ALLERGAN INC.
REGULATORY AFFAIRS
2525 Dupont Drive
Irvine, California 92612

FAX COVER SHEET

TO:	K. Bhatt	FROM:	T. Walton
FAX:	301 827 2091	FAX:	(714) 246-4272
TELEPHONE:	301 827 2056	TELEPHONE:	(714) 246- 4470
CC:		DATE:	9-25

Pages being sent including this cover page: 3

Message:

AVAGE

Tube + Carton 30g

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2

_____pages redacted from this section of the approval package consisted of draft labeling

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, HFD-540
Rockville, MD 20857

FACSIMILE TRANSMISSION RECORD

DATE: 9/24/02 Pages (including cover) 2

TO: Tom Walton

COMPANY:

ADDRESS:

FAX PHONE#: 714-246-4272 Our Fax # (301) 827-2075

Voice # (301) 827-2020

MESSAGE: Post Marketing Study Commitments

NOTE: We are providing the attached information via telephone facsimile for your convenience. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

FROM: /S/

TITLE: PM.

TELEPHONE: 301-827-2020

We remind you of your postmarketing study commitments:

1. "A commitment to summarize in the annual report all cases of lentigo maligna or melanoma that were exposed to topical tazarotene or are attributed to treatment with topical tazarotene."

2. The sponsor will agree 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. Potential errors include any reports of potential circumstances or events that have the capacity to cause error and should be reported in a quarterly summary. Actual errors include any preventable event that reached the patient and caused harm, reached the patient and did not cause harm, and errors that did not reach the patient, such as if the wrong drug was prepared but system checks prevented the drug from reaching the patient or being administered to the patient. All actual errors should be submitted as a 15-day report regardless of patient outcome. A name change could be requested following the receipt of two actual errors that resulted in the wrong drug being administered due to proprietary name confusion.

********** -COMM. JOURNAL- ********** DATE SEP-24-2002 ***** TIME 11:35 *********

MODE = MEMORY TRANSMISSION START=SEP-24 11:33 END=SEP-24 11:35

FILE NO.=192

STN NO.	COMM.	ONE-TOUCH/ ABBR NO.	STATION NAME/EMAIL ADDRESS/TELEPHONE NO.	PAGES	DURATION
001	OK	#	917142464272	002/002	00:00:41

-FDA/CDER/DDDDP/HFD540 -

********** -301 827 2091 - ***** - 301 827 2091- **********

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, HFD-540
Rockville, MD 20857

FACSIMILE TRANSMISSION RECORD

DATE: 9/24/02 **Pages (including cover)** 2

TO: Tom Walton

COMPANY:

ADDRESS:

FAX PHONE#: 714-246-4272 **Our Fax # (301) 827-2075**
Voice # (301) 827-2020

MESSAGE: Phase 4 Commitments

NOTE: We are providing the attached information via telephone facsimile for your convenience. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

FROM: /S/

TITLE: PM.O

TELEPHONE: 301-827-2020

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, HFD-540
Rockville, MD 20857

FACSIMILE TRANSMISSION RECORD

DATE: 9-30-02 Pages (including cover) 21

TO: Peter Kressel

COMPANY: ALLERGAN

ADDRESS:

FAX PHONE#: 714-246-4272 Our Fax # (301) 827-2075

Voice # (301) 827-2020

MESSAGE: Congratulations on your Approval letter for NDA 21-184 SCOZ.

NOTE: We are providing the attached information via telephone facsimile for your convenience. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

FROM: [signature]

TITLE: P.M.

TELEPHONE: 301-827-2020

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

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/s/

Jonathan Wilkin
9/30/02 04:27:53 PM

Division of Dermatologic and Dental Drug Products (HFD-540)
Pharmacology/Toxicology Forward Planning Meeting

NDA Number: 21-184 SE1 002 **Date:** 8/3/01
Drug Name: tazarotene cream, 0.1%
Reviewer: Amy Nostrandt
CAS Number: not provided
Drug Type: (i.e. NME, new formulation, new indication) new indication
Drug Class: retinoid
Indication:

Route of Administration: topical to the skin
Date CDER Received: 6/29/01
User Fee Date: 10-month 4/29/02
Expected Date of Draft Review: 1/2/02
Sponsor: Allergan

Fileability:

On initial overview of the NDA application: YES NO

(1) On its face, is the pharmacology/toxicology section of the NDA organized in a manner to allow substantive review to begin? _X_ ___
Comments?
The submission is entirely electronic.

(2) Is the pharm/tox section of the NDA indexed and paginated in a manner to allow substantive review to begin? __X__ ___
Comments?
The submission is entirely electronic.

(3) On its face, is the pharm/tox section of the NDA legible so that substantive review can begin? ___ _X__
Comments?
Many of the journal articles are printed with a font too small to be read on a computer monitor. However, paper copies were provided with supplement 001, so this should not be a problem.

(4) Are all required (*) and requested IND studies completed and submitted in this NDA (carcinogenicity, mutagenicity, teratogenicity*, effects on fertility*, juvenile studies, acute studies*, chronic studies*, maximum tolerated dosage determination, dermal irritancy, ocular irritancy, photocarcinogenicity, animal pharmacokinetic studies, etc)? ___ ___
Comments?
Not applicable; The current submission is an efficacy supplement for an approved drug for which all requirements have previously been met.

(5) If the formulation to be marketed is different from the formulation used in the toxicology studies, has the Sponsor made an appropriate effort to either repeat the studies using the to be marketed product or to explain why such repetition should not be required? _X_ ____
Comments?

The studies submitted are additional oral reproductive/developmental and general toxicology studies. Studies submitted to the original NDA were performed with the clinical formulation by the intended route of human exposure to bridge to existing data from oral and topical toxicology studies.

(6) Are the proposed labeling sections relative to pharm/tox appropriate (including human dose multiples expressed in either mg/m^2 or comparative serum/plasma levels) and in accordance with 201.57? _X_ ____
Comments?

It should be noted that the proposed indication —
— the exposure multiples used for comparison of animal toxicology data to human exposure are based on clinical use on the face only.

(7) Has the Sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the Sponsor? ____ ____
Comments?

Not applicable

(8) On its face, does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the Sponsor submitted a rationale to justify the alternative route? _X_ ____
Comments?

The studies submitted to this supplement are additional oral reproductive/developmental and general toxicology studies. Studies submitted to the original NDA were performed with the clinical formulation by the intended route of human exposure to bridge to existing data from oral and topical toxicology studies.

(9) Has the Sponsor submitted a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations? _X_ ____
Comments?

There is a statement that most studies were conducted in compliance with GLP's and that GLP compliance and QA statements were included with individual study reports.

(10) Has the Sponsor submitted the data from the nonclinical carcinogenicity studies, in the STUDIES electronic format, for the review by Biometrics? ___ ___
Comments?
Not applicable

(11) Has the Sponsor submitted a statement(s) that the pharm/tox studies have been performed using acceptable, state-of-the-art protocols which also reflect agency animal welfare concerns? ___ _X_
Comments?

(12) From a pharmacology perspective, is this NDA fileable? If "no", please state below why it is not. _X_ ____

(13) If the NDA is fileable, are there any issues that need to be conveyed to Sponsor? If so, specify: ___ _X_

(14) Issues that should not be conveyed to the Sponsor:
None

/S/ 8/1/01
Reviewing Pharmacology Officer

/S/ 8/2/01
Pharmacology Supervisor

Statistical Review and Evaluation
45 Day Fileability Review

NDA:	21-184/SE1-002
Name of Drug:	Tazarotene cream 0.1%
Applicant:	Allergan
Indication:	
Filing Date:	August 29, 2001
45 Day Meeting Date:	August 3, 2001
User Fee Date:	April 29, 2002
Statistical Reviewer:	Kathleen Fritsch, Ph.D., HFD-725
Clinical Reviewer:	Hon-Sum Ko, M.D., Ph.D., HFD-540

Clinical Studies: 190168-033C and 190168-034C are phase 3 randomized, double-blind, vehicle-controlled, multi-center safety and efficacy studies. 190168-025C is a phase 2 randomized, investigator-blind, vehicle-controlled dose ranging study. 190168-036C is a phase 2 randomized histological safety profile study. 190168-037C is an inter- and intra-rater reliability study of the photonumeric guidelines.

I. ORGANIZATION AND DATA PRESENTATION	YES/NO/NA
A. Is there a comprehensive table of contents with adequate indexing and pagination?	YES
B. Are the original protocols, protocol amendments, and proposed label provided?	YES
C. Are the following tables/listings provided in each study report?	
1. Patient profile listings by center, for all enrolled patients.	YES
2. Discontinued subject tables by center (includes reason and time of loss).	YES
3. Subgroup analysis summary tables (gender, age, race, etc.)	YES
4. Adverse event listings by center and time of occurrence.	YES
D. Have the data been submitted electronically?	YES
1. Has adequate documentation of the data sets been provided?	YES
2. Do the data appear to accurately represent the data described in the study reports?	YES
3. Can the data be easily merged across studies and indications?	YES

II. STATISTICAL METHODOLOGY	YES/NO/NA
A. Are all primary efficacy studies of appropriate design to meet basic approvability requirements within current Division policy, or to the extent agreed upon previously with the sponsor by the Division?	YES
B. For each study, is there a comprehensive statistical summary of the efficacy analyses which covers the intent-to-treat population, per protocol subject population, and other applicable subgroups (age, gender, race, etc.)?	No PP anal., other OK
C. Based on the summary analyses of each study,	
1. Are the analyses are appropriate for the type of data collected, the study design, and the study objectives (based on protocol objectives and proposed labeling claims?)	YES
2. Are the Intent-to-treat and per protocol patient analyses properly performed?	YES (No PP)
3. Has missing data been appropriately handled?	YES
4. Have multiplicity issues (regarding endpoints, timepoints, or dose groups) been adequately addressed?	YES (for prim endpt)
5. If interim analyses were performed, were they planned in the protocol and appropriate significance level adjustments made?	NA
D. Were sufficient and appropriate references included for novel statistical approaches?	YES
E. Are all of the pivotal studies complete?	YES
F. Has the safety data been comprehensively and adequately summarized?	YES

III. FILEABILITY CONCLUSIONS

From a statistical perspective this submission, or indications therein, is reviewable with only minor further input from the sponsor.

