

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

64-134

MICROBIOLOGY REVIEW

11-1-64

OFFICE OF GENERIC DRUGS

HFD-640

Microbiology Review #1

September 10, 1999

A. 1. ANDA 64-134a

APPLICANT Bausch & Lomb Pharmaceuticals, Inc.
Pharmaceutical Division
Attn: Peter Stoelze
8500 Hidden River Parkway
Tampa, FL 33637

2. PRODUCT NAME: Tobramycin & Dexamethasone Ophthalmic
Suspension USP, 0.3%/0.1%

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: eyedrops,
2.5 & 5 ML dropper bottles

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Antimicrobial and anti-
inflammatory

B. 1. DATE OF INITIAL SUBMISSION: December 10, 1998
Subject of this Review (Received Dec. 14, 1998)

2. DATE OF TELEPHONE AMENDMENT: September 9, 1999
Subject of this Review (Received Sept. 9, 1999)

3. RELATED DOCUMENTS: N/A

4. ASSIGNED FOR REVIEW: September 7, 1999

C. REMARKS: The original sterility assurance submission
was reviewed and determined to be recommended
for approval by J. McVey (11/27/96).

This amendment was filed to respond to
chemistry deficiencies, which included
production of a new exhibit batch and
accompanying test data from its production.
They also request the addition of
for production of their
commercial drug product lots.

A telecon was held with the applicant
(9/7/99) to clarify two issues regarding the
sterility assurance of the product, not
addressed in the 12/14/98 amendment. The
applicant responded to these issues with a
telephone amendment (faxed and received

9/9/99), which is also reviewed in this review.

- D. CONCLUSIONS: The submission **is recommended** for approval on the basis of sterility assurance. Specific comments regarding the aseptic filling process are provided in "E. Review Notes".

Lynne A Ensor 9/10/99
Lynne A Ensor, Ph. D.

cc: -----

ET
9/14/99

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releasable.

Micro Rev.)

9/10/99

Dosage Form / Route of Administration: Topical, sterile, ophthalmic solutions or suspensions in plastic dropper-tip bottles with caps.

Conclusions and Recommendations: Recommend approval of all supplements incorporated into this submission [4 NDA, 12 AADA, and 18 ANDA supplements] on the basis of sterility assurance.

See Review Notes, below.

cc:

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Carol K. Vincent, HFD-805

PKY 5/10/99 5-7-99

File:C:\CKV97\NDA19907.S10

This same information is also submitted to the following Bausch & Lomb applications, which are under the purview of the Office of Generic Drugs . This review will also apply to these same applications.

<u>AADAs</u>	64-046	64-052	64-063	64-067
	64-047	64-053	64-064	64-068
	64-048	64-055	64-065	64-120

<u>ANDAs</u>	40-063	40-069	74-188	74-449
	40-064	40-070	74-307	74-776
	40-065	40-073	74-326	74-778
	40-066	40-074	74-443	
	40-067	40-075	74-447	

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s/7/99

OFFICE OF GENERIC DRUGS, HFD630

Microbiologists Review #2

November 27, 1996

A. 1. ANDA: **64-134**

APPLICANT: Bausch & Lomb Pharmaceuticals, Inc.
Pharmaceutical Division
Attention: Peter Stoelze
8500 Hidden River Parkway
Tampa, FL 33637

2. PRODUCT NAMES: Tobramycin and Dexamethasone Ophthalmic
Suspension USP, 0.3% / 0.1%

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Eyedrops.
2.5 mL and 5 mL dropper bottles.

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Antimicrobial and anti-
inflammatory.

B. 1. DATE OF INITIAL SUBMISSION: July 29, 1994; Filed September 1,
1995.

2. DATE OF AMENDMENT: August 31, 1995
June 11, 1996 - Subject of this Review.
December 3, 1996- Subject of this Review.

3. RELATED DOCUMENTS: AADA 62-837

4. ASSIGNED FOR REVIEW: November 27, 1996.

C. REMARKS: Volumes 1 and 2 must be reviewed simultaneously.

D. CONCLUSIONS: The submission is recommended for approval on the basis of
sterility assurance. Specific comments are provided in "E. Review Notes".

