CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20379/S9

APPROVAL LETTER

NDA 20-379/S-009

MAR 26 1998

Pharmacia and Upjohn Company
Attention: Mr. Gregory G. Shawaryn
Regulatory Manager, Regulatory Affairs
7000 Portage Road
Kalamazoo, MI 49001

Dear Mr. Shawaryn:

Please refer to your supplemental new drug application dated November 21, 1997, received November 24, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act and the provisions of 21 CFR 314.70(c) for Caverject (alprostadil for injection) Sterile Powder.

The supplemental application provides for revisions to the **PATIENT INSTRUCTIONS** section of both the Physician Package Insert and Patient Instructions Insert as follows:

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 final printed labeling submitted on February 10, 1997. Accordingly, the supplemental application is approved. However, as a term of the supplemental approval, we request that a labeling supplement should be submitted to incorporate information on the new PenInject 2.25 device no later than 90 days from the date of receipt of this letter.

Should a letter communicating important information about this drug product (i.e., a "Dear Doctor" letter) be 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 20852-9787

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, please contact Terri Rumble, Project Manager, at (301) 827-4260.

Sincerely,

/S/ 3/24/98

Lisa D. Rarick, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Orig. NDA
HFD-580
HFD-580/LRarick/MHirsch
DISTRICT OFFICE
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)
HFD-580/CKish/3.19.98/n20379ap.s09
concurrence:MHirsch 3.20.98/DShames 3.23.98/LRarick 3.23.98

SUPPLEMENT APPROVAL (S/AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20379/S9

MEDICAL REVIEW(S)

ORIGINAL

DEC - 3 1997

NDA 20,379 **Supplement** 009
Sponsor: Pharmacia & Upjohn Company
Drug: Caverject Sterile Powder (alprostadil for injection)
Date: December 3, 1997
Regarding: Special Supplement - Changes Being Effected

Medical Officer's Memo

Background:
In this single volume submission, Pharmacia & Upjohn Company has enclosed a supplement to revise the physician and patient package inserts for Caverject Sterile Powder (alprostadil for injection). The changes are being made to strengthen safety information for the physician and patient. These revisions are in regard to the proper handling of the syringe during dose preparation. The sponsor's intention is to prevent needle damage with subsequent breakage and to facilitate injection of the diluent into the sterile powder vial. Post-marketing surveillance reveals that needle breakage, with lodging of the needle fragment in the shaft of the penis, has been reported on 10 occasions. Further, the sponsor has received reports of difficulty injecting the diluent into the sterile powder vial during dose preparation.

Label Revisions:

Reviewer comment:

The label revisions in this supplement are acceptable as submitted.

In the Quarterly Periodic Report for CAVERJECT Sterile Powder, on page 42, under the heading "Implementation of Corrective Actions", the sponsor reports that "a device called PenInject 2.25 Autoinjector has recently been made available for purchase to provide customers assistance in the injection of the reconstituted CAVERJECT solution." Further, "the device can be ordered from Pharmacia & Upjohn by pharmacists or physicians". However, there is no information concerning this device and its safe and effective use either in the physician or patient package insert.

Recommended regulatory action:

A regulatory letter should be drafted to the sponsor relating that the changes being effected in Supplement 009 are acceptable, however, the sponsor should revise the label further to include the new device called PenInject 2.25.

/S/

Mark S. Hirsch, MD
Medical Officer
DRUDP
cc: Orig NDA 20-379
HFD-580 Division File
HFD-580/LRarick/HJolson/MHirsch/TRumble

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20379/S9

CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-379/S-009

NOV 26 1997

Noted + received in memo Dec 3, 1997 MT

Pharmacia & Upjohn Company
7000 Portage Road
Kalamazoo, Michigan 49001

Attention: Gregory G. Shawaryn
Manager, Regulatory Affairs

Dear Gregory G. Shawaryn:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Caverject Sterile Powder(alprostadil for injection)

NDA Number: 20-379

Supplement Number: S-009

Date of Supplement: November 21, 1997

Date of Receipt: November 24, 1997

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on January 23, 1998 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 Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely. /S/

Lana D. Pauls, M.P.H.
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-379/S-009
HFD-580/Div. Files
HFD-580/CSO/

SUPPLEMENT ACKNOWLEDGEMENT

Pharmacia & Upjohn

ORIGINAL

Office of:

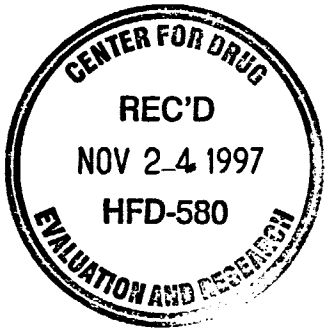
Gregory Shawaryn
Manager, Regulatory Affairs
U.S. Regulatory Affairs
Telephone No. (616) 833-8239

Facsimile No. (616) 833-8237

November 21, 1997

NDA NO. 20-379 REF. NO. 009

NDA SUPPL FOR SUI SS



Dr. Lisa Rarick
Division of Reproductive & Urological Drug Products HFD-580
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room 17B-30
5600 Fisher Lane
Rockville, MD 20857

Re: NDA 20-379
Caverject® Sterile Powder
alprostadil for injection

Special Supplement - Changes Being Effected

Dear Dr. Rarick,

In conformance with 21 CFR§ 314.70, Pharmacia and Upjohn Company is submitting the attached supplement to revise the physician and patient package inserts for the above product.

