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Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
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CITIZEN PETITION

The undersigned Andrx Pharmaceutical, Inc. ("Andrx") respectfully submits this petition pursuant to 21 C.F.R. §§ 10.30, 314.107(c)(4) and section 505(j) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 355(j), to request that the Commissioner of Food and Drugs determine that the ongoing marketing of loratadine in 10 milligram orally disintegrating tablets by Wyeth-Ayerst Laboratories ("Wyeth")[1] pursuant to an approval under section 505(b)(2) of the Act constitutes "commercial marketing" of generic loratadine within the meaning of section 505(j)(5)(B)(iv)(I).

A. Action Requested

On December 19, 2002, FDA gave effect to its approval of Wyeth's application, under section 505(b)(2), to market an over-the-counter allergy medication named Alavert, an orally disintegrating tablet in which the active ingredient is loratadine. Loratadine is also the active ingredient in Claritin, an allergy medication manufactured and sold by Schering Corporation ("Schering"). On December 19, 2002, or shortly thereafter, Wyeth commenced marketing Alavert.

On March 9, 2000, however, Wyeth had become the first manufacturer to file an Abbreviated New Drug Application under section 505(j) for a generic version of the orally disintegrating dosage

[1] Throughout this petition we refer only to "Wyeth," although various actions described herein were carried out by Wyeth's parent companies Whitehall-Robbins and American Home Products and by ESI-Lederle, a Wyeth subsidiary. The distinctions among these corporate entities have no bearing on the merits of the petition.

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form of Claritin. Since Wyeth also certified that it contested the validity or applicability of two of Schering's patents, under section 505(j)(5)(B)(iv), Wyeth is entitled to 180 days of generic exclusivity protection from competition by other manufacturers of the same generic drug product. Petitioner Andrx has also filed an ANDA for a generic orally disintegrating tablet in which the active ingredient is loratadine, and although it received tentative approval on November 15, 2002, it is precluded from marketing its product until 180 days after the date on which Wyeth's generic exclusivity commences.

The FDA recently declared that the "commercial marketing" prong of section 505(j)(5)(B)(iv) is triggered when a generic drug company markets a product that is equivalent to the product for which it received the first ANDA approval, and its position was upheld by a federal court. Mylan Pharmaceuticals, Inc. v. Thompson, 207 F. Supp. 2d 476, 488 (N.D. W. Va. 2001) (affirming in relevant part FDA's response to citizen petition in Docket No. 00P-1446/CP1). This Citizen Petition presents a similar question. The statute, the regulations as well as the agency's prior decision require that this Citizen Petition be resolved in the same manner as that earlier Citizen Petition.

Andrx therefore urges the Commissioner to declare that Wyeth has been commercially marketing generic loratadine under the name Alavert since December 19, 2002, and to declare further that 180 days after that date, petitioner's ANDA will be eligible for full approval.[2]

B. Statement of Grounds

1. Factual Background

On December 23, 1996, Schering received FDA approval to market Claritin Reditabs, the active ingredient in which is loratadine. Schering obtained three patents for the product, the expiration dates for which were December 19, 2002 ('233 patent), October 21, 2004 ('716 patent), and March 15, 2009 ('931 patent).

A number of drug companies filed ANDAs under section 505(j) to market generic loratadine in reditab form. Of relevance here, Wyeth filed on March 9, 2000 (ANDA 75-822) and Andrx filed on September 11, 2000 (ANDA 75-990). Schering sued Wyeth, Andrx and other companies for patent infringement in federal district court for the District of New Jersey. In an order dated August 8, 2002, the Chief Judge of that court found the '716 patent to contain invalid claims and dismissed

[2] The Orange Book lists the approval date for Alavert as December 19, 2002. Throughout this petition we presume that Wyeth began selling the product on that date, but the legal arguments supporting the petition would remain in force even if Alavert sales began on some later date.

Schering's claims of infringement.[3] Schering v. Geneva Pharmaceuticals, Inc., Civil Action Nos. 98-1259 (JWB), et. al., order reaffirmed August 29, 2002. Schering has appealed that order to the Court of Appeals for the Federal Circuit, but its appeal has not yet been decided.

