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March 25, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

CITIZEN PETITION

A. Action Requested

Endo Pharmaceuticals, Inc. (Endo) submits this petition to request that the Food and Drug Administration (FDA) declare abbreviated new drug applications (ANDAs) may be filed for orally disintegrating formulations of our Percocet® (oxycodone hydrochloride and acetaminophen) Tablets in the following combination strengths:

- 7.5 mg oxycodone hydrochloride/325 mg acetaminophen and
- 10.0 mg oxycodone hydrochloride/325 mg acetaminophen.

B. Statement of Grounds

1. Basis for Dosage Form Change

FDA has approved Percocet® Tablets in strengths of 7.5 mg/325 mg and 10 mg/325 mg for the treatment of moderate to moderately severe pain. See ANDA 40-434. Percocet® Tablets in those approved strengths are the reference listed drugs for the corresponding-strength orally disintegrating tablets proposed in this petition.

The petition requests a change from the reference listed drugs in *dosage form only*: i.e., change from tablets to orally disintegrating tablets. The proposed drug products would contain the same active ingredients, comprise the same dosage strengths, be intended for the same route of administration, and bear the same labeling (except for permitted differences) as the reference products. The change in dosage form would *not* affect the site of absorption, but rather would simply provide a dosage form that is more convenient for some patients, i.e., the tablet dissolves in the mouth after being placed on the tongue, allowing its contents to be swallowed with or without water.

The Federal Food, Drug, and Cosmetic Act and FDA regulations permit the submission of ANDAs for drug products that differ in dosage form compared to a listed drug. 21 U.S.C. § 355(j) (2) (C); 21 C.F.R. §§ 314.93, 5.10. FDA has recently approved a number of ANDA suitability petitions seeking comparable dosage form change from tablet to orally disintegrating tablet. On February 5, 2003, for example, FDA approved a petition to file an ANDA for hydrocodone bitartrate and acetaminophen orally disintegrating tablets, 5 mg/500 mg; the reference listed drug was Vicodin® (hydrocodone bitartrate and acetaminophen) Tablets USP, 5 mg/500 mg (ANDA 88-058). See Docket No. 02P-0233/CP-1 and PAV-1; see also Docket No. 02P-0078 (approval of petition to submit ANDA for baclofen orally disintegrating tablets 10 mg and 20 mg), Docket No. 02P-0033 (approval of petition to submit ANDA for carbidopa and levodopa orally disintegrating tablets 10/100 mg, 25/100 mg, and 25/250 mg), and Docket No. 00P-1433 (approval of petition to submit ANDA for famotidine orally disintegrating tablets 10 mg).

Endo is aware that FDA recently suspended approval of at least the first two referenced suitability petitions, pending review of a potential need for clinical studies in children under the Pediatric Research Equity Act of 2003. As discussed below, however, Endo requests a waiver of any requirement for pediatric testing of its orally disintegrating oxycodone hydrochloride and acetaminophen tablet dosage forms. Apart from the pediatric testing issue, FDA approval of the referenced petitions continues to support a determination that clinical studies are not required to establish safety or effectiveness of the petitioned new dosage form.

2. Labeling Information

In accordance with 21 C.F.R. § 314.93(d), the following labeling information and comparisons are attached to this petition:

1. Copies of the current prescribing information for the reference listed drugs, Percocet® Tablets 7.5/325 mg and 10/325 mg are Attachment 1.
2. Side-by-side comparisons of labeling for the reference and proposed products are Attachment 2. Labeling for the proposed products would be the same as that of the corresponding reference products, except for permitted deviations including the description of the dosage form and related administration information.
3. Draft package inserts for the proposed Percocet® Orally Disintegrating Tablets are Attachment 3.

3. Pediatric Assessment

Endo is aware that the Pediatric Research Equity Act of 2003 amended the Federal Food, Drug, and Cosmetic Act to require that certain drug applications seeking approval of a new dosage form include “data ... that are adequate (i) to assess the safety and effectiveness of the ... product for the claimed indications in all relevant pediatric subpopulations; and (ii) to support dosing and administration for each pediatric subpopulation for which the ... product is safe and effective.” New 21 U.S.C. § 355c (a) (2). Although FDA has not yet promulgated regulations or published general guidance announcing how it intends to interpret the new law in the context of ANDA suitability petitions, we assume based on recent letters posted to other suitability petition dockets that the pediatric assessment requirement may be applied to this petition.

In anticipation of such an interpretation, Endo requests that FDA consider the current ongoing pediatric study involving Percocet® Tablets to fully satisfy this legislation and, therefore, waive any pediatric assessment requirement relative to this petition for an orally disintegrating tablet dosage form.

Pursuant to agreement and ongoing dialogue with FDA’s Division of Anesthetic, Critical Care, and Addiction Drug Products, Endo is undertaking clinical assessment of oxycodone hydrochloride/acetaminophen combination products to treat acute pain in pediatric patients from zero to 16 years of age. The ongoing trial is designed to generate safety, efficacy, and pharmacokinetic/dosing information that will be included in the Pediatric Section of Percocet® Tablets labeling. Attachment 4 summarizes the parameters of this ongoing pediatric trial. This document reflects the major ongoing efforts undertaken by Endo to successfully conduct and complete this trial within a reasonable time frame.

Furthermore, Endo expects that the Agency will find the Percocet® Orally Disintegrating Tablets (contemplated under this petition) to be bioequivalent to Percocet® Tablets based on the results of an appropriately designed and executed bioequivalence trial, and (as indicated in Attachment 2) that labeling for the two products will be essentially identical. In other words, the pediatric information that currently is being developed for Percocet® Tablets will be fully relevant to, and appropriate for, presentation in the labeling of Percocet® Orally Disintegrating Tablets. It would therefore be redundant to require pediatric assessment as a condition of approval of the orally disintegrating tablet dosage form.

For the stated reasons, a pediatric study of the proposed orally disintegrating oxycodone and acetaminophen drug products would not add significantly to the ongoing study or impact the pediatric usage labeling; rather, performing a new pediatric study with the proposed products would be redundant and unnecessarily expose children to placebo administration and blood draws. If the Pediatric Research Equity Act is deemed applicable to this petition, we respectfully request that any pediatric study requirement be fully waived and this petition be approved.

C. Environmental Impact

In accordance with 21 C.F.R. § 25.31, neither an environmental assessment nor an environmental impact statement is required in support of this petition.

D. Economic Impact

In accordance with 21 C.F.R. § 10.30(b), economic impact information will not be submitted unless requested by the Commissioner following review of this petition.

E. Certification

The undersigned representative of Endo certifies that to her best knowledge and belief, this petition includes all information and views on which the petition relies, and that it includes representative data and information that are known to be unfavorable to the petition.

Sincerely,



Mary Alice Raudenbush
Vice President, Regulatory Affairs

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