CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
21-184/S-001

Correspondence

ALLERGAN

2525 Dupont Drive, P O. Box 19534, Irvine, California, USA 92623-9534 Telephone: (714) 246-4500 Website: www.allergan.com

October 10, 2001

Jonathan Wilkin, MD
Director,
Division of Dermatologic and Dental Drug Products
HFD-540/Room N115
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., Building 2
Rockville, MD 20850

REF: TAZORAC® (tazarotene) Cream 0.05%, 0.1%
NDA 21-184/S-001
Acceptance of Labeling Received by Electronic Mail on October 10, 2001

Dear Doctor Wilkin:

Allergan is formally notifying you of our acceptance of the labeling communicated to us by the Project Manager today.

The revised label called for the revision of 2 sentences in the CONTRAINDICATIONS and PRECAUTIONS: Pregnancy sections. Those revisions have now been completed.

We have attached the revised label to this submission. Should you have any comments or require any further information, please contact Thomas Walton at 714.246.4470, Pacific Time.

Sincerely,

Trudy A. Rumbaugh, MD
Director,
Global Regulatory Affairs, Retinoids

TR/tww

LERGAN

SE1-001/S4

Dupont Drive, P.O. Box 19534, Irvine, California, USA 92623-9534 Telephone: (714) 246-4500 Website: www.allergan.com

50 years
GROWTH & INNOV

April 24, 2001

Jonathan Wilkin, MD
Director,
Division of Dermatologic and Dental Drug Products
HFD-540/Room N115
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., Building 2
Rockville, MD 20850

see new original 7-15 JH

REF: TAZORAC® (tazarotene) Cream 0.05%, 0.1%
NDA 21-184/120 Day Safety Update for Supplement S-001

Dear Doctor Wilkin:

Allergan is amending the above-referenced New Drug Application with the 120 Day Safety Update according to 21 CFR 314.50(d)(5)(vi)(b) for Clinical Supplement S-001. The supplement seeks to add the indication of the topical treatment of acne vulgaris for TAZORAC® Cream 0.1%. There is currently one open-label study comparing the facial tolerance of tazarotene cream 0.1% with tretinoin gel microsphere 0.1% and adalalene gel 0.1% on-going

We have also included adverse event data from completed and on-going studies related to the indication of the topical treatment of the signs and symptoms of premature aging of the skin caused by overexposure to the sun. We intend to file a Clinical Supplement for this indication in June 2001.

On the basis of all information that we are aware of, no change is warranted to the Integrated Summary of Safety. No change to the contraindications, warnings, precautions and adverse events as described in the current, approved labeling for the indication of the topical treatment of plaque psoriasis is warranted. No change is likewise planned for the draft labeling accompanying Clinical Supplement S-001.

ORIGINAL

We ask that this additional safety information be reviewed and filed to NDA 21-184, TAZORAC® Cream. Should you have any questions or require further information, please call me at 714.246.4292 or Thomas Walton at 714.246.4470, Pacific Time.

Sincerely,

T. Rumbaugh MD

Trudy A Rumbaugh, MD
Director,
Global Regulatory Affairs, Retinoids

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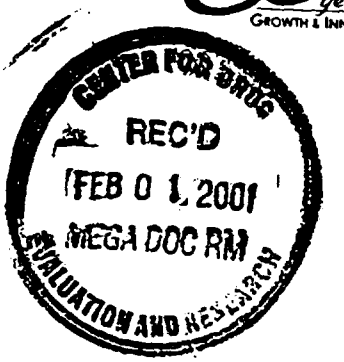
February 1, 2001



Jonathan Wilkin, MD
Director,
Division of Dermatologic and Dental Drug Products
HFD-540/Room N115
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., Building 2
Rockville, MD 20850

REF: TAZORAC® (tazarotene) Cream 0.05%, 0.1%
NDA 21-184
Withdraw Chemistry, Manufacturing and Controls (CMC) Section of S-001

Dear Doctor Wilkin:

Allergan is amending the above-referenced New Drug Application at the request of the Project Manager, Kalyani Bhatt and the Chemistry Reviewer, William Timmer, PhD. The amendment asks that the CMC section of Clinical Efficacy Supplement S-001, consisting of the . Month Stability Report for TAZORAC® Cream and the Environmental Impact Statement Update, be withdrawn.

The Chemistry Reviewer, Dr. Timmer, asked that this CMC data be submitted in the annual report to the NDA, rather than as a component of S-001.

This withdrawal affects *only* the CMC portion of S-001 as mentioned above. All other sections of S-001 remain as filed. Should this request for withdrawal by Allergan at the request of the Project Manager and the Chemistry Reviewer result in a change to the User Fee Action Date or resets the regulatory review period for S-001, Allergan will withdraw this amendment, preserving the original User Fee Date.

