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December 7, 1999

VIA FEDERAL EXPRESS

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room l-23
12420 Parklawn Drive
Rockville, Maryland 20857

Re: Petition for Stay of Approval of any ANDA for a generic version of Enalapril Other Than The One Submitted by TorPharm, a Division of Apotex Inc.

Dear Sir or Madam:

Pursuant to 21 C.F.R. § 10.35 and on behalf or our client TorPharm, a Division of Apotex Inc. ("TorPharm"), we submit this petition to seek a stay of approval of any Abbreviated New Drug Application ("ANDA") for a generic version of enalapril maleate ("enalapril") other than the ANDA submitted by TorPharm.

Petition for Stay of Action

The undersigned submits this petition requesting that the Commissioner of Food and Drugs stay the effective date of the following matter.

A. Decision Involved

The decisions involved are any decisions by the Food and Drug Administration ("FDA") to approve an ANDA for enalapril other than the one submitted by TorPharm, ANDA

99P-5317

PSA 1

No. 75-178, until the expiration of TorPharm's statutorily guaranteed 180-day generic marketing period.

B. Action Reauested

TorPharm asks that FDA stay the effective date of approval of any ANDA, regardless of the patent certification contained in that ANDA, for a generic version of enalapril other than ANDA No. 75-178 until 180 days after the earlier of either (1) the date of the first commercial marketing of the drug covered by ANDA No. 75-178, or (2) the date of a final decision of a court holding the enalapril patent to be invalid or not infringed. Moreover, given the immediate circumstances presented by this petition, TorPharm requests that the Commissioner consider TorPharm's petition on an expedited basis.

C. Statement of Grounds

I. Introductory Statement

TorPharm was the first company to file an ANDA for enalapril with a paragraph IV certification challenging the validity of the patent covering enalapril, U.S. Patent No. 4,374,829 (the "'829 patent"). TorPharm is, therefore, entitled to the 180-day generic marketing period provided for in 21 U.S.C. § 355(j)(5)(B)(iv). TorPharm's statutory exclusivity extends, if necessary, beyond expiration of the '829 patent. Accordingly, FDA should stay the effective date of approval of any enalapril ANDA, regardless of the patent certification contained in that ANDA, other than TorPharm's enalapril ANDA, until TorPharm's exclusivity period ends.

II. Background

On July 3 1, 1997, TorPharm filed an ANDA for enalapril. FDA accepted TorPharm's ANDA for filing on September 4, 1997 and assigned it No. 75-178. While its

ANDA initially contained a paragraph III certification, TorPharm amended its patent certification to a paragraph IV on March 12, 1999. At that time, TorPharm became the first company to file a paragraph IV certification with respect to the '829 patent. On May 28, 1999, TorPharm received notice that FDA had tentatively approved its enalapril ANDA.

On March 11, 1999, TorPharm provided the patent holder, Merck & Co., with the statutorily-required notice of its paragraph IV certification. On April 23, 1999, as provided for by statute, Merck filed an infringement action against TorPharm. Merck's infringement action is currently being litigated in the U.S. District Court for the Northern District of Illinois. While TorPharm is doing everything within its power to expedite this litigation, TorPharm simply cannot control the pace of Merck's infringement action.

The '829 patent is scheduled to expire on February 22, 2000.[1] Unless FDA grants TorPharm's petition on an expedited basis, companies other than TorPharm would be able to enter the enalapril market once the patent expires. TorPharm is, however, statutorily-entitled to exclusivity. Accordingly, TorPharm submits that FDA should grant TorPharm's stay petition immediately.

III. Discussion of Grounds

The Commissioner "may grant a stay in any proceeding if it is in the public interest and in the interest of justice." 21 C.F.R. § 10.35(e). The Commissioner "shall" grant a stay if: (1) the petitioner will otherwise suffer irreparable injury; (2) the petitioner's case is not frivolous and is being pursued in good faith; (3) the petitioner has demonstrated sound public

[1] TorPharm understands that enalapril might be entitled to pediatric exclusivity, in which case FDA could not approve an ANDA for generic enalapril until August 22, 2000.

policy grounds supporting the stay; and (4) the delay resulting from the stay is not outweighed by public health or other public interests. Id. In this case, a stay is appropriate.

A. TorPharm Would Be Irreparably Harmed By Denial Of The Stay

Without a stay, other ANDA applicants likely will begin to market a generic version of enalapril as soon as they receive FDA approval. If this marketing takes place, TorPharm will suffer economic injury because it will lose its "officially sanctioned head start" for its own generic enalapril product. Mova Pharmaceutical. Corn. v. Shalala, 955 F. Supp. 128, 131 (D.D.C. 1997), aff'd, 140 F.3d 1060 (D.C. Cir. 1998). The drug industry widely recognizes that "the earliest generic drug manufacturer in a specific market has a distinct advantage over later entrants." Id. Indeed, Congress recognized this very point when it created the generic exclusivity provision. No subsequent remedial measures can compensate TorPharm for the potential lost sales and market position it would have obtained with the 180-day exclusive marketing period for a TorPharm-manufactured enalapril product. Thus, TorPharm's injuries would be irreparable. See, e.g., Bracco Diagnostics, Inc. v. Shalala, 963 F. Supp. 20, 28 (D.D.C. 1997).

