CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: 020720, S12, S14

Trade Name: REZULIN TABLETS

Generic Name: TROGLITAZONE

Sponsor: PARKE-DAVIS PHARMACEUTICAL RESEARCH

Approval Date: 09/16/99

INDICATION(s): USE OF REZULIN IN COMBINATION WITH METFORMIN AND SULFONYLUREA IN PATIENTS WITH TYPE 2 DIABETES.

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APPLICATION: 020720, S12, S14

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tenative Approval Letter				X
Approvable Letter				X
Printed Labeling	X			
Medical Review(s)	X			
Chemistry Review(s)				X
EA/FONSI				X
Pharmacology Review(s)				X
Statistical Review(s)				X
Microbiology Review(s)				X
Clinical Pharmacology Biopharmaceutics Review(s)	X			
Bioequivalence Review(s)				X
Administrative/ Correspondence Document(s)	X			

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Application Number: 020720, S12, S14

APPROVAL LETTER

NDA 20-720/S-012
NDA 20-720/S-014

Parke-Davis Pharmaceutical Research
Attention: Ms. Mary E. Taylor, M.P.H.
Director, Worldwide Regulatory Affairs
2800 Plymouth Road
Ann Arbor, MI 48105

Dear Ms. Taylor:

Please refer to your supplemental new drug application (S-012) dated November 18, 1998, received November 19, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Rezulin® (troglitazone) Tablets.

We acknowledge receipt of your submissions dated December 8 and 15, 1998, and January 6, 11, 13, and 28, March 10, 18, and 31, May 4, and June 11 and 16, 1999.

This supplemental new drug application provides for the use of Rezulin® (troglitazone) in combination with metformin and sulfonylurea in patients with type 2 diabetes.

We also refer to your supplemental new drug application (S-014) dated June 11, 1999, received June 11, 1999. We acknowledge receipt of your submissions dated June 14 and 16, 1999. This supplement provides for a patient package insert.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon draft labeling. Accordingly, these applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the draft physician and patient labeling submitted June 16, 1999. Marketing the product with FPL that is not identical to the approved draft labeling may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplemental NDA 20-720." Approval of this submission by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55. We are deferring submission of your pediatric studies until December 2, 2000. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

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 (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov.cder/pediatric) for details.

If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. If you do not submit a Proposed Pediatric Study Request within 120 days from the date of this letter, we will presume that you are not interested in obtaining pediatric exclusivity [NOTE: You should still submit a pediatric drug development plan] and will notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity.

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

Please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Metabolic and Endocrine Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

We remind you that you must comply with the requirements for an approved supplemental NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Ms. Jena Weber, Regulatory Project Manager, at (301) 827-6422.

Sincerely,

John K. Jenkins, M.D., F.C.C.P.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research