/S/

Kathleen Fritsch, Ph.D.
Mathematical Statistician, Biometrics III

/S/

Concur: Mohamed Alosh, Ph.D.
Team Leader, Biometrics III

cc:
Archival NDA 21-184
HFD-540/Dr. Wilken
HFD-540/Dr. Walker
HFD-540/Dr. Ko
HFD-540/Ms. Bhatt
HFD-700/Dr. Anello
HFD-725/Dr. Huque
HFD-725/Dr. Alosh
HFD-725/Dr. Fritsch

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

/s/

Kathleen Fritsch
8/3/01 01:54:53 PM
BIOMETRICS

Mohamed Alosh
8/3/01 02:46:26 PM
BIOMETRICS
Concur with Memo to file

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA **21-184** **S-002**

Drug TAZORAC (tazarotene) 0.01% Applicant **ALLERGAN**
Indication:
RPM Kalyani Bhatt Phone 301-827-2056

☒ 505(b)(1)
☐505(b)(2) Reference listed drug

☐Fast Track ☐Rolling Review Review priority: ☒ S P

Pivotal IND(s)

Application classifications:
Chem Class Retinoid
Other (e.g., orphan, OTC)

PDUFA Goal Dates:
Primary 4-29-02
Secondary 6-29-02

Arrange package in the following order:

Indicate N/A (not applicable), X (completed), or add a comment.

GENERAL INFORMATION:

- User Fee Information: ☒User Fee Paid
  User Fee Waiver (attach waiver notification letter)
  ☐ User Fee Exemption

- Action Letter..... ☐AP ☒AE ☐NA

- Labeling & Labels
  FDA revised labeling and reviews..... X
  Original proposed labeling (package insert, patient package insert) X
  Other labeling in class (most recent 3) or class labeling..... N/A
  Has DMETS reviewed the labeling? ..... ☒Yes (include review) ☐ No
  Immediate container and carton labels X
  Nomenclature review ..... N/A

- Application Integrity Policy (AIP) ☐ Applicant is on the AIP. This application ☐ is ☒ is not on the AIP.
  Exception for review (Center Director's memo)..... _____
  OC Clearance for approval..... _____

- Status of advertising (if AP action) ☐ Reviewed (for Subpart H – attach review) ☐ Materials requested in AP letter

- Post-marketing Commitments N/A
  - Agency request for Phase 4 Commitments..... N/A
  - Copy of Applicant's commitments ..... N/A

- Was Press Office notified of action (for approval action only)?..... Yes X No
  - Copy of Press Release or Talk Paper..... N/A

- Patent
  - Information [505(b)(1)] :..... X
  - Patent Certification [505(b)(2)].....
  - Copy of notification to patent holder [21 CFR 314.50 (i)(4)].....

- Exclusivity Summary X

- Debarment Statement X

- Financial Disclosure X
  - No disclosable information .....
  - Disclosable information – indicate where review is located .....

- Correspondence/Memoranda/Faxes X

- Minutes of Meetings X
  - Date of EOP2 Meeting August 20, 1999
  - Date of pre NDA Meeting February 21, 2001
  - Date of pre-AP Safety Conference N/A

- Advisory Committee Meeting ..... N/A
  - Date of Meeting .....
  - Questions considered by the committee .....
  - Minutes or 48-hour alert or pertinent section of transcript .....

- Federal Register Notices, DESI documents ..... N/A

CLINICAL INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- Summary memoranda (e.g., Office Director's memo, Division Director's memo, Group Leader's memo) ..... N/A

- Clinical review(s) and memoranda X

- Safety Update review(s) .....

- Pediatric Information
  X Waiver/partial waiver (Indicate location of rationale for waiver) ☐ Deferred
  Pediatric Page..... N/A
  ☐ Pediatric Exclusivity requested? ☐ Denied ☐ Granted ☐ Not Applicable

- Statistical review(s) and memoranda X

- Biopharmaceutical review(s) and memoranda..... X

- Abuse Liability review(s) ..... N/A
  Recommendation for scheduling .....

- Microbiology (efficacy) review(s) and memoranda ..... N/A

- DSI Audits ..... N/A
  ☒Clinical studies ☐ bioequivalence studies .....

CMC INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- CMC review(s) and memoranda X

- Statistics review(s) and memoranda regarding dissolution and/or stability ..... N/A

- DMF review(s) ..... N/A

- Environmental Assessment review/FONSI/Categorical exemption ..... N/A

- Micro (validation of sterilization) review(s) and memoranda ..... N/A

- Facilities Inspection (include EES report)
  Date completed N/A ..... ☐ Acceptable ☐ Not Acceptable

- Methods Validation ..... Completed ☐ Not Completed

PRECLINICAL PHARM/TOX INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- Pharm/Tox review(s) and memoranda X

- Memo from DSI regarding GLP inspection (if any) ..... N/A

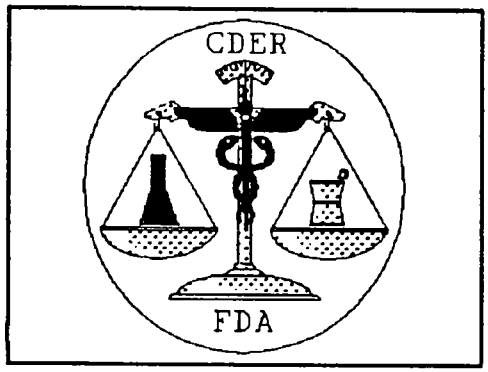
-

- Statistical review(s) of carcinogenicity studies ..... N/A

- CAC/ECAC report ..... N/A

U.S. FOOD AND DRUG ADMINISTRATION

FAX CONTROL SHEET



To: TO WHOM IT MAY CONCERN
Title:
Dept:
Company: ALLERGAN INC
FAX: 917142464272

Date: Tuesday, May 15, 2001

Our Ref:
Subject: USER FEES

Message No. 16593

From: U.S. Food and Drug Administration
FDA/CDER
5600 Fishers Lane
Rockville, MD 20857 U.S.A.
FAX:

Phone:

****
THE FOOD AND DRUG ADMINISTRATION
* USER FEE ID ASSIGNMENT SYSTEM *
****

****** SUBMISSION INFORMATION ******

APPLICATION: N021184

ORIGINAL OR SUPPLEMENT: S

RESUBMISSION?:

FAX NUMBER: 7142464272

COMPANY: ALLERGAN INC

REQUEST DATE: 15-MAY-2001

----------->> USER FEE ID#: 4148

The assigned User Fee ID number must be noted on the submission sent into the FDA for review and also noted on the submitted payment.

This FAX will be the only notification you will receive of this User Fee ID Assignment.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No 0910-0297
Expiration Date: February 29, 2004.

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

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

2 TELEPHONE NUMBER *(Include Area Code)*

(800) 347.4500

3. PRODUCT NAME

Tradename (tazarotene) Cream, 0.1%

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

N021184

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☒ YES ☐ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

4148

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE **EXCLUSIONS**? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☒ NO

(See Item 8, reverse side if answered YES)

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
T. Mamlouk, M.D.	Director, Global Regulatory Affairs, Retinoids	5/15/01

FORM FDA 3397 (3/01)

MEMORANDUM **DEPARTMENT OF HEALTH AND HUMAN SERVICES**
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: August 26, 2002

TO: Jonathan Wilkin, M.D., Director
HFD-540

FROM: Karen Lechter, J.D., Ph.D.
Social Science Analyst
Division of Surveillance, Research,
and Communication Support, HFD-410
Office of Drug Safety (ODS)

THROUGH: Anne Trontell, M.D., Director
Division of Surveillance, Research,
and Communication Support, HFD-410
Office of Drug Safety

SUBJECT: DSRCS PPI Review for Tazarotene Cream
NDA 21-184

The labeling that follows is a revised Patient Package Insert for tazarotene cream. It has been reviewed by our office and by DDMAC. We have simplified wording, made it consistent with the PI, removed promotional language and other unnecessary information, and put it in the format we are recommending for all patient information. Our proposed changes are known through research and experience to improve risk communication to a broad audience of varying educational backgrounds.

Outstanding questions or comments for the review division appear in brackets or parentheses in the text.

Please let us know if you have any questions.

