

April 6, 2007

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Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

RE: CITIZEN PETITION

The undersigned submits this petition under 21 CFR 10.30 to request the Commissioner of Food and Drugs to take administrative action.

A. Action Requested

To incorporate the full proprietary name, "Zanaflex Capsules", as the listed name in FDA's Approved Products with Therapeutic Equivalence Evaluations (Orange Book), for Acorda Therapeutic Inc.'s product, Zanaflex Capsules, instead of the truncated form of the name, "Zanaflex".

B. Statement of Grounds

Acorda Therapeutics Inc. (Acorda) holds two NDAs for two separate and distinct products having the active ingredient tizanidine hydrochloride:

Zanaflex®, 2 mg and 4 mg tablets (NDA 20-397)

And

Zanaflex Capsules™, 2 mg, 4 mg and 6 mg. (NDA 21-447)

B.1 Product Recognition and Identification

The 26th Edition of the Orange Book listed the above two products under the single name "Zanaflex" in the following sections (see Attachment 1):

- 3.0 Prescription Drug Product List
- Appendix A, Product Name Index

- Appendix B, Product Name Sorted By Applicant
- Prescription and OTC Drug Product Patent and Exclusivity List

Acorda notified the FDA Orange Book Staff of this error in a letter dated July 28, 2006 (see Attachment 2). The Orange Book Staff responded to the letter on September 12, 2006 (see Attachment 2). In their response, the Orange Book Staff stated that:

“Although your proprietary name encompasses the word “capsules” it is not our policy to add dosage form to the listed name. For this reason your product will remain listed in the Orange Book as Zanaflex”

The proprietary name of the Acorda capsule product is “Zanaflex Capsules” and the Orange Book Staff acknowledges this fact in their response letter. While the common word “Capsules” does imply a dosage form, it is used in this case as a distinguishing term in the proprietary name to specify two non-interchangeable products (the capsule and the tablet). Distinguishing terms in the proprietary name are commonly used in the Orange Book for this purpose. The following examples from the current edition of the Orange Book (Appendix A-Product Name Index, Page A-1 to A-21), while not exhaustive, show their common use:

- Adderall 10, Amphetamine Aspartate
- Adderall 12.5, Amphetamine Aspartate
- Aminosyn 10%, Amino Acids
- Aminosyn 3.5%, Amino Acids
- Anexsia 5/325, Acetaminophen
- Anexsia 7.5/325, Acetaminophen
- Atrovent HFA, Ipratropium Bromide
- Atrovent, Ipratropium Bromide
- Catapres-TTS-1, Clonidine
- Catapres-TTS-2, Clonidine
- Catapres-TTS-3, Clonidine
- DDAVP (Needs No Refrigeration), Desmopressin Acetate
- DDAVP, Desmopressin Acetate
- Flovent Diskus 50, Fluticasone Propionate
- Flovent Diskus 100, Fluticasone Propionate

As an example, the FDA Orange Book allows searching of products by “Proprietary Name” (<http://www.fda.gov/cder/ob/docs/querytn.htm>). An electronic search of the Orange Book by the proprietary name on the first example above, “Adderall 10”, results in a listing specific to only “Adderall 10” (<http://www.accessdata.fda.gov/scripts/cder/ob/docs/temptn.cfm> , see Attachment 3). An

electronic search by the abbreviated name “Adderall”, dropping the distinguishing term “10”, results in the complete list of Adderall products and strengths (XR 10, XR 15, XR 20, XR 25, XR 30, 10, 12.5, 15, 20, 30, etc.) (<http://www.accessdata.fda.gov/scripts/cder/ob/docs/temptn.cfm> , see Attachment 3).

A similar electronic search of the FDA Orange Book by proprietary name for “Zanaflex Capsules” resulted in:

“No matching records found. Use your browser's Back button to go back and enter a new search criteria.”

While a search using the abbreviated name “Zanaflex” results in the listing of Zanaflex Capsules and Zanaflex tablets. By not allowing the use of the full, market-recognized proprietary name, Zanaflex Capsules, searchers cannot locate the approved Zanaflex Capsules product in a proprietary name search of the FDA Orange Book.

In the “Frequently Asked Questions” section of the electronic Orange Book (<http://www.fda.gov/cder/ob/obfaqs.htm>), under the heading: “3. How Do I use the Electronic Orange Book to find approved generic drugs?”, it first specifies a search by proprietary name as follows:

“First, if you have the trade name, search the Electronic Orange Book Rx or OTC section using the Proprietary Name search. This determines the ingredient(s). Then use the Ingredient Search for all approved products that contain the ingredient(s). The resulting list will provide approved products by dosage form and route.”

Surely, the inclusion of an Orange Book search by proprietary name was intended to identify products specifically. This objective is not fulfilled by truncating the Zanaflex Capsules proprietary name to “Zanaflex” in the Orange Book.

