

FDA's Exclusivity Forfeiture Saga Continues

Thursday, May 15, 2008 --- Just when we were all starting to get a better understanding of the exclusivity forfeiture provisions added to the Hatch-Waxman Act by the 2003 Medicare Modernization Act (the "MMA"), the Food and Drug Administration ("FDA") has thrown us another curveball.

In its May 7, 2008 letter ruling on Cobalt's exclusivity period relating to its generic version of Bayer's Precose (acarbose) tablets, FDA determined that Cobalt had forfeited its exclusivity period under the MMA forfeiture provisions because Cobalt did not obtain final approval of its ANDA within 30 months and Bayer had delisted its patent from the Orange Book.

This letter ruling required FDA to revisit two previously settled issues.

Earlier this year, in FDA's Jan. 17, 2008 letter ruling on granisetron, we learned that it is FDA's position that a first filer will not forfeit its 180-day generic exclusivity period when it fails to market its product within 30 months of filing its ANDA if a court decision against the patent has not occurred. (See "FDA Removes Teeth from Exclusivity Forfeiture," *IPLaw360*, Jan. 25, 2008.)

And almost two years ago, in the D.C. Circuit's decision in *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120 (D.C. Cir. 2006), we learned that FDA could not delist a patent at the request of the brand company when a Paragraph IV certification had been filed under pre-MMA law.

The murky exclusivity forfeiture and patent listing provisions of the Hatch-Waxman Act seem to be in a constant state of flux these days. Cobalt has challenged FDA's acarbose letter ruling in court, and the district court denied its motion for a temporary restraining order on May 9 and set an expedited preliminary injunction briefing schedule. A hearing is scheduled to take place on June 12, which may provide more clarity on these issues.

The Hatch-Waxman Act

Before marketing a new drug in the United States, the Federal Food, Drug and Cosmetics Act ("FDCA") requires that a drug company submit to FDA a New Drug Application ("NDA"), demonstrating that the drug is safe and effective for its proposed use.

Once approved by FDA, a new drug is generally referred to as a "branded" (or "innovator") drug because NDA holders usually market such drugs under brand-name trademarks.

Along with clinical studies and other data submitted to FDA, an NDA

applicant is required to provide to FDA the patent number and expiration date of any patent covering the drug product or method of using such drug product. FDA lists this patent information in a publication commonly referred to as the “Orange Book.”

Under the Hatch-Waxman Act, the manufacturer of a generic drug may file an ANDA, relying on the safety and efficacy data submitted by the NDA holder, if the ANDA applicant can demonstrate that the proposed generic product is bioequivalent to the approved drug. An ANDA applicant must file, in addition to its proof of bioequivalence, a certification with respect to any patent covering the proposed generic product or a method of using such product.

The applicant must certify one of the following: (I) that patent information has not been filed for the approved drug; (II) that the listed patent has expired; (III) that the listed patent will expire on a particular date (and that the ANDA applicant is not seeking to market its generic product until the patent expires); or (IV) that the listed patent is invalid, unenforceable or would not be infringed by the manufacture, use or sale of the proposed generic product (a “Paragraph IV certification”).

To encourage patent challenges, Congress provided that the first applicant to file an ANDA with a Paragraph IV certification with respect to a particular branded drug (the “first filer”) is, under certain circumstances, entitled to a 180-day exclusivity period during which the first filer is the only ANDA applicant allowed to market a generic version of the branded product.

As originally enacted, the 180-day exclusivity period begins to run on the earlier of: (1) the date of the first commercial marketing by the first filer; or (2) the date of a decision by a court holding the listed patent invalid, unenforceable or not infringed.

Under the changes implemented by the MMA in 2003, however, the 180-day exclusivity period is triggered only by the first commercial marketing of the generic drug. The exclusivity period is now subject to numerous forfeiture events, including the failure to commence marketing within certain statutorily mandated time periods.

The “Failure To Market” Forfeiture Provision

In response to a perceived problem of “exclusivity parking” where a first filer and brand company would agree to a delayed market entry date, Congress created a set of conditions in the MMA under which a first filer forfeits its 180-day exclusivity period.

While some forfeiture provisions are relatively straightforward (e.g., withdrawal of the ANDA or expiration of the listed patent), the failure to market provision was created as a complex algorithm of conditions which requires the application of an “earlier-of/later-of” analysis:

(l) Failure To Market. The first applicant fails to market the drug by the later of –

(aa) the earlier of the date that is –

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).