Twelve copies of the Final Printed Labeling of the physician insert (copy code 816 442 004) and patient insert (copy code 816 175 004) are provided in Attachment 1. These inserts correspond to the pre-filled diluent syringe package presentation and will be the first to be implemented. For ease of review, mock-ups showing the changes made to the currently approved inserts are included in Attachment 2. Implementation is anticipated by January 1, 1998.

Similar changes will be made, with the exception of #2 below, to the physician and patient inserts supplied with the vials only package presentation at the next printing. Mock-ups showing the changes that will be made to the currently approved inserts are included in Attachment 3. These inserts will be provided to the Division in the next NDA Annual Report.

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA

Telephone (616) 833-4000

The revision affects the patient information that is contained at the end of the the physician text in the physician insert and as a separate insert intended for the patient.

The changes in the attached labeling are:

If you should have any questions regarding this information, please contact Gregory G. Shawaryn at (616) 833-8239. Please address correspondence to Unit 0635-298-110.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Gregory G. Shawaryn
Regulatory Manager
U.S. Regulatory Affairs

REVIEWS COMPLETED
AP letter sent 3/26/98
CSO ACTION:
☒ LETTER ☐ N.A.I. ☐ MEMO
3/30/98
CSO INITIALS DATE

GGS:crdt
Attachments

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

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001.
Expiration Date: 12/31/95
See OMB Statement on Page 3.

FOR FDA USE ONLY

DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314).*

NAME OF APPLICANT
Pharmacia & Upjohn Company

DATE OF SUBMISSION
November 21, 1997

ADDRESS *(Number, Street, City, State and Zip Code)*
7000 Portage Road
Kalamazoo, Michigan 49001

TELEPHONE NO. *(Include Area Code)*
(616) 833-8239

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (if previously issued)
20-379

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*
alprostadil for injection

PROPRIETARY NAME *(if any)*
CAVERJECT® Sterile Powder

CODE NAME *(if any)*

CHEMICAL NAME
11a, 13E, 15S)-11, 15-dihydroxy-9-oxoprost-13-en-1-oic acid

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
sterile powder	intracavernosal injection	5 mcg, 10 mcg 20 mcg, 40 mcg

PROPOSED INDICATIONS FOR USE
Treatment of erectile dysfunction

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21 CFR 314.420)* REFERRED TO IN THIS APPLICATION:

INDs DMFs OB-MF

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

☐ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)* ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG	HOLDER OF APPROVED APPLICATION

TYPE SUBMISSION *(Check one)*

☐ PRESUBMISSION ☐ AN AMENDMENT TO A PENDING APPLICATION ☒ SUPPLEMENTAL APPLICATION

☐ ORIGINAL APPLICATION ☐ RESUBMISSION

SPECIFIC REGULATION(S) TO SUPPORT CHANGE OF APPLICATION *(e.g., Part 314.70(b)(2)(iv))*_____

PROPOSED MARKETING STATUS *(Check one)*

☒ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)* ☐ APPLICATION FOR AN OVER-THE-COUNTER PRODUCT *(OTC)*

CONTENTS OF APPLICATION

This application contains the following items: *(Check all that apply)*

	1. Index
	2. Summary (21 CFR 314.50 (c))
	3. Chemistry, manufacturing, and control section (21 CFR 314.50 (d) (1))
	4. a. Samples (21 CFR 314.50 (e) (1)) (Submit only upon FDA's request)
	b. Methods Validation Package (21 CFR 314.50 (e) (2) (i))
	c. Labeling (21 CFR 314.50 (e) (2) (ii))
	i. draft labeling *(4 copies)*
	ii. final printed labeling (12 copies)
	5. Nonclinical pharmacology and toxicology section (21 CFR 314.50 (d) (2))
	6. Human pharmacokinetics and bioavailability section (21 CFR 314.50 (d) (3))
	7. Microbiology section (21 CFR 314.50 (d) (4))
	8. Clinical data section (21 CFR 314.50 (d) (5))
	9. Safety update report (21 CFR 314.50 (d) (5) (vi) (b))
	10. Statistical section (21 CFR 314.50 (d) (6))
	11. Case report tabulations (21 CFR 314.50 (f) (1))
	12. Case reports forms (21 CFR 314.50 (f) (1))
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. OTHER *(Specify)*

I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

1. **Good manufacturing practice regulations in 21 CFR 210 and 211.**
2. **Labeling regulations in 21 CFR 201.**
3. **In the case of a prescription drug product, prescription drug advertising regulations in 21 CFR 202.**
4. **Regulations on making changes in application in 21 CFR 314.70, 314.71, and 314.72.**
5. **Regulations on reports in 21 CFR 314.80 and 314.81.**
6. **Local, state and Federal environmental impact laws.**

If this application applies to a drug product that FDA has proposed for scheduling under the controlled substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Gregory G. Shawaryn, Regulatory Manager, Regulatory Affairs	Gregory Shawaryn	November 21, 1997

ADDRESS *(Street, City, State, Zip Code)*	TELEPHONE NO. *(Include Area Code)*
7000 Portage Road Kalamazoo, Michigan 49001	(616) 833-8239

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)