 patent listing in the Orange Book, or the accuracy of the use code submitted by Jazz, the FDA required Avadel to convert its patent statement to a patent certification. *See id*. Following the FDA's instruction, Avadel submitted a paragraph IV certification. Jazz promptly filed a patent infringement lawsuit, triggering the automatic 30-month stay of FDA's approval of Avadel's Lumryz NDA. *See Jazz Pharms. v. Avadel CNS Pharm.*, No. 22-941-GBW (D. Del. July 15, 2022).

Shortly thereafter, Avadel filed a counterclaim in the instant case seeking to delist the '963 patent from the Orange Book on the basis that it does not claim Xyrem or a method of using Xyrem—the only permissible statutory bases for listing. Avadel then filed a Motion for Partial Judgment on the Pleadings on delisting. (D.I. 21, July 23, 2021.) Jazz opposed the motion, arguing—among other things—that its complaint alleged that the '963 patent covers "methods of use and administration of sodium oxybate," and claim construction was therefore necessary to determine whether the patent could be listed as a "method of use" for Xyrem. (D.I. 159 at 10–13, Sept. 2, 2022 (original filed under seal on Aug. 26, 2022).) Viewing facts and inferences in the light most favorable to Jazz, the Court found that the delisting dispute depends on "the question

of whether the claimed 'system' includes methods of using [Xyrem]" and denied the motion without prejudice to renewing it. (D.I. 55, Oct. 19, 2021). Avadel has now renewed its motion for judgment on the pleadings (in tandem with claim construction), and the Court has expedited consideration of that motion. (D.I. 117, June 23, 2022; D.I. 212, Oral Order, Oct. 28, 2022.)

The '963 patent is the only Orange Book listed patent that Jazz has asserted against Avadel and provides the sole basis for the ongoing 30-month stay, which will expire on June 17, 2023, along with the expiration of the '963 patent and its accompanying regulatory exclusivity. *See Jazz Pharms*., No. 22-941-GBW. The FDA has granted tentative approval for the Lumryz NDA but is barred from granting final approval while the 30-month stay remains in effect. Thus, the listing of the '963 patent in the Orange Book and the associated Hatch-Waxman litigation is blocking final approval of Avadel's product.

ARGUMENT

Improper Orange Book listings raise serious competition concerns because they illegally block generic or 505(b)(2) entry. Under the Hatch-Waxman framework, a brand pharmaceutical company can obtain a 30-month stay to block a competitor simply by listing a patent in the Orange Book and suing for infringement. The Hatch-Waxman Act strictly limits the types of patents that can be listed in the Orange Book, but neither the FDA nor any other entity verifies that listed patents meet those criteria. Under the statute, the appropriate mechanism to remove an improperly listed patent is a delisting counterclaim. Given the enormous profit margins of many brand drugs, even small delays in competition can be extremely lucrative to the brand company—but cause substantial detriment to consumers.

The FTC takes no position on the specific scope of Jazz's '963 patent. As a general matter, however, patents that merely claim a pharmaceutical distribution system (including a REMS-mandated distribution system) do not meet the Orange Book criteria because they claim,

at most, a method of *distributing* a drug rather than a "method of *using* a drug."[17] Thus, to the extent that the '963 patent claims a REMS distribution system for dispensing a drug (not a method of using that drug), it should be delisted.

I. Improper Orange Book listings can harm competition

The Hatch-Waxman scheme reflects a careful balance between encouraging innovation in drug development and accelerating the availability of lower-cost competing drugs.[18] The Orange Book listing process is part of this balance. As the Third Circuit has observed, "[t]he automatic, 30-month stay creates tension with the Hatch Waxman Act's procompetitive goals." *AbbVie*, 976 F.3d at 340. As such, Congress did not intend for every patent owned by a brand to trigger the Hatch-Waxman litigation process and its automatic 30-month stay of FDA approval. Rather, Congress limited this special treatment to the specific set of patents described in 21 U.S.C. § 355(b)(1) and (c)(2)—those claiming "the drug for which the [brand] submitted the [NDA]" or "a method of using such drug." *See, e.g. Caraco*, 566 U.S. at 405.[19] And Congress confirmed this limitation in 2003 when it created a mechanism to remove any listed patent that does not claim either (a) the brand drug, or (b) "an approved method of using the drug." 21 U.S.C. § 355(j)(5)(C)(ii)(I).[20]

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[17] Avadel and Jazz also dispute whether the '963 patent claims a "method" at all as opposed to a system. The FTC takes no position on the specific claims of the '963 patent. Even a method patent, however, fails to meet Orange Book listing criteria if it covers a method of distributing—as opposed to using—a drug. *See infra* Section II.

