

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

**Application Number: 17703/S013**

**Trade Name: CYLERT CHEWABLE TABLETS**

**Generic Name: PEMOLINE**

**Sponsor: ABBOTT LABORATORIES**

**Approval Date: 12/12/97**

**Indication(s): TREATMENT OF ATTENTION DEFICIT  
DISORDER**

# CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION: 17703/S013**

## CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tentative Approval Letter				X
Approvable Letter				X
Final 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 Document(s)/ Correspondence	X			

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Application Number: 17703/S013**

**APPROVAL LETTER**



Food and Drug Administration  
Rockville MD 20857

NDA 16-832/S-015  
NDA 17-703/S-013

DEC 12 1997

Abbott Laboratories  
Attention: Matthew A. Biondi  
100 Abbott Park Road  
D-491, AP6B-1SW  
Abbott Park, Illinois 60064-3500

APPEARS THIS WAY  
ON ORIGINAL

Dear Mr. Biondi:

We acknowledge your supplemental new drug application dated November 4, 1997, received November 5, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cylert<sup>®</sup> (pemoline) Tablets and Chewable Tablets.

The supplemental application provides for new safety warnings concerning the occurrence of fatal and/or potentially fatal acute liver failure associated with pemoline's usage, as requested in our October 30, 1996, letter.

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drugs are safe and effective for use as recommended in the final printed labeling submitted on November 4, 1997. Accordingly, the supplemental applications are approved effective on the date of this letter.

If you have any questions, please contact Anna Marie Weikel, R.Ph., Project Manager, at (301) 594-5536.

Sincerely yours,

/S/

12/11/97

Paul Leber, M.D.  
Director  
Division of Neuropharmacological  
Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

APPEARS THIS WAY  
ON ORIGINAL

NDA 16-832/S-015  
NDA 17-703/S-013  
Page 2

cc:

- Original NDA 16-832 & 17-703 /S/ 12-11-97
- HFD-120/Div. files /S/ 12/1/97
- HFD-120/Leber /S/ 12/1/97
- HFD-120/Laughren/12.9.97/Mdsholder/12.8.97
- HFD-120/Purvis/12.8.97 /S/ 12/9/97
- HFD-120/Weikel /S/ 12/11/97
- DISTRICT OFFICE /S/ 12/11/97
- HF-2/Medwatch (with labeling)
- HFD-92/DDM-DIAB (with labeling)
- HFD-40/DDMAC (with labeling)
- HFD-613/OGD (with labeling)
- HFI-20/Press Office (with labeling)

APPEARS THIS WAY  
ON 12/11/97

Drafted by: AMW/12.05.97  
C:\WPFILES\NDA\CYLERTN16832S1.AP  
final: AMW/12.09.97

APPEARS THIS WAY  
ON 12/11/97

APPROVAL (AP)

APPEARS THIS WAY  
ON 12/11/97

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: 17703/S013**

**ADMINISTRATIVE DOCUMENTS/CORRESPONDENCE**

DEC 8 1997

1

Division of Neuropharmacological Drug Products

PROJECT MANAGER LABELING REVIEW

NDA#: 16-832/S-015  
17-703/S-013

APPEARS TO BE ON ORIGINALLY

Product Name:  
Cylert<sup>R</sup> (pemoline)

Date Review Completed: December 4, 1997

Date of Submissions: November 4, 1997

Provides for:

1. Addition of statements to the 'Indications and Usage' section cautioning against use of Cylert as first line drug therapy for ADHD.
2. Addition of a boxed warning to the 'Warnings' section regarding the occurrences of acute hepatic failure with Cylert usage.
3. Changes to the 'Precautions' section regarding the need for increased liver monitoring.
4. Changes to the 'Adverse Reactions' section regarding hepatic dysfunction.

Applicant's Name and Address:

Abbott Pharmaceutical Products Division  
100 Abbott Park Road  
Abbott Park, IL 60064

APPEARS TO BE ON ORIGINALLY

Dosage Form and Strength:

Oral Tablets, 18.75, 37.5 & 75 mg  
Chewable Tablets 37.5 mg

Material Reviewed:

1. FPL submitted in 16-832/S-015 & 17-703/S-013 dated November 4, 1997, and the February 12, 1997, general correspondence.

