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VIA HAND-DELIVERY

Dockets Management Branch
Food and Drug Administration
HFA - 305
Room 1061
5630 Fishers Lane
Rockville, MD 20857

Re: Docket No. 2007N-0389; Comments Regarding Exclusivity for Granisetron Hydrochloride Injection

Ranbaxy Inc. submits these comments regarding 180-day exclusivity for granisetron hydrochloride injection (granisetron). The question presented in comments submitted by Teva Parenteral Medicines is whether section 505(j)(2)(5)(D)(i)(I) of the Food, Drug, and Cosmetic Act (FDCA) requires forfeiture of exclusivity if, 30 months after submission of the ANDA, a first applicant has obtained a tentative approval but has failed to launch its product within 30 months of ANDA submission and the applicant has not been sued for infringement based on a paragraph IV certification that qualifies the applicant for exclusivity. Ranbaxy supports Teva's position that the statute cannot be read to require forfeiture in this situation.

A. The Plain Meaning of the "Later-Of" Clause

By its plain meaning, section 505(j)(2)(5)(D)(i)(I) provides for forfeiture of exclusivity only in the event of, with regard to each patent qualifying the first applicant for exclusivity (hereinafter "qualifying patent"), (1) a court decision or order containing a finding the patent is invalid or not infringed or (2) the delisting of the patent. Once such an event has occurred with regard to each qualifying patent, the first applicant forfeits exclusivity unless it launches the drug within certain prescribed timelines, which differ depending on the circumstances.

Section 505(j)(2)(5)(D)(i)(I) (hereinafter the "'Later-Of' Clause") achieves this end by requiring forfeiture if "[t]he first applicant fails to market the drug *by the later of*" two dates.[1]

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[1] Emphasis added. Section 505(j)(5)(D)(i)(I) provides as follows:

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

2007N-0389 C3

The first date is described in section 505(j)(2)(5)(D)(i)(I)(aa) as 75 days after approval or 30 months after submission of the ANDA, whichever comes first (hereinafter the "Subclause (aa) Date"). The second date (hereinafter the "Subclause (bb) Date") is described in section 505(j)(2)(5)(D)(i)(I)(bb) as 75 days after each qualifying patent is either (1) the subject of a final court decision, settlement order, or consent decree containing a finding that the patent is invalid or not infringed or (2) withdrawn from listing

Thus the predicate for forfeiture under the "Later-Of" Clause is the determination of the later of two dates. As a matter of simple logic, that determination cannot be made until both dates are determined. Because, in the case of granisetron, none of the events described in Subclause (bb) has occurred, the Subclause (bb) Date cannot be determined and the "Later-Of" Clause cannot be applied. Under the rule of *Chevron,* this plain meaning of the statute must govern.[2]

An alternative interpretation of the "Later-Of" Clause that would trigger forfeiture under Subclause (aa) prior to the occurrence of the Subclause (bb) Date would not only be contrary to the plain meaning of the statute, but would effectively reverse that plain meaning by triggering forfeiture on the *earlier* of the Subclause (aa) Date and the Subclause (bb) Date rather than on the "later" date as specified in the statute.

B. Giving Effect to the Tentative Approval Clause

An interpretation that would trigger forfeiture based solely on the determination of the Subclause (aa) date would also be precluded under principles of statutory construction requiring that each provision of a statute be given force and effect. A separate forfeiture provision, section 505(j)(5)(D)(i)(IV), requires forfeiture if "[t]he first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed" (hereinafter the "Tentative Approval Clause"). If exclusivity were forfeited under the "Later-Of" Clause based solely on the Subclause (aa) Date, the Tentative Approval Clause would have no effect. An applicant's failure to obtain a tentative approval within 30 months of ANDA filing would mean, by definition, that the applicant previously failed to launch its product by the Subclause (aa) Date (30 months after ANDA submission or 75 days after approval, whichever comes first).

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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).

