# CENTER FOR DRUG EVALUATION AND RESEARCH

# APPROVAL PACKAGE FOR:

# APPLICATION NUMBER

# 21-184/002

# Chemistry Review(s)

# CHEMISTRY REVIEW #2 ADDENDUM

**DIVISION OF DERMATOLOGICAL AND DENTAL DRUG PRODUCTS**
**HFD-540**
Review of Chemistry, Manufacturing, and Controls

| NDA #: 21-184 | CHEM. REVIEW #: 2 | REVIEW DATE: | 26-SEPT-2002 |
|---|---|---|---|

| SUBMISSION/TYPE | DOCUMENT DATE | CDER DATE | ASSIGNED DATE |
|---|---|---|---|
| 21-184/Y-001 | 7-APR-2002 | 9-APR-2002 | 10-APR- 2002 |
| 21-184/SE1-002/BL | 25-APR-2002 | 26-APR-2002 | 6 MAY-2002 |
| Telecon | 25-SEPT-2002 | 25 SEPT-2002 | 25-SEPT 2002 |

**NAME & ADDRESS OF APPLICANT:**

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

Trudy A. Rumbaugh, MD
Director, Global Regulatory Affairs
(714) 246-4292

**DRUG PRODUCT NAME**

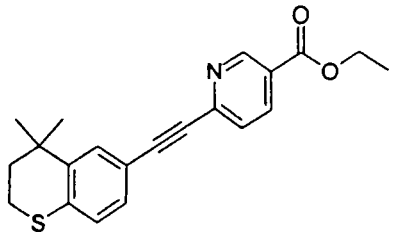
| | |
|---|---|
| Proprietary: | Avage™ Cream, 0.1% |
| Nonproprietary/USAN: | Tazarotene Cream, 0.1% |
| Code Names/#'s: | AGN 190168 |
| Chemical Type/ | 3 |
| Therapeutic Class: | S |

**PHARMACOLOGICAL CATEGORY/INDICATION:**

| | |
|---|---|
| **DOSAGE FORM:** | Cream |
| **STRENGTHS:** | 0.1% |
| **ROUTE OF ADMINISTRATION:** | Topical |
| **DISPENSED:** | _X_ Rx __ OTC |

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT:**

Ethyl 6-[(4,4-dimethylthiochroman-6-yl) ethynyl] nicotinoate




| | |
|---|---|
| Molecular Formula: | $C_{21}H_{21}NO_2S$ |
| Molecular Weight: | |
| CAS No.: | 118292-40-3 |

**SUPPORTING DOCUMENTS:**
None.

**REMARKS/COMMENTS:**

This is a follow-up to chemistry review # 1 of an efficacy supplement which provides for a new indication, [redacted] which was submitted in accordance with 21 CFR 314.70(b)(3)(g). The sponsor's initial proposal of [redacted] as a new proprietary name for their product (letter dated April 25, 2002), instead of the previously approved name, "TAZORAC", was found unacceptable. This follow-up reviews the carton and container label with the new proprietary name "AVAGE™", which was submitted by the sponsor on July 3, 2002 (21-184-SE1-002/NC dated July 3, 2002), and which was approved by the Division of Medication Errors and Technical Support on September 20, 2002 (with the proviso that the sponsor make a Phase 4 commitment to submit all medication error reports, both potential and actual, that occur with the drug Avage for a period of two years following the date of drug approval).

The final print carton and container label in the annual report (NDA 21-184/Y-001, Tazorac (tazarotene) Cream, 0.05 and 0.10%, (dated April 9, 2002) do not incorporate the changes to the established name (i.e., removal of "topical cream" from within the parentheses) which were requested in our fax of August 24, 2000. Upon request of the project manager , the sponsor submitted via facsimile a copy of the modified labeling using the new approved proprietary name, "AVAGE™", on the carton and container (see pages 3and 4 below). There were several deficiencies in the faxed submission which were relayed to the sponsor via telecon on September 25, 2002, and which are summarized below.

The prominence of the established name is not commensurate with the prominence of the proprietary name as required by 21 CFR 201.10(g)(2), which states: "The established name shall be printed in letters that are at least half as large as the letters comprising the proprietary name or designation with which it is joined, and the established name shall have a prominence commensurate with the prominence with which such proprietary name or designation appears, taking into account all pertinent factors, including typography, layout, contrast, and other printing features." Furthermore, the font of the dosage strength is not commensurate with the prominence of the established name.

