

LAW OFFICES

KLEINFELD, KAPLAN AND BECKER, LLP

1140 NINETEENTH STREET, N.W.

WASHINGTON, D. C. 20036-6606

TELEPHONE (202) 223-5120

FACSIMILE (202) 223-5619

www.kkblaw.com

WEST COAST OFFICE:
ONE MARKET STREET
STEUART TOWER, SUITE 1450
SAN FRANCISCO, CA 94105-1313
TELEPHONE (415) 538-0014
FACSIMILE (415) 538-0016

VINCENT A. KLEINFELD
1907-1993

ALAN H. KAPLAN
1930-2001

THOMAS O. HENTELEFF
RICHARD S. MOREY
KINSEY S. REAGAN
PETER R. MATHERS
ANTHONY L. YOUNG
ANNE V. MAHER
BONNIE A. BEAVERS
DANIEL R. DWYER
GLENN E. DAVIS
STACY L. EHRLICH
JENNIFER A. DAVIDSON
STACEY L. VALERIO
ROBERT O. WINTERS

OF COUNSEL:
HARVEY A. SUSSMAN
WILLIAM J. HARDY

February 17, 2004

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

**Re: Docket # 2004P-0006
Petition for Stay of Action**

On behalf of Purdue Pharma L.P. ("Purdue"), the undersigned submits this Response to the January 29, 2004 comments filed by Teva Pharmaceuticals USA, Inc. ("Teva") on the above-referenced Petition for Stay of Action. Purdue's Petition for Stay of Action requests that the Commissioner of Food and Drugs stay final approval and/or the effective date of approval of any and all abbreviated new drug applications ("ANDAs") for modified-release oxycodone HCl products that list OxyContin[®] (oxycodone HCl controlled-release) Tablets as the reference listed drug, unless and until the products covered by those ANDAs are the subject of appropriate risk management programs ("RMPs") consistent with the RMP for OxyContin. Teva has not shown that FDA should approve applications for generic versions of OxyContin unsupported by appropriate RMPs, and therefore Purdue's Petition should be granted.

Like Endo Pharmaceuticals' comments to this Docket, Teva's comments assert an unconditional right to sell its generic version of OxyContin without devising or implementing a risk management program. While Teva states that it is willing to implement a "voluntary" RMP, it demands approval of its ANDA first, and vaguely commits to implement risk management measures only when "FDA provides workable guidance with respect to Teva's program, or RMPs in general." Thus, despite acknowledging that, "[f]ollowing the introduction of OxyContin, abuse and diversion of the drug became an unexpectedly serious problem," Teva asserts that it has no obligation to take that problem seriously. Indeed, it does not even appear to acknowledge that the problem continues to be a serious one, stating only that abuse and diversion "to some degree still occurs." Then, like Endo, Teva naively suggests "even without immediate RMP related materials, [the availability of generic versions of OxyContin] will likely improve the abuse and diversion environment."

KLEINFELD, KAPLAN AND BECKER, LLP

Dockets Management Branch
February 17, 2004
Page 2 of 5

As we explained in our February 6, 2004 response to Endo's comments, the idea that generic products are immune from abuse and diversion because they are not "promoted" is totally unsupported and, indeed, contrary to experience which indicates that increasing availability of generic versions of similar opiate-based products is accompanied by increasing numbers of cases of abuse and diversion. Moreover, the refusal to acknowledge the role of generic firms in helping to monitor and prevent such abuse severely undercuts the sincerity of Endo's and Teva's commitments to implement "voluntary" risk management programs some time in the future.

Having recently responded to substantially similar comments by Endo, we do not repeat ourselves here. However, we do wish to respond to a few additional arguments offered by Teva in its comments.

1. Teva cites the recent GAO report as supporting its assertion that Purdue was responsible for the significant abuse and diversion of OxyContin and that Purdue only implemented its risk management program because it was forced to do so. But that is not what the GAO concluded. Contrary to Teva's argument, the GAO did not conclude that Purdue, or its promotional activities for OxyContin, was responsible for causing the abuse and diversion of the drug. Teva's citations are almost exclusively to the DEA's comments on the GAO report – comments which the GAO, after two years of investigation, did not corroborate.¹

Moreover, relying again on DEA statements, Teva mischaracterizes the manner in which Purdue and FDA agreed to the implementation of risk management measures for OxyContin. As the director of FDA's Office of Drug Evaluation II testified before a Congressional committee just this week:

