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October 10, 2001

VIA FEDERAL EXPRESS

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Petition for Stay of Action – Approval of ANDAs for Clonidine Transdermal Patch Products That Do Not Meet Appropriate Approval Standards

Dear Sir or Madam:

PETITION FOR STAY OF ACTION

We are submitting this Petition for Stay of Action on behalf of Boehringer Ingelheim Pharmaceuticals, Inc. ("BI"), which markets Catapres-TTS® clonidine transdermal patch products. Simultaneously with this Petition for Stay of Action, we are filing a Citizen Petition that asks the Food and Drug Administration ("FDA"), among other things: (1) to decline to approve a specific generic clonidine transdermal product that is allegedly substantially different than Catapres-TTS® patch products; (2) to decline to approve any new or pending abbreviated new drug application ("ANDA") or application submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for any generic clonidine transdermal product that has a controlled-release mechanism or inactive ingredients that differ from those in Catapres-TTS® patch products in the absence of an appropriate showing that the differences do not affect safety or effectiveness; (3) to decline to approve any such application if the product does not meet bioequivalence testing requirements proposed in the petition; (4) to decline to approve any such application for a generic product whose drug reservoir is substantially larger than that of the innovator product and (5) to determine whether 180-day exclusivity applies to any pending ANDAs. In this Petition, BI requests that the Commissioner of Food and Drugs stay the approval of any approved application or decision to approve any new or pending application for a product that falls in those categories until final resolution of the issues raised in the Citizen Petition.

01P-0470

PSA 1

A. Decision involved

Presently before the FDA is the question whether the Agency may approve or maintain approval of ANDAs or section 505(b)(2) applications for generic clonidine transdermal products if the products differ in identified ways from Catapres-TTS® patch products or do not meet the proposed bioequivalence requirements. This depends on issues addressed by the Citizen Petition submitted on the same date as this Petition for Stay of Action.

B. Action requested

In this Petition for Stay of Action, BI requests that FDA stay approval of all new or pending ANDAs or section 505(b)(2) applications for generic clonidine transdermal products that differ from Catapres-TTS® patch products in ways addressed in the accompanying Citizen Petition or do not meet the bioequivalence requirements contained in that petition. BI requests that the stay continue until resolution of the issues raised by the accompanying Citizen Petition. Should FDA deny that Citizen Petition in whole or in part, BI asks that the stay requested herein not expire until a reviewing court has ruled on the correctness of that decision so long as BI seeks court review within two weeks of its receipt of the adverse decision.

C. Statement of grounds

The accompanying Citizen Petition demonstrates that the marketing of generic clonidine transdermal products with different release mechanisms or inactive ingredients, or that do not meet the proposed bioequivalence requirements, would be contrary to law. In addition, because clonidine is a very potent antihypertensive drug product, underdosing could lead to hypertension. Delivering too much clonidine could lead to hypertension followed by hypotension, leading to potentially dangerous adverse events such as stroke or fainting, including, of particular concern, while operating automobiles or machinery or while exercising. Accordingly, it is crucial that such ANDAs not be approved unless FDA has resolved the issues presented by the Citizen Petition, and if those issues are resolved against BI, until BI has an opportunity for judicial review of that decision.

There is precedent for granting stays where, as here, significant legal and policy issues have been raised about FDA policies. *See, e.g.*, 45 Fed. Reg. 82,052 (Dec. 12, 1980) (reference to stay of "paper NDA" policy until 10 days after denial of citizen petition challenging that FDA policy).

This Petition for Stay of Action satisfies the prerequisites for a mandatory grant of a stay under FDA regulations. *See* 21 C.F.R. § 10.35(e)(1)-(4).

The petitioner will otherwise suffer irreparable injury. Here, BI will face diminution of the reputation of its Catapres-TTS® products if generic products with different characteristics or bioinequivalent generic products are approved and marketed. This injury would be even greater should adverse events result from the differences. In addition, BI will inappropriately lose sales of its Catapres-TTS® products to such generic products once they are marketed. There is no mechanism by which the harm to BI, if it occurs, can be repaired.

The petitioner's case is not frivolous and is being pursued in good faith. The accompanying Citizen Petition illustrates that the petitioner's case is not frivolous and is well grounded in applicable law. This matter is being pursued in good faith, with every attempt being made to seek resolution in an appropriate and expeditious manner based on the application of applicable law to the facts presented.

The petitioner has demonstrated sound public policy grounds supporting the stay. The ANDA provisions are premised on approval of products that are as safe and effective as innovator products. Particularly with respect to transdermal products for such important conditions as hypertension, FDA must pay special attention to differences in release mechanism or inactive ingredients that may affect the safety or efficacy of the product and to bioavailability. BI has tried to engage FDA more informally on this issue through the channels of scientific exchange and dialogue. The issue is clearly a significant one, whose prompt resolution is important to all concerned. A stay until FDA responds to BI's Citizen Petition addressing the questions raised is certainly justified.

The delay resulting from the stay is not outweighed by public health or other public interest. Once the issues presented by the Citizen Petition are addressed by FDA, petitioner is confident that FDA will conclude that generic clonidine transdermal products must be shown to meet the reasonable approval standards discussed in that Petition. There is no public interest in the marketing of products that are not clinically the same as the innovator product. More generally, there can, of course, be no public interest in having FDA rush into inappropriate approvals, without considering concerns that are scientifically valid and medically relevant to the propriety of those approvals.

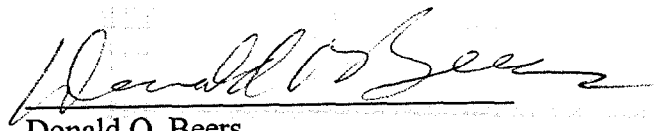
Even were FDA not to find that the criteria for mandatory stay discussed above had been satisfied, such a stay should be granted under the Agency's discretionary authority to stay any action "in the public interest and in the interest of justice." 21 C.F.R. § 10.35(e). The issues raised by BI's Citizen Petition are clearly substantial.

The interests of the public and of justice demand a fair and expeditious resolution of those issues in an orderly process.

Based on publicly available information, including notices of paragraph IV certification received by BI from Elan Pharmaceutical Research Corp. and Hercon Laboratories, BI believes that ANDAs for generic clonidine transfermal products may be pending at FDA and that FDA may be considering approval of such an application.

Accordingly, BI asks that the requested stay be entered and that notice thereof be issued to the parties as soon as possible.

Respectfully submitted,



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