CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-755

ADMINISTRATIVE DOCUMENTS

Kasturi

JUN 18 1997

Memorandum

Date: 18 June 1997

From: Kasturi Srinivasachar, Ph.D., Review Chemist, HFD-580

6/18/97

Subject: NDA 20-755 Environmental Assessment

To: NDA 20-755

The non-confidential Environmental Assessment submitted in Appendix A, pages 3.6/16-3.6/44, vol. 1.7, is a copy of the Environmental Assessment submitted to NDA 20-379 (Caverject Sterile Powder). Many sections of this are not relevant to alprostadil aqueous injection since this is a different formulation manufactured at another location. A revised non-confidential Environmental Assessment should be submitted with information pertinent to the formulation for which marketing approval is being sought.

An estimate of the maximum possible environmental concentration should be provided in the confidential Environmental Assessment. This information is missing on page 3.6/10, vol. 1.7, where only the equation used in arriving at this number is given.

Conclusions and Recommendations: The Applicant should be requested to resubmit an Environmental Assessment section with the revisions detailed above. It is recommended that this information be submitted as soon as possible to facilitate the review of this NDA.

cc: Orig. NDA 20-755
HFD 580/ Div. Files
HFD 580/ K. Srinivasachar/Rhee/CSO
R/D initialed by: 6/18/97

Filename: nda20755.me2

CAVERJECT Injection NDA 20-755

XIII. PATENT INFORMATION

A. PATENT CERTIFICATION

1.	Active Ingredient(s)	Alprostadil (Prostaglandin E_1, PGE_1)
2.	Strength(s)	5, 10 and 20 mcg/mL and 40 mcg in 2 mL
3.	Trade Name	CAVERJECT Injection (alprostadil aqueous injection)
4.	a. Dosage Form	Sterile isotonic solution
	b. Route of Administration	Intracavernosal injection
5.	Applicant Firm Name	Pharmacia & Upjohn Company
6.	NDA Number	20-755
7.	NDA Approval Date	To be determined
8.	Exclusivity - Date first ANDA could be approved and length of exclusivity period	Three (3) years after date of NDA approval or March 16, 1997, whichever occurs last
9.	Applicable patent numbers and expiration date of each	4,127,118 (3/16/97)

To the best of my knowledge, this is to certify that the above information is accurate.

Robert A. Paarlberg
Director
Regulatory Affairs

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NDA/PLA # 20-755 Supplement # _____ Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HF____ Trade (generic) name/dosage form: Caverject (alprostadil injection) aqueous Action: (AP) AE NA

Applicant Pharmacia & Upjohn Therapeutic Class 55

Indication(s) previously approved _____ Pediatric labeling of approved indication(s) is adequate X inadequate __

Indication in this application erectile dysfunction (For supplements, answer the following questions in relation to the proposed indication.)

__ 1. **PEDIATRIC LABELING IS ADEQUATE.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric subgroups. Further information is not required.

__ 2. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

__ a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

__ b. The applicant has committed to doing such studies as will be required.

__ (1) Studies are ongoing,

__ (2) Protocols were submitted and approved.

__ (3) Protocols were submitted and are under review.

__ (4) If no protocol has been submitted, explain the status of discussions on the back of this form.

__ c. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

X 3. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in children. Explain, on the back of this form, why pediatric studies are not needed.

__ 4. **EXPLAIN.** If none of the above apply, explain, as necessary, on the back of this form.

EXPLAIN, AS NECESSARY, ANY OF THE FOREGOING ITEMS ON THE BACK OF THIS FORM.

_____ 10/24/97

Signature of Preparer and Title (PM, CSO, MO, other) Date

cc: Orig NDA/PLA # 20-755
HFD-510/Div File
NDA/PLA Action Package
HFD-510/GTroendle (plus, for CDER APs and AEs, copy of action letter and labeling)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

3/96

DEBARMENT CERTIFICATION FOR NDA 20-755

CAVERJECT® Injection (alprostadil agueous injection)
5, 10, 20 mcg/mL and 40 mcg in 2 mL

Pursuant to section 306(k)(1) of the Federal Food, Drug and Cosmetic Act, the applicant certifies that, to the best of its knowledge and belief, the applicant did not and will not use in any capacity the services of any person listed pursuant to section 306(e) as debarred under subsections 306(a) or (b) of the Act in connection with this application.

Angel L. Canales
Director, Regulatory Compliance

July 24, 1996
Date

NDA 20-755
Caverject® injection (alprostadil injection) aqueous
Pharmacia & Upjohn, Inc.

Division Director's Memo

The application will be signed off at the Division level. No memo is necessary.

NDA 20-755
Caverject® injection (alprostadil injection) aqueous
Pharmacia & Upjohn, Inc.

Group Leader's Memo

No Group Leader's memo will be prepared; the medical review has been done in conjunction with both the Deputy Director and the Division Director; neither of which felt a memo was required.

NDA 20-755 Volume 1.14

OCT 31 1997

Medical Officer Memorandum

Date: October 30, 1997

OCT 31 1997

Sponsor: Pharmacia & Upjohn
700 Portage Road
Kalamazoo, MI 49001-0199

Drug: Caverject® Injection
(alprostadil injection) aqueous

Dosage: 2.5 mcg, 5 mcg, 10 mcg, 20 mcg, 40 mcg
Route of Administration: intracavernosal
Indication: erectile dysfunction

Background: In reviewing Volume 1.14 (clinical data section) of NDA 20-755 (Caverject® Injection) and the previous medical review of Protocol M/5650/007 from NDA 20-379 (Caverject® Sterile Powder), a minor discrepancy has been noted.

Brief Summary: On page 49 of the previous medical review (Dr .Jean Fourcroy), a table appears, summarizing the incidence rates of penile pain in the three arms of the study. The overall incidence rates of penile pain in the Alprostadil Sterile Powder group, Alprostadil Sterile Solution group and Prostin VR Pediatric Solution group were noted as 17%, 14% and 9%, respectively.

Data presented in tabular format on page 23 of Volume 1.14 of NDA 20-755 reveal that the true incidence rates of penile pain in the Alprostadil Sterile Powder group, Alprostadil Sterile Solution group and Prostin VR Pediatric Solution group were 14%, 17% and 9%, respectively.

Therefore, the true incidence rate of penile pain reported in the Alprostadil Sterile Solution group was 17% , whereas the true incidence rate reported in the Alprostadil Sterile Powder group was 14%.

This minor difference would appear to have no significant clinical impact.

As a secondary note, in Protocol M/5650/007 (page 24, volume 1.14, NDA 20-755), there is a suggestion that the incidence rate of moderate to severe penile pain reported in the Alprostadil Sterile Solution group was slightly higher than that reported in the Alprostadil Sterile Powder group (11 of 166 patients versus 4 of 166 patients). The incidence of mild penile pain was similar in the two groups (19 of 166 patients versus 20 of 166 patients).