[18] H.R. REP. NO. 98-857, at 14–15 (1984), 1984 U.S.C.C.A.N. 2647, 2647–48.

[19] As noted above, the Orange Book Transparency Act of 2020 amended the language of 21 U.S.C. § 355(b)(1) and 355(c)(2) in 2021, but did not expand the categories of covered patents.

[20] In 2020, the Orange Book Transparency Act of 2020 clarified that "[p]atent information that is not the type of patent information required by [the listing statute] shall not be submitted [for listing in the Orange Book.]" Jazz argues that, prior to this clarification, patents that did not meet the statutory criteria could be freely listed unless they had been specifically highlighted by the (Continued…)

Brand manufacturers can, however, evade the statutory limitation and improperly obtain a stay by "exploit[ing] the FDA's determination that it cannot police patent claims." *Caraco*, 566 U.S. at 424. Indeed, the FDA takes a "purely ministerial" role in the listing process. *Organon*, 293 F. Supp. 2d at 458–59.[21] It accepts the brand's patent descriptions and "does not independently assess the patent's scope or otherwise look behind the description authored by the brand." *Caraco*, 566 U.S. at 406–07. It similarly "does not attempt to verify the accuracy of the use codes that the brand manufacturers supply." *Id.* at 405. Nor does the FDA have any tools to remove improperly listed patents. The only mechanism to do so is the statutory delisting counterclaim underway here. *See Caraco*, 566 U.S. at 425 ("The statutory counterclaim we have considered enables courts to resolve disputes so that the FDA can fulfill its statutory duty to approve generic drugs that do not infringe patent rights.").[22] There is thus no gatekeeper to prevent a company from inappropriately listing patents that do not meet the Orange Book criteria.

FDA as inappropriate. (D.I. 159 at 10–13, Sept. 2, 2022 (original filed under seal on Aug. 26, 2022).) This interpretation is impossible to square with Congress's enactment of the delisting procedure in 2003. In any event, the delisting procedure contains no requirement that a currently listed patent was barred from being listed when it was submitted.

[21] *See also Am. Biosci, Inc. v. Thompson*, 269 F.3d 1077, 1084 (D.C. Cir. 2001) (FDA "administers the Hatch-Waxman Amendments in a ministerial fashion simply following the intent of the parties that list patents"); *In re Buspirone Patent Litig.*, 185 F. Supp. 2d 363, 371 (S.D.N.Y. 2002) ("[T]he FDA's actions are non-discretionary and do not reflect any decision as to the validity of the representations in an Orange Book listing.").

[22] The FDA's regulations allow any person to "dispute the accuracy of patent information listed in the Orange Book," but FDA will then only "request that the brand verify the information." *Caraco*, 566 U.S. at 407 n.1. "[U]nder 21 C.F.R. 314.53(f)(1)(i)(B)(1), FDA will not change the patent information in the Orange Book for a listed method-of-use patent if the NDA holder confirms the correctness of the patent information and complies with certain other applicable requirements under FDA's regulations." FDA Patent Decision at 13.

An improper listing harms competition and consumers: By listing a patent in the Orange Book and then filing an infringement suit, a brand can block competition for up to two-and-a-half years regardless of the scope or validity of the patent and regardless of whether it meets the statutory listing criteria. *AbbVie*, 976 F.3d at 371 (noting the "the collateral injury the Hatch-Waxman Act's 30-month stay invariably inflicts"); *Caraco*, 566 U.S. at 419 ("An overbroad use code therefore throws a wrench into the FDA's ability to approve generic drugs as the statute contemplates."). Indeed, as early as the late 1990s, "evidence mounted that some brands were exploiting this statutory scheme to prevent or delay the marketing of generic drugs." *Caraco*, 566 U.S. at 408; *see also* FTC Study (identifying numerous instances in which the 30-month stay was abused to block competition).[23] Consumers suffer both because they are forced to continue