{See appended electronic signature page}

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

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/s/

Karen Lechter
9/11/02 01:13:19 PM
UNKNOWN

Anne Trontell
9/12/02 02:36:10 PM
MEDICAL OFFICER

Office of Drug Safety

Memo

To: Jonathan Wilkin, MD
Director, Division of Dermatologic and Dental Drug Products
HFD-540

From: Carol Holquist, R.Ph.
Deputy Director, Division of Medication Errors and Technical Support
HFD-400

Through: Jerry Phillips, R.Ph.
Associate Director, Office of Drug Safety
HFD-400

CC: Kalyani Bhatt
Project Manager
HFD-540

Date: September 20, 2002

Re: ODS Consult: 02-0039-6; Avage (Tazarotene Cream) 0.1%; 21-184/S-002

This memorandum is in response to a September 20, 2002, request from your Division to prepare a Phase IV Commitment for the proposed proprietary name, Avage. The proposed proprietary name, Avage, was found unacceptable by DMETS in the initial name review on August 9, 2002 (ODS Consult 02-0039-4). In a telecon on September 20, 2002 between DMETS and your Division, an agreement was made to consider the proposed proprietary name, Avage, acceptable with the following Phase IV commitment incorporated into the final approval package.

Phase IV Commitment:

The sponsor will agree 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. Potential errors include any reports of potential circumstances or events that have the capacity to cause error and should be reported in a quarterly summary. Actual errors include any preventable event that reached the patient and caused harm, reached the patient and did not cause harm, and errors that did not reach the patient, such as if the wrong drug was prepared but system checks prevented the drug from reaching the patient or being administered to the patient. All actual errors should be submitted as a 15-day report regardless of patient outcome. A name change could be requested following the receipt of two actual errors that resulted in the wrong drug being administered due to proprietary name confusion.

If you have any questions or need clarification, please contact the medication errors project manager, Sammie Beam at 301-827-3242.

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

/s/

Carol Holquist
9/20/02 03:43:56 PM
PHARMACIST

Jerry Phillips
9/20/02 03:52:02 PM
DIRECTOR

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: 8/23/02	DUE DATE: 8/30/02	ODS CONSULT: 02-0039-5

TO:

Jonathan Wilkin, MD
Director, Division of Dermatologic and Dental Drug Products
HFD-540

THROUGH:

Kalyani Bhatt
Project Manager
HFD-540

PRODUCT NAME:	NDA SPONSOR:
Avage — (Tazarotene Cream) 0.1% **NDA #:** 21-184/S-002	Allergan

SAFETY EVALUATOR: Alina R. Mahmud, RPh.

SUMMARY: In response to a consult from the Division of Dermatologic and Dental Drug Products (HFD-540), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name "Avage — to determine the potential for confusion with approved proprietary and established names as well as pending names.

DMETS RECOMMENDATION:
DMETS does not object to the use of the proprietary name Avage —

/S/

Carol Holquist, RPh
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: 301-827-3242 Fax: 301-443-5161

/S/

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Rm. 15B32
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: August 26, 2002

NDA NUMBER: 21-184/S-002

NAME OF DRUG: **Avage** —
(Tazarotene Cream) 0.1%

NDA HOLDER: Allergan

I. INTRODUCTION:

This consult was written in response to a request from the Division of Dermatologic and Dental Drug Products (HFD-540), for assessment of the tradename "Avage" regarding potential name confusion with other proprietary and established drug names.

Currently, the applicant holder, Allergan, markets tazarotene cream (0.5% and 0.1%) under the proprietary name Tazorac. Tazorac is indicated for the treatment of plaque psoriasis and acne vulgaris. Allergan also wishes to market tazarotene cream 0.1% using the proprietary name Avage. Avage is indicated for

DMETS was consulted on the first proposed proprietary name on March 28, 2002 (ODS Consult 02-0039) and April 16, 2002 (ODS Consult 02-0039-1). DMETS did not recommend the use of the proposed proprietary name in either consult since was being proposed in addition to the marketed drug product Tazorac. Based on the proposed CDER draft guidance, DMETS discouraged the use of two proprietary names for the same active ingredient by the same applicant holder. However, this matter is currently being revisited and possibly reconsidered by the Agency. Therefore, DMETS conducted a Tradename Review on the proposed proprietary name on June 24, 2002 (ODS Consult 02-0039-2).

Because the Division had concerns about an implied claim, The Division requested that DMETS review the name as an alternate. From a safety perspective, DMETS did not object to the use of or However, from a promotional perspective, DDMAC did not recommend the use of the name

The sponsor proposed three additional tradenames Avage) because there is discussion between the firm and the Agency on the acceptability of the name DMETS reviewed the proposed name on August 5, 2002 (ODS Consult 02-0039-3) and found the name acceptable from a safety perspective. Similarly, from a promotional perspective, DDMAC had no objections to the use of the name However, from a promotional perspective, the Division of Dermatologic and Dental Drug Products did not recommend the use of the name Therefore, DMETS performed a review for the proposed proprietary names and "Avage" and did not recommend either name. The name "Avage" was found to have look-alike similarity to the currently marketed drug products Amerge and Amaryl. Consequently, the sponsor submitted the name

"Avage[redacted] to assist in differentiating the proposed product from the drug products Amerge and Amaryl.

PRODUCT INFORMATION

Avage[redacted] is the proposed proprietary name for tazarotene cream 0.1%. The cream is indicated for [redacted]. A pea-sized amount of cream is to be applied once a day to lightly cover the entire face. Avage[redacted] will be available in 15 gram and 30 gram tubes.

II. RISK ASSESSMENT:

The proprietary name "Avage" was not recommended by DMETS on August 9, 2002 (ODS consult 02-0039-5). Avage was found to have look-alike similarities with the currently marketed drug products Amerge and Amaryl.

In order to minimize the look-alike confusion with Amerge and Amaryl, the sponsor has proposed the modifier[redacted] to be used in conjunction with the proprietary name "Avage". The proposed modifier [redacted] has been used to convey medical terminology. For example, Procter and Gamble's Pharmacist's Handbook defines [redacted]. Dorland's Medical Dictionary defines [redacted] as [redacted] and the abbreviation [redacted] as [redacted] Although DMETS has concerns with the inadvertent misinterpretation of the modifier[redacted] as any of the above mentioned definitions, the likelihood of confusion and error as a result of this misinterpretation is minimal especially since the modifier will be scripted with the proprietary name Avage. Additionally, the use of the modifier[redacted] in conjunction with the proposed proprietary name "Avage" will decrease the potential for confusion with the currently marketed drug products Amerge and Amaryl.

III. RECOMMENDATIONS:

DMETS does not object to the use of the proprietary name Avage[redacted]

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

/S/

Alina Mahmud, RPh
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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

/s/

Alina Mahmud
8/27/02 03:54:47 PM
PHARMACIST

Carol Holquist
8/27/02 04:00:40 PM
PHARMACIST

Jerry Phillips
8/28/02 08:22:19 AM
DIRECTOR

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: 8/6/02	**DUE DATE:** 8/9/02	**ODS CONSULT:** 02-0039-4

TO:

Jonathan Wilkin, MD
Director, Division of Dermatologic and Dental Drug Products
HFD-540

THROUGH:

Kalyani Bhatt
Project Manager
HFD-540

PRODUCT NAME:	**NDA SPONSOR:**
[redacted] (Primary Name) **Avage** (Secondary Name) (Tazarotene Cream) 0.1% **NDA #:** 21-184/S-002	Allergan

SAFETY EVALUATOR: Nora Roselle, PharmD

SUMMARY: In response to a consult from the Division of Dermatologic and Dental Drug Products (HFD-540), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary names [redacted] and "Avage" to determine the potential for confusion with approved proprietary and established names as well as pending names.

DMETS RECOMMENDATION:
DMETS does not recommend the use of the proprietary names, [redacted] or Avage.

/S/ /S/

Carol Holquist, RPh
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: 301-827-3242 Fax: 301-443-5161

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Rm. 15B32
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: August 9, 2002

NDA NUMBER: 21-184/S-002

NAME OF DRUG: [redacted] (Primary Name) **or Avage** (Secondary Name)
(Tazarotene Cream) 0.1%

NDA HOLDER: Allergan

*****NOTE: This review contains proprietary and confidential information that should not be released to the public.*****

I. INTRODUCTION:

This consult was written in response to a request from the Division of Dermatologic and Dental Drug Products (HFD-540), for assessment of the tradenames [redacted] and "Avage", regarding potential name confusion with other proprietary and established drug names.

Currently, the applicant holder, Allergan, markets tazarotene cream (0.5% and 0.1%) under the proprietary name Tazorac. Tazorac is indicated for the treatment of plaque psoriasis and acne vulgaris. Allergan also wishes to market tazarotene cream 0.1% under one of the following proprietary names: [redacted] or Avage. [redacted] Avage is indicated for [redacted]

DMETS was consulted on the first proposed proprietary name, [redacted] on March 28, 2002 (ODS Consult 02-0039) and April 16, 2002 (ODS Consult 02-0039-1). DMETS did not recommend the use of the proposed proprietary name in either consult since [redacted] was being proposed in addition to the marketed drug product Tazorac. Based on the proposed CDER draft guidance, DMETS discouraged the use of two proprietary names for the same active ingredient by the same applicant holder. However, this matter is currently being revisited and possibly reconsidered by the Agency. Therefore, DMETS conducted a Tradename Review on the proposed proprietary name [redacted] on June 24, 2002 (ODS Consult 02-0039-2).

