CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-632/S004

Trade Name: Meridia Capsules

Generic Name: sibutramine hydrochloride monohydrate

Sponsor: Knoll Pharmaceutical Company

Approval Date: July 6, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-632/S004

CONTENTS

Reviews / Information Included in this NDA Review.	
Approval Letter	X
Approvable Letter	
Labeling	
Medical Review(s)	
Chemistry Review(s)	X
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative/Correspondence Document(s)	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-632/S004

APPROVAL LETTER

NDA 20-632/S-004

JUL 6 1999

Knoll Pharmaceutical Company
Attention: Robert J. Mandetta
Associate Director, Regulatory Affairs
3000 Contintental Dr., North
Mount Olive, NJ 07828-1234

Dear Mr. Mandetta:

Please refer to your supplemental new drug application dated March 15, 1999, received March 16, 1999, submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Meridia (sibutramine hydrochloride monohydrate) 5, 10, and 15 mg Capsules.

This supplemental new drug application provides for the use of an additional container closure system for the blister packaging of the 5, 10, and 15 mg capsules of Meridia. Specifically, a six count sample blister package will be used for physician samples.

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 immediate container and carton labels submitted March 15, 1999.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-632/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.

If you have any questions, contact Maureen Hess, MPH, RD, Regulatory Health Project Manager, at (301) 827-6411.

Sincerely yours,

7/6/99

Solomon Sobel, M.D.
Director
Division of Metabolic and Endocrine Drug Products (HFD-510)
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Cc:
NDA 20-632
HFD-510/Div. File
HFD-510/MHess/MHaber/DWu
HFD-820/JGibbs
DISTRICT OFFICE

Drafted by: MAH/6.25.99
Initialed by: MHaber/6.30.99/DWu/7.2.99/EGalliers/7.2.99
Final: MAH/7.5.99

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-632/S004

CHEMISTRY REVIEW(S)

JUN 22 1999

CHEMIST'S REVIEW	1.ORGANIZATION	2. NDA NUMBER
	DMEDP, HFD-510	20-632

NAME AND ADDRESS OF APPLICANT	4. SUPPLEMENT NUMBER, DATE
Knoll Pharmaceutical Co. 199 Cherry Hill Road Parsippany, NJ 07054 (973) 331-7570	SCP-004, 3/15/99 User Fee Goal Date, 7/16/99

5. NAME OF THE DRUG	6. NONPROPRIETARY NAME	8. AMENDMENTS/REPORT, DATE
Meridia	sibutramine HCl monohydrate	

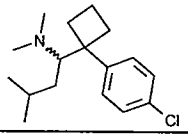
7. SUPPLEMENT PROVIDES FOR:	
The use of an additional container closure system (blister packaging).	N/A

9. PHARMACOLOGICAL CATEGORY	10 HOW DISPENSED	11. RELATED IND/NDA/DMF
anti-obesity	Oral	

12. DOSAGE FORM	13. POTENCY	
Capsules	5, 10, and 15 mg	N/A

14. CHEMICAL NAME AND STRUCTURE.

Cyclobutanemethanamine, 1-(4-chlorophenyl)-
N,N-dimethyl-(2-methylpropyl)- hydrochloride, monohydrate (±)



15. COMMENTS

This prior approval supplement provides for the use of an additional container closure system (blister packaging). Specifically, a 6 count sample blister package will be used for physician sampling. Blister packaging will be done at Knoll Pharmaceutical Co., 30 North Jefferson Road, Whippany, NJ 07981. A satisfactory inspection report dated 4/9/99 has been received, see attachment. For specific chemistry comments, see Review Notes.

16. CONCLUSION AND RECOMMENDATION

The CMC information provided is satisfactory. Issue an **Approval** letter. Request FPL.

17. REVIEWER NAME	18. REVIEWER SIGNATURE	19. DATE COMPLETED
Martin Haber, Ph.D.	Martin Haber	June 22, 1999

AP DISTRIBUTION: ORIGINAL JACKET M. Hess M. Haber DIVISION FILE

R/D Init by: Dr. Duu-Gong Wu, Team Leader Chemist

Duugong Wu 6/22/99

1 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-632
S004

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 20632/004**
Stamp: **16-MAR-1999** Regulatory Due: **16-JUL-1999**
Applicant: **KNOLL PHARM**
199 CHERRY HILL RD
PARSIPPANY, NJ 07054

