CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 20-583

MICROBIOLOGY REVIEW(S)

JUL 26 1995

CONSULTATIVE REVIEW TO HFD-540
DIVISION OF MEDICAL IMAGING, SURGICAL, and DENTAL DRUG PRODUCTS; HFD-160
MICROBIOLOGIST'S REVIEW OF NDA

July 26, 1995

A. 1. **NDA 20,583**

APPLICANT: Pharmos Corporation
2 Innovation Drive
Suite A
Alachua, FL 32615

2. **PRODUCT NAMES:** Loteprednol Etabonate 0.5% ophthalmic suspension
Lotemax
P-5604

3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:**
Ophthalmic Suspensions for Topical (Ocular) Administration

4. **METHODS OF STERILIZATION:**

5. **PHARMACOLOGICAL CATEGORY:**
Ophthalmic Inflammation and Allergic Conditions of the Eye

B. 1. **DATE OF INITIAL SUBMISSION:** March 31, 1995

2. **RELATED DOCUMENTS:**

3. **ASSIGNED FOR REVIEW**: April 1, 1995

C. **REMARKS**: The NDA 20-583 provides for the use Loteprednol Etabonate in a sterile preserved formulation for the relief of ocular inflammation. The drug product is packaged in a multiuse eye drop container.

The drug product is manufactured by an aseptic fill process by Bausch & Lomb in Tampa, Florida for Pharmos Corporation.

D. **CONCLUSIONS**: The NDA 20-583 for Loteprednol Etabonate is not recommended for approval from the standpoint of microbiology. The submission contains insufficient data to assure the sterility and safety of the product. Specific comments are provided in section E. "Review Notes" and in the Microbiologist's Draft Letter to the Applicant".

Jul 26, 1995

Patricia F. Hughes, Ph.D.
Review Microbiologist

PFH 7/26/95

cc: Original NDA 20,583

HFD-160/Consult File
HFD-160/P.F.Hughes, 07/26/95
HFD-540/Division File
HFD-540/CSO/K.Chapman

Drafted by P.F.Hughes, 07/26/95
R/D initialed by P. Cooney, 07/26/95

HFD 540 ~~CHAPMAN~~ HOLMES
OCT 21 1996

NOV - 1 1996

REVIEW TO HFD-540
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY TEAM; HFD-805
REVIEW OF AMENDMENT
October 11, 1996

A. 1. **NDA 20,583** **APPLICANT:** Pharmos Corporation
2 Innovation Drive
Suite A
Alachua, FL 32615

2. **PRODUCT NAMES:** Loteprednol Etabonate 0.5% ophthalmic suspension
Lotemax
P-5604

3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:**
Ophthalmic Suspensions for Topical (Ocular) Administration

4. **METHODS OF STERILIZATION:**

5. **PHARMACOLOGICAL CATEGORY:**
Ophthalmic Inflammation and Allergic Conditions of the Eye

B. 1. **DATE OF INITIAL SUBMISSION:** March 31, 1995
2. **DATE OF AMENDMENT:** July 30, 1996
3. **ASSIGNED FOR REVIEW:** August 12, 1996

C. **REMARKS:** The amendment is in response to deficiencies identified in the original NDA submission.

D. **CONCLUSIONS:** The NDA 20-583 for Lotemax is recommended for approval from the standpoint of microbiology. Specific comments are provided in section E. "Review Notes".

10/16/96

Patricia F. Hughes, Ph.D.
Microbiology Reviewer

10/21/96

cc: Original NDA 20,583
HFD-160/Consult File
HFD-160/P.F.Hughes
HFD-540/Division File
HFD-540/CSO/K.~~Chapman~~ Holmes

Drafted by P.F.Hughes, 10/11/96
R/D initialed by P. Cooney, 10/11/96

Rec'd FEB -2 1998

REVIEW FOR HFD-550
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #4 OF NDA

January 22, 1998

JAN 28 1998

A. 1. NDA 20-583

SPONSOR Pharmos Corporation (represented by Bausch & Lomb)
2 Innovation Drive
Alachua, FL 32615

2. PRODUCT NAMES: Loteprednol Etabonate Ophthalmic Suspension 0.5%

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Plastic ophthalmic dropper bottles

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Topical steroid for the treatment of signs and symptoms of seasonal allergic conjunctivitis

6. DRUG PRIORITY CLASSIFICATION: 1S

B. 1. DATE OF INITIAL SUBMISSION: 29 March 1995 (subject of Microbiology Review #1, 26 July 1995)

2. DATE OF AMENDMENT(s): 30 July 1996 (subject of Microbiology Review #2 dated 21 October 1996), 27 August 1997 (subject of Microbiology Review #3 dated 23 September 1997), and 11 December 1997 (subject of this review).

3. RELATED DOCUMENTS: NDA 20-803 (Lotemax 0.2% suspension) and its Microbiologist's Review #1, 30 May 1997.

4. ASSIGNED FOR REVIEW: 22 December 1997

C. REMARKS: This product at 0.5% strength is to be manufactured by Bausch and Lomb at their facility in Tampa, Florida. This same facility manufactures Loteprednol Etabonate 0.2% (NDA 20-803) and Loteprednol Etabonate 0.5% (NDA 20-841). The formulation of the 0.5% and the 0.2% products are similar, and microbiologically there is no difference except for an additional fill volume (15 mL) for the 0.5% strength. In the review of NDA 20-803, it was noted there was a suspicious practice of dissolving the product in methanol as

part of the sterility test. Since the 3 related NDAs use the same protocol, the question was relevant to this NDA and is addressed in this amendment.

D. CONCLUSIONS: The application is approvable. Specific comments are provided in section "E. Review Notes," and the "Microbiologist's Draft of Letter to the Applicant."

01-22-98

David Hussong, Ph.D.

1/28/98

cc:

HFD-550/Consult File
HFD-550/CSO/LoBianco
HFD-550/Chemist/Fenselau
HFD-160/Consult File
HFD-805/D. Hussong

Drafted by: D. Hussong, 01/22/98
R/D initialed by: P. Cooney

Filename, c:\d\nda\20-583r4.wpd