# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER: NDA 20-649

## MICROBIOLOGY REVIEW(S)

SEP 30 1996

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF STABILITY DATA
30 September 1996

A. 1. NDA 20-649
APPLICANT: Schwartz Pharma
P.O. Box 2038
Milwaukee, WI 53201

2. PRODUCT NAMES: SPM 691/EDEX (alprostadil for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile lyophilized powder for intracavernous injection after reconstitution with sterile isotonic saline. The product is supplied in single dose vials containing either 5, 10, 20, or 40 μg of the active.

4. METHODS OF STERILIZATION:
The active drug portion of the product is prepared, filled, and lyophilized using aseptic fill conditions. The diluent portion of the product is also aseptically filled.

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is used for the diagnosis and treatment of male erectile dysfunction.

B. 1. DATE OF INITIAL SUBMISSION: 13 December 1995

2. DATE OF AMENDMENTS: 16 September 1996

3. RELATED DOCUMENTS: DMF's

4. ASSIGNED FOR REVIEW: 30 September 1996

C. REMARKS: The lyophilized active drug portion of the product is manufactured, tested, and released by Abbott Laboratories. The sterile syringe is manufactured by

aseptically fills the syringe with Sodium Chloride for Injection, USP, tests, and releases the prefilled syringe. The syringe and active drug components are shipped to the applicant for determination of conformance to specifications, assembly into the trade kit, and release of the product for distribution.

Amendment 14 contains further stability data on product and diluent. These data have been generated in the stability program since the original submission.

D. CONCLUSIONS: Review of Amendment 14 does not alter the previous recommendations transcribed in italics, below:

*The use of bacteriostatic sodium chloride injection (or other appropriate bacteriostatic diluent), rather than sodium chloride injection is still recommended for product reconstitution.*

*The product is recommended for approval following resolution of the diluent to be packaged with the lyophilized product.*

30 September 1996

Paul Stinavage, Ph.D.

cc: Original NDA 20-649
HFD-510/T. Rumble
HFD-805/Consult File/Stinavage

DAC 9/30/96

Drafted by: P. Stinavage, 30 September 1996
R/D initialed by P. Cooney

SEP 12 1996

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW AMENDMENT 6 TO NDA 20-649
11 September 1996

A. 1. NDA 20-649
APPLICANT: Schwartz Pharma
P.O. Box 2038
Milwaukee, WI 53201

2. PRODUCT NAMES: Viridal® (alprostadil for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile lyophilized powder for intracavernous injection after reconstitution with sterile isotonic saline. The product is supplied in single dose vials containing either 5, 10, 20, or 40 μg of the active.

4. METHODS OF STERILIZATION:
The active drug portion of the product is prepared, filled, and lyophilized using aseptic fill conditions. The diluent portion of the product is also aseptically filled.

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is used for the diagnosis and treatment of male erectile dysfunction.

B. 1. DATE OF INITIAL SUBMISSION: 13 December 1995

2. DATE OF AMENDMENTS: 28 March 1996

3. RELATED DOCUMENTS: DMF's

4. ASSIGNED FOR REVIEW: 30 July 1996 and 12 August 1996

C. REMARKS: The lyophilized active drug portion of the product is manufactured, tested, and released by Abbott Laboratories. The sterile syringe is manufactured by

aseptically fills the syringe with Sodium Chloride for Injection, USP, tests, and releases the prefilled syringe. The syringe and active drug components are shipped to the applicant for determination of conformance to specifications, assembly into the trade kit, and release of the product for distribution.

Amendment 6 contains documentation reflecting a request for increased fill volume for the drug product and prefilled syringes and updated test methods for bacterial endotoxins.

D. CONCLUSIONS: Review of Amendment 6 does not alter the previous recommendations transcribed in italics, below:

*The use of bacteriostatic sodium chloride injection (or other appropriate bacteriostatic diluent), rather than sodium chloride injection is still recommended for product reconstitution.*

*The product is recommended for approval following resolution of the diluent to be packaged with the lyophilized product.*

11 September 1996

Paul Stinavage, Ph.D.