During the pendency of its ANDA patent litigation in the District Court, Wyeth sought an alternative route to market generic loratadine in reditab form. On August 23, 2001, Wyeth filed a new drug application pursuant to section 505(b)(2) for an over-the-counter version of Schering's Claritin Reditabs, which was only sold by prescription at the time Wyeth filed its NDA. On December 12, 2002, FDA approved this NDA effective December 19, 2002, the day that Schering's '233 patent expired. (The '716 patent had already been declared invalid.)

About the same time that Wyeth's NDA was approved, Schering itself won approval to shift Claritin from a prescription medication to an over-the-counter product. See FDA Letter to Schering Corp. dated November 27, 2002, approving NDA 19-670/S-018, et. al. Thus, upon information and belief, the section 505(b)(2) product for which Wyeth won approval last December and began marketing on December 19, 2002 is in every respect a generic version of the drug Schering itself markets as over-the-counter Claritin.

The petitioner also asserts, upon information and belief, that Alavert and Claritin are bioequivalent.[4] Petitioner is unaware if the FDA formally ascertained the bioequivalence of the two products at the time Alavert was approved for sale. If not, FDA should make the determination at this time in response to this petition. If Alavert and Claritin are bioequivalent, there is no meaningful difference between Alavert and the generic loratadine product for which Wyeth, on February 10, 2003, obtained final marketing approval under ANDA 75-822.

Meanwhile Andrx received tentative approval of its ANDA on November 15, 2002, but it cannot market its generic product until Wyeth's 180 days of marketing exclusivity has expired. For the reasons stated below, petitioner urges the FDA to declare that Wyeth's 180-day exclusivity runs from the date on which Wyeth began marketing generic loratadine in its product Alavert pursuant to its approval under section 505(b)(2). A contrary result – that the 180 days will not begin to run until Wyeth notifies the FDA that it has commenced commercial marketing of the product referenced

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[3] Both Wyeth and Andrx agreed to await the December 19, 2002 expiration of the '233 patent and both represented that they would not infringe the '931 patent, which relates to Schering's manufacturing process. Consequently, Schering did not sue the generic drug companies with respect to those patents and the only issue litigated was the validity of the '716 patent.

[4] Wyeth's advertising evidences the equivalence of Schering's brand-name product (Claritin) and Wyeth's section 505(b)(2) product (Alavert). On its website, Wyeth describes Alavert as follows: "Alavert contains prescription strength loratadine, the ingredient in the #1 prescribed non-sedating antihistamine, and is now available without a prescription." (http://www.alavert.com (last visited Feb. 14, 2003)). This claim plainly equates Alavert and Claritin.

in its ANDA – would be contrary to the goals of the Hatch-Waxman Act and the agency's prior interpretations of the Act.

2. Legal Argument

In the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman" or "the Act"), Congress sought to "make available more low cost generic drugs." H.R. Rep. No. 98-857, pt. 1, at 14 (1984). The Act creates an incentive for generic drug companies to challenge brand-name drug patents, namely the 180 days of generic exclusivity in section 505(j)(5)(B)(iv). But this 180-day period represents a careful balance between the need for such an incentive and the danger that lengthier generic exclusivity would harm consumers by preventing competition *among* generic companies. The Act must be implemented in a manner that provides a first ANDA filer with the full 180 days to which it is entitled but no more.