In response to reports of abuse and misuse of OxyContin, FDA worked with Purdue Pharma to develop a RMP. The program included strengthening OxyContin's warning label, educating healthcare professionals and Purdue Pharma's sales staff, and developing a tracking system to identify and monitor abuse. In July 2001, Purdue Pharma, working in cooperation with FDA, significantly strengthened the warning and precaution sections in the labeling for OxyContin. The labeling now includes a "black box" warning, the strongest warning for an FDA approved product, which warns patients and physicians of the potentially lethal consequences of crushing the controlled-release tablets and injecting or snorting the contents. The

¹ *Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem*, General Accounting Office, GAO-04-110 (Dec. 2003), published Jan. 22, 2004 (available at: <http://www.gao.gov/>).

KLEINFELD, KAPLAN AND BECKER, LLP

Dockets Management Branch
February 17, 2004
Page 3 of 5

indication for use was clarified to reflect that it is approved for the treatment of moderate to severe pain in patients who require around the clock narcotics for an extended period of time.²

Purdue was thus an active and cooperative collaborator with the FDA in devising the RMP for OxyContin. Of course, had Purdue failed to take additional responsible action to monitor and attempt to reduce the incidence of abuse and diversion of the product, as it did in its RMP, FDA could have decided to seek to withdraw the NDA approval. Indeed, in discussions between FDA representatives and Purdue it was clear that not only the RMP itself, but the effectiveness of the RMP, would be considered in deciding whether new information warranted withdrawal of the NDA approval. In this respect, although Purdue and FDA were in full agreement on the need to implement risk management measures, it does not appear to be critical whether the actions taken by Purdue are described as “voluntary” or not. What is critical is that the actions were taken and that it would have been irresponsible and inappropriate, under the circumstances, if they had not been, just as it would be irresponsible and inappropriate, under current circumstances, if Teva and/or Endo were allowed to begin selling generic versions of OxyContin without also implementing appropriate RMPs consistent with that which has been implemented by Purdue.

2. Teva attempts to distinguish the precedent set by the Agency’s action on ANDAs for generic versions of Accutane[®], but this effort fails. Teva argues that the abuse and diversion of OxyContin is outside of the labeled “conditions of use” of the product and that there is, therefore, no basis on which the FDA could claim that a RMP aimed at monitoring or preventing abuse and diversion is necessary to the safety and effectiveness of OxyContin for its labeled “conditions of use.” Teva tries to contrast this with Accutane, which is contraindicated for use by pregnant women. According to Teva, this distinction means that imposing RMP requirements on Accutane is legally appropriate, but imposing them on OxyContin is not. Teva’s theory does not bear scrutiny. In both cases, the risk-benefit considerations on which the safety of the drug is assessed turn on the adequacy of the labeling, and other ancillary measures, to effectively warn against and hopefully prevent inappropriate and potentially harmful use of the drug. Both cases involve precisely the same problem – helping to assure proper patient selection and monitoring, and physician and patient education, so that people who should not use the drug, or will not use it properly, are not given access to it and people who are given access to it are aware of the proper way to use it. For this same reason, the RMPs for each drug include measures to assess the effectiveness of the RMPs in preventing improper use. In the case of drugs which carry

² See Statement of Robert J. Meyer, M.D., Director, Office of Drug Evaluation II, Center for Drug Evaluation and Research, Food and Drug Administration, Before U.S. House of Representatives, Committee on Government Reform, Subcommittee on Criminal Justice, Drug Policy, and Human Resources (Feb. 9, 2004) (available at: <http://www.fda.gov/ola/2004/oxycontin0209.html>).

KLEINFELD, KAPLAN AND BECKER, LLP

Dockets Management Branch
February 17, 2004
Page 4 of 5

significant risks when used inappropriately, FDA has properly found that RMPs are critical to the risk-benefit analysis that underlies the continued approval of the product.

Teva also attempts to distinguish the Accutane precedent because, in that case, FDA clearly and unambiguously affirmed that the “same labeling” requirement for ANDAs applies to all risk management provisions reflected in approved labeling. Based on its comments, it appears that Teva has not made a commitment to meet the standard set by the Purdue RMP. Indeed, it says that it is waiting for “workable” guidance from the FDA before it takes steps to implement any RMP. Moreover, while arguing under the “same labeling” requirement that it has the right to an immediate approval before FDA approves Purdue’s pending supplements, Teva also argues that the “same labeling” requirement would not apply to it if those supplements were approved. Teva can point to no distinction or precedent under Hatch-Waxman that would support such disparate treatment of products on such a fundamental requirement.