Moreover, unless the Commissioner grants this petition immediately, TorPharm could suffer additional injury. The current U.S. market for enalapril is approximately 750 million tablets. Manufacturing the tablets necessary to supply the entire generic market for enalapril will require TorPharm make significant commitments of both human and financial resources. It would thus be unwise for TorPharm to begin this process without the current stay. If TorPharm does not begin manufacturing tablets soon, however, it might not have the inventory necessary to meet the U.S. market need for generic enalapril immediately upon expiration of the

'829 patent. Accordingly, TorPharm will suffer significant economic injury if it does not receive the requested stay immediately.

B. TorPharm's Case Is Not Frivolous And Is Being Pursued In Good Faith On The Plain Language Of The Statute And Congress' Unambiguous Intent When Passing The Hatch-Waxman Amendments

The first company to file an ANDA containing a paragraph IV certification has a statutory right to 180 days of generic exclusivity. The expiration of the relevant patent does not impact that right. The plain and unambiguous statutory language, as well as Congress' clear intent when passing the Hatch-Waxman Amendments, mandate this result.

1. The Statutory Language Requires Exclusivity To Survive Patent Expiration

Section 355(j)(5)(B) governs FDA's approval of ANDAs. The plain language of this provision makes clear that generic exclusivity survives patent expiration, and that such exclusivity can delay the approval of both paragraph IV and paragraph III ANDAs:

> (B) The approval of an [ANDA] application . , . shall be made effective ~~on the~~ last applicable date determined under the following:
>
> * * *
>
> (ii) If the applicant made a [paragraph III] certification . . ., the approval may be made effective on the date certified under subclause (III).
>
> (iii) If the applicant made a [paragraph IV] certification . . ., the approval shall be made effective immediately unless an action is brought for infringement . . . . If such an action is brought . . ., the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice . . ., except that--
>
> (1) if . . . the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,

(II) if. . . the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders . . ., or

(III) if . . . the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

* * *

(iv) If the application contains a [paragraph IV] certification . . . and is for a drug on which a previous application has been submitted under this subsection continuing [sic: containing] such a certification, the application shall be made effective not earlier than one hundred and eighty days after -

(I) the date the [FDA] 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) (emphasis added).

The statute thus expressly provides that approval of paragraph IV ANDAs cannot be made effective until 180 days after first commercial marketing by the first paragraph IV filer or a decision of a court holding the patent invalid or not infringed. 21 U.S.C. §§ 355(j)(5)(B)(iv)(I), (II). The statute does not provide for approval of paragraph IV ANDAs upon patent expiration. Similarly, the statute states that approval of paragraph III ANDAs "may be made effective on the date" of patent expiration. The statute specifically does not require approval of paragraph III ANDAs to be effective upon patent expiration. Accordingly, Congress

has, therefore, spoken directly -- and favorably -- on the issue of whether exclusivity survives patent expiration.

When "the intent of Congress is clear, that is the end of the matter; for . . . the agency, must give effect to the unambiguously expressed intent of Congress." Chevron, U.S.A., Inc. v. Natural Resources Defense Counsel, Inc., 467 U.S. 837, 842-43 (1984); accord Amalgamated Transit Union v. Skinner, 894 F.2d 1362, 1368 (D.C. Cir. 1990). FDA, therefore, has no choice but to follow Congress' directive. Indeed, the courts have repeatedly held that FDA cannot adopt a regulation that imposes a requirement on an applicant's right to generic market exclusivity that is not found in the statute. See Purepac Pharmaceutical Co. v. Friedman, 162 F.3d 1201 (D.C. Cir. 1998); Mova Pharmaceutical Corp. v. Shalala, 140 F.3d 1060 (D.C. Cir. 1998) (invalidating FDA's so-called "successful defense" requirement); Granutec, Inc. v. Shalala, 139 F.3d 889, 1998 WL 153410 (4th Cir. Apr. 3, 1998) (same) (unpublished). For the Agency to conclude that exclusivity vanishes upon patent expiration is just as impermissible as its successful defense requirement -- as both place restrictions on exclusivity that Congress did not intend and that the statutory language does not support. Any decision to deny TorPharm exclusivity if the '829 patent expires would thus be as invalid as the successful defense requirement.

Accordingly, the Agency must award TorPharm its 180 days of generic marketing exclusivity, regardless of whether or not the enalapril patent expires before TorPharm concludes its infringement action with Merck.

