# CENTER FOR DRUG EVALUATION AND RESEARCH

**Approval Package for:**

***APPLICATION NUMBER:***

# 20-786 /S009

***Trade Name:*** Allegra D-Extended Release Tablets

***Generic Name:*** Fexofenadine HCl/pseudoephedrine HCl

***Sponsor:*** Aventis Pharmaceuticals

***Approval Date:*** January 19. 2001

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

# 20-786 /S009

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## Reviews / Information Included in this NDA Review.

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| Approval Letter | X |
| Approvable Letter | X |
| Labeling | |
| Summary Review | |
| Officer/Employee List | |
| Office Director Memo | |
| Cross Discipline Team Leader Review | |
| Medical Review(s) | |
| Chemistry Review(s) | X |
| Environmental Assessment | |
| Pharmacology Review(s) | |
| Statistical Review(s) | |
| Microbiology Review(s) | |
| Clinical Pharmacology/Biopharmaceutics Review(s) | |
| Risk Assessment and Risk Mitigation Review(s) | |
| Proprietary Name Review(s) | |
| Administrative/Correspondence Document(s) | X |

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**20-786 /S009**

# APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-786/S-009

Aventis Pharmaceuticals
10236 Marion Park Drive
PO Box 9627
Kansas City, MO 64134-0627

Attention: Carol Childers, PharmD
US Drug Regulatory Affairs - CMC

Dear Dr. Childers:

Please refer to your supplemental new drug application dated July 19, 2000, received July 20, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra-D (fexofenadine hydrochloride and pseudoephedrine hydrochloride) Extended Release Tablets.

We acknowledge receipt of your submission dated September 27, 2000. Your submission of September 27, 2000, constituted a complete response to our August 10, 2000, action letter.

This "Changes Being Effected in 30 days" supplemental new drug application provides for a change in the synthesis [redacted]

We have completed the review of this supplemental application, and it is approved.

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, call Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

*{See appended electronic signature page}*

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary and Allergy Drug Products
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

/s/
---
Craig Bertha
1/19/01 06:54:13 AM
for G. Poochikian

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**20-786 /S009**

# APPROVABLE LETTER

NDA 20-786/S-009

Aventis Pharmaceuticals
10236 Marion Park Drive
P.O. Box 9627
Kansas City, MO 64134--0627

Attention: Dhiren N. Shah, Ph.D.
Director-CMC, US Drug Regulatory Affairs

Dear Dr. Shah:

We acknowledge receipt of your supplemental new drug application dated July 19, 2000, received July 20, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra-D (fexofenadine HCl/pseudoephedrine HCl) Extended-release Tablets.

This "Changes Being Effected in 30 days" supplemental new drug application proposes a change in the synthesis [redacted]

We have completed our review and find the information presented is inadequate, and the supplemental application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). You may not put the proposed changes into effect until the following deficiencies have been addressed.

1. [redacted]

2. [redacted]

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, call Mrs. Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary and Allergy Drug Products, HFD-570
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

cc:
Archival NDA 20-786
HFD-570/Div. Files
HFD-570/G.Trout
HFD-570/Rogers
HFD-570/Poochikian
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: GST/August 1, 2000
Initialed by: S. Barnes 8/9/00
B. Rogers 8/9/00
G. Poochikian 8/9/00
final:S. Barnes 8/10/00
filename: n:\staff\troutg\20786na

NOT APPROVABLE (NA)

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**20-786 /S009**

# CHEMISTRY REVIEW(S)

# CHEMIST'S REVIEW

| | | |
|---|---|---|
| | 1. ORGANIZATION<br>HFD-570 DPADP | 2. NDA NUMBER<br>20-786 |
| 3. NAME AND ADDRESS OF APPLICANT (City and State)<br>Aventis Pharmaceuticals, Inc.<br>10236 Marion Park Drive<br>PO Box 9627<br>Kansas City, MO 64134-0627 | 4. AF NUMBER | 5. SUPPLEMENT(S)<br>NUMBER DATE<br>SCS-009 7/19/00<br>SCS-009 9/27/00*<br>*Subject of this review |
| 6. NAME OF DRUG<br>Allegra-D™ Extended-release Tablets | 7. NONPROPRIETARY NAME<br>fexofenadine hydrochloride and pseudoephedrine hydrochloride extended-release tablets | |
| 8. SUPPLEMENT PROVIDES FOR:<br>Change in the synthesis of the [redacted] in the synthesis of the drug substance | | 9. AMENDMENT(S), REPORT(S), ETC. |
| 10. PHARMACOLOGICAL CATEGORY<br>Histamine $H_1$-receptor antagonist/decongestant for treatment of symptoms associated with seasonal allergic rhinitis | 11. HOW DISPENSED<br>RX X OTC _ | 12. RELATED IND/NDA/DMF<br>X |
| 13. DOSAGE FORM(S)<br>Extended-release Tablet | 14. POTENCY<br>60 mg immediate-release fexofenadine HCl and 120 mg extended-release pseudoephedrine HCl | |
| 15. CHEMICAL NAME AND STRUCTURE<br>(±)-4-[1-Hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-dimethylbenzeneacetic acid HCl and [S-(R*,R*)]-α-[1-(Methylamino)ethyl]-benzenemethanol HCl (for structures see USAN) | | 16. RECORDS AND REPORTS<br>CURRENT YES_ NO_<br>REVIEWED YES_ NO_ |

