

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**21-437/S-002**

**Approval Letter(s)**



NDA 21-437/S-002

G.D. Searle LLC  
Attention: Lynne E. Weissberger, Ph.D.  
4901 Searle Parkway  
Skokie, IL 60077

Dear Dr. Weissberger:

Please refer to your supplemental new drug application dated April 4, 2003, received April 7, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Inspra (eplerenone) 25, 50 & 100-mg Tablets.

We acknowledge receipt of your submissions dated April 4; May 8; July 16; and August 22, 2003.

This supplemental new drug application provides for the use of Inspra (eplerenone) Tablets to improve survival of stable patients with left ventricular systolic dysfunction (ejection fraction  $\leq 40\%$ ) and clinical evidence of congestive heart failure after an acute myocardial infarction.

We have completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We note the 50-mg Hospital Unit Dose and the 100-mg Tablet are no longer listed in your package insert. Please report these changes in the next annual report for NDA 21-437 Inspra (eplerenone) Tablets.

The final printed labeling (FPL) must be identical to the enclosed labeling text for the package insert. Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-437/S-002." Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must submit patent information on form FDA 3542, *Patent Information Submitted Upon and After Approval of an NDA or Supplement*, within 30 days of the date of this letter as required by 21 CFR 314.53(c)(2)(ii) and 314.53(d)(2) at the address provided by 21 CFR 314.53(d)(4). The form may be obtained at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>. To expedite review of this patent declaration form, we request you submit an additional copy of the form to this application and to the Center for Drug Evaluation and Research "Orange Book" staff at:

Food and Drug Administration  
Office of Generic Drugs, HFD-610  
Orange Book Staff  
7500 Standish Place  
Metro Park North II  
Rockville, MD 20855-2773

FDA's Pediatric Rule [at 21 CFR 314.55/21 CFR 601.27] was challenged in court. On October 17, 2002, the court ruled that FDA did not have the authority to issue the Pediatric Rule and has barred FDA from enforcing it. Although the government decided not to pursue an appeal in the courts, it will work with Congress in an effort to enact legislation requiring pharmaceutical manufacturers to conduct appropriate pediatric clinical trials. In addition, third party interveners have decided to appeal the court's decision striking down the rule. Therefore, we encourage you to submit a pediatric plan that describes development of your product in the pediatric population where it may be used. Please be aware that whether or not this pediatric plan and subsequent submission of pediatric data will be required depends upon passage of legislation or the success of the third party appeal. In any event, we hope you will decide to submit a pediatric plan and conduct the appropriate pediatric studies to provide important information on the safe and effective use of this drug in the relevant pediatric populations.

The pediatric exclusivity provisions of FDAMA as reauthorized by the Best Pharmaceuticals for Children Act are not affected by the court's ruling. Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products. You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at [www.fda.gov/cder/pediatric](http://www.fda.gov/cder/pediatric)) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request". FDA generally does not consider studies submitted to an NDA before issuance of a Written Request as responsive to the Written Request. Applicants should obtain a Written Request before submitting pediatric studies to an NDA.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Cardio-Renal Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call:

Mr. Daryl Allis  
Regulatory Health Project Manager  
(301) 594-5309

Sincerely,

*{See appended electronic signature page}*

Douglas C. Throckmorton, M.D.  
Director  
Division of Cardio-Renal Drug Products  
Office for Drug Evaluation I  
Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
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/s/

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Doug Throckmorton  
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