James L. McVey 12/5/96
James L. McVey

Q. O. P. 12/6/96

initialed by F. Fang or F. Holcombe

cc:

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Micro Review R

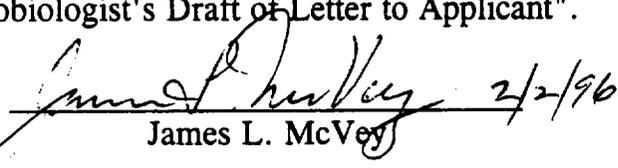
11/27/96

OFFICE OF GENERIC DRUGS, HFD630

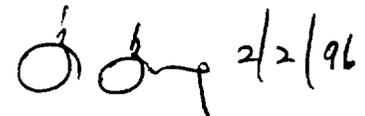
Microbiologists Review #1

February 2, 1996

- A. 1. ANDA: 64-134
- APPLICANT: Bausch & Lomb Pharmaceuticals, Inc.
Pharmaceutical Division
Attention: Peter Stoelze
8500 Hidden River Parkway
Tampa, FL 33637
2. PRODUCT NAMES: Tobramycin and Dexamethasone Ophthalmic Suspension USP, 0.3% / 0.1%
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Eyedrops. 2.5 mL and 5 mL dropper bottles.
4. METHOD(S) OF STERILIZATION:
5. PHARMACOLOGICAL CATEGORY: Antimicrobial and anti-inflammatory.
- B. 1. DATE OF INITIAL SUBMISSION: July 29, 1994; Filed September 1, 1995. - Subject of this Review.
2. DATE OF AMENDMENT: August 31, 1995 - Subject of this Review.
3. RELATED DOCUMENTS: AADA 62-837
4. ASSIGNED FOR REVIEW: January 22, 1996.
- C. REMARKS: Volumes 1 and 2 must be reviewed simultaneously.
- D. CONCLUSIONS: The submissions are not recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes" and "Microbiologist's Draft of Letter to Applicant".


James L. McVey 2/2/96

initialed by F. Fang or F. Holcombe


2/2/96

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Micro Rev 1

2/2/96

Medical Officer Review of ANDA 64-134
Ophthalmology Consultation

NDA 64-134

Submission date: 10/3/97
Review date: 11/2/97

Sponsor: Bausch & Lomb
8500 Hidden River Parkway
Tampa, FL 33637
(813) 975-7700

Drug: Tobramycin and Dexamethasone Ophthalmic Suspension
0.3% / 0.1%

Pharmacologic Category: Steroid

Submitted: Proposed Protocols 1. Pilot Study and 2. Definitive Study

Title: Pilot Study: A Pilot Evaluation Assessing Five Loading Regimens with TobraDex Ophthalmic Suspension

OBJECTIVE

The objective of the pilot study is to evaluate the effect of five loading regimens on the efficacy of TobraDex in reducing the signs and symptoms associated with acute allergic conjunctivitis induced by topical allergen challenge. The five loading regimens (2, 5, 8, 11 and 14 days) will be analyzed to identify the optimal loading period required to produce a 0.5 unit change and a statistically significant reduction from placebo in both conjunctival hyperemia and ocular itching.

Reviewer's Comments: *The study should attempt to determine the dosing regimen necessary to elicit a 1 unit change in itching and a 1 unit change in redness.*

STUDY DESIGN

This pilot study is a randomized, double-masked, placebo-controlled, contralateral eye comparison evaluation of TobraDex ophthalmic suspension in approximately 60 volunteers exposed to allergen challenge. Subjects will be treated four times daily with TobraDex in one eye and placebo in the contralateral eye. Five loading regimens will be compared (2, 5, 8, 11 and 14 days) with 12 subjects per regimen. The study consists of three visits; Visit 1 (Day 0), Visit 2 (Day 7), and Visit 3 (Day 21).

Reviewer's Comments: *Acceptable, although in general it is preferable to have each eye treated independently instead of a paired comparison.*

NDA 64-134 Tobramycin-Dexamethasone Suspension 0.3%/0.1%