

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: 020607, S004

Trade Name: ARTHROTEC TABLETS

Generic Name: DICLOFENAC SODIUM/MISOPROSTOL

Sponsor: G.D. SEARLE & COMPANY

Approval Date: 02/22/99

INDICATION(s): TREATMENT OF THE SIGNS AND SYMPTOMS OF OSTEOARTHRITIS OR RHEUMATOID ARTHRITIS.

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APPLICATION: 020607, S004

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tentative 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: 020607, S004

APPROVAL LETTER

NDA 20-607/S-004

G.D. Searle & Company
Attention: Peter F. East
Associate Director, Regulatory Affairs
4901 Searle Parkway
Skokie, Illinois 60077

FEB 22 1999

Dear Mr. East:

Please refer to your supplemental new drug application dated August 27, 1999, received August 28, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Arthrotec (diclofenac sodium/misoprostol) Tablets.

This supplemental new drug application provides for the revision of the Geriatric Use subsection of the PRECAUTIONS section of the package insert in accordance with the Final Rule on Specific Requirements on Content and Format of Labeling for Prescription Human Drugs; Addition of "Geriatric Use" Subsection in the Labeling [21 CFR Part 201], published in the Federal Register, Vol. 62, No

We have completed the review of this supplemental application 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 labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted August 27, 1998).

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 supplement NDA 20-607/S-004." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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

NDA 20-607/S-004

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If you have any questions, contact Brian Strongin, Project Manager, at (301) 827-7310.

Sincerely,

/S/ 2-22-99

Lilia Talarico, M.D.

Director

Division of Gastrointestinal and Coagulation Drug
Products

Office of Drug Evaluation III

Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020607, S004

ADMINISTRATIVE/CORRESPONDENCE DOCUMENTS

Division of Gastrointestinal & Coagulation Drug Products

PROJECT MANAGER REVIEW

Application Number: NDA 20-607/SLR-004
Name of Drug: Arthrotec (diclofenac sodium/misoprostol) Tablets
Sponsor: G.D. Searle & Company

FEB 22 1999

Material Reviewed

Submission Date: August 27, 1998

Receipt Date: August 28, 1998

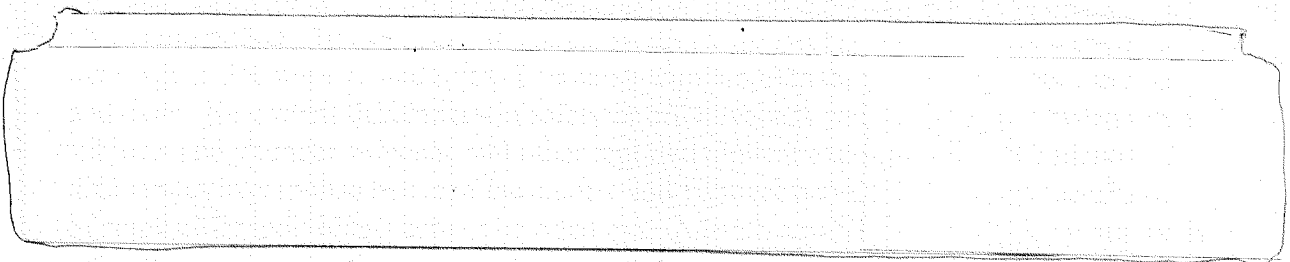
Background and Summary Description: NDA 20-607 for Arthrotec (diclofenac sodium/misoprostol) Tablets was approved December 24, 1997 for treatment of the signs and symptoms of osteoarthritis and rheumatoid arthritis in patients at high risk of developing NSAID-induced gastric and duodenal ulcers and their complications. SLR-004 provides for a revised Geriatric Use subsection of the PRECAUTIONS section of the package insert in accordance with the Final Rule on Specific Requirements on Content and Format of Labeling for Prescription Human Drugs; Addition of "Geriatric Use" Subsection in the Labeling [21 CFR Part 201], published in the Federal Register, Volume 62, Number 166. The labeling provided in SLR-004 was compared to the currently approved labeling and the differences noted below.

