



November 17, 2006

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*BY HAND DELIVERY*

Division of Dockets Management  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

**Re: Docket No. 2006P-0209**

Dear Sir or Madam:

Valeant Pharmaceuticals International ("Valeant") submits the following response to the September 29, 2006 reply comments from Lachman Consultant Services, Inc. ("Lachman").

Lachman has petitioned FDA to determine whether the 5 mg/mL, 10 mg/2 mL, 15 mg/3 mL, and 20 mg/4 mL fixed-dose Diastat® (diazepam rectal gel) products were withdrawn from the market for reasons of safety or effectiveness. In comments previously submitted to this docket, Valeant has shown that the risk of medication errors led FDA to require Valeant to quickly and completely withdraw these fixed-dose products from the market.<sup>1</sup> In essence, FDA has already determined that the Diastat® products were withdrawn for reasons of safety.

In its reply, Lachman asserts that withdrawal of the fixed-dose product cannot have been for reasons of safety or effectiveness, because the approval letter for Diastat® AcuDial™ makes no mention of it.<sup>2</sup> This is faulty logic. Withdrawal of the fixed-dose products was an integral part of Valeant's risk management program (RMP), implementation of which was a condition of FDA's approval of Diastat® AcuDial™. The approval letter made reference to the RMP, but not the market

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<sup>1</sup> Valeant Comments, Aug. 7, 2006 (Docket 2006P-0209/C1).

<sup>2</sup> Lachman Reply, Sept. 29, 2006 (Docket 2006P-0209/RC1) at 1, 3 (noting that approval letter "is devoid of any statement regarding the removal of the fixed-dose configurations from the market" and presuming that the RMP therefore does not "identify or address any risks associated with the concurrent availability of a fixed-dose syringe and a flexible-dose syringe").

withdrawal component, simply because Valeant had already addressed that issue to the agency's satisfaction.

Attached is a redacted copy of FDA's March 2005 approvable letter for Diastat® AcuDial™, in which FDA made clear that, to avoid confusion between products and the risk of medication error, the overlapping fixed-dose products must be removed quickly and completely:

We recognize that, under your current plan, the new and old syringes will be in the marketplace at the same time for between three and six months. ***We recommend that this duration of overlap be as short as possible, and would like to discuss with you the possibility that this can be avoided.*** If the products are to be available at the same time (regardless of the duration), we believe that you will need to be aggressive about informing the relevant parties about this co-existence, to avoid confusion. ***We would like to see the details of this portion of the plan.***<sup>3</sup>

As the highlighted portions indicate, it was clear that the fixed-dose products were going to be removed from the market. The only question was whether there would be a temporary overlap and, if so, what its duration would be. The six-month phase-out initially proposed was certainly too long, in FDA's view. The agency wanted Valeant to completely eliminate any period of overlap, but if that were not possible, the period during which both products would be available needed to be as short as possible. And if there was going to be even a short overlap, the risks of confusion would require an aggressive campaign to educate doctors, pharmacists, caregivers and patients about the two products and their differences.

In response, Valeant developed a program intended to avoid any meaningful market overlap. We answered the approvable letter with a revised RMP that, among other things, proposed "an inventory reduction plan and returns program with a goal of reducing wholesaler inventory to zero, which [was] estimated to result in a maximum of 1- to 2-day inventory in the retail channel at the time of launch."<sup>4</sup>

Lachman further argues that the continued marketing of a 2.5 mg Diastat® product proves that the existence of fixed-dose products poses no safety

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<sup>3</sup> March 2, 2005 Approvable Letter at 2 (attached at Tab A) (emphases added).

<sup>4</sup> Diastat® AcuDial™ Risk Management Program at 11-12 (relevant excerpt attached at Tab B).

risk.<sup>5</sup> In this regard, Lachman misses the point. FDA's insistence on prompt and complete market withdrawal was driven by the agency's concern about the confusion and medication error that would result from the availability of fixed-dose products that would *duplicate* doses provided by Diastat® AcuDial™. Because it does not overlap with any dose available with Diastat® AcuDial™, the 2.5 mg Diastat® poses no such risk to patient safety, and its continued availability is irrelevant.

Lachman also asserts that the risks created by marketing generic fixed-dose products that overlap doses of Diastat® AcuDial™ "can be managed by way of the [product] labeling."<sup>6</sup> Here, Lachman is wrong on the law. The labeling for a generic product must be the "same as" the labeling for the reference listed drug.<sup>7</sup> Accordingly, even if the fixed-dose Diastat® products had not been withdrawn for reasons of safety, a generic diazepam rectal gel would require labeling that is the same as that for the withdrawn products. Neither the statute nor FDA regulations allow for the addition of warnings or other information that might seek to mitigate the risk of medication error that would result from concurrent marketing of overlapping fixed-dose products and Diastat® AcuDial™.<sup>8</sup>

The Lachman reply comments reflect mistaken assumptions as to the facts and the law. FDA recognized the unavoidable risk of confusion and medication error that would result from having on the market fixed-dose diazepam rectal gel products that duplicate the doses available with Diastat® AcuDial™. That is why the agency urged Valeant to withdraw the fixed-dose products in a way that avoided any overlap in the marketplace. Because the fixed-dose Diastat® products were withdrawn for reasons of patient safety, they cannot serve as a reference listed drug.

Respectfully submitted,



Greg J. Kricorian, M.D.  
Director, Medical Affairs

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<sup>5</sup> Lachman Reply at 3.

<sup>6</sup> Lachman Reply at 4, n.1.

<sup>7</sup> 21 USC 355(j)(2)(A)(v); 21 CFR 314.94(a)(8)(iv). The exceptions to this rule are not applicable here.

<sup>8</sup> See Valeant Citizen Petition, Docket 2006P-0392/CP1 at 4-5.

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**Attachments**

cc: Russell Katz, M.D.  
Docket 2006P-0392