PTK 9/12/96

cc: Original NDA 20-649
HFD-510/C. Kish
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 11 September 1996
R/D initialed by P. Cooney

KLS/1

SEP 1 1 1996

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #3 OF NDA 20-649
11 September 1996

A. 1. NDA 20-649
APPLICANT: Schwartz Pharma
P.O. Box 2038
Milwaukee, WI 53201

2. PRODUCT NAMES: Viridal® (alprostadil for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile lyophilized powder for intracavernous injection after reconstitution with sterile isotonic saline. The product is supplied in single dose vials containing either 5, 10, 20, or 40 μg of the active.

4. METHODS OF STERILIZATION:
The active drug portion of the product is prepared, filled, and lyophilized using aseptic fill conditions. The diluent portion of the product is also aseptically filled.

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is used for the diagnosis and treatment of male erectile dysfunction.

B. 1. DATE OF INITIAL SUBMISSION: 13 December 1995

2. DATE OF AMENDMENTS: 1 August 1996 and 12 July 1996 (Subjects of this Review)

3. RELATED DOCUMENTS: DMF's

4. ASSIGNED FOR REVIEW: 30 July 1996 and 12 August 1996

C. REMARKS: The lyophilized active drug portion of the product is manufactured, tested, and released by Abbott Laboratories. The sterile syringe is manufactured by

aseptically fills the syringe with Sodium Chloride for Injection, USP, tests, and releases the prefilled syringe. The syringe and active drug components are shipped to the applicant for determination of conformance to specifications, assembly into the trade kit, and release of the product for distribution.

D. CONCLUSIONS: The use of bacteriostatic sodium chloride injection (or other appropriate bacteriostatic diluent), rather than sodium chloride injection is still recommended for product reconstitution.

The product is recommended for approval following resolution of the diluent to be packaged with the lyophilized product.

11 September 1996

Paul Stinavage, Ph.D.

cc: Original NDA 20-649
HFD-510/C. Kish
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 11 September 1996
R/D initialed by P. Cooney

JUL 22 1996

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #4 OF NDA 20-649 (Request for Guidance)
22 July 1996

A. 1. NDA 20-649
APPLICANT: Schwartz Pharma
P.O. Box 2038
Milwaukee, WI 53201

2. PRODUCT NAMES: Viridal® (alprostadil for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile lyophilized powder for intracavernous injection after reconstitution with sterile isotonic saline. The product is supplied in single dose vials containing either 5, 10, 20, or 40 µg of the active.

4. METHODS OF STERILIZATION:
The active drug portion of the product is prepared, filled, and lyophilized using aseptic fill conditions. The diluent portion of the product is also aseptically filled.

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is used for the diagnosis and treatment of male erectile dysfunction.

B. 1. DATE OF INITIAL SUBMISSION: 13 December 1995

2. DATE OF AMENDMENT: 19 June 1996 (Subject of this Review)

3. RELATED DOCUMENTS: DMF's

4. ASSIGNED FOR REVIEW: 15 July 1996

C. REMARKS: The Amendment requests guidance on the Reviewer's response to Amendment 010 to the application. The applicant has requested guidance on a proposed microbial growth test for the reconstituted product. This Amendment is a request for guidance and does not address the deficiencies cited in the 23 May 1996 review of the new drug application.

D. CONCLUSIONS: The information presented in the 19 June 1996 Amendment does not alter the *"Not Recommended for Approval"* recommendation of the 23 May 1996 review of the New Drug Application. The protocol to determine growth promotion appears adequate.

22 July 1996

Paul Stinavage, Ph.D.

7/22/96

cc: Original NDA 20-649
HFD-510/C. Kish
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 22 July 1996
R/D initialed by P. Cooney

JUN 20 1996

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #3 OF NDA 20-649
19 June 1996

A. 1. NDA 20-649
APPLICANT: Schwartz Pharma
P.O. Box 2038
Milwaukee, WI 53201

2. PRODUCT NAMES: Viridal® (alprostadil for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile lyophilized powder for intracavernous injection after reconstitution with sterile isotonic saline. The product is supplied in single dose vials containing either 5, 10, 20, or 40 µg of the active.

4. METHODS OF STERILIZATION:
The active drug portion of the product is prepared, filled, and lyophilized using aseptic fill conditions. The diluent portion of the product is also aseptically filled.

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is used for the diagnosis and treatment of male erectile dysfunction.