The sponsor was informed that the final print carton and container label in the annual report (NDA 21-184/Y-001, Tazorac (tazarotene) Cream, 0.05 and 0.10%, (dated April 9, 2002) do not incorporate the changes to the established name (i.e., removal of "topical cream" from within the parentheses) which were requested in our fax of August 24, 2000 (See minutes of September 25, 2002 telecon). The sponsor was requested to modify the font and spacing of the established name to adhere to the requirements of 21 CFR 201.10(g)(2). The sponsor was also requested to modify the font of the dosage strength to be commensurate with the prominence of the established name, after modification of the established name to conform to the regulatory requirements as requested.

The sponsor agreed to make the requested changes.

**CONCLUSIONS & RECOMMENDATIONS:**

The supplemental application is recommended for APPROVAL under section 505(b) of the Federal Food, Drug, and Cosmetic Act, on condition that the sponsor include with the final printed insert the requested modifications as requested in the telecon of September 25, 2002.

S. A. Turujman, Ph.D.
Review Chemist

cc: Orig. NDA 21-184
HFD-540/Division File
HFD-540/DivDir/JKWilkin
HFD-540/ProjMan/KBhatt
HFD-540/Pharm/ANostrandt
HFD-540/MedOffr/HKo
HFD-540/Chem/SATurujman
HFD-540/TeamLdr/WHDeCamp

C:\DATA\MY DOCUMENTS\TURUJMAN\REVIEWS\SUPPLEMENTS\SUPPL 2002\21-184 TAZAROTENE CREAM\21-184 SE1-002 CARTON.DOC

2 pages redacted from this section of the approval package consisted of draft labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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Saleh Turujman
9/26/02 03:38:01 PM
CHEMIST

For your concurrence

Wilson H. DeCamp
9/26/02 04:01:32 PM
CHEMIST
concur with review

# CHEMISTRY REVIEW #1 ADDENDUM

**DIVISION OF DERMATOLOGICAL AND DENTAL DRUG PRODUCTS**
**HFD-540**

Review of Chemistry, Manufacturing, and Controls

| NDA #: 21-184 | CHEM. REVIEW #: 1 | REVIEW DATE: | 15-APR-2002 |
|---|---|---|---|
| **SUBMISSION/TYPE** | **DOCUMENT DATE** | **CDER DATE** | **ASSIGNED DATE** |
| 21-184/SE1-002 | 28-JUN-2001 | 29- JUN-2001 | 3-AUG- 001 |

**NAME & ADDRESS OF APPLICANT:**

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

Trudy A. Rumbaugh, MD
Director, Global Regulatory Affairs
(714) 246-4292

**DRUG PRODUCT NAME**

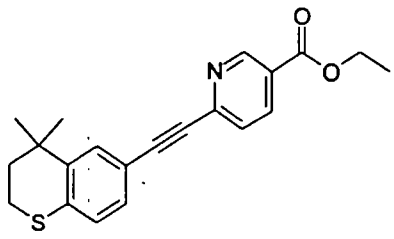
| | |
|---|---|
| Proprietary: | Tazorac Cream, 0.1% |
| Nonproprietary/USAN: | Tazarotene Cream, 0.1% |
| Code Names/#'s: | AGN 190168 |
| Chemical Type/ | 3 |
| Therapeutic Class: | S |

**PHARMACOLOGICAL CATEGORY/INDICATION:**

| | |
|---|---|
| **DOSAGE FORM:** | Cream |
| **STRENGTHS:** | 0.1% |
| **ROUTE OF ADMINISTRATION:** | Topical |
| **DISPENSED:** | _X_ **Rx** __ **OTC** |

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT:**

Ethyl 6-[(4,4-dimethylthiochroman-6-yl) ethynyl] nicotinoate




| | |
|---|---|
| Molecular Formula: | $C_{21}H_{21}NO_2S$ |
| Molecular Weight: | |
| CAS No.: | 118292-40-3 |

**SUPPORTING DOCUMENTS:**
None.

**REMARKS/COMMENTS:**

This is an efficacy supplement which provides for the [redacted] in accordance with 21 CFR 314.70(b)(3)(i). The sponsor submits a claim of categorical exclusion, stating that the exposure due to the proposed indication will be less than 1 ppb.

The sponsor proposed [redacted] " as a new proprietary name for their product, instead of the current name, "TAZORAC". The request was denied. The modified labeling will use the proprietary name "TAZORAC".

**CONCLUSIONS & RECOMMENDATIONS:**

The supplemental application is recommended for APPROVAL under section 505(b) of the Federal Food, Drug, and Cosmetic Act.