Because the Division had concerns about an implied claim, [redacted] The Division requested that DMETS review the name [redacted] as an alternate. From a safety perspective, DMETS did not object to the use of [redacted] or [redacted] However, from a promotional perspective, DDMAC did not recommend the use of the name [redacted]

The sponsor proposed three additional tradenames [redacted] and Avage) because there is discussion between the firm and the Agency on the acceptability of the name [redacted] DMETS reviewed the proposed name [redacted]" on August 5, 2002 (ODS Consult 02-0039-3) and found the name acceptable from a safety perspective. Similarly, from a promotional perspective, DDMAC had no objections to the use of the name [redacted] However, from a promotional perspective, the Division of Dermatologic and Dental Drug Products did not recommend the use of the name [redacted]

PRODUCT INFORMATION

[redacted] is the proposed proprietary name for tazarotene cream 0.1%. The cream is indicated for [redacted]. A pea-sized amount of cream is to be applied once a day to lightly cover the entire face [redacted] will be available in 15 gram and 30 gram tubes.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3] for existing drug names that sound-alike or look-alike to [redacted] Avage to a degree where potential confusion between drug names could occur under the usual clinical practice settings. The Saegis[4] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name. At this time, only the results for the [redacted] study are available. Studies were not performed on Avage, due to the short time frame for review.

A. EXPERT PANEL DISCUSSION

An Expert Panel Discussion was held by DMETS to gather professional opinions on the safety of the proprietary name [redacted] Avage. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

Several product names were identified in the Expert Panel Discussion (EPD) and through independent review that were thought to have potential for confusion with [redacted] Avage. These products are listed in Table 1 and Table 2 (see page 4), along with the dosage forms available and usual FDA-approved dosage.

DDMAC did not have concerns about the name with regard to promotional claims.

[1] MICROMEDEX Healthcare Intranet Series, 2002, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2002).
[2] Facts and Comparisons, 2002, Facts and Comparisons, St. Louis, MO.
[3] The Division of Medication Errors and Technical Support [DMETS] database of proprietary name consultation requests, New Drug Approvals 98-02, and the electronic online version of the FDA Orange Book.
[4] Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Generic name	Usual adult dose*	Other
[redacted]	Tazarotene Cream 0.1%	Apply pea-sized amount to entire face once daily	
Vivelle	Estradiol, Transdermal Patch 0.0375 mg/day, 0.05 mg/day, 0.075 mg/day , 0.1 mg/day	Apply one patch twice weekly	Look-alike
*Frequently used, not all-inclusive. ***Not marketed, not approved in the United States.			

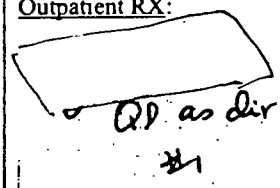
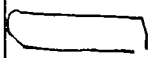
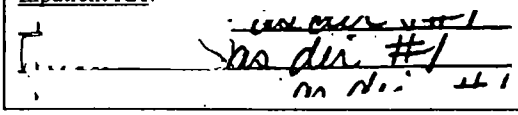
Table 2: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Generic name	Usual adult dose*	Other
Avage	Tazarotene Cream 0.1%	Apply pea-sized amount to entire face once daily	
Amerge	Naratriptan, 1 mg, 2.5 mg Tablets	1 mg to 2.5 mg at the onset of headache; dose may be repeated after 4 hours	Look-alike
Amaryl	Glimepiride, 1 mg, 2 mg, 4 mg Tablets	1 mg to 4 mg once daily	Look-alike
*Frequently used, not all-inclusive.			

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name [redacted] to determine the degree of confusion with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 106 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for [redacted] (see page 5). These prescriptions were optically scanned and delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

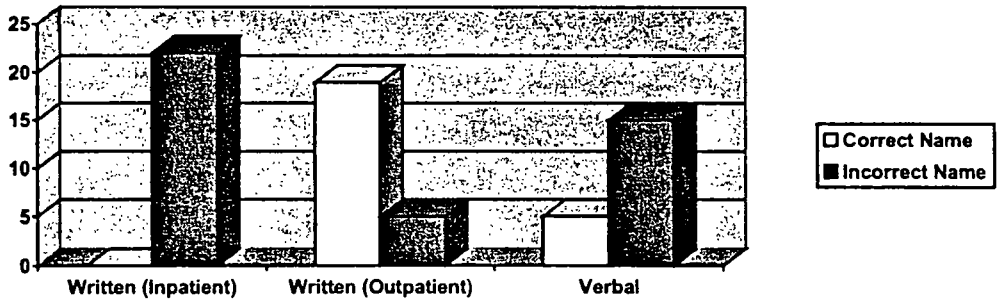
HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
Outpatient RX: 	 Apply daily as directed. Dispense one container.
Inpatient RX: 	

2. Results

The results are summarized in Table II.

Table II

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Inpatient	35	22 (63%)	0 (0%)	22 (100%)
Written Outpatient	32	24 (75%)	19 (79%)	5 (21%)
Verbal Outpatient	39	20 (51%)	5 (25%)	15 (75%)
Total	106	66 (62%)	24 (36%)	42 (64%)



Among the written outpatient prescriptions, 5 of 24 (21%) respondents interpreted the name incorrectly. Incorrect interpretations included .

When examining the interpretations from the written inpatient prescriptions, none of the respondents interpreted the name correctly. Respondents incorrectly interpreted the name to be

In addition, 15 of 20 (75%) respondents from the verbal outpatient prescriptions interpreted the name incorrectly. Incorrect interpretations included

NOTE: This review contains proprietary and confidential information that should not be released to the public.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name [redacted] the marketed product considered to have the greatest potential for name confusion with [redacted] was Vivelle. [redacted] three additional names also thought to have look-alike potential with [redacted] are currently under review in the Agency.

[redacted]

Vivelle (Estradiol Transdermal) is indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause. Vivelle is available as a transdermal patch in the following strengths: 0.0375 mg/day, 0.05 mg/day, 0.075 mg/day, and 0.1 mg/day. The recommended dosage of Vivelle is the application of one patch to the skin twice weekly. Vivelle is contraindicated in patients with known or suspected pregnancy; porphyria; abnormal genital bleeding of unknown etiology; known or suspected carcinoma of the breast; estrogen-dependent tumors; and history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with estrogen use. Vivelle and [redacted] have similar look-alike characteristics.

[redacted]

Vivelle and [redacted] have overlapping numerical strengths (0.1 mg vs. 0.1%). Prescriptions are often written with non-specific directions for use such as "use as directed" or take as directed". The more generalized a prescription is, the less information there is to help pharmacists differentiate one drug from another.

One possible scenario involving misinterpretation and possible misadministration of [redacted] for Vivelle is if a prescription is written for [redacted] 0.1, use as directed, #1":

[redacted] 0.1
use as dir
#1

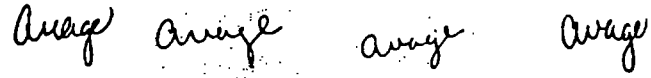
In this example [redacted] may be misinterpreted as Vivelle, the numerical strength 0.1 can be interpreted as 0.1% or 0.1 mg, and #1 could be interpreted as 1 box of patches or 1 tube of cream. Therefore, a prescription written for [redacted] 0.1, use as directed, #1" may be incorrectly filled as "Vivelle 0.1, use as directed, #1".

If a prescription for [redacted] is misinterpreted, dispensed, and administered as Vivelle in a patient with porphyria; abnormal genital bleeding of unknown etiology; breast cancer; estrogen-dependent tumors; or a history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with estrogen use, severe medical consequences may occur because Vivelle is contraindicated in these patient groups.

AVAGE

The marketed products considered having the greatest potential for name confusion with Avage were Amerge and Amaryl.

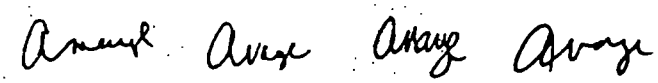
Amerge (Naratriptan) is a serotonin agonist used in the treatment of acute migraine headache with or without aura. Amerge is available as 1 mg and 2.5 mg oral tablets in blister packs of 9 tablets per box. The usual dose of Amerge is 1 mg to 2.5 mg at the onset of a migraine. If the headache returns or does not fully resolve, the dose may be repeated after four hours to a maximum of 5 mg in 24 hours. Amerge is contraindicated in patients with cerebrovascular or peripheral vascular disease, ischemic heart disease, uncontrolled hypertension, or in patients who have received either another serotonin agonist or ergotamine-containing product within 24 hours. Patients should be advised that blood pressure increases may result with the administration of Amerge. Amerge has look-alike characteristics to Avage in that each name contains similar upstroke and downstroke letter combinations.



In addition to look-alike similarities, Amerge and Avage share other characteristics. Both medications share similar numerical strengths (1 mg and 0.1%). Similarly, both Amerge and Avage may be prescribed with the directions "take as directed" and the quantity "#1". In this example, #1 can be interpreted as 1 box of tablets (i.e., Amerge is available in quantities of nine tablets per box) or 1 tube of cream. If a patient with heart disease was inadvertently given Amerge instead of Avage, increases in blood pressure and serious adverse reactions may occur (EKG changes, coronary artery vasospasms, premature ventricular contractions, palpitations, etc.).

We note that differences do exist between the two drug products, however DMETS believes that in addition to the mentioned similarities the two names look significantly alike when scripted increasing the risk for confusion and error.

Amaryl (Glimepiride) is an antidiabetic agent used in the management of noninsulin-dependent diabetes mellitus (type II) as an adjunct to diet and exercise to lower blood glucose and may also be used in combination with insulin. Amaryl is available as 1 mg, 2 mg, and 4 mg oral tablets. The usual dose of Amaryl in the treatment of type II diabetes mellitus is 1 mg to 4 mg once daily. Amaryl has look-alike characteristics to Avage in that each name contains similar upstroke and downstroke letter combinations.



In addition to look-alike similarities, Amaryl and Avage share many other characteristics. Both medications share similar numerical strengths (1 mg and 0.1%) and dosing schedules ("qd" = once daily). Also, both Amaryl and Avage may be prescribed with the quantity "#30" (#30 can be interpreted as 30 tablets or a 30 gram tube of cream). The similar strength, dosing directions, and quantity may increase the potential for confusion and error in the dispensing process.