[23] These early abuses were exacerbated by two loopholes in the original law: First, a brand company could repeatedly list new patents and obtain an *additional* 30-month stay for each one, extending the potential length of the stay well beyond 30 months. *See* FTC Study at 40. Second, there was originally no procedure to challenge or remove inappropriately listed patents from the Orange Book. *See* FTC Study at 40; *Caraco*, 566 U.S. at 408. As a result, brand companies could list new patents on the eve of a competitor's approval and block competition with virtually no accountability as to whether the listing was appropriate. *See, e.g.*, *Mylan Pharms., Inc. v. Thompson*, 268 F.3d 1323 (Fed. Cir. 2001) (a brand company listed a new patent at the eleventh hour and obtained an additional 30-month delay—even though the new late-listed patent did not actually cover the relevant drug); Order, *In re Biovail Corp.*, FTC No. C-4060 (Oct. 2, 2002) (a brand company obtained a second 30-month stay by listing a patent for the current version of a drug when that patent covered only potential reformulations). In the 2003 MMA, Congress limited NDA holders to one 30-month stay per drug and created the delisting mechanism. 21 U.S.C. § 355(c)(3)(C), 355(j)(5)(B)(iii), 355(c)(3)(D)(ii)(I), 355(j)(5)(C)(ii)(I). Though these amendments curbed some of the worst listing abuses, the lack of verification for patent listings and the incentive of a 30-month stay still elicit improper listings by brands trying to protect their products from competition. *See, e.g., In re Lantus Direct Purchaser Antitrust Litig.*, 950 F.3d 1 (1st Cir. 2020) (finding that brand company's listing of a medical device patent failed to meet the statutory criteria); *United Food & Com. Workers Loc. 1776 & Participating Emps. Health & Welfare Fund v. Takeda Pharm. Co. Ltd.*, 11 F.4th 118, 134–35 (2d Cir. 2021) ("[A] patent claim that fails to explicitly include the drug actually makes *neither* type of claim on the drug."); *see also* Orange Book Transparency Act of 2020, H.R. REP. 116-47 at 4 (2020) (noting that as of 2020 some manufacturers "are submitting patents potentially for the purpose of blocking generic competition").

paying non-competitive prices and because they are deprived of the ability to choose between products. *See* FTC Study (outlining the lower prices and substantial savings that typically result from generic or follow-on competition); *United States v. Brown Univ.*, 5 F.3d 658, 675 (3d Cir. 1993) ("Enhancement of consumer choice . . . has [] been acknowledged as a procompetitive benefit"), *citing NCAA*, 468 U.S. 85, 102, 104 (1984).

In this case, if the '963 patent is improperly listed, it appears to be causing significant harm to competition. The FDA has tentatively approved Avadel's product, indicating that Avadel will receive final approval once the 30-month stay is resolved. The entry of Avadel's product would not only potentially introduce price competition, but also increase consumer choice by offering a different and more favorable dosing regimen that does not require the patient to wake up in the middle of the night. *Accord In re Suboxone (Buprenorphine Hydrochloride & Naloxone) Antitrust Litig.*, No. 13-MD-2445, 2022 WL 3588024, at *20 (E.D. Pa. Aug. 22, 2022) (consumers should have been free to decide "whether the benefits of the new, higher-priced, once-daily version of the drug outweighed the benefits of adhering to the old, twice-daily, lower-priced regimen").[24] The parties seem to agree that the '963 patent will expire before trial in this case. (*See* D.I. 43 at 2 n.1, Aug. 20, 2021.) Thus, to the extent the '963 patent is improperly listed, the only way to remedy a potentially significant harm to consumers is for this Court to order it removed from the Orange Book.

[24] *See also New York ex rel. Schneiderman v. Actavis PLC*, 787 F.3d 638, 655 (2d Cir. 2015) (finding that the hard product switch, which removed the original product formulation from the market, deprived consumers of deciding "whether the benefits of switching to once-daily Namenda XR would outweigh the benefits of adhering to twice-daily therapy using less-expensive generic IR").

