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Dockets Management
Food and Drug Administration
5630 Fishers Lane
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CITIZEN PETITION

Action Requested

The undersigned counsel respectfully submit this citizen petition on behalf of Mylan Laboratories Inc. and Mylan Pharmaceuticals Inc. (collectively "Mylan") requesting that the FDA not delist U.S. patent 4,879,303 ("the '303 patent") during any period that Mylan is entitled to market exclusivity under 21 U.S.C. §355(j)(5)(B)(iv).

Introduction and Statement of Facts

The '303 patent currently is listed by Pfizer Inc. ("Pfizer") in connection with its Norvasc® amlodipine besylate product. The '303 patent expired on March 25, 2007. Three days prior to its expiration, a panel of the Court of Appeals for the Federal Circuit held three of its eleven claims to be invalid. *Pfizer Inc. v. Apotex, Inc.*, No. 2006-1261, 2007 U.S. App. LEXIS 6623 (Fed. Cir. Mar. 22, 2007). Pfizer has petitioned the Court to rehear the case *en banc*. The '303 patent remains listed in the Orange Book post-expiration because Pfizer is entitled to pediatric exclusivity at least until the Federal Circuit's decision becomes final through issuance of its mandate. Ex. 1, April 18, 2007 Letter from G. Buehler to ANDA Applicants.

Mylan filed an Abbreviated New Drug Application ("ANDA") seeking approval to market a generic version of Pfizer's approved product nearly five years ago in May 2002. That ANDA contained a certification under 21 U.S.C. §355(j)(2)(A)(vii)(IV) certifying that Mylan believed the '303 patent to be invalid or not infringed ("Paragraph IV certification"). Mylan timely served Pfizer with notice of its Paragraph IV filing, and, although Pfizer did not sue Mylan within forty-five days, it did sue Mylan in September 2002 in the U.S. District Court for the Western District of Pennsylvania alleging infringement of the '303 patent. Mylan has been engaged in protracted and expensive litigation with Pfizer since that time. Earlier this year, the Pennsylvania court entered judgment that the '303 patent was valid, enforceable and infringed by Mylan's product. Mylan appealed that decision to the U.S. Court of Appeals for the Federal

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Circuit. Based on the Federal Circuit's decision in *Pfizer v. Apotex*, Mylan promptly moved the appeals court to stay the effect of the Pennsylvania court's judgment pending appeal. That motion was granted.

Mylan was the first company, by more than a year, to develop a generic amlodipine besylate product and file a Paragraph IV certification challenging the '303 patent. Because of its first-filer status, Mylan is entitled to 180 days of market exclusivity. Mylan received final FDA approval of its ANDA and, on March 23, 2007, commenced commercial marketing of its product, thereby triggering the commencement of its market exclusivity. Mylan's hard-earned exclusivity is in jeopardy if Pfizer requests the Agency to delist the '303 patent and the Agency complies with that request. Delisting the '303 patent prior to expiration of Mylan's 180-day exclusivity would be contrary to the policy underlying the exclusivity statute – to provide an incentive for early development of lower cost generic drugs and for early challenges to patents that block the sale of such drugs to consumers – and would also allow the NDA holder to deprive the first-to-file generic company of its 180-day exclusivity. As discussed below, such delisting also would be inconsistent with the Agency's own regulations and precedent.

Statement of Grounds

The Hatch-Waxman statute provides that the first company to file an ANDA containing a paragraph IV certification to a patent listed in the Orange Book is entitled to 180 days of exclusivity:

> If the application contains a [paragraph IV certification] and is for a drug for which a previous application has been submitted under this subsection, [containing] such a certification, the application shall be made effective not earlier than one hundred and eighty days after
>
> (I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application; or
>
> (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed,
>
> whichever is earlier.

21 U.S.C. §355(j)(5)(B)(iv).[1] "This period of exclusivity is an important component of the Hatch-Waxman Amendments because it 'encourages generic drug makers to incur the potentially substantial litigation costs associated with challenging pioneer drug makers' patents and bringing generic drugs to the market faster." *Ranbaxy Laboratories, Ltd. v. Leavitt*, 459 F. Supp. 2d 1, 3 (D.D.C. 2006) (quoting *Mylan Pharmaceuticals Inc. v. Shalala*, 81 F. Supp. 2d 30, 33 (D.D.C. 2000)). Mylan has incurred such substantial litigation costs through its litigation with Pfizer for nearly five years.[2]

The policy underlying these statutory provisions would be frustrated if an NDA holder such as Pfizer could extinguish a first-filer's market exclusivity by delisting its patent. Indeed, the Agency's regulations recognize the harm that will result from such delisting:

> A patent that is the subject of a lawsuit under §314.107(c) shall not be removed from the list until FDA determines either that no delay in effective dates of approval is required under that section as a result of the lawsuit, that the patent has expired, or that any such period of delay in effective dates of approval is ended.

21 C.F.R. §314.94(a)(12)(viii)(B). The FDA has acknowledged that this regulation precludes it from delisting a patent when there is an outstanding claim of 180 day exclusivity – particularly in a case in which the paragraph IV certification has resulted in litigation:

> This regulation recognizes a limited exception to this delisting and amendment requirement when the patent is the subject of a lawsuit. . . . The reason for this limited exception is to avoid an unjust result that would occur if an ANDA applicant who is eligible for exclusivity prevails in the patent litigation but lost exclusivity if the NDA holder decided to delist.