The inadvertent administration of Avage instead of Amaryl (glimepiride) in a newly diagnosed diabetes patient picking up a new prescription for Amaryl may perpetuate elevated glucose levels due to the lack of the antidiabetic medication. In this situation a patient may experience hyperglycemia associated with extreme thirst, excessive hunger, frequent urination, fatigue, nausea, vomiting, and abdominal pain. Likewise, the inadvertent administration of Amaryl instead of Avage may increase the risk of hypoglycemia. Symptoms associated with hypoglycemia include tachycardia, palpitations, shakiness, sweating, inability to concentrate, dizziness, hunger, blurred vision, and even impairment of motor function, seizure, or coma.

Generally, one would assume that confusion would be unlikely between drug products that differ in dosage form. However, post-marketing experience has demonstrated that errors do occur between drugs that share few commonalties other than a similar name.

POST-MARKETING EXPERIENCE

We searched the FDA Adverse Event Reporting System (AERS) database for all post-marketing safety reports of medication errors between solid oral dosage forms and topical products. The Drug Quality Reporting System (DQRS) database was also searched for similar reports. One actual error report involving an oral tablet (Desogen) and topical cream (DesOwen) was identified through the DQRS database search.

A report was submitted involving a prescription from a physician that was written for "Desogen, use as directed #1" with 5 refills. The order was actually filled for DesOwen topical cream. The error was discovered when the patient picked up the prescription and knew that she was not supposed to get a cream. The reporter stated that "because of poor handwriting and the 'use as directed' statement the prescription was interpreted as DesOwen". (DQRS Report U050016)

In this case the patient knew that she was not prescribed a cream and the error was corrected, but this may not always occur. Often times pharmacists are given incomplete or generalized information and when there is a lack of information about the drug or patient, there is the opportunity for confusion and error. The above mentioned report just reinforces that the

potential for error between names goes beyond the context for use (indication, strengths, dosage forms, etc.) when the names are very similar.

While we believe that many scenarios will result in the verification of a prescription order with the prescriber or pharmacist, we question whether it is appropriate to introduce a proprietary drug name that may potentially generate confusion in an area already burdened by confusion, error and patient safety concerns.

III. COMMENTS TO THE SPONSOR

DMETS does not recommend the use of the proposed proprietary names, [redacted] and Avage.

In reviewing the proprietary name [redacted] the marketed product considered to have the greatest potential for name confusion with [redacted] was Vivelle.

[redacted]

Vivelle (Estradiol Transdermal) is indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause. Vivelle is available as a transdermal patch in the following strengths: 0.0375 mg/day, 0.05 mg/day, 0.075 mg/day, and 0.1 mg/day. The recommended dosage of Vivelle is the application of one patch to the skin twice weekly. Vivelle is contraindicated in patients with known or suspected pregnancy; porphyria; abnormal genital bleeding of unknown etiology; known or suspected carcinoma of the breast; estrogen-dependent tumors; and history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with estrogen use. Vivelle and [redacted] have similar look-alike characteristics.

Vivelle [redacted] [redacted]

Vivelle and [redacted] have overlapping numerical strengths (0.1 mg vs. 0.1%). Prescriptions are often written with non-specific directions for use such as "use as directed" or take as directed". The more generalized a prescription is, the less information there is to help pharmacists differentiate one drug from another.

One possible scenario involving misinterpretation and possible misadministration of [redacted] for Vivelle is if a prescription is written for [redacted] 0.1, use as directed, #1":

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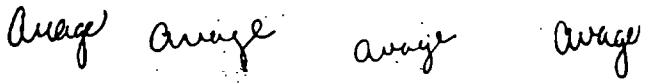

In addition to look-alike similarities, Amerge and Avage share other characteristics. Both medications share similar numerical strengths (1 mg and 0.1%). Similarly, both Amerge and Avage may be prescribed with the directions "take as directed" and the quantity "#1". In this example, #1 can be interpreted as 1 box of tablets (i.e., Amerge is available in quantities of nine tablets per box) or 1 tube of cream. If a patient with heart disease was inadvertently given Amerge instead of Avage, increases in blood pressure and serious adverse reactions may occur (EKG changes, coronary artery vasospasms, premature ventricular contractions, palpitations, etc.).

We note that differences do exist between the two drug products, however DMETS believes that in addition to the mentioned similarities the two names look significantly alike when scripted increasing the risk for confusion and error.

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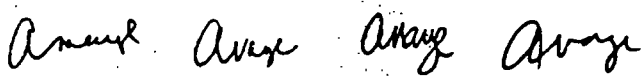

In addition to look-alike similarities, Amaryl and Avage share many other characteristics. Both medications share similar numerical strengths (1 mg and 0.1%) and dosing schedules ("qd" = once daily). Also, both Amaryl and Avage may be prescribed with the quantity "#30" (#30 can be interpreted as 30 tablets or a 30 gram tube of cream). The similar strength, dosing directions, and quantity may increase the potential for confusion and error in the dispensing process.

The inadvertent administration of Avage instead of Amaryl (glimepiride) in a newly diagnosed diabetes patient picking up a new prescription for Amaryl may perpetuate elevated glucose levels due to the lack of the antidiabetic medication. In this situation a patient may experience hyperglycemia associated with extreme thirst, excessive hunger, frequent urination, fatigue, nausea, vomiting, and abdominal pain. Likewise, the inadvertent administration of Amaryl instead of Avage may increase the risk of hypoglycemia. Symptoms associated with hypoglycemia include tachycardia, palpitations, shakiness, sweating, inability to concentrate, dizziness, hunger, blurred vision, and even impairment of motor function, seizure, or coma.

Generally, one would assume that confusion would be unlikely between drug products that differ in dosage form. However, post-marketing experience has demonstrated that errors do occur between drugs that share few commonalties other than a similar name.

POST-MARKETING EXPERIENCE

We searched the FDA Adverse Event Reporting System (AERS) database for all post-marketing safety reports of medication errors between solid oral dosage forms and topical products. The Drug Quality Reporting System (DQRS) database was also searched for similar reports. One actual error report involving an oral tablet (Desogen) and topical cream (DesOwen) was identified through the DQRS database search.

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In this case the patient knew that she was not prescribed a cream and the error was corrected, but this may not always occur. Often times pharmacists are given incomplete or generalized information and when there is a lack of information about the drug or patient, there is the opportunity for confusion and error. The above mentioned report just reinforces that the potential for error between names goes beyond the context for use (indication, strengths, dosage forms, etc.) when the names are very similar.

While we believe that many scenarios will result in the verification of a prescription order with the prescriber or pharmacist, we question whether it is appropriate to introduce a proprietary drug name that may potentially generate confusion in an area already burdened by confusion, error and patient safety concerns.

LABELING, PACKAGING AND SAFETY RELATED ISSUES:

No comments at this time.

IV. RECOMMENDATIONS:

DMETS does not recommend the use of the proprietary names, [redacted] and Avage.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

/S/

Nora Roselle, PharmD
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

/S/

Alina Mahmud, RPh
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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

/s/

Nora L. Roselle
8/9/02 01:17:36 PM
CSO

Alina Mahmud
8/9/02 01:41:36 PM
PHARMACIST

Carol Holquist
8/9/02 02:07:08 PM
PHARMACIST

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: 7/5/02	**DUE DATE:** 8/9/02	**ODS CONSULT:** 02-0039-3

TO:

Jonathan Wilkin, MD
Division of Dermatologic and Dental Drug Products
HFD-540

THROUGH:

Kalyani Bhatt
Project Manager
HFD-540

PRODUCT NAME: [redacted] (Tazarotene Cream) 0.1% **NDA #:** 21-184/S-002	**NDA SPONSOR:** Allergan

SAFETY EVALUATOR: Nora Roselle, PharmD

SUMMARY: In response to a consult from the Division of Dermatologic and Dental Drug Products (HFD-540), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name [redacted] to determine the potential for confusion with approved proprietary and established names as well as pending names.

DMETS RECOMMENDATION:
DMETS has no objections to the use of the proprietary name [redacted]. This name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.

/S/

Carol Holquist, RPh
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: 301-827-3242 Fax: 301-443-5161

/S/

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Rm. 15B32
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: August 5, 2002

NDA NUMBER: 21-184/S-002

NAME OF DRUG: [redacted]
(Tazarotene Cream) 0.1%

NDA HOLDER: Allergan

*****NOTE: This review contains proprietary and confidential information that should not be released to the public.*****

I. INTRODUCTION:

This consult was written in response to a request from the Division of Dermatologic and Dental Drug Products (HFD-540), for assessment of the tradename [redacted] regarding potential name confusion with other proprietary and established drug names.

Currently, the applicant holder, Allergan, markets tazarotene cream (0.5% and 0.1%) under the proprietary name Tazorac. Tazorac is indicated for the treatment of plaque psoriasis and acne vulgaris. Allergan also wishes to market tazarotene cream 0.1% under one of the following proprietary names: [redacted] or Avage. [redacted] Avage is indicated.

DMETS was consulted on the first proposed proprietary name, [redacted] on March 28, 2002 (ODS Consult 02-0039) and April 16, 2002 (ODS Consult 02-0039-1). DMETS did not recommend the use of the proposed proprietary name in either consult since [redacted] was being proposed in addition to the marketed drug product Tazorac. Based on the proposed CDER draft guidance, DMETS discouraged the use of two proprietary names for the same active ingredient by the same applicant holder. However, this matter is currently being revisited and possibly reconsidered by the Agency. Therefore, DMETS conducted a Tradename Review on the proposed proprietary name [redacted] on June 24, 2002 (ODS Consult 02-0039-2).