We ask that this information be filed to NDA 21-184, TAZORAC® Cream. Should you have any questions or require additional information, please call me at 714.246.4292 or Thomas Walton at 714.246.4470, Pacific Time.

Sincerely,

Thomas Walton / for

Trudy A. Rumbaugh, MD
Director
Global Regulatory Affairs, Retinoids

TR/tww

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SE1-001 / BN

LERGAN

Tupont Drive, P.O. Box 19534, Irvine, California, USA 92623-9534 Telephone: (714) 246-4500 Website: www.allergan.com

Grow

January 31, 2001

Jonathan Wilkin, MD
Director,
Division of Dermatologic and Dental Drug Products
HFD-540/Room N115
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., Building 2
Rockville, MD 20850

REF: TAZORAC® (tazarotene) Cream 0.05%, 0.1%
NDA 21-184/Missing CRFs from Clinical Efficacy Supplement (S-001)

Dear Doctor Wilkin:

Allergan is amending the above-referenced New Drug Application with the inclusion of two Case Reports Forms (CRF) that were inadvertently omitted from the Clinical Efficacy Supplement (Acne) submitted on December 8, 2000.

The missing CRFs are from Study 190168-030: An open-label, multi-center, pharmacokinetics study of tazarotene *gel* 0.1% after a single dose and after 6, 13, 26 and 42 repeat topical applications once-daily over 15% body surface area in female patients with acne vulgaris. This study was intended as providing supportive, rather than pivotal, data for the use of tazarotene *cream* 0.1% in the treatment of acne.

Allergan apologizes for any inconvenience caused by this omission.

We ask that this information be filed to NDA 21-184 in support of S-001. Should you have any questions or require further information, please call me at 714.246.4292 or Thomas Walton at 714.246.4292, Pacific Time.

Sincerely,

Thomas Walton /Rr

Trudy A. Rumbaugh, MD
Director,
Global Regulatory Affairs, Retinoids

TR/tww

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ɔont Drive, P.O. Box 19534, Irvine, California, USA 92623-9534 Telephone: (714) 246-4500 Website: www.allergan.com

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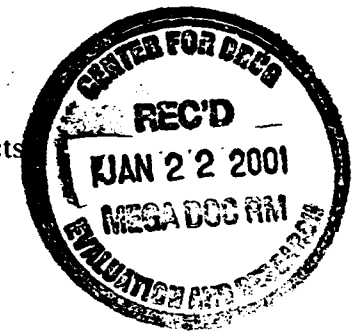
January 19, 2001



Jonathan Wilkin, MD
Director,
Division of Dermatologic and Dental Drug Products
HFD-540/Room N115
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., Building 2
Rockville, MD 20850

S21-001/NC

REF: TAZORAC® (tazarotene) Cream, 0.05%, 0.1%
NDA 21-184/Clinical Efficacy Supplement (S-001) of December 8, 2000
Replacement of Misdirected Volume 1 (Review Copy)

Dear Doctor Wilkin:

Allergan is supplementing the above-referenced NDA with another Review Copy of Volume 1 of the Clinical Efficacy Supplement (S-001) previously filed to the NDA.

In a teleconference with the Project Manager, Kalyani Bhatt, it was reported that the original Review Copy of Volume 1 had been misdirected within FDA.

We ask that the above information be reviewed and filed to NDA 21-184. Should you have any questions or require additional information, please call me at 714.246.4292 or Thomas Walton at 714.246.4470, Pacific Time.

Sincerely,

Trudy A. Rumbaugh, MD
Director,
Global Regulatory Affairs, Retinoids

TR/tww

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-184/S-001

DEC 21 2000

Allergan Inc.
2525 Dupont Drive
Irvine, CA 92623-9534

Attention: Trudy A. Rumbaugh, MD, Director, Global Regulatory Affairs

Dear Dr. T. A. Rumbaugh:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Tazorac®(Tazarotene) Cream 0.05%, 0.10%

NDA Number: 21-184

Supplement Number: S-001

Date of Supplement: December 8, 2000

Date of Receipt: December 11, 2000

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on February 16, 2000, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Food and Drug Administration
Division of Dermatologic and Dental Drug Products, HFD-540
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Attention: Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

/S/

Mary J. Kozma-Fornaro
Supervisor, Project Management Staff

Section VI - Labeling

Submissions

ALLERGAN

P.O. Box 19534, Irvine, California, USA 92623-9534 Telephone: (714) 246-4500 Website: www.allergan.com