Secondly, contrary to the statement made in the response letter from the Orange Book Staff that it is not their policy to add dosage form to listed names, the Orange Book contains dosage forms in listed names. These dosage forms are either the full dosage form name or abbreviated names for dosage forms. The following list of examples from the current edition of the Orange Book (Appendix A: Product Name Index, page A-1 to A-26), while not exhaustive, refutes the position of the Orange Book Staff:

- Advil Liqui-gels, Ibuprofen Potassium
- Azulfadine EN-Tabs, Sulfasalazine
- Balanced Salt Solution, Calcium Chloride
- Beconase AQ, Beclomethasone Dipropionate Monohydrate

- Bronitin Mist, Epinephrine Bitartrate
- Cefoxitin and Dextrose in Duplex Container, Cefoxitin Sodium
- Chloraprep Single Swabstick, Chlorhexidine Gluconate (OTC)
- Chlorascrub Swabstick, Chlorhexidine Gluconate (OTC)
- Chlorascrub Swab, Chlorhexidine Gluconate (OTC)
- Dialyte Concentrate w/dextrose 30% in Plastic Container, Calcium Chloride
- Dermatop E Emolient, Prednicarbate
- Elliotts B Solution, Calcium Chloride
- Ery-Tab, Erythromycin
- Foradil Certihaler, Formoterol Fumarte
- FS Shampoo, Fluocinolone acetonide
- Gonal-F Rff Pen, Follitropin Alfa/Beta
- H.P. Acthar Gel, Corticotropin
- Ibu-Tab 200, Ibuprofen
- Lidosite Topical System Kit, Epinephrine
- Nitrolingual Pumpspray, Nitroglycerin
- Pepcid AC (Geltab), Famotidine (OTC)
- Phoslo Gelcaps, Calcium Acetate
- Prevacid IV, Lansoprazole
- Promethazine with codeine syrup, codeine phosphate
- Tobramycin (Pharmacy Bulk), Tobramycin Sulfate
- Tylenol (Caplet), Acetaminophen (OTC)
- Tylenol (Geltab), Acetaminophen (OTC)

B.2 Product Substitution Errors

The Orange Book is the primary FDA source of information on product substitution. The product, Zanaflex (tizanidine hydrochloride), available as tablets, is substitutable and there are multiple listed suppliers of generic tizanidine hydrochloride tablets in the Orange Book.

However, Zanaflex Capsules are a different product. Zanaflex Capsules are not AB rated and can not be substituted with Zanaflex or generic tizanidine hydrochloride tablets.

Zanaflex Capsules prescriptions have been mistakenly filled with the tablet dosage form –either Zanaflex or generic tablets, because the product name “Zanaflex” is common to both the substitutable tablet and the not substitutable Zanaflex Capsules.

This inappropriate substitution contributes to the hundreds of medication errors that occur each year, many of which result in serious patient harm. It is estimated that 50% of all medication errors are due to similar drug names, labeling, or packaging. In addition, 13% of medication errors are due to nomenclature issues. Finally, approximately 5% of fatal medication errors result

from proprietary name confusion (<http://www.fda.gov/cder/drug/MedErrors/mixed.pdf>; referenced March 2007).

Having the full proprietary name listed in the Orange Book will help ameliorate these substitution errors and may prevent these serious events.

B.3 Patient Safety and Product Identification

While Zanaflex[®] and Zanaflex Capsules[™] are bioequivalent under fasting conditions; they are not bioequivalent when administered with food. As a result, they are not interchangeable and the approved product labeling includes statements to this effect (see Attachment 4). The package insert labeling includes a bolded statement on page 1 that states:

**PHARMACOKINETIC DIFFERENCES BETWEEN ZANAFLEX CAPSULES[™] AND ZANAFLEX[®] TABLETS:
ZANAFLEX CAPSULES[™] ARE NOT BIOEQUIVALENT TO ZANAFLEX[®] TABLETS IN THE FED STATE. THE PRESCRIBER SHOULD BE THOROUGHLY FAMILIAR WITH THE COMPLEX EFFECTS OF FOOD ON TIZANIDINE PHARMACOKINETICS (see PHARMACOKINETICS and DOSAGE AND ADMINISTRATION).**

In addition, the DOSAGE and ADMINISTRATION section specifically informs prescribers about possible adverse events and clinical effects that may result if the products are switched.

“Food has complex effects on tizanidine pharmacokinetics, which differ with the different formulations. These pharmacokinetic differences may result in clinically significant differences when [1] switching administration of the tablet between the fed or fasted state, [2] switching administration of the capsule between the fed or fasted state, [3] switching between the tablet and capsule in the fed state, or [4] switching between the intact capsule and sprinkling the contents of the capsule on applesauce. These changes may result in increased adverse events or delayed/more rapid onset of activity, depending upon the nature of the switch. For this reason, the prescriber should be thoroughly familiar with the changes in kinetics associated with these different conditions (see CLINICAL PHARMACOLOGY: Pharmacokinetics).”

For reasons of patient safety, efficacy, and for specific product identification, Acorda believes that Zanaflex Capsules should be listed separately from Zanaflex in the Orange Book at the sections referenced above and included in Attachment 1.

Based on the arguments presented in this section, Acorda requests that the FDA take action to have Zanaflex Capsules listed by its full proprietary name, and separately from Zanaflex, in the next opportunity for revision to the Orange Book.

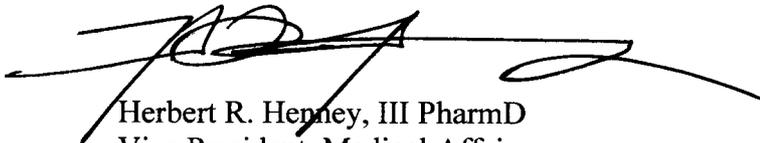
C. Environmental impact

Acorda claims categorical exclusion under 21 CFR 25.30 and therefore will not be preparing an EA or EIS for this action.

The Petitioner warrants that, to the best of the Petitioner's knowledge, information, and belief, the statements made in the submission are true and accurate.

Should you have questions or comments regarding this petition, please do not hesitate to contact me at (914) 347-4300.

Sincerely,



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