



# PHARMACEUTICAL LAW & INDUSTRY



## REPORT

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### Exclusivity

#### **FDA Says Hi-Tech Forfeited Exclusivity; Way Paved for Approval of All Cosopt ANDAs**

**H**i-Tech Pharmacal Co. forfeited its 180-day period of exclusivity for a generic version of Merck & Co.'s eye disease treatment Cosopt (dorzolamide hydrochloride and timolol maleate), the Food and Drug Administration told the company in a letter released Oct. 29.

FDA gave final approval Oct. 28 to Hi-Tech's abbreviated new drug application (ANDA) to make a generic version of Cosopt and to Apotex Inc.'s ANDA for generic Cosopt—the opposite of the result that Hi-Tech was seeking.

Meanwhile, Prasco Laboratories said Oct. 28 it had begun shipping an authorized generic version of Cosopt under an agreement with Merck. The brand-name drug had annual sales of \$342 million for the 12 months ending June 2008.

Hi-Tech earlier sought a preliminary injunction banning FDA from approving any other generic copies of Cosopt during Hi-Tech's exclusivity period under the Hatch-Waxman Act, but a federal court rejected its request Oct. 10 (6 PLIR 1202, 10/24/08).

Cosopt is a brand-name ophthalmic drug marketed by Merck to reduce elevated intraocular pressure (IOP) in certain patients with open-angle glaucoma or ocular hypertension. The agency said that Hi-Tech can be found to have failed to market the generic drug by a certain deadline if a triggering forfeiture event occurs, which, in this case, is the brand-name company's request to delist relevant patents from the FDA *Orange Book*.

**Third MMA Forfeiture Exclusivity Decision.** FDA's latest exclusivity decision is its third decision to address the forfeiture provisions of the 180-day exclusivity period under the Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA). It follows ear-

lier exclusivity decisions on acarbose (FDA Docket No. 2007-N-0445, 5/7/08) and granisetron (FDA Docket No. 2007-N-0389, 1/17/08).

The latest decision "certainly cuts back on the availability of the 180-day exclusivity period," Steven H. Sklar of Leydig, Voit & Mayer, Chicago, told BNA.

"The key point," Sklar said, "is [the] harshness of FDA's interpretation involving the failure of an ANDA filer to get to market within 30 months of the date of submission of the ANDA. According to FDA, this 30-month deadline is not stayed or otherwise delayed if an ANDA filer can't get to market due to another patent or exclusivity."

Sklar observed that it is not "uncommon" for an ANDA filer to file a Paragraph III certification on a molecule patent and a Paragraph IV on a later-expiring formulation or polymorph patent. Under a Paragraph III certification under the Hatch-Waxman Act, an applicant certifies that it will not seek to market the generic drug until the patent expires. With a Paragraph IV certification, an ANDA applicant seeks to market a generic before the patent at issue expires, certifying that the patent is invalid or not infringed. But Sklar said, "Based on FDA's decision in this case over Cosopt, it would appear that there is no way to hold onto any 180-day exclusivity based on the Paragraph IV [certification] for the later-expiring patents."

Mitchell M. Wong, of counsel in Morrison & Foerster LLP's New York office, told BNA that the Hi-Tech decision appears to solidify FDA's position that "the delisting of patents from the *Orange Book* starts the forfeiture clock even if the first Paragraph IV certificant is unable to market the generic drug lawfully."

The *Orange Book* is formally known as FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*.

"FDA's position . . . injects substantial uncertainty into the marketing processes of generic drug companies that hold the first Paragraph IV certifications," Wong said, adding that "the uncertainties are magnified, as was the case here in Hi-Tech, by the FDA's

practice of withholding a [n exclusivity] decision until the last permissible day.”

**FDA Letter Decision.** In its letter to Hi-Tech explaining the agency’s exclusivity forfeiture decision, Gary Buehler of FDA said that Merck’s request to FDA to withdraw two of its Cosopt patents, U.S. Patent Nos. 6,248,735 (the ’735 patent) and 6,316,443 (the ’443 patent) from the FDA’s *Orange Book*, constitutes a “failure to market” forfeiture event under MMA. Thus, FDA said, Hi-Tech forfeited its eligibility for 180-day marketing exclusivity as the first ANDA applicant for dorzolamide/timolol, and the agency now can approve any ANDA for dorzolamide/timolol that is otherwise eligible for approval. Buehler is director of the Office of Generic Drugs at FDA’s Center for Drug Evaluation and Research.

The MMA added exclusivity forfeiture provisions to the Drug Price Competition and Patent Term Restoration Act of 1984 (known as the Hatch-Waxman Act) to curb potential roadblocks to competition that Hatch-Waxman exclusivity periods could create.