December 8, 2000

FEDERAL EXPRESS

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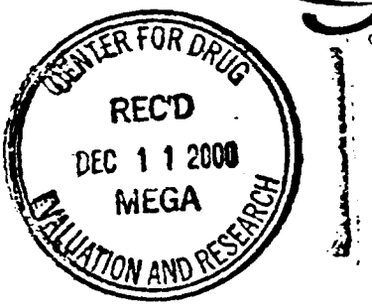

Jonathan Wilkin, MD
Director.
Division of Dermatologic and Dental Drug Products
HFD-540/Room N115
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., Building 2
Rockville, MD 20850

REF: TAZORAC® (tazarotene) Cream, 0.05%, 0.1%
NDA 21-184
Clinical Efficacy Supplement/Treatment of Acne Vulgaris

User Fee Number: 4061

Dear Doctor Wilkin:

Allergan is supplementing the above-referenced NDA with a clinical efficacy supplement for the use of TAZORAC® Cream, 0.1% in the once-daily treatment of acne vulgaris. As you know TAZORAC® (tazarotene) Gel, 0.1% has been previously approved for the once-daily treatment of acne vulgaris (NDA 20-600).

This supplement is being filed according to the provisions of **21 CFR §314.70(b)(3)**, **21 CFR §314.71(a)-(c)**, the Prescription Drug User Fee Act, and the agreements and commitments made between Allergan and your Division at the PreNDA Meeting of September 11, 2000. We have included a copy of the Meeting Minutes for your reference.

In addition to the nonclinical safety and clinical safety and efficacy data that support the new indication and labeling, we have, as agreed in the PreNDA Meeting, included an updated Environmental Assessment and an updated Stability Report (months) for the Drug Product.

Three clinical studies support the safety (Studies 190168-029C, 190168-031C and 190168-035C) and two, Phase 3 clinical studies support the efficacy (Studies 190168-029C and 190168-031C) of TAZORAC® (tazarotene) Cream, 0.1% in the once-daily treatment of acne vulgaris. The Phase 3 studies were conducted in the United States. Both studies were multi-center, double-blind, randomized, vehicle-controlled studies that evaluated the safety and efficacy of tazarotene cream, 0.1% for 12-weeks in the once-daily treatment of acne vulgaris. The results of both studies indicated that TAZORAC® (tazarotene) Cream, 0.1% was safe and significantly more effective than vehicle cream in the reduction of lesion counts for the primary efficacy variable: the percent reduction from baseline for total lesions. The secondary efficacy variables were also achieved: the percent reduction from baseline for the individual components of the total lesions:

inflammatory (papules, pustules and nodules) lesions and noninflammatory (open and closed comedones) lesions.

This supplement consists of both Archival and Review copies. Most of this supplement is presented in paper only except for the Case Report Tabulations (Section 11) and Case Report Forms (Section 12) which are presented in electronic format on a CD in accordance with the agreements from the PreNDA Meeting and **21 CFR § 11.** (The CD containing the electronic portion is located in a sleeve in the front of Volume 1 in the Archival copy.) See *Attachment 1* to this Cover Letter that describes in greater detail the contents of the electronic portion of the supplement. Also included is a verification that Allergan has performed a scan of the submission for virus protection. See *Attachment 2* that describes in detail the FDA locations receiving the submission and which sections.

In addition to the Archival and Review copies of this supplement, Allergan is sending eleven additional Desk Copies of Volume 1 that contains Sections 1, 2 and 3 to aid the Division in its review. The Desk Copies are identical in content and format to the Archival and Review copies officially submitted. A Field Copy of Volume 1 that contains Sections 1, 2, and 3, and Volume 2 containing Section 4 (Month Stability Report and Environmental Assessment) has been forwarded to the Dallas District Office, as the Drug Product is manufactured at the Allergan Waco, Texas facility.

In addition to the acne clinical safety and efficacy information modifications, the Draft Labeling also includes a correction to the psoriasis pharmacokinetics information. A review of the Phase 3 studies conducted for psoriasis discovered that 3 patients (rather than 6) had detectable plasma tazarotenic acid concentrations greater than 1 ng/mL during the treatment period. We have modified the package insert for the acne indication to reflect this discovery.

At this time, all Allergan facilities utilized in the development, validation, manufacturing and quality assurance of TAZORAC® (tazarotene) Cream, 0.1% (Irvine, California; Waco, Texas;) are prepared for pre-approval inspections.

We ask that this Clinical Efficacy Supplement be filed to NDA 21-184, TAZORAC® Cream, 0.05%, 0.1%. Should you have any questions or require additional information, please call me at 714.246.4292 or Thomas Walton at 714.246.4470, Pacific Time.

Sincerely,

Trudy A. Rumbaugh, MD
Director,
Global Regulatory Affairs, Retinoids