

PHASE V PHARMACEUTICALS

A VALUE-DRIVEN DRUG COMPANY

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Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services, Rm. 1-23
12420 Parklawn Dr.
Rockville, MD 20857

Citizen Petition

The undersigned submits this petition under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of Food and Drugs to take an administrative action.

A. Action requested

Section 505(j)(2)(C) states that: "If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application." This Petition requests permission to file an abbreviated new drug application for Baclofen Oral Solution, 10 mg/ 5 mL.

B. Statement of grounds

Characteristics of the new drug change only dosage form—Baclofen Oral Solution will use the same active ingredient (baclofen), route of administration (oral), and strength (10 mg) as several generic drugs currently on the market. The intended dosage of Baclofen Oral Solution is 10 mg per standard 5 mL dose. The only difference will be the dosage form, which is changed to a liquid oral solution, and the accompanying inactive ingredients.

Inactive ingredients are commonly used, with excellent safety records—The planned formulation includes purified water USP, glycerin (co-solvent), methylparaben and propylparaben (preservatives), sucralose (sweetener), cherry flavoring (flavor #825.382 from Flavors of North America, Inc.), and FD&C Red Dye #40. All of these excipients have excellent safety records and Phase V Pharmaceuticals is not aware of any safety problems. Thus, they are not expected to alter the safety or efficacy of Baclofen Oral Solution.

Clinical studies will demonstrate bioequivalence of Baclofen Oral Solution to currently marketed drugs—This formulation is being developed to ease the delivery of baclofen to spastic patients with dysphagia. These disabled persons cannot swallow tablets and are currently receiving doses of crushed tablets which have unknown pharmacokinetics. In addition, they often have feeding tubes, which can be obstructed by crushed tablets. As the route of administration is oral, the site of absorption of Baclofen Oral Solution will be identical to that of currently marketed baclofen tablets. Metabolism and excretion will not be affected. Because it is a liquid, dispersion is not an issue, although it may make absorption more rapid.

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than uncrushed tablets. Absorption is most likely to be the same as that of the orally disintegrating tablets, since they also are delivered to the gut in liquid form suspended in saliva. Baclofen Oral Solution will be tested for bioequivalence against the reference listed drug from Ivax Pharmaceuticals.

Other marketed products have a good safety and effectiveness record—The Orange Book, as of March 23, 2005, listed four approved generic oral tablets of baclofen 10 mg:

- #072234 (RLD); Ivax Pharmaceuticals; approved July 21, 1988
- #074584; USL Pharmaceuticals; approved August 19, 1996
- #073092; Watson Pharmaceuticals; approved January 28, 1994
- #072824; Watson Pharmaceuticals; approved September 18, 1991

and one approved branded orally disintegrating tablet of baclofen 10 mg:

- #021589; Kemstro; Schwarz Pharmaceuticals; approved October 30, 2003

Phase V Pharmaceuticals is not aware of any problems with safety and efficacy for these products.

Additional studies of safety and effectiveness are not needed—The safety and effectiveness of baclofen is well documented based on over 30 years of use, with 16 years in generic status, and delivery of millions of doses. A bioequivalent liquid formulation will not alter the safety and effectiveness of this drug.

Potentially unfavorable information—Filing of a NDA means the FDA can require testing of the safety and effectiveness of baclofen in children prior to approval. This is of special interest because a liquid formulation is most likely to be used off-label in children. Thus, the FDA would have an interest in denying permission to file an ANDA in order to increase the probability that safety and effectiveness data in children is generated. Offsetting this interest is the following:

- 1) The NIH is initiating a clinical trial of baclofen in children to assess safety and effectiveness via the Best Pharmaceuticals for Children Act (RFP-NIH-NICHD-2005-13, "Use of Oral Baclofen for Treatment of Spasticity of Cerebral Palsy in Children," 3/22/05). Thus, the data is likely to be generated anyway.
- 2) Phase V Pharmaceuticals is cooperating with the NIH clinical trial, to help supply liquid baclofen for research use (see Additional Information/Clarifications for RFP-NIH-NICHD-2005-13).
- 3) The most recent baclofen NDA (#021589) was not required to perform clinical trials of safety and effectiveness in children.
- 4) Phase V Pharmaceuticals is a very small company with limited resources. The development of Baclofen Oral Solution is being supported by a NIH SBIR grant, which does not contain funds for a clinical trial. If a clinical trial is required before approval, at best the drug will be delayed for several years as additional NIH funding is sought, and in all likelihood the product will simply fail to reach the market and the clinical studies will not be done (except by the NIH).
- 5) Phase V Pharmaceuticals is planning to perform clinical trials in children after initial approval, using revenues from sales to adults to fund the new research.

Thus, we suggest that the course of action that has the highest probability of generating data in children is to permit such data to be acquired after approval of an ANDA.

C. Environmental impact

A claim for categorical exclusion is made under 21 CFR Section 25.31(a), which allows a categorical exclusion for: "Action on an NDA, abbreviated application, application for marketing approval of a biologic product, or a supplement to such applications, or action to an OTC monograph, if the action does not increase use of the active moiety." Permission to submit an abbreviated new drug application for Baclofen Oral Solution will not result in the drug being administered at higher dosages, for longer durations, or for different indications presently in effect in the marketplace.

D. Economic impact

To be submitted only when requested.

E. Certification

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

(Signature)



(Name of petitioner)

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