17. COMMENTS: See attached

cc:
Orig. NDA #20-786
HFD-570/div. File
HFD-570/BRogers/1/8/00
HFD-570/GPoochikian
HFD-570/GTrout
R/D Init. by:_____
F/T by: B. Rogers/1/8/00
doc # 20786.A09.DOC

18. CONCLUSIONS AND RECOMMENDATIONS: This supplement is APPROVED.

| 19. REVIEWER NAME | 20. SIGNATURE | 21. DATE COMPLETED |
|---|---|---|
| Brian D. Rogers, Ph.D. | | 1/8/00 |

1 Page(s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

*Withheld Track Number: Chemistry-* 20-786 5009

/s/
---
Brian Rogers
1/17/01 02:46:05 PM
CHEMIST

Craig Bertha
1/17/01 03:10:31 PM
CHEMIST

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**20-786 /S009**

# ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ORIGINAL

NDA NO. 20786 REF NO. 5009
NDA SUPPL FOR SCS

Aventis Pharmaceuticals

Aventis

July 19, 2000

CENTER FOR DRUGS
RECD
JUL 20 2000
HFD-570
EVALUATION AND RESEARCH

Division of Pulmonary Drug Products (HFD-570)
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room 10B-03
5600 Fishers Lane
Rockville, MD 20857

***Attention: Ms. Gretchen Trout, SupervisoryRegulatory Health Project Manager***

Subject: NDA 20-786
Allegra-D® Tablets
(fexofenadine HCl/
pseudoephedrine HCl
extended release tablets)

**Special Supplement**
Changes Being Effected-30
Chemistry, Manufacturing, and Controls
Drug Substance
Synthesis Change

Dear Ms. Trout:

In accordance with the Guidance for Industry, Changes to an Approved NDA or ANDA, dated November 1999, section VII.C.1.b., Aventis Pharmaceuticals Inc. (Aventis) is submitting, in duplicate, a Changes Being Effected in 30 Days (CBE-30) supplement for the above referenced NDA.

The supplement provides for a change in the synthesis of [redacted] is the current approved supplier in the NDA for [redacted]

The following information is provided in support of the supplement:

- [redacted]
- [redacted]
- A letter from [redacted] which states that the FDA has determined that a CBE-30 supplement is the type of notification required for of the synthesis [redacted] (See Appendix III)

In support of this change, Aventis commits to place the [redacted] of Allegra-D tablets manufactured using [redacted] on long-term stability using the NDA approved stability protocol and submit the stability data to the Agency in subsequent Annual Reports.

Pursuant to 21 CFR §314.71(b), we are providing a copy of this supplement to the Kansas City FDA District Office.

We appreciate your review of this supplement. Should you have any comments or questions on this supplement, please contact the undersigned at (816) 966-7914.

Sincerely,
Aventis Pharmaceuticals Inc.

Dhiren N. Shah
Dhiren N. Shah, Ph.D.
Director – CMC, US Drug Regulatory Affairs

Attachments

cc: Kansas City FDA District Office – 11630 W. 80th St., Lenexa, KS 66214

Aventis Pharmaceuticals Inc.
Kansas City, Missouri 64137

NDA 20-786
ALLEGRA-D® Tablets
(fexofenadine hydrochloride and pseudoephedrine hydrochloride)

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Chemistry, Manufacturing, and Controls

# Appendix I

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**
**PUBLIC HEALTH SERVICE**
**FOOD AND DRUG ADMINISTRATION**

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

# USER FEE COVER SHEET

***See Instructions on Reverse Side Before Completing This Form***

1. APPLICANT'S NAME AND ADDRESS

Aventis Pharmaceuticals Inc.
PO Box 9627, H4-M2316
Kansas City, MO 64134-0627

2. TELEPHONE NUMBER *(Include Area Code)*

( 816 ) 966-5000

3. PRODUCT NAME

Allegra-D

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? No
IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____
(APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

6. LICENSE NUMBER / NDA NUMBER

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE **EXCLUSIONS**? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

**FOR BIOLOGICAL PRODUCTS ONLY**

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☐ NO
*(See reverse side if answered YES)*

***A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.***

**Public reporting burden for this collection of information** is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please **DO NOT RETURN** this form to this address.

| SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE | TITLE | DATE |
|---|---|---|
| [signature] | Vice President<br>US Drug Regulatory Affairs | July 19, 2000 |

FORM FDA 3397 (5/98)