Under the statute, the 180-day period of marketing exclusivity is triggered by one of two events: the "first commercial marketing" of the generic product, 505(j)(5)(B)(iv)(I), or the "date of a decision of a court" invalidating the patent in question, 505(j)(5)(B)(iv)(II). Because the Wyeth ANDA for generic Claritin was filed before the publication of the FDA's March 2000 "Guidance for Industry: Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act," FDA has determined that the "decision of a court" trigger will be the date Schering's appeal in the patent infringement case is decided by the Court of Appeals. See FDA letter to Andrx Pharmaceuticals dated November 15, 2002, tentatively approving ANDA 75-990. That has not yet occurred. At issue here, then, is whether the 180 days has started to run under the "commercial marketing" prong of the statute.[5]

Ordinarily the "first commercial marketing" trigger is activated when the generic drug company entitled to marketing exclusivity notifies the FDA it has started selling the drug for which it filed its ANDA. But the agency has recognized that notice may not always be provided in a timely manner and has therefore established a mechanism for finding "commercial marketing" in the absence of notice from the company. 21 C.F.R. § 314.107(c)(4).

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[5] Since FDA acquiesced to the holding in Mylan Pharmaceuticals v. Shalala, 81 F. Supp. 2d 30 (D.D.C. 2000), to the effect that exclusivity begins to run from any court decision (rather than from a final unappealable court decision), Andrx could argue that the court trigger applicable to all reditab loratadine ANDAs, including Wyeth's ANDA, should be the district court decision. Thus, Andrx could argue that the 180-days of exclusivity should have begun running from August 8, 2002, the date the court in the ANDA litigation issued a final judgment in favor of the defendants. Moreover, if it prevailed in such an argument, Andrx would also contend that the August 8, 2002 decision triggered the 180-day exclusivity as to both the '716 and '931 patents. Andrx recognizes that FDA has recently decided these issues, and it does not seek a specific ruling on them in response to this petition. Nevertheless, Andrx respectfully preserves its right to raise these issues in any further proceedings.

Regulations implementing the Hatch-Waxman Act state that the FDA may "deem" commercial marketing to have occurred, even if the first ANDA filer attempts to postpone initiation of the 180-day generic exclusivity. Section 314.107(c)(4) requires the first ANDA filer to notify FDA of the date that it commences commercial marketing of its drug product, and defines that date, in relevant part, as "the first date of introduction or delivery for introduction into interstate commerce outside the control of the manufacturer of a drug product."[6] The regulation then provides: "If an applicant does not promptly notify FDA of such date, the effective date of approval *shall be deemed to be* the date of the commencement of first commercial marketing." Id. (emphasis added).

In other words, FDA may determine whether commercial marketing has occurred. A drug manufacturer may engage in activity that it contends is not "commercial marketing" under section 505 (j)(5)(B)(iv), but the agency reserves to itself authority to conclude otherwise. Thus, FDA has authority to determine whether and when Wyeth began "commercial marketing" of generic loratadine for purposes of 505(j). The agency should make that determination in a manner that affords Wyeth its statutory benefit but prevents it from obtaining more than 180 days of marketing exclusivity.

Moreover, the relief sought in this petition is compelled by the agency's recent action in a parallel proceeding: the agency's adjudication of the citizen petition filed by Teva Pharmaceuticals USA, Inc. in Docket No. 00P-1446/CP1. In that instance, Mylan Pharmaceuticals was the first company to file an ANDA with respect to extended release nifedipine tablets for which Pfizer was the NDA holder. When it won final approval to market generic nifedipine, however, Mylan did not market the product approved in its ANDA. Instead, it settled its patent litigation with Pfizer by entering into a licensing agreement that enabled Mylan to market Pfizer's generic nifedipine product. Teva filed a citizen petition requesting, inter alia, that FDA deem Mylan's marketing of the Pfizer product to constitute "commercial marketing" under section 505(j)(5)(B)(iv)(I), even though Mylan was not marketing its ANDA version of generic nifedipine.

In a decision dated February 6, 2001, the FDA granted Teva's petition. In relevant part, the agency found that Mylan's exclusivity started to run with its commercial marketing of Pfizer's generic product. The agency wrote:

> Whether Mylan markets the product approved in its ANDA or the product approved in Pfizer's NDA is of little import to the statutory scheme; Mylan has begun commercial marketing of generic

[6] It is significant that the regulation defines commercial marketing as introduction "of a drug product" into interstate commerce. 21 C.F.R. § 314.107(c)(4). This regulation could have been written to refer, for example, to introduction of "the product for which ANDA approval was granted." Instead, the regulation utilizes the more general term "a drug product" which focuses attention on the chemical properties of the product itself, not on whether it came to market under section 505(j) or 505(b)(2).