Because the Division had concerns about an implied claim, [redacted] The Division requested that DMETS review the name [redacted] as an alternate. From a safety perspective, DMETS did not object to the use of [redacted] or [redacted] However, from a promotional perspective, DDMAC did not recommend the use of the name [redacted]

Now, the sponsor is proposing three additional tradenames because there is discussion between the firm and the Agency on the acceptability of the name [redacted]

PRODUCT INFORMATION

[redacted] is the proposed proprietary name for tazarotene cream 0.1%. The cream is indicated for [redacted] A pea-sized amount of cream is to be applied once a day to lightly cover the entire face [redacted] will be available in 15 gram and 30 gram tubes.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3] for existing drug names that sound-alike or look-alike to [redacted] to a degree where potential confusion between drug names could occur under the usual clinical practice settings. The Saegis[4] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel Discussion was held by DMETS to gather professional opinions on the safety of the proprietary name [redacted] Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

Several product names were identified in the Expert Panel Discussion (EPD) and through independent review that were thought to have potential for confusion with [redacted] These products are listed in Table 1 (see page 4), along with the dosage forms available and usual FDA-approved dosage.

DDMAC did not have concerns about the name with regard to promotional claims.

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[1] MICROMEDEX Healthcare Intranet Series, 2002, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2002).

[2] Facts and Comparisons, 2002, Facts and Comparisons, St. Louis, MO.

[3] The Division of Medication Errors and Technical Support [DMETS] database of proprietary name consultation requests, New Drug Approvals 98-02, and the electronic online version of the FDA Orange Book.

[4] Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Generic name	Usual adult dose*	Other
[redacted]	Tazarotene Cream 0.1%	Apply pea-sized amount to entire face once daily	
Amaryl	Glimepiride, 1 mg, 2 mg, 4 mg Tablets	1 mg – 4 mg once daily	Look-alike
Uvadex	Methoxsalen, 20 mcg/mL Solution (10 mL vials)	0.6 mg/kg by mouth given 2 hours prior to UVA exposure	Look-alike

*Frequently used, not all-inclusive.
***Not marketed, not approved in the United States.

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of [redacted] with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug names. These studies employed a total of 106 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for [redacted] (see page 5). These prescriptions were optically scanned and delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

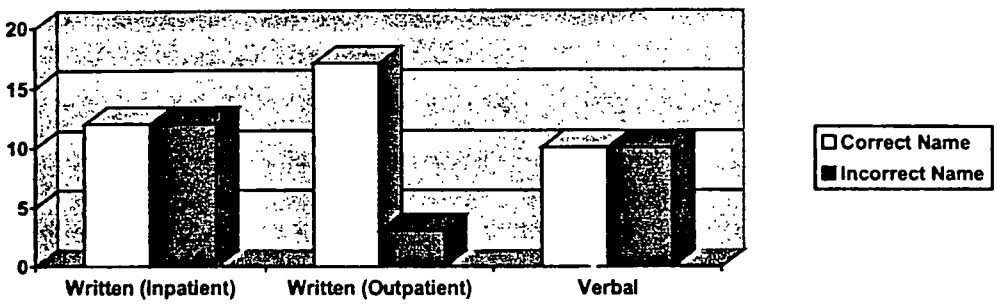
HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
Outpatient RX: [redacted] Sig: Apply qd-bid dr. # 1	[redacted] Apply daily as directed. Dispense one container.
Inpatient RX: [redacted] apply daily as directed.	

2. Results - [redacted]

The results are summarized in Table I.

Table I

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Inpatient	39	24 (62%)	12 (50%)	12 (50%)
Written Outpatient	35	20 (57%)	17 (85%)	3 (15%)
Verbal Outpatient	32	20 (63%)	10 (50%)	10 (50%)
Total	106	64 (60%)	39 (61%)	25 (39%)



Among the written outpatient prescriptions, 3 of 20 (15%) respondents interpreted the name incorrectly. Incorrect interpretations included

When examining the interpretations from the written inpatient prescriptions, 12 of 24 (50%) respondents interpreted the name incorrectly. Respondents incorrectly interpreted the name to be and

In addition, 10 of 20 (50%) respondents from the verbal outpatient prescriptions interpreted the name incorrectly. Many of the incorrect name interpretations were misspelled/phonetic variations of Incorrect interpretations included

*****NOTE: This review contains proprietary and confidential information that should not be released to the public.**

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name the primary concerns raised were related to sound-alike, look-alike names that already exist in the U.S. marketplace. The products considered having the greatest potential for name confusion with were Amaryl and Uvadex. Another name thought to have slight sound-alike similarity with is

Amaryl (Glimepiride) is an antidiabetic agent used in the management of noninsulin-dependent diabetes mellitus (type II) as an adjunct to diet and exercise to lower blood glucose and may also be used in combination with insulin. Amaryl is available as 1 mg, 2 mg, and 4 mg oral tablets. The usual dose of Amaryl in the treatment of type II diabetes mellitus is 1 mg to 4 mg once daily. Amaryl has similar look-alike characteristics to that each name contains similar upstroke and downstroke letter combinations.

In addition to look-alike similarities, Amaryl and share similar numerical strengths (0.1% and 1 mg) and dosing schedules (once daily). However, Amaryl and have different routes of administration (topical vs. oral), indications for use, and directions for use. DMETS believes that the differences in route of administration, indication for use, and directions for use help decrease the potential for confusion and error between these two drug names.

Uvadex (Methoxsalen) is prescription drug used in the treatment of psoriasis and skin symptoms associated with cutaneous T-cell lymphoma (extracorporeal administration). Uvadex is available

as a 20 mcg/mL (10 mL vial) oral solution. The usual dosage of Uvadex is 0.6 mg/kg by mouth given two hours prior to UVA exposure. Uvadex and [redacted] have look-alike similarities to one another in that the names contain the [redacted] However, Uvadex and [redacted] have different strengths that do not overlap (0.1% vs. 20 mcg/mL). In addition, Uvadex is available as an oral solution while [redacted] will be available in a cream formulation. Likewise, Uvadex is used with ultraviolet light (UVA) for the treatment of psoriasis and would be administered orally before a scheduled medical procedure in a doctor's office or inpatient setting. [redacted] is a topical cream that would most likely be prescribed in a physician's office and filled in an outpatient pharmacy for use on an outpatient basis. DMETS believes the potential for confusion between these two drug names is minimal.

[redacted]

and [redacted] have similar sound-alike characteristics, but do not share overlapping strengths, routes of administration, indications for use, or dosage formulations. Thus, DMETS believes the risk for error is minimal between these two proposed names.

IV. LABELING, PACKAGING AND SAFETY RELATED ISSUES:

No comments at this time.

IV. RECOMMENDATIONS:

A. DMETS has no objections to the use of the proprietary name [redacted]

B. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from this date forward.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

/S/

Nora Roselle, PharmD
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

/S/

Alina Mahmud, RPh
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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

/s/

Nora L. Roselle
8/5/02 01:50:45 PM
CSO

Alina Mahmud
8/5/02 01:59:54 PM
PHARMACIST

Carol Holquist
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8/6/02 12:16:38 PM
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CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: 5/30/02	DUE DATE: 07/05/02	ODS CONSULT #: 02-0039-2

TO:

Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
HFD-540

THROUGH:

Kalyani Bhatt
Project Manager
HFD-540

PRODUCT NAME:	**NDA SPONSOR:** Allergan
(Tazarotene Cream) 0.1% **NDA #:** 21-184/S-002	

SAFETY EVALUATOR: Alina R. Mahmud, RPh.

SUMMARY: In response to a consult from the Division of Dermatologic and Dental Drug Products (HFD-540), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name to determine the potential for confusion with approved proprietary and established names as well as pending names. The Division was also concerned that was promotional. Therefore, the Division requested DMETS review the proprietary name as an alternate.

DMETS RECOMMENDATION:

From a safety perspective, DMETS has no objections to the use of the proprietary name if it is approved before the proposed propietary name However, from a promotional perspective, DDMAC does not recommend the use of the name Because of the promotional concerns raised by DDMAC and the Division, DMETS has evaluated the alternate name as well. DMETS has no objection to the use of the name in lieu of the proposed name

*****NOTE: This review contains proprietary and confidential information that should not be released to the public.**

/S/

Carol Holquist, R.Ph.
Deputy Director,
Division of Medication Errors and Technical Support
Office of Drug Safety
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/S/

Jerry Phillips, R.Ph.
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Rm. 15B32
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: June 24, 2002

NDA NUMBER: 21-184/S0-002

NAME OF DRUG: (Tazarotene Cream) 0.1%

NDA HOLDER: Allergan

***** NOTE: This review contains proprietary and confidential information that should not be released to the public.**

I. INTRODUCTION:

This consult was written in response to a request from the Division of Dermatologic and Dental Drug Products (HFD-540) for assessment of the tradename , regarding potential name confusion with other proprietary/established drug names. The Division has concerns about an implied claim, Because of these concerns, the Division would like DMETS to review the name as an alternate. The Division provided the example since the modifier is being used to specify an indication separate from the indications of use for The draft container labels, carton and insert labeling for were provided for review and comment as well.