2. 16-832/S-013 & 17-703/S-011: Agency approval letter dated April 11, 1996, and the FPL contained in the January 5, 1996, FPL submission (last approved FPL).

3. The October 30, 1996, Agency letter requesting labeling changes.

Background:

This 'Special Supplement - Changes Being Effected' labeling supplement was requested in a October 30, 1996, Agency letter due to concerns about acute hepatic failure in children.

Labeling Review:

Conclusion:

A side-by-side comparison between the most recently approved package insert FPL (03-4633-R17-Rev. December 1995), approved on April 11, 1996, and the FPL (03-4735-R18-Rev. December 1996) provided in this supplement, shows the exact revisions that were requested in the Agency 10/30/96 letter.

Therefore, with the concurrence of the clinical reviewers, a supplement approval letter seems appropriate for these new revisions to the labeling.

**/S/**

Anna Marie H. Weikel  
Project Manager

Concur:

**/S/**

John S. Purvis  
Supervisory CSO

12/8/97

cc:  
Orig NDA 16-832 & 17-703  
HFD-120  
HFD-120/Weikel

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4 Page(s) Redacted

DRAFT  
Labeling



DEPARTMENT OF HEALTH & HUMAN SERVICES

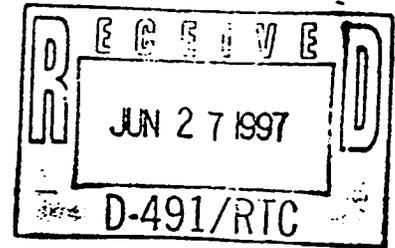
Public Health Service

Food and Drug Administration  
Rockville MD 20857

JUN 20 1997

NDA's 19-204, 19-057, 11-971, 18-279, 12-524, 12-775,  
20-347, 05-545, 16-832, 17-703  
05-378, 10-021, 10-841, 19-080, 17-105,  
05-856, 20-680, 20-471, 50-662, 50-611

ANDA's 61-904, 61-905, 62-746, 61-621,  
60-359, 62-298, 83-245, 84-093, 83-220



Abbott  
Pharmaceutical Products Division  
Abbott Laboratories  
100 Abbott Park Road  
Abbott Park, Illinois 60064-3500

Attention: Richard Poska  
Senior Regulatory Affairs Administrator  
Abbott Laboratories

Dear Mr. Poska:

Please refer to your letters dated April 17 and May 13, 1997. We also refer to your April 8, 1997, telephone conversation with Dr. Eric Sheinin and your May 13 and 19, 1997, telephone conversations with Dr. Yuan-yuan Chiu, both of this Agency.

In your letters you have provided information to support proposed changes as "Special Supplements - Changes Being Effectuated" for several of your approved New Drug Applications (NDA's) and Abbreviated New Drug Applications (ANDA's).

It is our opinion that the changes as proposed may be submitted as "Special Supplements - Changes Being Effectuated".

In addition, the packaging should also be tested according to Consumer Product Safety Commission regulations. We understand that you will specify the package sizes and configurations applicable to each product in each supplement since not all package sizes and configurations will be used for every drug product.

Data from stability studies are not required for the submission of the supplements. However, stability testing should be initiated on the first production batch based on the approved protocol for selection of batches of different strengths and packaging sizes and configurations. The data from the stability studies should be submitted in the annual reports for each NDA and ANDA.

It would be helpful to each review division if you included a copy of this letter with each supplement.