> nifedipine. Permitting Mylan to market nifedipine without triggering the beginning of exclusivity would be inconsistent with the intent of the statutory scheme.

Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, to Deborah Jaskot, Senior Director, Regulatory Affairs, Teva Pharmaceuticals USA, Inc., dated February 6, 2001, at 7-8.

In reaching this conclusion about the "commercial marketing" trigger, the agency relied on the D.C. Circuit's interpretation of the parallel "decision of a court" trigger. In that earlier dispute involving Teva, the court had directed the agency to employ a broader interpretation of the statutory phrase "decision of a court" to prevent one company from "manipulat[ing] the system in order to block or delay generic competition." Teva Pharmaceuticals v. FDA, 182 F.3d 1003, 1009 (D.C. Cir. 1999) (citation omitted). In adjudicating Teva's citizen petition two years later, the agency recognized that the "commercial marketing" trigger was susceptible to the same type of manipulation as the "decision of a court" trigger and acted to prevent that outcome.

The agency's ruling in Teva's favor in Docket 00P-1446/CP1 was upheld by the federal court that reviewed it. That court specifically found the agency's interpretation of section 505(j) to be "a reasonable one." Mylan Pharmaceuticals, Inc. v. Thompson, 207 F. Supp. 2d 476, 488 (N.D. W. Va. 2001).

This case presents at least as compelling circumstances for finding that commercial marketing has occurred as those presented in Teva's Citizen Petition. In that petition, the active ingredient, dosage and dosage form of the product for which Mylan had received its ANDA approval and the product that it was marketing were the same. Similarly, here, the active ingredient, dosage and dosage form of the product for which Wyeth filed an ANDA and the product it is currently marketing as Alavert under a section 505(b)(2) approval are the same. By definition, the ANDA is for generic Claritin. Alavert, the section 505(b)(2) product, is also generic Claritin. And here, unlike the earlier petition, Wyeth itself is manufacturing the product that it is marketing. To paraphrase the agency's response to the Teva petition, whether Wyeth markets the product approved in its ANDA or the product approved in its section 505(b)(2) NDA is of little import to the statutory scheme; Wyeth has begun commercial marketing of generic loratadine.

The relief sought by petitioner herein would provide Wyeth with its 180-day period of marketing exclusivity while appropriately denying it the market "windfall" that would undermine Hatch-Waxman and deny consumers competition in the generic loratadine market.

3. Request for Expeditious Ruling

Petitioner respectfully requests that the Commissioner adjudicate this petition in an expeditious fashion. If Wyeth's 180-day period of market exclusivity began to run in mid-December, it will expire in mid-May. Wyeth, Andrx and perhaps other companies have a strong interest in having this matter resolved promptly so they can plan manufacturing, sales, marketing and other corporate activities. If the relief sought is granted, consumers would benefit from the advent of competition in the generic anti-allergy drug market as soon as the law allows.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 C.F.R. § 25.31.

D. Economic Impact

Petitioner is not providing economic information because no economic information has been requested by the Commissioner. 21 C.F.R. § 10.30.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

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To Whom it May Concern:

On behalf of Andrx Pharmaceutical, Inc., I enclose a Citizen Petition submitted pursuant to 21 C.F.R. §§ 10.30, 314.107(c)(4) and section 505(j) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 355(j), to request that the Commissioner of Food and Drugs determine that the ongoing marketing of loratadine in 10 milligram orally disintegrating tablets by Wyeth-Ayerst Laboratories pursuant to an approval under section 505(b)(2) constitutes "commercial marketing" of generic loratadine within the meaning of section 505(j)(5)(B)(iv)(I).

Please regard me as a point of contact on this matter.

Sincerely,

William B. Schultz
Attorney for Petitioner

cc: Daniel E. Troy, Chief Counsel
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