

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-275**

**CHEMISTRY REVIEW(S)**

**Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs  
DAAODP**

**Review of Chemistry, Manufacturing, and Controls**

**NDA #: 21-275**

**REVIEW # 3**

**DATE REVIEWED: March 15, 2001**

| <b><u>SUBMISSION TYPE</u></b> | <b><u>DOCUMENT DATE</u></b> | <b><u>CDER DATE</u></b> | <b><u>ASSIGNED DATE</u></b> |
|-------------------------------|-----------------------------|-------------------------|-----------------------------|
| Original                      | 9/18/00                     | 9/19/00                 | 9/21/00                     |
| Amendment                     | 10/10/00                    | 10/11/00                | 10/13/00                    |
| Amendment                     | 10/26/00                    | 11/24/00                | 12/1/00                     |
| Amendment                     | 12/8/00                     | 12/12/00                | 12/19/00                    |
| Amendment                     | 12/29/00                    | 1/02/01                 | 1/02/01                     |
| Amendment                     | 2/1/01                      | 2/2/01                  | 2/7/01                      |
| Amendment                     | 2/5/01                      | 2/6/01                  | 2/11/01                     |
| Amendment                     | 2/12/01                     | 2/13/01                 | 2/14/01                     |
| Amendment                     | 2/20/01                     | 2/22/01                 | 2/22/01                     |

**NAME & ADDRESS OF APPLICANT:**

Allergan  
2525 Dupont Drive  
P. O. Box 19534  
Irvine, CA 92623-9534

**DRUG PRODUCT NAME**

|                                |                  |
|--------------------------------|------------------|
| <u>Proprietary:</u>            | Lumigan          |
| <u>Established:</u>            | Bimatoprost      |
| <u>Code Name/#:</u>            | AGN 192024       |
| <u>Chem. Type/Ther. Class:</u> | Prostaglandin/1P |

**PHARMACOL. CATEGORY:**

Prostamide

**DOSAGE FORM:**

Solution

**STRENGTHS:**

0.03%

**ROUTE OF ADMINISTRATION:**

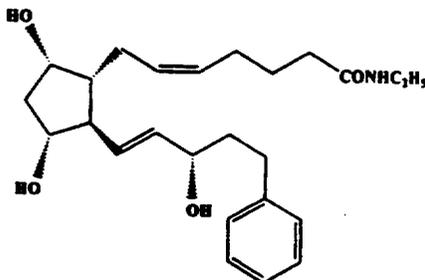
Topical/ocular, one drop/day/eye

**DISPENSED:**

Rx  OTC

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:**

(1) Chemical Structure



(2) Molecular Weight

415.58

(3) Chemical Name

(Z)-7-[(1R, 2R, 3R, 5S)-3, 5-dihydroxy-2-[(1E, 3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-N-ethyl-5-heptenamide

(4) USAN Name

Bimatoprost

(5) Chemical Abstract Number

CAS 155206-00-1

(6) Other Names

Prostamide; prostaglandin analog

**SUPPORTING DOCUMENTS:**

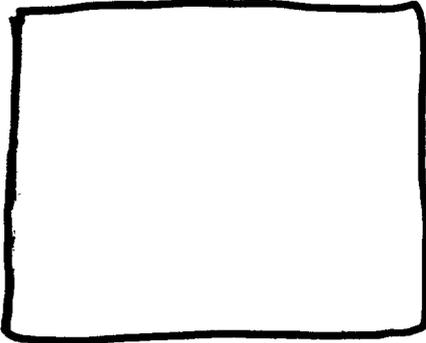
[Redacted]

| DMF#       | Type | Holder     | Item/Component | Review Date              | Status     | Letter date |
|------------|------|------------|----------------|--------------------------|------------|-------------|
| [Redacted] | III  | [Redacted] | [Redacted]     | Last reviewed<br>10/5/00 | Adequate   | 1/17/00     |
| [Redacted] | III  | [Redacted] | [Redacted]     | Last reviewed<br>8/8/00  | Adequate   | 1/17/00     |
| [Redacted] | III  | Allergan   | [Redacted]     | Not reviewed*            | Adequate*  | ---         |
| [Redacted] | III  | [Redacted] | [Redacted]     | Last reviewed<br>10/5/00 | Adequate** | 2/3/00      |

\* Allergan in NDA 21-275 has provided adequate data for the components of the packaging system. These data includes the source of the resins, coloring materials and extensive extractable studies.

\*\* Also refer to evaluation of FDA's question #13 in chemistry review No. 2.

**RELATED DOCUMENTS:**



**CONCLUSIONS & RECOMMENDATIONS:**

From CMC standpoint, NDA 21-275 is approvable at this time.

The approvability of this NDA pending receipt of the satisfactory inspection results from the OC for all requested sites.

cc:  
Orig. NDA : 21-275  
HFD-550/Division File  
HFD -550/Chemist/STso  
HFDD-550/CSO/Puglisi  
HFD-830/Cchen  
HFD-550/Boyd  
HFD-550/Zhou Chen  
HFD-550/Linda Ng  
HFD-550/Hkhorshidi  
HFD-550/WChambers

/S/

3/15/01

\_\_\_\_\_  
Chemist, HFD-550/830  
Hossein S. Khorshidi, Ph.D.

/S/

3/15/01

\_\_\_\_\_  
Chemistry Team Leader, HFD-550/830  
Linda Ng, Ph.D.

**Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs  
DAAODP**

**Review of Chemistry, Manufacturing, and Controls**

**NDA #: 21-275**

**REVIEW # 2**

**DATE REVIEWED: February 26, 2001**

| <b><u>SUBMISSION TYPE</u></b> | <b><u>DOCUMENT DATE</u></b> | <b><u>CDER DATE</u></b> | <b><u>ASSIGNED DATE</u></b> |
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\* Subject of this review

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**DOSAGE FORM:**

Solution

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0.03%

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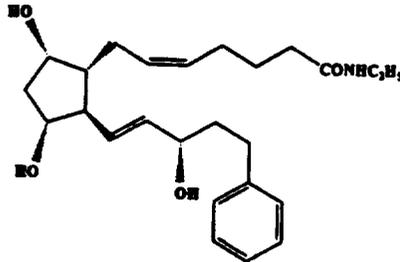
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(2) Molecular Weight  
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(3) Chemical Name  
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(5) Chemical Abstract Number  
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(6) Other Names  
Prostamide; prostaglandin analog

**SUPPORTING DOCUMENTS:**

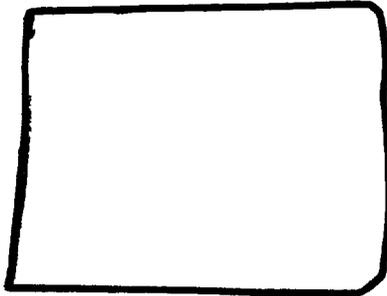
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\*\* Also refer to evaluation of FDA's question #13 in this review.

**RELATED DOCUMENTS:**



**CONCLUSIONS & RECOMMENDATIONS:**

From CMC standpoint, this NDA application is approved pending receipt of the satisfactory inspection results for all proposed sites from the OC.

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Orig. NDA - 21-275  
HFD-550/Division File  
HFD -550/Chemist/STso  
HFDD-550/CSO/Puglisi  
HFD-830/Cchen  
HFD-550/Boyd  
HFD-550/Zhou Chen  
HFD-550/Linda Ng  
HFD-550/Hkhorshidi  
HFD-550/WChambers

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Chemist, HFD-550/830  
Hossein S. Khorshidi, Ph.D.

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Chemistry Team Leader, HFD-550/830  
Linda Ng, Ph.D.

**Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs  
Review of Chemistry, Manufacturing, and Controls**

**NDA #:** 21-275

**REVIEW # 1**

**DATE REVIEWED:** January 9, 2001

| <b><u>SUBMISSION TYPE</u></b> | <b><u>DOCUMENT DATE</u></b> | <b><u>CDER DATE</u></b> | <b><u>ASSIGNED DATE</u></b> |
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| Amendment                     | 10/26/00                    | -----                   |                             |

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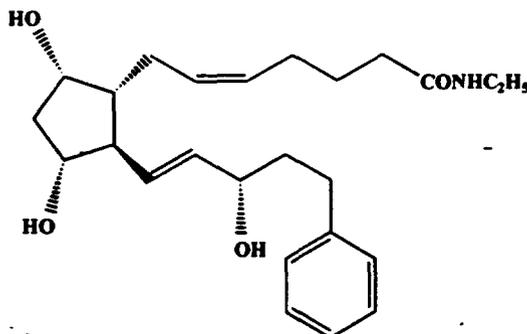
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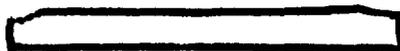
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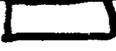
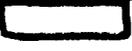
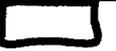
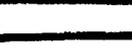
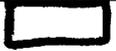
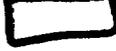
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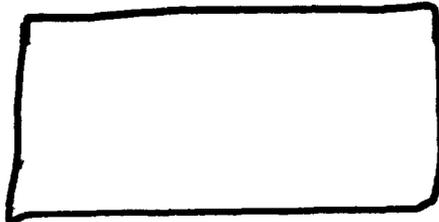
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|  | III  |  |  | Last reviewed<br>10/5/00 | Adequate   | 1/17/00     |
|  | III  |  |  | Last reviewed<br>8/8/00  | Adequate   | 1/17/00     |
|  | III  | Allergan  |  | Not reviewed             | N/A        | 3/28/00     |
|  | III  |  |  | Last reviewed<br>10/5/00 | Inadequate | 2/3/00      |

**RELATED DOCUMENTS:**



**REMARKS:**

This drug is classified as 1P. It is a 0.03% solution of bimatoprost for lowering intraocular pressure in patients with glaucoma or ocular hypertension. Bimatoprost is a synthetic analog of prostaglandin. The drug product has not been marketed before.

**CONCLUSIONS & RECOMMENDATIONS:**

From a chemistry, manufacturing and controls perspective, the NDA is recommended for an approvable action. Firm should address all outstanding issues that were submitted as facsimiles and listed in the draft letter of this review. Other issues for the reviewer to follow up are a) the impurity specifications were sent to pharmacologist and medical officer for comment (memo dated 11/29/00), b) methods validation to FDA labs, and c) EES.

**APPEARS THIS WAY  
ON ORIGINAL**

cc:

Orig. NDA - 21-275  
HFD-550/Division File  
HF -550/Chemist/STso  
HFDD-550/CSO/Puglisi  
HFD-830/Cchen  
HFD-550/Boyd  
HFD-550/Zhou Chen  
HFD-550/Linda Ng  
HFD-550/HKhorshidi

**/S/**

\_\_\_\_\_  
Chemist, HFD-550/830  
Su C. Tso, Ph.D.

*9/10/00, 2001*

**/S/**

\_\_\_\_\_  
Linda Ng, Ph.D. ✓  
Chemistry Team Leader, HFD-550/830

*1/10/01*

**APPEARS THIS WAY  
ON ORIGINAL**