Should you have any questions, please contact:

For NDAs: Susan Lange, M.P.H.  
Consumer Safety Officer  
Office of New Drug Chemistry  
(301) 827-5173

For ANDAs: Mark Anderson, R.P.H.  
Project Manager  
Office of Generic Drugs  
(301) 827-5848

Sincerely,

/S/

Eric B. Sheinin, Ph.D.  
Director  
Office of New Drug Chemistry  
Office of Pharmaceutical Sciences  
Center for Drug Evaluation  
and Research

Sincerely,

/S/

Douglas L. Šprn  
Director  
Office of Generic Drugs  
Office of Pharmaceutical Science  
Center for Drug Evaluation  
and Research



**ABBOTT**

ORIGINAL

**Pharmaceutical Products Division**

Abbott Laboratories  
100 Abbott Park Road  
D-491, AP6B-1SW  
Abbott Park, Illinois 60064-3500

November 25, 1997

APPEARS THIS WAY  
ON ORIGINAL

CENTER FOR DRUG EVALUATION  
AND RESEARCH

NOV 26 1997

RECEIVED HFD-120

Paul D. Leber, M.D.  
Division of Neuropharmacological Drug Products  
Woodmont II, HFD-120  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, Maryland 20852

APPEARS THIS WAY  
ON ORIGINAL

**SPECIAL SUPPLEMENT-Changes Being Effected**

Re: **Cylert® (pemoline)**  
**NDA No. 17-703**

NDA NO. 17-703 REF. NO. SCP-014

**Packaging Change**

REASON FOR Packaging

Dear Dr. Leber:

APPEARS THIS WAY  
ON ORIGINAL

The sponsor, Abbott Laboratories, submits this change to our approved NDA No. 17-703 for Cylert Chewable as a Changes Being Effected supplement in accordance with an agreement reached with Agency personnel as explained below.

Reference is made to the letter from Dr. E.B. Sheinin, Director, Office of New Drug Chemistry and Mr. D.L. Sporn, Director, Office of Generic Drugs dated June 20, 1997 regarding Abbott's proposal to implement

A copy of this letter is enclosed herein.

We have generated sufficient data to meet the requirements outlined in the referenced letter to allow us to supplement our NDA No. 17-703 for Cylert Chewable Tablets, 37.5 mg. This product is an orange monogrammed, grooved tablet provided in via a Changes Being Effected filing. In accordance with the June 20, 1997 FDA letter, we commit to place the first production lot of each product (and each strength and packaging configuration, as appropriate) on long-term stability using the approved product protocol. This submission provides data and information pertaining to all bottles and caps being converted

This change is being implemented to comply with the Poison Prevention Act covered by the Consumer Product Safety Commission (CPSC) in 16 CFR section 1700 by January, 1998. It is also expected to have a positive impact on the customer complaints that Abbott has received regarding the difficulty in opening the current child resistant closure.

APPEARS THIS WAY  
ON ORIGINAL



Paul D. Leber, M.D.  
Division of Neuropharmacological Drug Products  
November 25, 1997  
Page 2

Should you have any questions or comments on this information, please contact me at the phone number listed below. We will plan to implement this change 30 days from the date of this letter if we are not notified of any concerns from you.

Sincerely,

ABBOTT LABORATORIES

Steven I. Engel, M.S., Pharm.D.  
Director, PPD Regulatory Affairs  
(847) 937-7739  
Fax: (847) 937-8068

APPEARS THIS WAY  
ON ORIGINAL

SIE/wet

Encl.: 1) June 20, 1997 Letter; E.B. Sheinin and D.L. Sporn to R. Poska  
2) Technical Information, "Conversion to Induction Seal Closure System"

CC: Chicago/FDA District Offices - cover only  
R. Poska - cover only  
S. Self - cover only



**ABBOTT**

**Pharmaceutical Products Division**

Abbott Laboratories  
100 Abbott Park Road  
D-491, AP6B-1SW  
Abbott Park, Illinois 60064-3500

February 5, 1998

Paul Leber, M.D., Director  
Division of Neuropharmacological Drug Products  
Woodmont II, HFD-120  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, MD 20852

CENTER FOR DRUG EVALUATION  
AND RESEARCH

FEB 06 1998

RECEIVED HFD-120

DUPLICATE

PAI

5/11/98

/S/

**SPECIAL SUPPLEMENT-Changes Being Effected  
Amendment to a Pending Supplement**

Re: **Cylert® (pemoline)**  
**NDA No. 17-703/ Supplement S-014**

**Packaging Change**

NDA SUPPL AMEND  
SCP-014  
(BL)

APPEARS THIS WAY  
ON ORIGINAL

Dear Dr. Leber:

Abbott Laboratories submits this amendment to our pending Supplement S-014 for approved NDA No. 17-703 for Cylert® (pemoline) submitted on November 25, 1997.