2 *Chevron U.S.A., Inc., v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842-43 (1984).

Thus the Subclause (aa) events cannot be deemed an independent basis for forfeiture. Subclause (aa) does not embody a general congressional intent to require launch or exclusivity forfeiture within 30 months of ANDA submission. It is rather intended to protect a first applicant from being forced into an even earlier launch or forfeiture as a result of a Subclause (bb) occurring within that 30-month period and prior to the approval of the product. Where the Subclause (bb) Date occurs during that period and prior to approval, the Subclause (aa) Date may enable first applicant to delay launch until 75 days after approval or the end of the 30-month period, whichever comes first.

C. The Coherent Approach Embodied in the Plain Meaning of the Statute

The "Later-Of" Clause and Tentative Approval Clause, read together and in accordance with their plain meaning, reflect a clear and coherent approach by Congress to concerns over unwarranted delays in generic competition resulting from 180-day exclusivity. The approach is designed to prevent parking of exclusivity after removal of a barriers posed by listed patents and ensure that first applicants can meet substantive requirements for approval.

The "Later-Of" Clause is an anti-parking provision designed to force a first applicant to launch or forfeit after either a court decision/order that removes the patent barrier for one or more paragraph IV applicants or a delisting with regard to each qualifying patent. It is clearly not designed to require an applicant to launch at risk – within 30 months of submission or at any other time – prior to a final court decision on a listed patent.

The Tentative Approval Clause serves a different purpose. It ensures that, where there is no early Subclause (bb) event requiring launch within 30 months of ANDA filing, the applicant demonstrates active pursuit of approval and ability to meet substantive approval requirements by obtaining a tentative approval.

The scheme thus operates as follows:

1. Generally, if the qualifying patent (or each of the qualifying patents) has either been the subject of a court decision or order with a finding of invalidity or noninfringement or been delisted per Subclause (bb), the first applicant will be required to launch within 75 days or forfeit exclusivity.
2. If, however, the 75-day clock under Subclause (bb) would require launch within 30 months of ANDA submission, the launch/forfeiture clock may be extended until the end of the 30-month period or until 75 days after the product's approval, whichever comes first, per Subclause (aa).
3. If there has been no Subclause (bb) event requiring launch within 30 months of ANDA filing, the first applicant will be required to demonstrate active and capable pursuit of approval by having obtained tentative approval in order to avoid exclusivity forfeiture.

D. Forcing an Applicant to Launch at Risk

An interpretation of the "Later-Of" Clause that would require product launch under Subclause (aa) (within 30 months of ANDA submission) in the absence of a final court decision or order or delisting with regard to the qualifying patent(s) would essentially require the first applicant to gain full approval within the 30-month timeframe and to launch at risk. Even if made sense to require an applicant to obtain final approval prior to the occurrence of a Subclause (bb) event – which is not the case – a requirement that the first applicant launch at risk would be contrary to Congress' clearly expressed intent in the MMA.

This intent is manifest by Congress' reinstatement in the MMA of FDA's original interpretation of the pre-MMA exclusivity provisions. The agency had initially interpreted the court decision trigger of the pre-MMA exclusivity provisions[3] to apply only with regard to a final court decision from which no appeal has been or can be taken.[4] This interpretation was based on the agency's view that "[i]t serves the public interest to permit a prudent ANDA holder in [an infringement suit] to stay off the market until the litigation is resolved, thereby minimizing potential damages."[5] The agency was forced to amend its regulations implementing this approach, however, based on court decisions holding that the 180-day exclusivity period is triggered by a district court decision of invalidity or noninfringement, even if that decision is appealed.[6] The legislative history of the MMA reflects that the agency brought this issue before squarely before Congress.[7] In section 1102(b)(3) of the MMA, Congress demonstrated its agreement with FDA's concern over requiring first applicants to

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3 FDCA § 505(j)(5)(B)(iv)(II) as in effect prior to passage of the MMA.