/S/

S. A. Turujman, Ph.D.
Review Chemist

cc: Orig. NDA 21-184
HFD-540/Division File
HFD-540/DivDir/JKWilkin
HFD-540/ProjMan/KBhatt
HFD-540/Pharm/ANostrandt
HFD-540/MedOffr/HKo
HFD-540/Chem/SATurujman
HFD-540/TeamLdr/WHDeCamp

C:\DATA\MY DOCUMENTS\TURUJMAN\REVIEWS\SUPPLEMENTS\SUPPL 2002\21-184 TAZAROTENE CREAM\21-184 SE1-002'.DOC

**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

/s/

Wilson H. DeCamp
4/16/02 10:08:23 AM
concur with review

**Bhatt, Kalyani**

| | |
|---|---|
| **From:** | Decamp II, Wilson H |
| **Sent:** | Friday, August 03, 2001 3:23 PM |
| **To:** | Bhatt, Kalyani; Turujman, Saleh; Jacobs, Abigail C; Bashaw, Edward D; Luke, Markham C; Walker, Susan J; Al Osh, Mohamed A; Fritsch, Kathleen; Ghosh, Tapash; Nostrandt, Amy C; Wilkin, Jonathan K; Ko, Hon Sum |
| **Cc:** | Kozma-Fornaro, Mary J |
| **Subject:** | RE: EDR - NDA 021184 S-002 from ALLERGAN drug name Tradename (TAZAROTENE)/0.1% TOPICAL CR |

On an overview of this submission, I find that:
(1) a categorical exclusion is claimed for the EA, which is based on the approved EA, and which does not require a review;
(2) there are no new package sizes or other manufacturing changes; and
(3) the carton and label are submitted for our review.

Therefore, the chemistry recommendation is that the application be filed. We will defer initiating any chemistry review until we have a response from OPDRA on the tradename issue. At that time, if appropriate, we will initiate a review of the labeling only. My estimate of review completion is 60 days after we receive the results from OPDRA, or the end of November, whichever is later.

Of course, if any discipline identifies an issue that requires chemistry review, we will promptly initiate a review including that issue.

an additional point, I find it interesting that

is a business decision, which only needs to be reported in the annual report, and over which we have no approval authority.

As a thinking point, consider how we might have handled this application if the other

Tony

-----Original Message-----
From: Bhatt, Kalyani
Sent: Friday, August 03, 2001 2:30 PM
To: Decamp II, Wilson H; Turujman, Saleh; Jacobs, Abigail C; Bashaw, Edward D; Luke, Markham C; Walker, Susan J; Al Osh, Mohamed A; Fritsch, Kathleen; Ghosh, Tapash; Nostrandt, Amy C; Wilkin, Jonathan K; Ko, Hon Sum
Cc: Kozma-Fornaro, Mary J
Subject: FW: EDR - NDA 021184 S-002 from ALLERGAN drug name Tradename(TAZAROTENE)/0.1% TOPICAL CR

ello Review Team
ice again this is a efficacy supplement with a new indication. This is an electronic submission which you can have access to below. Please look through this and see if you are having a difficulty in having access to the data. If so, send me a list things you may need which I will forward to the sponsor. Allergan has access to the security email.
Thanks,
Kalyani
-----Original Message-----
From: EDRAdmin@cder.fda.gov [mailto:EDRAdmin@cder.fda.gov]
Sent: Monday, July 02, 2001 11:35 AM
To: BHATTK@cder.fda.gov; KOH@cder.fda.gov; NOSTRANDTA@cder.fda.gov; FRITSCHK@cder.fda.gov; BOYDK@cder.fda.gov; ALLENS@cder.fda.gov; BROWNEWELLS@cder.fda.gov; NGUYENH@cder.fda.gov; KOZMAFORNARO@cder.fda.gov
Cc: levinr@cder.fda.gov; henigp@cder.fda.gov; selnekovic@cder.fda.gov; nathanj@cder.fda.gov; SCHAPIROP@cder.fda.gov
Subject: EDR - NDA 021184 from ALLERGAN drug name TAZORAC(TAZAROTENE) 0.05%/0.1% TOPICAL CR

Hi!

The EDR has received an Electronic Document on CD-ROM For division HFD-540:

NDA # N21184
Incoming Document type SE1
Incoming Document Type Sequence Number 002
Supplement Modification Type
Letter Date 6/28/01

It has item's 1, 2, 3, 4, 5, 6, 8, 11, 12

It is now available on the network. You can review this submission by entering EDR in your browser.
Thanks,
Nathan