Currently, the applicant holder, Allergan, markets the tazarotene cream 0.5% and 0.1% under the proprietary name Tazorac. Tazorac is indicated for the treatment of plaque psoriasis and acne vulgaris. Allergan wishes to also market tazarotene cream 0.1% under the proprietary name is

DMETS was consulted on the proposed proprietary name on April 16, 2002 (ODS Consult 02-0039-1) and March 28, 2002 (ODS Consult 02-0039). DMETS did not recommend the use of the proposed proprietary name in either consults since is being proposed in addition to the marketed drug product Tazorac. Based on the proposed CDER draft guidance, DMETS discouraged the use of two proprietary names for the same active ingredient by the same applicant holder. However, this matter is currently being revisited and possibly reconsidered by the Agency. Therefore, the proposed proprietary name must undergo a Tradename Review for potential sound-alike and/or look-alike drug names.

PRODUCT INFORMATION

[redacted] is the proposed proprietary name for tazarotene cream 0.1%. [redacted] is indicated for [redacted] A pea-sized amount of cream is to be applied once a day to lightly cover the entire face [redacted] will be available in 15 gm, 30 gm and 60 gm tubes.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3] for existing drug names which sound alike or look alike to [redacted] to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the data provided by Thomson & Thomson's SAEGIS™ Online Service[4] was also conducted. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies of each proposed proprietary name consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name [redacted] Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. Five product names were identified in the Expert Panel Discussion (EPD) that were thought to have potential for confusion with [redacted] These products are listed in Table 1 (page 4) along with the dosage forms available and usual FDA-approved dosage.

2. DDMAC objects to the use of the proposed proprietary name [redacted] from a promotional perpective because [redacted]

[1] MICROMEDEX Healthcare Intranet Series, 2001, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2001).

[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

[3] The Established Evaluation System [EES], the Division of Medication Errors and Technical Support proprietary name consultation requests, New Drug Approvals 98-00, and the electronic online version of the FDA Orange Book.

[4] WWW location http://www.thomson-thomson.com.

Table 1

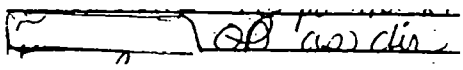
Product Name	Dosage form(s), Generic name	Usual adult dose*	Other**
[redacted]	Tazarotene Cream 0.1%	Apply pea-sized amount to entire face once daily	
[redacted]			
Preven	Levonorgesterol/Ethinyl Estradiol Tablets 0.25 mg/0.05 mg (Rx)	0.5 to 1 mL per minute given IV	**S/A
Prevpac	Lansoprazole 30 mg, Amoxicillin 500 mg and Clarithromycin 500 mg combination (Rx)	30 mg Lansoprazole, 1 gm Amoxicillin, 500 mg Clarithromycin twice daily	**LA
Provigil	Modafinil 100 mg and 200 mg (Rx- CIV)	One application of solution with one dose of illumination per treatment site per 8-week treatment session	**SA/LA
Precose	Acarbose 50 mg and 100 mg (Rx)	Dose must be individualized three times daily	**SA/LA

*Frequently used, not all-inclusive.
**SA (sound-alike), LA (look-alike)
*** NOTE: This review contains proprietary and confidential information that should not be released to the public.

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

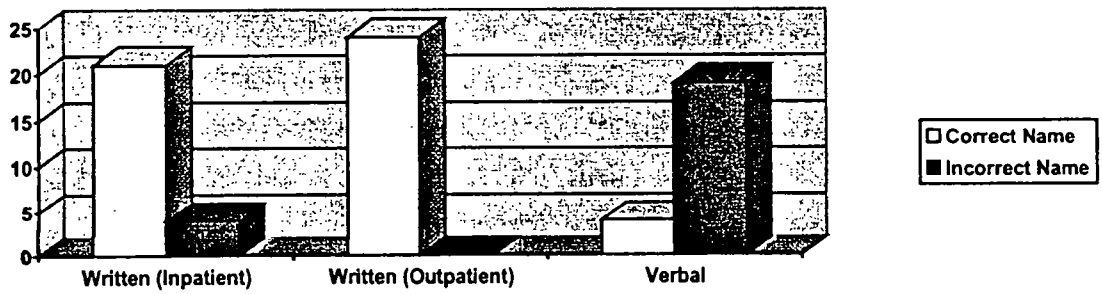
Three studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of [redacted] with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the name. These studies employed 108 health care professionals comprised of pharmacists, physicians, and nurses. This exercise was conducted in an attempt to simulate the prescription ordering process. DMETS staff members wrote an inpatient order and outpatient prescriptions, each consisting of a combination of marketed and unapproved drug products and a prescription for [redacted] (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, one DMETS staff member recorded a verbal outpatient prescription that was then delivered to a random sample of the participating health care professionals via telephone voicemail. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
Outpatient Rx: 	Use once daily as directed
Inpatient Rx: 	

2. Results:

Results of the exercises are summarized below:

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Inpatient	36	25 (69%)	21 (84%)	4 (16%)
Written Outpatient	32	24 (75%)	24 (100%)	0 (0%)
Verbal: Outpatient	39	23 (59%)	4 (17%)	19 (83%)
Total	107	72 (67%)	49 (68%)	23 (12%)



Among the written inpatient prescriptions, 4 of 25 (16%) respondents interpreted incorrectly. Incorrect interpretations included , and

Among the written outpatient prescriptions, all (100%) respondents interpreted correctly.

Among the verbal outpatient prescriptions, 19 of 23 (83%) respondents interpreted incorrectly. Interpretations included , and

3. AERS Search

Since the Division would like DMETS to comment on the use of modifier [redacted] in conjunction with the approved proprietary name [redacted] DMETS searched the FDA Adverse Event Reporting System (AERS) database in order to determine any post-marketing safety reports of medication errors associated with [redacted] The Meddra Preferred Term (PT), "Medication Error", and the drug name, [redacted] were used to perform the search. No reports of confusion were identified between [redacted] However, [redacted] has only been on the market since April 2002, which may account for the lack of reports in the AERS database.

C. SAFETY EVALUATOR RISK ASSESSMENT

1. Look-alike and sound-alike names to [redacted]

In reviewing the proprietary name [redacted] the primary concerns raised were related to sound-alike, look-alike names that already exist in the U.S. marketplace. Although the Expert Panel identified five drug products, the products considered having the greatest potential for confusion include *Provigil* and [redacted]

Provigil is the proposed proprietary name for modafinil and is indicated to improve wakefulness in patients with excessive daytime sleepiness associated with narcolepsy. Provigil is available as 100 mg and 200 mg tablets and is dosed as 200 mg once daily in the morning. Provigil and [redacted] look and sound somewhat similar depending on how the name is pronounced. The names share identical consonants other than the letter [redacted] at the [redacted] of Provigil. Although the vowels differ, when written, the vowels sound similar when pronounced. In addition, Provigil and [redacted] share an overlapping once daily dosing interval. However, Provigil and [redacted] differ with regard to other aspects. For example, Provigil and [redacted] differ in strength (100 mg and 200 mg vs. 0.1%) and dosage form (tablets vs. cream). Therefore, given the differences in strength and dosage form with a lack of convincing look-alike and sound-alike potential, there is insufficient evidence at this time to conclude that [redacted] would cause confusion with Provigil.

[redacted]

2. Tazorac

The Division would like DMETS to comment on the use of the modifier in conjunction with the proprietary name "Tazorac" since the proposed indication A search in the AERS database did not identify any reports of confusion between and that no errors were reported between . DMETS does not have any objections to the use of the name in lieu of the proposed proprietary name

III. LABELING, PACKAGING AND SAFETY RELATED ISSUES:

No comments at this time.

IV. RECOMMENDATIONS:

From a safety perspective, DMETS has no objections to the use of the proprietary name if it is approved before the proposed proprietary name However, from a promotional perspective, DDMAC and the Division object to the use of the name Because of the promotional concerns raised by DDMAC and the Division, DMETS has evaluated the alternate name as well. DMETS has no objection to the use of the name in lieu of the proposed name .

***NOTE: This review contains proprietary and confidential information that should not be released to the public.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, Project Manager, at 301-827-3242.

/S/

Alina R. Mahmud, RPh.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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

/s/

Alina Mahmud
7/3/02 07:29:45 AM
PHARMACIST

Carol Holquist
7/3/02 12:59:45 PM
PHARMACIST

Jerry Phillips
7/3/02 02:35:35 PM
DIRECTOR

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secret and/or

confidential

commercial

information

OFFICE OF DRUG SAFETY

Memo

To: Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
HFD-540

From: Carol Holquist, R.Ph.
Deputy Director, Division of Medication Errors and Technical Support (DMETS)
HFD-400

Through: Jerry Phillips, R.Ph.
Associate Director, Office of Drug Safety
HFD-400

CC: Kalyani Bhatt
Project Manager, HFD-540

Date: March 28, 2002

Re: ODS Consult 02-0039; Tazarotene Cream 0.1%; NDA 21-184/S-002

This memorandum is in response to a March 13, 2002, expedited request from your Division for a review of the proposed proprietary name [redacted]. The sponsor, Allergan, has submitted this supplement for a second trademark to the drug TAZORAC®. The sponsor intends to market the product under the tradename [redacted] providing for a new indication of use namely, [redacted]

I. Introduction

The proprietary name TAZORAC® was approved on June 13, 1997 under NDA 20-600 for Tazarotene Gel (0.05% and 0.1%) followed by the approval of NDA 21-184 on September 20, 2000, for a cream formulation (0.05% and 0.1%). Both the gel and cream formulations are indicated for the topical treatment of patients with stable plaque psoriasis of up to 20% body surface area involvement. TAZORAC® (tazarotene topical gel) 0.1% is also indicated for the topical treatment of patients with facial acne vulgaris of mild to moderate severity.