Priority: **1S** Org Code: **510**
Action Goal: District Goal: **11-JUN-1999**
Brand Name: **MERIDIA (SIBUTRAMINE HCL MONOHYDRATE)**
Established Name:
Generic Name: **SIBUTRAMINE HCL MONOHYDRATE**
Dosage Form: **CAP (CAPSULE)**
Strength: **5,10, 15, 20 MG**

FDA Contacts:

M. HESS	**(HFD-510)**	**301-827-6411**	**, Project Manager**
M. HABER	**(HFD-510)**	**301-827-6420**	**, Review Chemist**
D. WU	**(HFD-510)**	**301-827-6375**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 09-APR-1999 by M. EGAS (HFD-322) 301-594-0095

Establishment: **2211084**
KNOLL PHARMACEUTICALS
30 NORTH JEFFERSON RD
WHIPPANY, NJ 07981

DMF No:
AADA No:

Profile: **CHG** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **09-APR-1999**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE PACKAGER**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-632/S004

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-632/S-004

MAR 19 1999

Knoll Pharmaceutical Company
3000 Continental Drive- North
Mount Olive, New Jersey 07828-1234

Attention: Robert J. Mandetta
Associate Director, Regulatory Affairs

Dear Mr. Mandetta:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	Meridia® (sibutramine hydrochloride monohydrate)
NDA Number:	20-632
Supplement Number:	S-004
Date of Supplement:	March 15, 1999
Date of Receipt:	March 16, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on May 15, 1999, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Attention: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine
Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-632/S-004
HFD-510/Div. Files
HFD-510/CSO/M. Hess

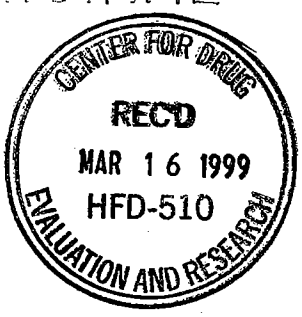
filename: C:\DATA\WPFILES\20632ACK

SUPPLEMENT ACKNOWLEDGEMENT / PA

Knoll Pharmaceutical Company

ORIGINAL

SCP-004



knoll®

BASF Pharma

March 15, 1999

Solomon Sobel, M.D., Director
Division of Metabolism and Endocrine Drug Products
HFD-510, Document Control Room 14B-04
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857-1506

NDA NO. 20-632 REF NO. 004
NDA SUPPL FOR SCP

RE: MERIDIA® (sibutramine hydrochloride monohydrate) Capsules
NDA 20-632/S-004
Additional Container/Closure System

3/22/99

Dear Dr. Sobel:

In accordance with 21 CFR § 314.70(b)(2)(vii), Knoll Pharmaceutical Company submits a supplemental application to provide for the use of an additional container/closure system for the blister packaging of the 5, 10, and 15 mg capsules of MERIDIA.

The original application for MERIDIA Capsules, NDA 20-632 provided for the use of the [redacted] as well as stability data in support of the [redacted] At the time of final approval of the NDA, [redacted] We now desire to use blister packaging in physician sampling.

The packaging components of the proposed blister package, provided for by this supplement, are identical to the those in the original NDA (Vol. 1.4, pages 0163 and 0183 - 0198). We are proposing the use of a 6-count sample blister package. The blister packaging would be used in addition to the currently approved 100-count bottles of 5, 10 and 15 mg capsules of MERIDIA.

To facilitate your review of this supplement, we have enclosed the appropriate information from the original NDA (Vol. 1.3, pages 060-0161 and Vol. 1.4, pages 0163 and 0183 - 0198) relating to the master formulas for packaging blisters and the container/closure system. As stated in our original NDA (Vol. 1.5, page 0415), an [redacted] s proposed for product packaged [redacted] blister configuration. Supporting stability data and draft labeling are enclosed.

Please note that the packaging of the blister samples will be performed at Knoll Pharmaceutical Company, 30 North Jefferson Road, Whippany, New Jersey 07981.

REVIEWS COMPLETED
CSO ACTION:
☑ LETTER ☐ N.A.I. ☐ MEMO
MAH 4-16-99
SIGNATURE DATE

3000 Continental Drive-North, Mount Olive, New Jersey 07828-1234 (973) 426-2600

In accordance with 21 CFR § 314.71(b), a field copy of this supplement will be concurrently submitted to the New Jersey District Office of the Food and Drug Administration.

We would appreciate your prompt and expeditious review of this supplemental application. We would like to have this container/closure system available for use as soon as possible. If you have any questions, please call me at (973) 426-6022.

Sincerely,

Robert J. Mandetta
Associate Director, Regulatory Affairs

Enc.