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Food and Drug Administration
Office of Generic Drugs, HFD-600
Attention: Gary J. Buehler, Director
7519 Standish Place
Rockville, Maryland 20855

April 4, 2007

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ANDA-77-262

Amlodipine Besylate
Response to Request for Comments
Controlled Correspondence

Dear Mr. Buehler,

Roxane Laboratories, Inc. is responding to your letter of March 29, 2007 soliciting comments regarding approval of abbreviated new drug applications for amlodipine besylate products.

General Comment: Mylan's ANDA was filed on May 22, 2002, and Pfizer sued for infringement of their '303 patent on September 20, 2002 (after the 45 day window). According to the Orange Book, Mylan's ANDA received effective approval on October 3, 2005. On February 27, 2007 the district court ruled in favor of Pfizer and issued an injunction to prevent Mylan from commercializing its product until after the expiration of the '303 patent and its pediatric exclusivity. Roxane asserts that once the district court ordered that the effective date for Mylan's approval be no earlier than the expiration of the pediatric exclusivity the effective approval should have been withdrawn. Consequently, Mylan should not have launched. Since the mandate could not have been issued before the patent expired, Mylan should not receive 180-day exclusivity.

With regard to the Agency's specific questions, Roxane has the following comments:

Question 1: What date controls FDA's giving effect to the decision in *Pfizer Inc. v Apotex*, Inc., No. 2006-1261 (Fed. Cir. March 22, 2007) ("*Apotex* decision") holding that Pfizer's patent 4,879,303 ("the '303 patent") is invalid? Can FDA treat the '303 patent as invalid as of March 22, 2007, or must FDA await the issuance of the mandate? Is the answer the same for all purposes, that is, for determining the applicability of pediatric exclusivity, the triggering of 180-day exclusivity, and the eligibility of other ANDA applicants for final approval?

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Comment 1: FDA must await the issuance of a mandate before the March 22nd opinion can be used in determining applicability of pediatric exclusivity, the triggering of 180-day exclusivity and the eligibility of other ANDA applicants for final approval.

Question 2: If FDA must await the issuance of the mandate, does pediatric exclusivity bar approval of all unapproved ANDAs in the meantime?

Comment 2: Yes, all of the tentative approvals are subject to pediatric exclusivity until the issuance of the mandate. Once the mandate is issued, it would then be proper for the FDA to review the ANDAs to confirm that the standards for approval continue to be met and issue approval letters where applicable.

Question 3: If and when the *Apotex* decision is implemented, what is the effect of the decision that the '303 patent is invalid on the obligation of an ANDA applicant to change its certification? Must Pfizer delist its patent, so that certifications can be withdrawn? Or can FDA treat an invalid patent as delisted as a matter of law, and presume the withdrawal of the certifications? Or must the ANDA applicants file paragraph II certifications stating the '303 patent has expired?

Comment 3: FDA can delist the patent as a matter of law, and ANDA applicants are not required to refile certifications.

Question 4: If and when the Apotex decision is implemented and the patent is treated as invalid, does pediatric exclusivity attach to the '303 patent with respect to any unapproved ANDAs? Does it matter whether the ANDA applicant filed a paragraph III or IV certification before patent expiration?

Comment 4: When the patent is invalidated, the pediatric exclusivity should expire with regard to all unapproved ANDAs regardless of the filed certification.

Question 5: Does 180-day exclusivity triggered before a patent expires continue to bar approvals of other ANDAs after the patent expires, even if other ANDA applicants change their certifications to paragraph II or withdraw their certifications altogether?

Comment 5: With respect to 180-day exclusivity, in this particular instance since an approval letter could not have been re-issued until after the patent expired on March 25, 2007, Mylan did not have approval to market before the patent expiration date and therefore Mylan should lose the 180-day exclusivity.

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It is Roxane's belief that once the mandate is issued and the Apotex decision is implemented then no pediatric exclusivity is granted and all ANDA holders should receive approval.

Correspondence concerning this correspondence should be directed to Elizabeth Ernst, Associate Director, DRA-Multisource Products, Roxane Laboratories, Inc. I can be reached at (614) 272-4785 and by telefax at (614) 276-2470. In my absence, please contact Marilynn Davis, Regulatory Affairs Manager at (614) 241-4123.

Respectfully,

Elizabeth A. Ernst
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