Pursuant to a January 30, 1998 letter to Mr. Steven Townsend, Project Manager, Abbott Laboratories from Dr. Donald Klein, Review Chemist, FDA, please find enclosed the requested product specific draft labeling for Cylert® (pemoline) for the above-referenced supplement. The draft labeling contains our proposed induction seal text.

APPEARS THIS WAY  
ON ORIGINAL

Should you have any questions or comments on this information, please contact me at the phone number listed below.

Sincerely,

APPEARS THIS WAY  
ON ORIGINAL

ABBOTT LABORATORIES

Steven I. Engel, M.S., Pharm.D.  
Director, PPD Regulatory Affairs  
D-491, AP6B-1, (847) 937-7739  
Fax: (847) 937-8002

SIE/wet  
Enclosure



Cylert®  
NDA 17-703/Supplement S-014  
February 5, 1998  
Page 2

**Copy of this Submission to:**  
Donald Klein, Ph.D.  
Division of Neuropharmacological Drug Products  
Woodmont II, HFD-120  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, MD 20852

**Copy of This Cover Letter to:**  
Anne Marie Weikel, Project Manager  
Division of Neuropharmacological Drug Products  
Woodmont II, HFD-120  
Food and Drug Administration  
1451 Rockville Pike  
Rockville, MD 20852

APPEARS THIS WAY  
1998 0211

RECEIVED  
FEB 11 1998



**ABBOTT**

**Pharmaceutical Products Division**

Abbott Laboratories  
100 Abbott Park Road  
D-491, AP6B-1SW  
Abbott Park, Illinois 60064-3500

February 10, 1998

ORIGINAL

Donald Klein, Ph.D.  
Division of Neuropharmacological Drug Products  
HFD-120, Woodmont Office Complex 2  
Food and Drug Administration  
Center for Drug Evaluation and Research  
1451 Rockville Pike  
Rockville, MD 20852

NDA SUPPL AMEND

SCP-014  
(BC)

CENTER FOR DRUG EVALUATION  
AND RESEARCH

FEB 11 1998

Re: NDA 16-832/S-016  
~~NDA 17-703/S-014~~  
NDA 18-081/S-030  
  
NDA 19-680/S-013

RECEIVED HFD-120

APPEARS THIS WAY  
ON ORIGINAL

Dear Dr. Klein:

The sponsor, Abbott Laboratories, submits the enclosed information in support of our pending Supplemental New Drug Applications for the above referenced NDA products, submitted as changes-being-effected supplements

Reference is made to your telephone call today in which you requested information on the manufacturing, packaging, and control sites for drug substance and drug product for these NDAs.

APPEARS THIS WAY  
ON ORIGINAL

Enclosed is the requested information.

Should you have any questions or comments regarding this submission, please contact me at the number listed below

Sincerely,

ABBOTT LABORATORIES

APPEARS THIS WAY  
ON ORIGINAL

*James D. Steck*

James D. Steck  
Director, PPD Regulatory Affairs  
Phone: (847) 937-0335  
Fax: (847) 937-8002



**NDA No. 16-832/S-016**

**NDA No. 17-703/S-014**

**NDA No. 18-081/S-030**

**NDA No. 19-680/S-013**

**February 10, 1998**

**Page 2**

SET:kdh

Enclosures

**Copy of this Cover Letter to:**

Jackie Ware, Pharm. D., Project Manager  
Division of Neuropharmacological Drug Products  
HFD-120, Woodmont Office Complex 2  
Food and Drug Administration  
Center for Drug Evaluation and Research  
1451 Rockville Pike  
Rockville, MD 20852