2. Permitting Exclusivity to Survive Patent Expiration Is Consistent with Congress' Intent in Creating the 180-Day Exclusivity Period

Congress' intent when creating generic exclusivity further confirms that the statute permits exclusivity to survive patent expiration. Both FDA and the courts have recognized that Congress created the 180-day exclusivity period as an incentive for generic companies to challenge patents. See, e.g., Apotex Inc. v. Shalala, 53 F. Supp. 2d 454, 457 (D.D.C.) ("The 180-day exclusivity period provides an incentive for generic manufacturers to file paragraph IV certifications challenging patents that may be invalid, not infringed upon by the product that is the subject of the ANDA, or unenforceable."), aff'd, No. 99-523 1, 1999 WL 956686 (D.C. Cir. Oct. 8, 1999).

When it created the exclusivity provision, Congress was well-aware of the competing interests involved, i.e., "to increase the availability of low-cost generic drugs and to provide a period of exclusivity for the company that is the first to 'risk' the possibility of a patent infringement lawsuit." Apotex, 53 F. Supp. 2d at 462. Despite the short delay in generic competition the generic exclusivity causes, Congress nevertheless created that exclusivity because it correctly believed exclusivity to be critical to opening the door to generic competition.

Generic companies do not and cannot control the length of the infringement actions that patentees invariably bring. As the length of time to resolve complex patent cases increases, the more likely it becomes that litigation will not conclude prior to patent expiration. Eliminating exclusivity in such instances clearly frustrates Congressional intent and undermines the ability of the Hatch-Waxman Amendments to serve their intended purpose.

Patent cases typically take more than two years to resolve at the district court level alone.* As FDA has recognized, a "prudent" applicant will then wait for an affirmance by the Federal Circuit before marketing, which adds another 12 months. 59 Fed. Reg. 50338, 50354 (Oct. 4, 1994) (stating that "construe 'the court' as a district court, regardless of any appeal of the district court decision, would deny the benefits of exclusivity to a prudent applicant that delayed marketing its product until resolution of an appeal by the patent holder."). Then, of course, the applicant's 6 months of generic exclusivity must be considered.

If FDA concludes that patent expiration eliminates generic marketing exclusivity, companies will become reluctant to challenge any patent that could expire prior to an applicant's ability to fully use its exclusivity. As a result, FDA will decrease, if not eliminate entirely, the incentive to challenge patents that expire 40 to 42 months before the applicant is ready to file its ANDA. Congress simply could not have intended this result when it passed legislation intended to encourage patent challenges. Indeed, Congress intended to reward the first company to expend the substantial time and money necessary to advance the first patent challenge -- that the relevant patent expired prior to resolution of that challenge does not alter this result. Accordingly, permitting exclusivity to survive patent expiration is consistent with Congress' express intent to reward the first-filer its patent challenge.

[2] In 1998, the median time between the filing of the complaint and resolution at trial was, for example, 22 months in the Northern District of Illinois (where TorPharm's suit is pending), 32 months in the Northern District of California, 21 months in the Southern District of New York, 3 1 months in the Eastern District of New York, and 2.5 months in the District of New Jersey. Indeed, ten percent of the cases in these districts take between 48 and 54 months to be resolved.

C. Sound Public Policy Supports The Requested Stay

Public policy supports TorPharm's petition. FDA has acknowledged that unpredictability concerning the rules governing the 180-day exclusivity provision "makes it difficult for the industry to make business plans and other arrangements." 62 Fed. Reg. 63268, 63269 (Nov. 28, 1997). In this instance, FDA would best achieve predictability by adhering to the plain words of the statute.

D. The Delay Resulting Prom The Stay Is Not Outweighed By Public Health Or Other Public Interests

The delay of other generic companies' entry into the market resulting from a stay is not outweighed by public health or other public interests. First, there is no public health issue at stake because TorPharm and Merck together are more than capable of supplying the enalapril market. Second, the public's interest in the "faithful application of the laws" by FDA weighs in favor of staying approval of all other enalapril ANDAs. See Mova, 140 F.3d at 1066. Finally, the public has an interest in the predictability that would be served with FDA's adherence to the ANDA statute's plain language.

IV. Conclusion

For the reasons stated, TorPharm, a Division of Apotex Inc., asks that FDA not approve any ANDA for a generic version of enalapril other than ANDA No. 75-178 until 180 days after either (1) the first commercial marketing of the drug covered by ANDA No. 75-178 or (2) the date of a final decision of a court holding the enalapril patent invalid or not infringed. Moreover, TorPharm asks the Commissioner to consider its petition on an expedited basis. Finally, if FDA decides to approve any other ANDA before the expiration of TorPharm's

exclusivity period, TorPharm asks that it be notified so that it can seek timely judicial review of that decision.

Respectfully submitted,

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