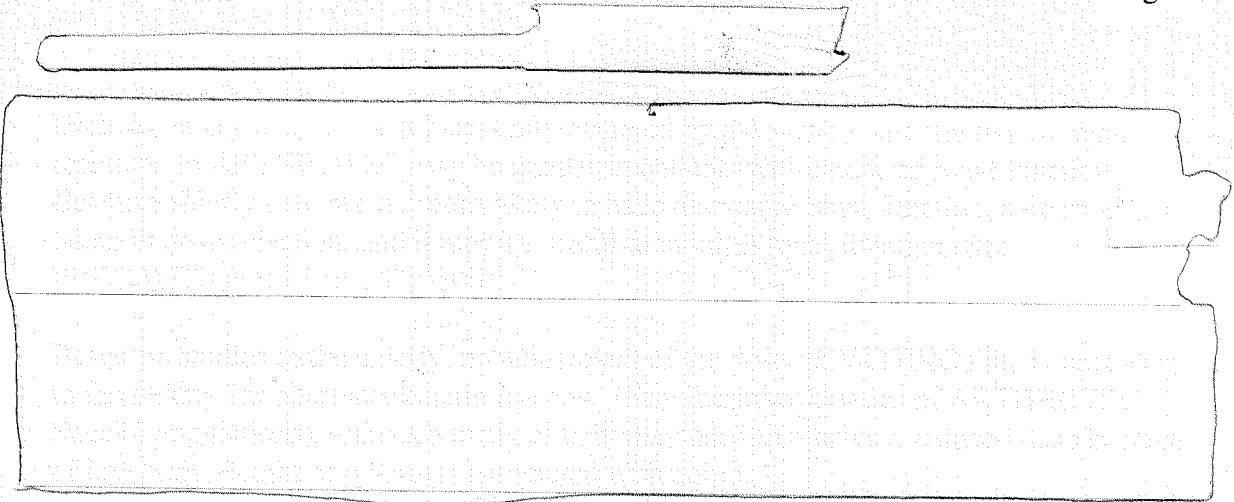
Review

The Geriatric Use subsection of the PRECAUTIONS section was changed from:

Approximately 1800 patients treated with diclofenac in U.S. trials and 500 patients treated with ARTHROTEC in multinational trials were older than 65 years of age. No overall differences were observed between efficacy, adverse events or pharmacokinetic profiles of older and younger patients. However, as with any NSAID, the elderly are likely to tolerate adverse events less well than younger patients.

to;





The language proposed in paragraph one is consistent with that recommended in 21 CFR 201.57(f)(10)(ii)(b). The language proposed in paragraph two is similar to that used in the PRECAUTIONS section, Renal Effects subsection in the currently approved labeling. The language proposed in paragraph three is similar to that used in the CLINICAL PHARMACOLOGY section, Special Populations subsection in the currently approved labeling.

No new data or analyses were submitted in support of these changes. As stated in the Guidance for Industry, entitled, Content and Format for Geriatric Labeling, "Labeling that simply relocated information already in the approved labeling does not require a reanalysis of the original data that supported this information."

Hugo Gallo-Torres, M.D., Ph.D., GI Medical Team Leader, reviewed the proposed changes and concluded that they are acceptable.

Conclusions

An approval letter will be drafted for SLR-004.

/S/

Project Manager

2/19/99

65 2-22-98

SEARLE

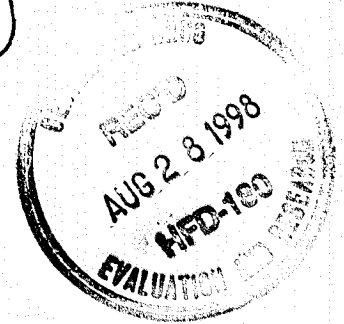
August 27, 1998

NDA NO. 20607 SUPP. NO. 004
NDA SUPPLEMENT FOR SLR

SEARLE
4901 SEARLE PARKWAY
SKOKIE, ILLINOIS 60077
PHONE (847) 982-7000
FAX (847) 982-4701

Lilia Talarico, M.D., Acting Director
Division of Gastrointestinal and Coagulation Drug Products
Center for Drug Evaluation and Research (HFD-180)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

(Geriatric Use)