II. Patents on REMS distribution systems do not meet the Orange Book listing criteria

An assessment of whether a patent is properly listed in the Orange Book under the Hatch-Waxman Act begins "'where all such inquires must begin: with the language of the statute itself.'" *Caraco*, 566 U.S. at 412 (quoting *United States v. Ron Pair Enterprises, Inc.*, 489 U.S. 235, 241 (1989)). The unambiguous language of the statute specifies that only patents covering "a drug" or "a method of using" a drug can be listed.[25] And the statute further provides that any patent "not claiming either—(aa) the drug for which the application was approved; or (bb) an approved method of using the drug" can be delisted pursuant to a court order. 21 U.S.C. § 355(c)(3)(D)(ii)(I), 355(j)(5)(C)(ii)(I). These clear statutory limits demonstrate that the Orange Book is not intended to be a repository for every patent relating to a brand product. To the extent the '963 patent is directed to the implementation of a REMS distribution system, it plainly does not cover "a drug," nor does Jazz contend that it does.[26]

A REMS distribution system cannot plausibly be considered a "method of using a drug." In the pharmaceutical context, a "method of use" means a method of using the drug to treat a patient. Method of use patents "generally cover a method of using the drug to treat a particular medical indication/condition." Shashank Upadhye, *Generic Pharmaceutical Patent and FDA*

[25] Prior to the Orange Book Transparency Act amendments, 21 U.S.C. § 355(b)(1) and 355(c)(2) required submission of patent information for any patent which "claims the drug" or which "claims a method of using such drug." Sections 355(b)(1) and 355(c)(2) now require submission of patent information for each patent that "(I) claims the drug . . . and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or (II) claims a method of using such drug." Section 355(c)(2) now also states that "a patent that is identified as claiming a method of using such drug shall be filed only if the patent claims a method of use approved in the application."

[26] To "claim[ ] the drug for which the NDA was submitted," a patent must "'contain[] a product claim that reads on the drug that is the subject of the NDA . . ..'" *United Food & Com. Workers Loc. 1776*, 11 F.4th at 132 (quoting *Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1344 (Fed. Cir. 2003) (emphasis omitted).

Law, § 3:14 Methods of Use (rev. ed. 2022) (patents on method of using a drug "usually cover[] a way of using [a] drug to treat someone for something"). A method of use patent might reflect an innovative way of using a drug to treat a new condition for which it was not previously prescribed. Or it might reflect a discovery about a new way to dose or administer a drug. To take one example, Jazz obtained a method of use patent that claims the preparation of an oral solution of Xyrem and oral administration to a narcolepsy patient.[27] These types of patents are consistent with the ordinary, common sense meaning of the phrase "using a drug": When a doctor prescribes a drug to treat a patient's condition, and selects the appropriate dosage and route of administration, the doctor is *using* that drug to treat the patient. And when a patient takes a drug as directed by their doctor, the patient is *using* the drug to treat their condition. *See, e.g., United States v. Dauray*, 215 F.3d 257, 260 (2d Cir. 2000) (considering "the ordinary, common-sense meaning of the words" where Congress provided no definition).

A method of *distributing* a drug, however, does not fall within the plain meaning of "using" that drug. Checking a computer system to make sure a patient has a valid prescription for a drug is not "using" that drug under any reasonable understanding of the word. Nor is following safety protocols when shipping a drug from the manufacturer to a pharmacy, or creating, maintaining, or monitoring databases of approved patients or authorized prescribers. Defining

[27] U.S. Patent No. 8,324,275 (claiming, in part, "1. A method of treating cataplexy or daytime sleepiness in a patient who has been diagnosed with narcolepsy, comprising: (i) diluting an aqueous solution comprising about 500 mg/mL of sodium gamma-hydroxybutyrate with an aqueous medium to provide a first dose of about 4.5 to about 9 grams sodium gamma-hydroxybutyrate; (ii) diluting an aqueous solution comprising about 500 mg/mL of sodium gamma-hydroxybutyrate with an aqueous medium to provide a second dose of about 4.5 to about 9 grams of sodium gamma-hydroxybutyrate; (iii) orally administering to a patient having narcolepsy the first dose within an hour prior to initial sleep onset; and (iv) orally administering to the patient having narcolepsy the second dose within 2.5 to 4 hours following initial sleep onset").

these types of logistical processes as "methods of using a drug" would stretch the plain meaning of the statutory text past its breaking point. It would also open the floodgates to a torrent of extraneous Orange Book listings based on artful claim drafting, such as a patent on a particular method of shipping a drug on an airplane, or a patent on a method of packing the drug into a box for shipment to a pharmacy. But claims that merely relate to these types of processes are not appropriate to list as a "method of *using*" the drug in question.