FDA's Granisetron Letter Ruling

In FDA's January 2007 granisetron letter ruling, FDA determined that a first filer does not forfeit its exclusivity even if the first filer fails to obtain final approval within 30 months as long as a court decision triggering event had not occurred. Specifically, the agency stated that:

"180-day exclusivity is not forfeited for failure to market when an event under subpart (aa) has occurred, but – as in this case – none of the events in subpart (bb) has occurred. The 'failure to market' provision results in forfeiture when there are two dates on the basis of which FDA may identify the 'later' event as described in section 505(j)(5)(D)(i)(I). The provision does not effect a forfeiture when an event under subpart (aa) has occurred, but no event under subpart (bb) has yet occurred."

In other words, even if 30 months have passed since the first filer submitted its ANDA to FDA, the first filer will not forfeit its exclusivity unless there has been an appellate court decision against the Orange Book patent or a district

court settlement order or consent decree against the patent.

Patent Delisting In Ranbaxy V. Leavitt

In September 2006, the D.C. Circuit addressed the issue of patent delisting by the brand company.

Specifically, the D.C. Circuit found that FDA was precluded from delisting two patents relating to Merck's Zocor (simvastatin) upon Merck's request because two ANDA filers had submitted Paragraph IV certifications and were entitled to the 180-day generic exclusivity period. *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120 (D.C. Cir. 2006).

FDA's Acarbose Letter Ruling

Cobalt filed the first ANDA with a Paragraph IV certification to U.S. Patent Number 4,904,769 ("the '769 patent"), which Bayer had listed in the Orange Book in connection with its Precose (acarbose) tablets.

Cobalt did not obtain final approval of its ANDA within 30 months. Before Cobalt received final approval and before the 30 months had run, Bayer sent a letter to FDA, requesting that the '769 patent be delisted from the Orange Book.

In October and November 2007, Cobalt filed citizen petitions with FDA, requesting, among other things, that subsequently-filed ANDA's be delayed from receiving final approval until Cobalt's exclusivity period had run.

FDA rejected Cobalt's petitions, finding that Cobalt had forfeited its exclusivity under the MMA's marketing forfeiture provisions.

Specifically, FDA found that the patent at issue was delisted when Bayer's delisting request was filed, resulting in a forfeiture under Section 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC).

FDA rejected the argument that *Ranbaxy v. Leavitt* precluded the delisting, finding that the D.C. Circuit's decision was limited to situations falling under pre-MMA law.

FDA also rejected the argument that only a delisting resulting from a counterclaim asserted in an infringement action – as set forth in 21 U.S.C. § 355(j)(5)(C)(ii) – could lead to a forfeiture. Because the 30 months from the filing of Cobalt's ANDA occurred after the delisting of the patent, FDA determined that Cobalt forfeited its exclusivity as of the 30 month deadline in September 2007.

An interesting side-note in this case involved another forfeiture provision directed towards the first filer's inability to obtain tentative approval "within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the

application imposed after the date on which the application is filed.” 21 U.S.C. § 355(j)(5)(D)(i)(IV).

In deciding that there was no forfeiture under this provision, FDA had to address two discrete issues.

First, FDA determined that the date of “filing” for purposes of this provision is the “date that qualifies the applicant as a first applicant for 180-day exclusivity purposes: the date the ANDA is sufficiently complete to permit a substantive review.” This issue was significant because Cobalt received a refuse to file letter relating to certain deficiencies in its original ANDA.

After resolving this issue, FDA then determined that Cobalt’s failure to obtain tentative approval was caused by a change in bioequivalence requirements by FDA. As a result, FDA concluded that Cobalt did not forfeit its exclusivity period by failing to obtain tentative approval within 30 months.

What Now?

Through the acarbose letter ruling, FDA has staked out additional positions relating to the MMA forfeiture provisions. Cobalt has challenged FDA’s decision in court, although the district court has denied Cobalt’s motion for a temporary restraining order and established an expedited preliminary injunction briefing schedule.

It’s possible that we may have a decision by the district court by the end of June, which may provide more clarity to the MMA forfeiture provisions. Until then, any analysis of the forfeiture provisions and their impact on market exclusivity and entry should be undertaken with great caution.

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