Ex. 2, FDA's Mem. in Opp. to Plaintiffs' Motion for Summary Judgment in *Ranbaxy v. Leavitt*, No. 05-1838 (D.D.C.) at 11.

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[1] Mylan filed its ANDA before December 8, 2003; therefore, this version of the statute applies to Mylan's ANDA.

[2] Although Apotex's ANDA was filed long after Mylan's, Apotex got its case to appeal earlier because of delays in Mylan's case resulting, *inter alia*, from the substitution of the trial judge and a heavy court docket. Apotex was able to benefit from the fact discovery and expert testimony already developed by Mylan to streamline its case preparation and get it to trial sooner.

> [T]he agency agrees that the protection offered by 180-day exclusivity should not be undermined by changes from paragraph IV certification or by the filing of original certifications other than paragraph IV certifications. If a patent were removed from the list immediately upon a court decision that the patent is invalid or unenforceable, an applicant with a subsequently filed application might seek to certify that there is no relevant patent and seek an immediately effective approval. To ensure that this does not occur, the agency has required that a patent remain on the list after being declared invalid or unenforceable *until the end of any applicable 180-day exclusivity period.* This means that a patent is deemed to be relevant under §314.94(a)(12)(ii) until the end of the term of the patent or applicable 180-day exclusivity period, whichever occurs first. Thus, where there is a patent that has been challenged by a paragraph IV applicant, a subsequent applicant will not be able to file a certification that there is no relevant patent or seek an immediately effective approval until either the patent or the 180-day exclusivity period expires.

59 Fed. Reg. 50,338, 50348 (Oct. 3, 1994).

The Agency's actions following patent litigation involving the drug mirtazapine also followed the longstanding practice of not destroying exclusivity by patent delisting. After the district court in that case held that the method claimed in the listed patent was not an approved use of the drug, the NDA holder, Organon, asked the FDA to delist the patent. FDA properly refused the request because of outstanding claims to 180 day exclusivity, explaining,

> [i]n the normal course, FDA would require ANDA applicants with paragraph IV certifications to maintain the certification and leave the patent in the Orange Book for the 180-day period beginning with the court decision, even when the patent holder requests that the patent be removed from the Orange Book, as has happened with Organon.

Ex. 3, Feb. 24, 2003 Letter from G. Buehler to T. Gilbert at 3.

After a similar court decision regarding the brimonidine tartrate patents, Alcon argued to the FDA that the patents could not be used as the basis of a claim to 180-day exclusivity. The FDA correctly rejected this argument:

> FDA's practice under 505(j)(5)(B)(iv) and 21 C.F.R. §314.107(c) is to grant 180-day exclusivity to the ANDA applicant that was first to file a valid paragraph IV certification to a listed patent, and for that exclusivity to be triggered in certain

> cases, by a court decision in litigation resulting from a paragraph IV certification finding the patent invalid or not infringed. It would be unreasonable, and contrary to FDA regulations and practice, to either remove challenged patents from the Orange Book or require a change from paragraph IV certification to section viii statement for the ANDA applicants on the basis of a district court decision of non-infringement, where that decision was the result of the ANDA applicant's submission of a paragraph IV certification and successful litigation of the patent claim. To do so would vitiate the 180-day exclusivity.

Ex. 4, May 28, 2004 Letter from G. Buehler to D. Tomasch at 4.

While 21 C.F.R. §314.94(a)(12)(viii)(B) would allow delisting after patent expiration, Mylan is currently challenging the Agency's position that 180-day market exclusivity ends with patent expiration. *Mylan Labs. Inc. and Mylan Pharms. Inc. and Mutual Pharm. Co., Inc. v. Michael O. Leavitt in his official capacity as Secretary of Health and Human Services, Andrew C. Von Eschenbach, M.D., in his official capacity as Commissioner of Food and Drugs, and United States Food and Drug Administration*, No. 07-579 (D.D.C. 2007). Just as FDA has recognized that patents should remain listed after a holding of invalidity, so as to preserve the first filer's 180-day market exclusivity, in a case such as this, the patent should remain listed after patent expiration. Until that issue has been finally resolved in the courts, it would be improper for the Agency to delist the '303 patent, thereby destroying Mylan's 180-day exclusivity and irreparably prejudicing Mylan's right to have the issue decided by the courts.

There are sound policy reasons behind the exclusivity provisions of the Hatch-Waxman Amendments, and there are sound bases for not allowing hard-earned exclusivity to be destroyed by the arbitrary delisting of a patent. Mylan relied on the incentives promised by Hatch-Waxman and committed enormous resources to challenging an invalid patent. The Agency should not frustrate the policies of the statute by delisting the '303 patent prior to judicial resolution of the question of whether 180-day exclusivity ends with patent expiration.

Conclusion

For the reasons set forth herein, Mylan requests that FDA not delist the '303 patent until after the expiration of Mylan's 180 day exclusivity.

Environmental Impact

The actions requested by this Petition are subject to categorical exclusion pursuant to 21 C.F.R. §25.30.

Economic Impact

An Economic Impact Statement will be provided at the request of the Commissioner.

Certification

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

Respectfully submitted,

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