

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-257**

**CHEMISTRY REVIEW(S)**

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

**NDA #:** 21-257

**REVIEW #** 1

**DATE REVIEWED:** 09-NOV-00

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Original pre-submission	05-MAY-00	11-MAY-00	XX-MAY-00
Original submission	06-JUN-00	07-JUN-00	XX-JUN-00
Amendment	04-AUG-00	07-AUG-00	17-AUG-00
Amendment	10-AUG-00	11-AUG-00	17-AUG-00
Amendment	12-SEP-00	13-SEP-00	25-SEP-00
Amendment	14-SEP-00	15-SEP-00	25-SEP-00
Amendment	15-SEP-00	18-SEP-00	25-SEP-00
Amendment	19-OCT-00	23-OCT-00	02-NOV-00
Amendment	24-OCT-00	25-OCT-00	XX-NOV-00
Amendment	06-NOV-00	XX-NOV-00	XX-NOV-00

**NAME & ADDRESS OF APPLICANT:**

Alcon Universal, Ltd.  
6201 South Freeway  
Fort Worth, TX 76134

**DRUG PRODUCT NAME**

Proprietary: Travatan  
Established: Travoprost  
Code Name/#: CAS-157283-68-6  
Chem.Type/Ther.Class: 1P

**PHARMACOL. CATEGORY:** Lowering of intraocular pressure

**DOSAGE FORM:** Solution

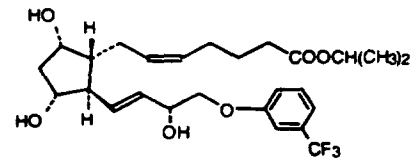
**STRENGTHS:** 0.004% and 0.0015%

**ROUTE OF ADMINISTRATION:** Topical/ocular (1 drop daily/eye)

**DISPENSED:**  Rx  OTC

**SPECIAL PRODUCTS/SPOTS:**  Yes  No

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



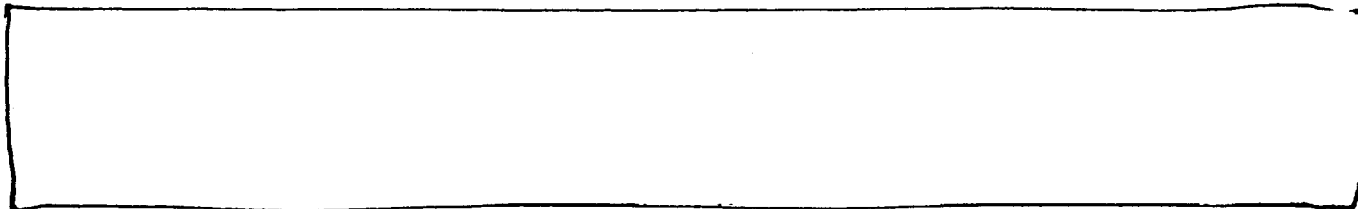
$C_{26}H_{35}F_3O_6$   
M.W.: 500.56

Isopropyl (Z)-7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3R)-3-hydroxy-4-[( $\alpha,\alpha,\alpha$ -trifluoro-*m*-tolyl)oxy]-1-butenyl]cyclopentyl]-5-heptenoate

**TRAVOPROST**

**APPEARS THIS WAY  
ON ORIGINAL**

**SUPPORTING DOCUMENTS:**



**RELATED DOCUMENTS:**

Chemistry Reviews of [redacted] (Alcon Lab., Inc.)

**CONSULT REVIEWS:**

Review of Tradenames (CDER Labeling and Nomenclature Committee, Consult # 00-00XX)  
Sterility Assurance Report (V. Pawar, HFD-160)

cc:

Orig. NDA 21-257

HFD-550/Division File

HFD-550/CSO/M.Puglisi

HFD-550/Chem/ A.Fenselau

HFD-550/TeamLdr./L.Ng

HFD-550/Pharm./Z.Chen

HFD-550/MO/L.Lim

HFD-550/Dep.Div.Dir./W.Chambers

HFD-830/Div.Dir.DNDCIII/C.-w.Chen

\_\_\_\_\_  
Allan Fenselau, Review Chemist, HFD-550

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Linda Ng, Chemistry Team Leader, HFD-550  
[redacted]

**APPEARS THIS WAY  
ON ORIGINAL**

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

**NDA #: 21-257**

**REVIEW # 2**

**DATE REVIEWED: 28-FEB-01**

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Original pre-submission	05-MAY-00	11-MAY-00	18-MAY-00
Original submission	06-JUL-00	07-JUL-00	20-JUL-00
Amendment, AZ	26-DEC-00	27-DEC-00	02-JAN-01
Amendment, BL	17-JAN-01	22-JAN-01	29-JAN-01
Amendment, BC	01-FEB-01	02-FEB-01	12-FEB-01
Amendment, BC	09-FEB-01	12-FEB-01	22-FEB-01
Amendment, BC	16-FEB-01	20-FEB-01	26-FEB-01
Amendment, BC	28-FEB-01	01-MAR-01	08-MAR-01

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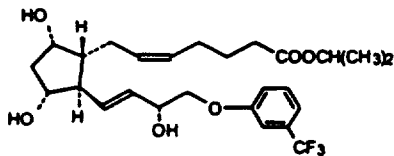
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**SPECIAL PRODUCTS/SPOTS:**  Yes  No

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



$C_{26}H_{35}F_3O_6$   
M.W.: 500.56

Isopropyl (Z)-7-[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(1E,3R)-3-hydroxy-4-[( $\alpha,\alpha,\alpha$ -trifluoro-*m*-tolyl)oxy]-1-butenyl]cyclopentyl]-5-heptenoate

**TRAVOPROST**

**CONCLUSIONS & RECOMMENDATIONS:** Based on a review of chemistry, manufacturing and control issues that pertain to the drug substance travoprost and its drug product travoprost ophthalmic solution, 0.004% (Travatan™), the application can be recommended for APPROVAL. The sponsor has committed to provide the analytical methods and their validation studies by 15-MAR-01 for all methods, except the one for [REDACTED]. In this case, the method validation package will be submitted as an NDA supplement by 01-OCT-01.

cc:

Orig. NDA 21-257

HFD-550/Division File

HFD-550/CSO/M.Puglisi

HFD-550/Chem/ A.Fenselau

HFD-550/TeamLdr./L.Ng

HFD-550/Pharm./Z.Chen

HFD-550/MO/L.Lim

HFD-550/Dep.Div.Dir./W.Chambers

HFD-830/Div.Dir.DNDCIII/C.-w.Chen

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Allan Fenselau, Review Chemist, HFD-550

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Linda Ng, Chemistry Team Leader, HFD-550