The FDA's Orange Book implementing regulations confirm the plain meaning of the statutory text. The FDA has specified that, "[f]or patents that claim a method of use, the applicant must submit information only on those patents that claim indications or other conditions of use for which approval is sought or has been granted in the NDA." 21 C.F.R. § 314.53(b)(1). Patents claiming elements of a distribution system do not claim methods of use involving "indications" for a drug, which are the medical conditions for which the FDA has approved the drug as a treatment.[28] Nor does a REMS distribution patent claim, as Jazz contends, "other conditions of use" for the drug.[29] (D.I. 159 at 10–13, Sept. 2, 2022 (original filed under

[28] Merely reciting "for the treatment of . . ." in the preamble of a method claim without including method steps relating to treating does not transform the scope of a claim whose body merely recites steps unrelated to treatment. *See, e.g.*, *Cochlear Bone Anchored Sols. AB v. Oticon Med. AB*, 958 F.3d 1348, 1353–55 (Fed. Cir. 2020).

[29] Jazz further argues that the FDA recently confirmed that its REMS patent is required to be listed in the Orange Book because it covers a condition of use. (D.I. 159 at 10–13, Sept. 2, 2022 (original filed under seal on Aug. 26, 2022).) But this misrepresents the FDA's ministerial role in the listing process. The FDA's statement that "Avadel is seeking approval of a condition of use that is claimed by the '963 patent, as described by the U-1110 use code" (FDA Patent Decision at 10), is premised on FDA's assumption that the patent is properly listed and that the use code is accurate. *See id.* at 3 ("FDA does not review the applicable patent to evaluate the appropriateness of the NDA holder's patent listing or the accuracy of its use codes."). The FDA recently reiterated that it did not assess Jazz's submitted patent information for accuracy. *See* Transcript of Oral Argument Proceedings at 82:17-23, *Avadel CNS Pharmaceuticals v. Becerra*, No. 1:22-cv-02159 (D.D.C. Oct.7, 2022) ("Under *Purepac* and under the FDA's longstanding practice, it takes what the applicant, what the NDA holder, Jazz, submits to it at face value. And part of (Continued…)

seal on Aug. 26, 2022).) The FDA has explained that "conditions of use" are those that encompass "how a drug is used [], to whom it is prescribed[], [or] for what purposes[]." *ViroPharma, Inc. v. Hamburg*, 898 F. Supp. 2d 1, 22 n.24 (D.D.C. 2012).[30] In other words, and consistent with the statutory text, a condition of use is a condition of using the drug for medical treatment; it does not encompass conditions on distribution.[31] A patent on a REMS distribution system is not a patent on how a drug is taken, or for what purpose. Nor is it a patent relating to who the drug can be prescribed to. It simply covers the logistical process of disseminating the drug through the supply chain to patients who already have a prescription.

To be sure, a REMS distribution system is a condition of FDA *approval* for certain drugs. But that does not make it a condition of the drug's *use*. This common-sense distinction is illustrated by the treatment of packaging patents in the FDA's regulations. REMS commonly include strict conditions on a drug's packaging that must be followed pursuant to the label, but "patents claiming packaging . . . are not covered by [the listing regulations], and information on these patents must not be submitted to FDA." 21 C.F.R. § 314.53(b).[32] In other words, although packaging requirements (like distribution requirements) may be a condition of approval for a

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what Jazz submitted here is a representation that this is a method-of-use patent. And a method-of-use patent, by definition, claims the use of a drug. That's what a method-of-use patent is.").

[30] This definition is consistent with the way the term is used elsewhere in related regulations. *See, e.g.*, 21 C.F.R. § 310.3(h)(5) (definition of new drug includes a new "dosage, or method or duration of administration or application, or other condition of use prescribed").

