

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*    **21-066**

**MICROBIOLOGY REVIEW(S)**

HFD-550/Rodriguez

/SI REVIEW

FEB - 9 1998

REVIEW TO HFD-550  
OFFICE OF NEW DRUG CHEMISTRY  
MICROBIOLOGY TEAM  
MICROBIOLOGIST REVIEW OF A NDA  
February 3, 1999

A. NDA 21-066

PRODUCT NAME: Ketotifen Fumarate Ophthalmic Solution

APPLICANT: Ciba Vision Corporation - A Novartis Company  
11460 Johns Creek Parkway  
Duluth, Georgia 30097-1556

DOSAGE FORM: Topical Solution for the Eyes, 0.025%

METHOD OF STERILIZATION: Aseptic processing

PHARMACOLOGICAL CATEGORY: For the prevention of itching of the  
eye due to allergic conjunctivitis

B. INITIAL APPLICATION DATE: 31 December 1998  
ASSIGNED FOR REVIEW: 25 January 1999

C. REMARKS: The validation information for the aseptic manufacturing process for this  
multidose preserved sterile eye drop drug product is the subject of this review.

D. CONCLUSIONS: The NDA 21-066, which provides for Ketotifen Fumarate  
Ophthalmic Solution (KFOS), is not recommended for approval from the standpoint  
of product quality microbiology.

SI 3 Feb 1999  
Patricia F. Hughes, Ph. D.  
Review Microbiologist

cc.: Original NDA 21-066  
HFD-160 /Consult File  
HFD-805/PFHughes  
HFD-550/R.Rodriguez  
HFD-550/Division File  
Drafted by PFHughes/3 February, 1999  
R/D Initialed by PHCooney

SI 2/9/99

APPEARS THIS WAY  
ON ORIGINAL

550- Rodriguez

2<sup>ND</sup>  
REVIEW

REVIEW TO HFD-550  
OFFICE OF NEW DRUG CHEMISTRY  
MICROBIOLOGY TEAM  
MICROBIOLOGIST REVIEW OF A NDA  
7 April 1999

APR 13 1999

A. NDA 21-066

PRODUCT NAME: Ketotifen Fumarate Ophthalmic Solution

APPLICANT: Ciba Vision Corporation - A Novartis Company  
11460 Johns Creek Parkway  
Duluth, Georgia 30097-1556

DOSAGE FORM: Topical Solution for the Eyes, 0.025%

METHOD OF STERILIZATION: Aseptic processing

PHARMACOLOGICAL CATEGORY: For the prevention of itching of the  
eye due to allergic conjunctivitis

B. INITIAL APPLICATION DATE: 31 December 1998  
DATE OF AMENDMENT # 1: 5 March 1999  
ASSIGNED FOR REVIEW: 15 March 1999

C. REMARKS: The amendment dated 5 March 1999 contains responses to microbiology deficiencies found in the initial NDA submission.

D. CONCLUSIONS: The NDA 21-066, which provides for Ketotifen Fumarate Ophthalmic Solution (KFOS), is not recommended for approval from the standpoint of product quality microbiology.

/S/ - 7/13/99

Patricia F. Hughes, Ph. D.  
Review Microbiologist

/S/ 4/13/99

cc.: Original NDA 21-066

HFD-160 /Consult File  
HFD-805/PFHughes  
HFD-550/R.Rodriguez  
HFD-550/Division File  
Drafted by PFHughes/7 April 1999  
R/D Initialed by PHCooney

1.1  
3RD REVIEW

REVIEW TO HFD-550  
OFFICE OF NEW DRUG CHEMISTRY  
MICROBIOLOGY TEAM  
MICROBIOLOGIST REVIEW OF AN AMENDMENT  
10 MAY 1999

MAY 10 1999

A. NDA 21-066

PRODUCT NAME: Ketotifen Fumarate Ophthalmic Solution  
APPLICANT: Ciba Vision Corporation - A Novartis Company  
11460 Johns Creek Parkway  
Duluth, Georgia 30097-1556  
DOSAGE FORM: Topical Solution for the Eyes, 0.025%  
METHOD OF STERILIZATION: Aseptic processing  
PHARMACOLOGICAL CATEGORY: For the prevention of itching of the eye due to allergic conjunctivitis

B. INITIAL APPLICATION DATE: 31 December 1998  
DATE OF AMENDMENT # 1: 5 March 1999  
DATE OF AMENDMENT # 2: 5 May 1999

ASSIGNED FOR REVIEW: 6 May 1999

C. REMARKS: The amendment dated 5 May 1999 contains responses to microbiology deficiencies found in the initial NDA submission and not fully addressed in the 5 March 1999 amendment.

D. CONCLUSIONS: The NDA 21-066, which provides for Ketotifen Fumarate Ophthalmic Solution (KFOS), is recommended for approval from the standpoint of product quality, microbiology

[Redacted]

ISI 10 May 1999  
Patricia F. Hughes, Ph. D.  
Review Microbiologist

cc.: Original NDA 21-066  
HFD-160 /Consult File  
HFD-805/PFHughes  
HFD-550/R.Rodriguez  
HFD-550/Division File  
Drafted by PFHughes/10 May 1999  
R/D Initialed by PHCooney

ISI 5/10/99

APPROVED FOR RELEASE  
CONFIDENTIAL