Specifically, the MMA provides that the 180-day exclusivity period “shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.” Failure to market forfeiture events, listed at 21 U.S.C. § 355(j)(5)(D)(i)(I)(aa) and (bb), can supply such a forfeiture trigger.

**No-Fault Basis.** According to FDA, the MMA’s “failure to market” forfeiture provisions operate on a no-fault basis: that is, even if Hi-Tech did not “fail” to do anything, it can still be found to have failed to market under the MMA if a triggering forfeiture event occurs, such as Merck’s withdrawal request. The failure to market forfeiture events, FDA said in the letter, “must be read as establishing a ‘no-fault’ forfeiture when an applicant fails to market by one of the identified dates.”

In this case, Hi-Tech filed a Paragraph IV certification against all three patents Merck listed for Cosopt in FDA’s *Orange Book*: U.S. Patent No. 4,797,413 (the ’413 patent), the ’735 patent, and the ’443 patent. The ’413 patent expired on April 28, 2008, with pediatric exclusivity extending the term to Oct. 28, 2008.

Meanwhile, the ’735 patent and the ’443 patents were scheduled to expire on April 17, 2011. Merck sued Hi-Tech for patent infringement based on its ANDA filing, but only sued on the ’413 patent, not on the ’735 or the ’443 patents. During the course of the litigation over the ’413 patent, Merck asked FDA to remove the ’735 and ’443 patents from the *Orange Book*.

Merck won the patent litigation over the ’413 patent, which blocked Hi-Tech from marketing its generic—and FDA from approving it—until Oct. 28, 2008.

**Forfeiture Dates.** The “failure to market” provisions of the MMA consist of two subparts: (aa) and (bb). A forfeiture occurs upon “the later of” subparts (aa) or (bb). The statute sets the forfeiture date by identifying the relevant dates for subparts (aa) and (bb), and selecting the later date.

Under Subpart (bb), there are three subitems, any of which can set a forfeiture event in motion. One of the subitems, invoked by FDA in this case, is Subitem (CC),

which provides a forfeiture date upon the new drug application holder’s delisting of all patents that were the subject of an earlier Paragraph IV certification.

The date set under subpart (aa) is “the earlier of” either 75 days after final approval of the ANDA following any Paragraph IV certification, or 30 months from the date of submission. In this case, FDA said the (aa) date was April 11, 2008, which is 30 months after Hi-Tech submitted its ANDA to FDA. The (bb) date was July 10, 2006: 75 days after Merck withdrew the information on the ’735 and ’443 patents, FDA said.

In this case, FDA said, the later date, for forfeiture purposes, was April 11—30 months after Hi-Tech submitted its ANDA to FDA. Thus, Hi-Tech forfeited its exclusivity under the MMA on April 11, 2008, FDA concluded.

**Hi-Tech’s Arguments Rejected.** In the letter, FDA rejected Hi-Tech’s argument that it should not lose exclusivity for circumstances beyond its control—such as when it is blocked from marketing by patents or exclusivity. Congress, FDA said, knew how to fashion exceptions for such events, but chose not to create such an exception in the failure-to-market provision.

“In accordance with the specific language in the statute, we apply the forfeiture under section 505(j)(5)(D)(i)(I) when an applicant fails to market, even when that failure to market is not the fault of the applicant but instead is a result of some outside factor (i.e., patent or exclusivity) over which the first applicant may have no control,” FDA said.

In addition, FDA discounted Hi-Tech’s argument that the 180-day exclusivity tolling provisions under the Best Pharmaceuticals for Children Act (Merck’s six-month period of pediatric exclusivity on the brand name drug expired Oct. 28) operated to bar the forfeiture of its generic exclusivity. But FDA said that those tolling provisions did not apply to cases, like this one, where the 2003 MMA was in effect. “[T]here is,” FDA said, “no statutory basis on which to toll the failure-to-market forfeiture event because of the innovator’s pediatric exclusivity.”

Finally, FDA also found unconvincing Hi-Tech’s argument that the agency had mishandled Merck’s delisting request by continuing to list the ’735 and ’443 patents in the *Orange Book* while treating the delisting request itself as a failure-to-market forfeiture event. Among other things, FDA said that its approach of continuing to list the patents “appropriately preserved potential exclusivity for Hi-Tech until FDA determined that there could be no exclusivity based on the patents that Merck had withdrawn.”

Thus, FDA said, after considering Hi-Tech’s ANDA, applicable law and comments of interested parties, “we have concluded that Hi-tech was eligible for 180-day exclusivity for the ’735 and ’443 patents, but that exclusivity was forfeited under the failure-to-market provisions at section 505(j)(5)(D)(i)(I) of the Act.”

BY DANA A. ELFIN

*The FDA’s exclusivity decision letter to Hi-Tech, FDA Docket No. 2008-N-0483, 10/28/08, is available on the Web at <http://op.bna.com/hl.nsf/r?Open=deln-7kvlcl>.*