[31] An example of a patent claiming a condition of use for a drug product is U.S. Patent No. 7,772,209, related to the chemotherapy drug Alimta, which claims administering folic acid and Vitamin B12 along with the drug to reduce toxicity. *See* Altima Label at 2.3 (Premedication Regimen), available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021462s015lbl.pdf

[32] This regulation also states that process patents, another type of method patent, must not be submitted. 21 C.F.R. § 314.52(b). Like distribution patents, process patents claim a method of manufacturing the drug rather than a method of using it to treat an indication, or a condition on the use of the drug in treating a patient.

REMS drug, the FDA has explained that they are not a condition of *using* that drug and patents pertaining to them cannot be listed in the Orange Book. REMS conditions on distributing a drug are likewise not conditions on the *use* of that drug under the listing regulations.

In addition to contravening the plain text of the Orange Book listing statute, improperly listing a REMS distribution patent may also violate the governing REMS statute: When Congress enacted the FDAAA in 2007, it explicitly prohibited brand sponsors from using REMS requirements to "block or delay" ANDA and 505(b)(2) approval. 21 U.S.C. § 355-1(f)(8). The FDA has similarly stated publicly that REMS programs should not be used to block or delay generic competition.[33] There has nonetheless been an unfortunate history of brand pharmaceutical companies misusing REMS programs to block competitors, sometimes for years. *See, e.g.*, *Mylan Pharms. Inc. v. Celgene Corp.*, No. 14-cv-2094 (ES) (MAH), 2018 WL 11299447, at *2–4, *10–18 (D.N.J. Oct. 3, 2018) (brand company allegedly misused REMS to prevent generic applicant from obtaining product samples needed for FDA-mandated testing).[34] Improperly submitting a REMS distribution patent for listing in the Orange Book and obtaining a

[33] *See* Center for Drug Evaluation and Research, FDA, Risk Evaluation and Mitigation Strategy (REMS) Public Meeting (July 28, 2010), at 270–71 (statement by Jane Axelrad, Associate Director of Policy, Center for Drug Evaluation and Research), *available at* http://www.fda.gov/downloads/Drugs/NewsEvents/UCM224950.pdf; FDA, Risk Evaluation and Mitigation Strategies; Notice of Public Meeting; Reopening of Comment Period, 75 Fed. Reg. 34453, at 34456 (June 17, 2010) (noting FDAAA subsection f(8) and requesting input on steps FDA could take "to ensure that REMS are not used to block or delay generic competition").

[34] The FTC has filed multiple amicus briefs on this issue. *See* Federal Trade Commission's Brief as *Amicus Curiae*, *Mylan Pharms., Inc. v. Celgene Corp.*, No. 2:14-cv-2094-ES (D.N.J. June 17, 2014) (Doc. No. 26-3); Federal Trade Commission's Brief as *Amicus Curiae*, *Actelion Pharms. Ltd. v. Apotex Inc.*, No. 1:12-cv-5743-NLH (D.N.J. Mar. 11, 2013) (Doc. No. 61-2). Some brand companies also abused a requirement—since removed by Congress—that any generic or 505(b)(2) applicants and brand share a single REMS by prolonging or even stonewalling the shared REMS negotiations. *See*, *e.g.*, *In re Suboxone*, 2022 WL 3588024, at *8-10, *42-44. In 2019, Congress passed the CREATES Act to provide additional tools to redress some abusive strategies. *See* 21 U.S.C. § 355-2. But REMS abuse remains a serious competition concern.

30-month stay based on that listing may constitute a misuse of the REMS to "block or delay" the approval of ANDA or 505(b)(2) products in violation of the FDAAA.

Leveraging distribution safeguards to hinder competition was never what Congress intended. But providing a remedy for competitors blocked or delayed by an improperly listed patent is exactly what Congress intended with the delisting statute. If the Court determines that the '963 patent covers only a REMS distribution system and does not claim an approved method of using Xyrem, the Court should order Jazz to delist it.

CONCLUSION

For the foregoing reasons, to the extent Jazz's '963 patent claims a REMS distribution system rather than a method of using Xyrem, it is improperly listed in the Orange Book and the Court should order it delisted.

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