3. Teva tries to avoid the public health implications of its inability to implement an adequate RMP at this time by arguing that Purdue’s Petition is improperly timed and that Purdue is attempting to impose on generic applicants RMP requirements that it does not itself meet. With respect to the timing of Purdue’s petition, Purdue stands by the fact that it submitted its Petition for Stay and labeling supplements in a timely manner, following a series of discussions with the Agency regarding RMPs.³ It stands by the fact that it filed the Petition in an attempt to preserve, if and when generic copies of its product are approved, the public health protections afforded by the RMP that Purdue has developed and put into place. It stands by the fact that the relief sought in the Petition would do no more than to implement the recommendations of the GAO, FDA, and DEA alike, that all drug products like OxyContin be the subject of appropriate risk management plans at the time of launch. For Teva to assert that it should be exempted from having a risk management program in place at the time of launch because Purdue is the Petitioner belies Teva’s total lack of understanding of the importance of the relief being sought.⁴

³ See Purdue Response to Endo Pharmaceuticals’ submission to this Docket, pp. 7-9 (Feb. 6, 2004).

⁴ In attempting to divert attention from the fact that it seeks to sell a generic version of OxyContin without having a risk management program in effect, Teva also claims that Purdue’s RMP for OxyContin is not yet in effect – supporting this assertion by misrepresenting the substance of an apparently staged phone inquiry to Purdue’s Medical Department. Although Teva provides no details about the time of the call or the person who placed it, Purdue has identified what it believes to be the referenced call – the only call placed to Purdue’s Medical Department during the month of January that referred to OxyContin risk management. In that call, placed on January 16, the caller was offered, and was subsequently sent, material relating to Purdue’s RMP. The caller did not request a copy of the RMP itself and the Purdue representative certainly did not state that Purdue had no risk management program. Indeed, the Purdue RMP for OxyContin has been in effect for over two years.

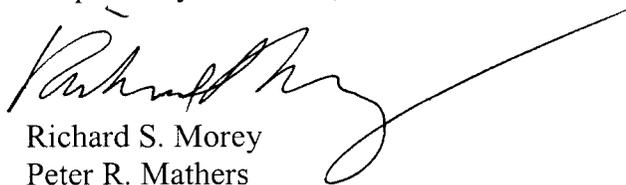
KLEINFELD, KAPLAN AND BECKER, LLP

Dockets Management Branch
February 17, 2004
Page 5 of 5

4. Finally, Teva argues that the regulatory criteria for a stay have not been satisfied. In fact, Purdue's Petition demonstrated that each of the relevant criteria is met⁵, and Teva's distortion of those criteria and Purdue's discussion of them should be disregarded. In particular, Teva's narrow emphasis on availability of generic versions of OxyContin fails to take into account the broader public interest in ensuring that all drugs, whether generic or branded, are at all times sold under conditions that are intended to optimize their risk/benefit ratio. While Teva appears to agree that RMPs, in principle, can be in the public interest, it ignores the potentially severe ramifications of launching a generic version of OxyContin without an adequate RMP. Approving generic controlled-release oxycodone products on the assumption that generic applicants would at some unspecified time later develop and implement some form of a RMP would open a gap – potentially a wide gap, based on historical performance of generic products – in existing risk management efforts. Such a gap would necessarily undermine Purdue's risk management efforts and potentially reverse the progress that has been made to date. To undermine risk management efforts at the time of first generic launch would be particularly detrimental to the public health, given the distribution system turmoil and increase in supply that typically accompanies initial generic launch. In short, Teva's suggestion that Purdue has not shown that a stay would benefit the public interest is wholly without merit.

Ultimately, Teva's comments serve only to emphasize the importance of Purdue's Petition. Based on those comments, it seems that Teva is willing to launch its generic oxycodone product unaccompanied by any risk management tools. It therefore appears that Teva, like Endo, fails completely to understand, and is currently unprepared to meet, the challenges presented by selling a generic version of OxyContin. Purdue urges the Agency ensure that generic applicants such as Teva and Endo *are* prepared to meet these challenges before they begin selling their products by staying final approval and/or the effective date of final approval until all ANDA applicants have developed and fully implemented RMPs, supported by appropriate staff and resources that are consistent with that for OxyContin.

Respectfully submitted,



Richard S. Morey
Peter R. Mathers
Jennifer A. Davidson
Counsel for Purdue Pharma L.P.

⁵ See Petition for Stay of Action, pp. 11-12 (Jan. 6, 2004).