B. 1. DATE OF INITIAL SUBMISSION: 13 December 1995

2. DATE OF AMENDMENT: 24 May 1996 (Subject of this Review)

3. RELATED DOCUMENTS: DMF's

4. ASSIGNED FOR REVIEW: 11 June 1996

C. REMARKS: The Amendment requests guidance on the Reviewer's response to Amendment 007 to the application. The applicant has also requested guidance on a proposed container/closure integrity test for the syringe portion of the product.

D. CONCLUSIONS: The information presented in the 24 May 1996 Amendment does not alter the *"Not Recommended for Approval"* recommendation of the 23 May 1996 review of the New Drug Application.

19 June 1995

Paul Stinavage, Ph.D.

Pstz 6/19/96

cc: Original NDA 20-649
HFD-510/C. Kish
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 19 June 1996
R/D initialed by P. Cooney

MAY 2 8 1996

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #2 OF NDA 20-649
23 May 1996

A. 1. NDA 20-649
APPLICANT: Schwartz Pharma
P.O. Box 2038
Milwaukee, WI 53201

2. PRODUCT NAMES: Viridal® (alprostadil for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile lyophilized powder for intracavernous injection after reconstitution with sterile isotonic saline. The product is supplied in single dose vials containing either 5, 10, 20, or 40 μg of the active.

4. METHODS OF STERILIZATION:
The active drug portion of the product is prepared, filled, and lyophilized using aseptic fill conditions. The diluent portion of the product is also aseptically filled.

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is used for the diagnosis and treatment of male erectile dysfunction.

B. 1. DATE OF INITIAL SUBMISSION: 13 December 1995

2. DATE OF AMENDMENT: 29 April 1996 (Subject of this Review)

3. RELATED DOCUMENTS: DMF's

4. ASSIGNED FOR REVIEW: 9 May 1996

C. REMARKS: The lyophilized active drug portion of the product is manufactured, tested, and released by Abbott Laboratories. The sterile syringe is manufactured by

aseptically fills the syringe with Sodium Chloride for Injection, USP, tests, and releases the prefilled syringe. The syringe and active drug components are shipped to the applicant for determination of conformance to specifications, assembly into the trade kit, and release of the product for distribution.

D. CONCLUSIONS: The use of bacteriostatic sodium chloride injection (or other appropriate bacteriostatic diluent), rather than sodium chloride injection is recommended for product reconstitution.

The application is not recommended for approval.

23 May 1996
Paul Stinavage, Ph.D.

5/23/96

cc: Original NDA 20-649
HFD-510/S. Trostle
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 23 May 1996
R/D initialed by P. Cooney, 23 May 1996

APR - 2 1996

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #1 OF NDA 20-649
25 March 1996

A. 1. NDA 20-649
APPLICANT: Schwartz Pharma
P.O. Box 2038
Milwaukee, WI 53201

2. PRODUCT NAMES: Viridal® (alprostadil for injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile lyophilized powder for intracavernous injection after reconstitution with sterile isotonic saline. The product is supplied in single dose vials containing either 5, 10, 20, or 40 μg of the active.

4. METHODS OF STERILIZATION:
The active drug portion of the product is prepared, filled, and lyophilized using aseptic fill conditions. The diluent portion of the product is also aseptically filled.

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is used for the diagnosis and treatment of male erectile dysfunction.

B. 1. DATE OF INITIAL SUBMISSION: 13 December 1995

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: DMF's

4. ASSIGNED FOR REVIEW: 21 December 1995

C. REMARKS: The lyophilized active drug portion of the product is manufactured, tested, and released by Abbott Laboratories. The sterile syringe is manufactured by

aseptically fills the syringe with Sodium Chloride for Injection, USP, tests, and releases the prefilled syringe. The syringe and active drug components are shipped to the applicant for determination of conformance to specifications, assembly into the trade kit, and releases the product for distribution.

D. CONCLUSIONS: The use of bacteriostatic sodium chloride injection (or other appropriate bacteriostatic diluent), rather than sodium chloride injection is recommended for product reconstitution.

The application is not recommended for approval.

25 March 1996

Paul Stinavage, Ph.D.

4/2/96

cc: Original NDA 20-649
HFD-510/S. Trostle
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 25 March 1996
R/D initialed by P. Cooney, 25 March 1996