According to a letter addressed to the Division of Dermatologic and Dental Drug Products on February 19, 2002, the sponsor proposes the alternate proprietary name [redacted] for the following reasons:

A. Patient Safety

"...Allergan believes that there are some causes for concern should the medical claims on the labeling for Tazorac. Allergan's main concern is that patients may overuse or share their medication inappropriately. For instance, patients who might be undergoing treatment with tazorotene gel or cream for the treatment of psoriasis or acne, may consider treating but not necessarily under the guidance of a physician.... The situation whereby claims share the same label on a product is an invitation to potential problems of misuse or overuse."

B. Reimbursement

"...Currently, tazarotene creams and gels are, for the most part, reimbursed under the trade name of Tazorac for the treatments of acne vulgaris and plaque psoriasis, as is customary for those disease-state conditions. requiring medical intervention and therefore, is not likely to be reimbursed by a third-party payer. It is also likely that many, if not most or all formularies might remove Tazorac from its reimbursable status should a condition be approved under the same trade name..."

C. Precedents

"Although most products that have a different tradename while containing the same dose or concentration of active drug substance have a slightly different vehicle (minor change in one or more of the excipients), there are several examples where identical products have been marketed under different brand names. Photoplex® Broad Spectrum Sunscreen Lotion...was also marketed as Filteray® Sunscreen. Erygel®...was also marketed as A/T/S® (erythromycin 2% Gel...."

II. Risk Assessment:

We disagree with the sponsor's proposal to market tazarotene cream under two proprietary names. The sponsor has cited three reasons for which they believe the proposal is acceptable: patient safety, third party reimbursement, and Agency precedent.

A. Patient Safety

We disagree with the sponsor's notion that "the situation whereby claims share the same label on a product is an invitation to potential problems of misuse or overuse". DMETS believes having all indications of use and safety information in one label would be less confusing to health care providers and consumers and be more informative by listing all uses and adverse events. One proprietary name with concise labeling decreases the likelihood of having the same drug product prescribed by different physicians or incorrect dosing regimens utilized for each indication of use. Moreover, practitioners and consumers may be misled to believe the drug product intended for a benign treatment such as is not associated with the same adverse events as the other indications for use. Common labeling will provide all information on the adverse events and risks associated with the active moiety. There are numerous examples of NDA applications that are safely managed and labeled with expanded/different indications for use and dosages.

B. Reimbursement

The sponsor has identified the potential failure of third-party reimbursement for a claim under the existing proprietary name as a reason for an alternate proprietary name. We recognize this potential; however, the Agency's primary concern is one of patient safety and not commercial gain.

C. Precedents

In support of the proposal to market tazarotene cream under two different names, the sponsor cited examples of other drug products that have been approved by the Agency with two proprietary names. Such examples include Photoplex/Filteray and Erygel/A/T/S. An additional example not noted by the sponsor is that of Retin-A and Renova. Despite these precedents, the Agency has reconsidered their approach in approving alternate proprietary names. Pursuant to a December 1, 2000, CDER policy meeting with the Center Director, Janet Woodcock, M.D. and senior management, DMETS will no longer recommend approval of different proprietary names by the same applicant or manufacturer for products that are essentially identical unless there is a public health risk or stigma associated with the use of the drug product. The Agency is concerned that the proliferation of proprietary names may be misleading and may also lead to product confusion resulting in medication errors and/or patient harm for the following reasons:

Safety Concerns:

•*Overdose:* Practitioners may become confused and not understand that the two products (with 2 different trade names) are identical. This may increase the risk of a patient being prescribed the same drug product by different physicians, resulting in an overdose or inadvertent exposure.

•*Confusion/Misleading*: Trivialization of the adverse events and risks associated with the use of different proprietary names for the same active moiety. Patients may be falsely assured that the medication does not carry significant risks because the FDA has allowed its use for a relatively benign condition.

•*Medication errors:* The creation of a new proprietary name for a new indication of an essentially identical drug product adds unnecessarily to the growing number of proprietary names in the United States. This proliferation of numerous proprietary names may increase the likelihood of occurrence of medication errors resulting in patient injury due to sound-alike and/or look-alike confusion between products.

Additionally, there are several consequences associated with the labeling and packaging of two identical drug products with two different proprietary names because this would require two sets of labeling. This poses problems when it comes to generic substitution. Once an NDA patent expires, a generic applicant would have to decide whether to file a new ANDA in order to market the "same product" for an expanded indication. We predict that generic firms will not find any incentive in filing another application and thus the generic drug labeling would lack important safety information. The creation of two separate package inserts for an essentially identical drug product will not prohibit nor discourage formulary decisions to purchase and utilize Agency approved and bio-equivalent formulations of the same drug product. The only situation in which a substitution would not occur is when the physician specifies "Dispense as Written". Moreover, most generic products do not use a proprietary name and would simply label the product with the established name (Tazarotene Cream). If a generic firm does decide to market the "same product" for the expanded indication, it would be extremely difficult to select the correct product for the intended indication of use.

You will have a situation where the same or even different generic manufacturers of tazarotene cream sitting side-by-side on a pharmacy shelf which are both labeled "Tazarotene Cream". However, the labeling accompanying the product will be different depending on the approved indication of use.

Other Concerns:

•*Management of ADE:* The increasing complexity to manage (regulatory) reports of adverse drug events associated with one active ingredient with 2 or more proprietary names.

In summary, there are no public health risks or stigmas associated with the use of one proprietary name for Tazarotene Cream. Therefore, the safe use of this product is best managed under one proprietary name. DMETS believes the most effective strategy will be in direct-to-consumer advertising and educational campaigns about this newly approved indication utilizing the existing proprietary name, Tazorac®.

If you have any questions or need clarification, please contact the project manager, Sammie Beam at 301-827-3242.

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

/s/

Carol Holquist
3/27/02 12:17:05 PM
PHARMACIST

Jerry Phillips
3/27/02 12:26:35 PM
DIRECTOR

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

vision/Office):
S/Sammie Beam

FROM: DDDDP(Division of Dermatologic and Dental Drug Products)HFD-540
Kalyani Bhatt, Project Manger

DATE:	IND #:	NDA #:	TYPE OF DOCUMENT :	DATE OF DOCUMENT:
3-7-02	[redacted]	21-184 S002	Consult for Tradename	

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
[redacted](tazarotene) Cream 0.1%		Retinoid	ASAP

NAME OF FIRM: Allergan

REASION FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- **X OTHER *(SPECIFY BELOW)*:** Tradename for OPASS

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ TOCOL REVIEW ☐ ER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW): New NDA Submission

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISION RICK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS:
1.) Sponsor is requesting the tradename [redacted] for tazarotene cream for [redacted]

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Kalyani Bhatt, Project Manager **DDDDP, HFD-540** **301-827-2056**	☒ **Electronic & Internal MAIL** ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

ision/Office):
/RA HFD - 400
Sammie Beam

FROM:
KALYANI BHATT, REGULATORY PROJECT MANAGER
DDDDP, HFD-540 301-827-2049

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
10-24-01		21-184 S-002	Consult for Tradename	June 29, 2001

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Tradename (Tazarotene) Cream 0.1%		Acetylenic Retinoid	

NAME OF FIRM: ALLERGAN

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE–NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- x OTHER *(SPECIFY BELOW)*:

NEW NDA EFFICACY SUBMISSION

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ PE A OR B NDA REVIEW ☐ D OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
KALYANI BHATT PROJECT MANAGER HFD-540 827-2049	☐X MAIL ☐X HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

Memorandum of Teleconference

Date: September 26, 2002

Time: 11:00 AM

Proposed Drug Product: AVAGE (Tazarotene) Cream, 0.1%

Proposed Indication: As an adjunctive agent for use in the mitigation (palliation) of facial fine wrinkling, facial mottled hyper- and hypopigmentation, and benign facial lentigines in patients who use comprehensive skin care and sunlight avoidance programs.

Allergan Teleconference Members:

Peter Kressel, Vice President Regulatory Affairs
Dave Garby, Allergan

FDA-Division of Dermatologic and Dental Products:

Wilson Decamp, Ph.D., Chemistry Team Leader DNDC III, HFD-830
Saleh Turujman, Ph.D., Chemistry Reviewer, DNDC, HFD-830
Kalyani Bhatt, Project Manager, DDDDP, HFD-540

Subject:

The use of a narrow-pitch font makes the established name not commensurate with the presentation of the trademark [21 CFR 201.10(g)(2)]. The carton and container label for Avage (tazarotene) Cream should be appropriately revised.

NDA 21-184/Y-001, Tazorac (tazarotene) Cream, 0.05 and 0.10%, (dated 4/9/2002):
The final print carton and container label for Tazorac (tazarotene) Cream 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. In addition, the established name lacks prominence commensurate with the trademark. Finally, the strength declaration on both label and carton is in a font that is even smaller than the established name; this, in conjunction with its position at the edge of the background banner, makes it nearly invisible, and may lead to medication errors. We understand that the carton and container label have been revised since the date of the Annual Report, and request that they be submitted as an amendment to Y-001.

NDA 20-600, Tazorac (tazarotene) Gel, 0.05 and 0.10%:
The final print carton and container label for Tazorac (tazarotene) Gel do not incorporate the changes to the established name (i.e., removal of "topical gel" from within the parentheses) which were requested in our letter of September 27, 2000. Please make this change, and include it in your next Annual Report.

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

/s/

Kalyani Bhatt
9/27/02 11:20:22 AM
CSO