4 *See* 65 Fed. Reg. 43,233, 43,234 (2000).

5 54 Fed. Reg. 28,872, 28,894 (1989)

6 65 Fed. Reg. at 43,234.

7 The Acting FDA Commissioner explained the agency's concern as follows:

> . . . FDA had interpreted the "court decision" that could begin the running of 180-day exclusivity (and the approval of the ANDA) as the final decision of a court from which no appeal can be or has been taken - generally a decision of the Federal Circuit. FDA's interpretation had meant that an ANDA applicant could wait until the appeals court had finally resolved the patent infringement or validity question before beginning the marketing of the generic drug.
>
> FDA had taken this position so that the generic manufacturer would not have to run the risk of being subject to potential treble damages for marketing the drug, if the appeals court ruled in favor of the patent holder. The current interpretation means that if the 180-day exclusivity is triggered by a decision favorable to the ANDA applicant in the district court, the ANDA sponsor who begins to market during that exclusivity period now may run the risk of treble damages if the district court decision is reversed on appeal to the Federal Circuit. As a practical matter, it means that many generic applicants may choose not to market the generic and thus the 180-day exclusivity period could run during the pendency of an appeal.

Statement of The Honorable Lester Crawford, D.V.M., Ph.D., Acting Commissioner, Food and Drug Administration, Committee on House Energy and Commerce Subcommittee on Health, 107th Cong. (October 9, 2002).

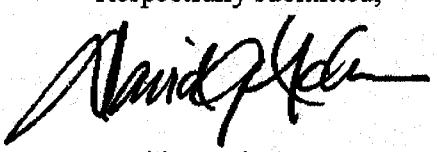
launch at risk or lose their exclusivity by reinstating FDA original interpretation of the "court decision" that triggers exclusivity under the pre-MMA provisions.[8]

Congress further evidenced its intent to protect first applicants from being forced to launch at risk in the "Later-Of" Clause of the MMA exclusivity provisions. The 75-day forfeiture clock under Subclause (bb) is triggered only after a patent delisting or 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."[9] An interpretation of the "Later-Of" Clause that would require an applicant to launch at risk within 30 months from ANDA submission – in the absence of even an initial district court decision – would be contrary to the clearly expressed intent of Congress, and would be unfair to the applicant who would be forced to forfeit exclusivity in the face of unresolved patent liability.

E. Assuming the Subclause (bb) Date Will Not Occur

FDA cannot interpret the "Later-Of" Clause to require forfeiture on the Subclause (aa) Date based on a determination that the events described in Subclause (bb) cannot occur. First, the wording of the statute would not permit such a construction. A agency determination that the Subclause (bb) events cannot not occur would mean that there is no Subclause (bb) Date. A date that can never come to pass cannot be deemed to have occurred earlier than the Subclause (aa) date. The Subclause (bb) Date must be determined before the "Later-Of Clause can be applied. Second, there is no evident basis in this docket, or under any foreseeable set of facts, for FDA to determine that no Subclause (bb) event can occur with regard to granisetron after the Subclause (aa) Date. Even where there is no lawsuit pending against any ANDA applicant on the Subclause (aa) Date, there is always some residual possibility that (1) a drug company will file a new paragraph IV ANDA, sue for declaratory judgment or be sued for infringement, and obtain a decision or settle the case with a finding of invalidity or noninfringement[10] or (2) the NDA holder will request that the patent be delisted.

Respectfully submitted,



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8 MMA § 1102(b)(3) provides as follows:

(3) EFFECTIVE DATE OF APPROVAL- The amendments made by subsections (a)(2)(A)(ii)(I) and (b)(2)(B)(i) apply with respect to any patent information submitted under subsection (b)(1) or (c)(2) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) on or after August 18, 2003.

9 FDCA § 505(j)(5)(D)(i)(I)(bb)(AA).

10 A lawsuit by or against any paragraph IV applicant could result in a decision or settlement that could constitute a Subclause (bb) event.