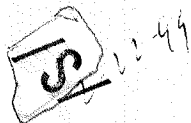
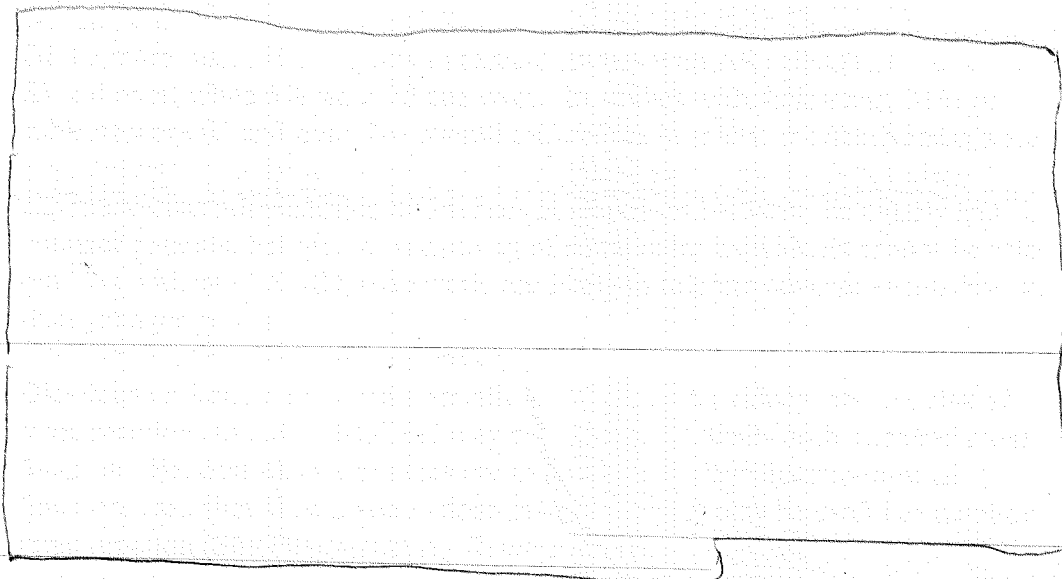


Re: **NDA 20-607/S-004**
Arthrotec® (diclofenac Na/misoprostol)

Dear Dr. Talarico:

Please refer to our approved New Drug Application for Arthrotec (diclofenac sodium/misoprostol) Tablets and to the Final Rule on Specific Requirements on Content and Format of Labeling for Prescription Human Drugs; Addition of "Geriatric Use" Subsection in the Labeling [21 CFR Part 201], published in the Federal Register, Vol. 62, No. 166.

Pursuant to the provisions of 21 CFR 314.70(b)(3), we hereby submit this supplemental new drug application providing revised draft physician labeling for Arthrotec Tablets. The "Geriatric Use" sub-section of the Precautions section has been revised in compliance with §201.57(f)(10) of the Final Rule. Specifically, the text has been revised to read as follows:



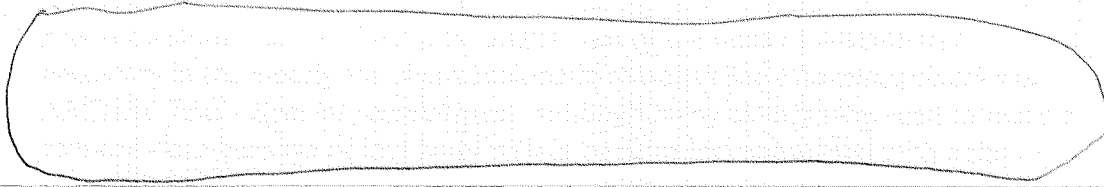
a MONSANTO  company

ORIGINAL

Arthrotec Tablets
(diclofenac Na/misoprostol)
NDA 20-607

Page 2

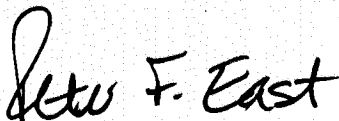
August 27, 1998



A copy of the current labeling (A05440-1) marked-up with the proposed changes is included to aid in your review.

Please address any questions or concerns regarding this submission to my attention.

Sincerely,



Peter F. East
Associate Director,
Regulatory Affairs
Tel.: (847) 982-8606
Fax: (847) 982-8152

enclosure

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Page(s) Redacted

DRAFT

Labeling