CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-184/002

Administrative Documents

EXCLUSIVITY SUMMARY for NDA # 21-184 SE1-002

Trade Name Tazorac®_ Generic Name:_(tazaortene)topical cream 0.1%
Applicant Name ALLERGAN_
Approval Date April 29, 2002 September 30, 2002

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

a) Is it an original NDA? YES/_ / NO /__X /

b) Is it an effectiveness supplement? YES /_X__/ NO /__/

If yes, what type(SE1, SE2, etc.)? SE1-002

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

YES /_X_/ NO /___/

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /_X_/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?
3 years of exclusivity

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No – Please indicate as such).

YES /___/ NO /_X_/

If yes, NDA # Drug Name

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /X/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 20-600 Tazarotene gel 0.5%, 0.1%

NDA # 21-184 Tazorac (tazarotene)topical cream 0.5% & 0.1%

NDA #

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /_X__/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in

another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /_X__/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /_X__/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /_ __/ NO /X_/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /_X_/

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /_X_/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # 190168 25C
Investigation #2, Study # 190168-036C
Investigation #3, Study # 190168-037C
Investigation #4 Study # 190168-038C

In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1	YES /___/	NO /_X_/
Investigation #2	YES /___/	NO /__X_/
Investigation #3	YES /___/	NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA #	Study #
NDA #	Study #
NDA #	Study #

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the

agency to support the effectiveness of a previously approved drug product?

Investigation #1	YES /___/	NO /X___/
Investigation #2	YES /___/	NO /_X__/
Investigation #3	YES /___/	NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # Study #

NDA # Study #

NDA # Study #

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation # , Study # 190168 25C;

Investigation # , Study # 190168-036C

Investigation # , Study # 190168-037C 190168-038C

To be eligible for exclusivity, a new investigation that is
essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study. Yes
(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND #[redacted] YES /_X__/ ! NO /___/ Explain:

Investigation #2

IND # YES /_X__/ ! NO /___/ Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

Investigation #2
YES /___/ Explain _____ ! NO /___/ Explain _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

_____

Signature of Preparer
Title: Project Manager

Date: April 25, 2002

Signature of Office of Division Director

Date

Memo to File NDA 21-184 AVAGE (Tazarotene) Cream 0.1%
Pediatric Waiver

September 25, 2002

The Sponsor requests a waiver of pediatric study requirements for tazarotene cream 0.1% for the indication of mitigation of fine facial wrinkles, facial mottled hyper and hypopigmentation, and facial lentigenes. This condition is not commonly found in the pediatric patient population. Therefore, it is appropriate to have a full waiver of tazarotene cream 0.1% for this specific indication.

/S/

Markham C. Luke, M.D., Ph.D.
Clinical Team Leader, Dermatology

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

/s/

Markham Luke
9/25/02 11:20:41 AM
MEDICAL OFFICER

Jonathan Wilkin
9/29/02 02:06:33 PM
MEDICAL OFFICER

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA/BLA # 21-184 Supplement Type (e.g. SE5): S-11 Supplement Number: 202

Stamp Date: July 30, 2002 Action Date: Sept 30, 2002

HFD 540 Trade and generic names/dosage form: AVAGE™ (Tazarotene) Cream, 0.1%

Applicant: ALLERGAN Therapeutic Class: 35

Indication(s) previously approved: plaque psoriasis & acne vulgaris

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: _____

Is there a full waiver for this indication (check one)?

☑ Yes: Please proceed to Section A.

☐ No: Please check all that apply: ____Partial Waiver ____Deferred ____Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ Products in this class for this indication have been studied/labeled for pediatric population
- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease to study
- ☐ There are safety concerns
- ☐ Other: The safety & efficacy of tazarotene cream have not been established in patients under the age of 18 years with facial fine wrinkling mottled hypo-/hyperpigmentation, and benign facial lentigines.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min____	kg____	mo.____	yr.____	Tanner Stage____
Max____	kg____	mo.____	yr.____	Tanner Stage____

Reason(s) for partial waiver:

- ☐ Products in this class for this indication have been studied/labeled for pediatric population
- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease to study
- ☐ There are safety concerns
- ☐ Adult studies ready for approval
- ☐ Formulation needed
- ☐ Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min ____	**kg____**	**mo.____**	**yr.____**	**Tanner Stage____**
Max____	**kg____**	**mo.____**	**yr.____**	**Tanner Stage____**

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

ion D: Completed Studies

Age/weight range of completed studies:

Min ____	**kg____**	**mo.____**	**yr.____**	**Tanner Stage____**
Max____	**kg____**	**mo.____**	**yr.____**	**Tanner Stage____**

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 21-184 S002
HFD-950/ Terrie Crescenzi
HFD-960/Grace Carmouze
(revised 9-24-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is there a full waiver for this indication (check one)?

- ☐ **Yes: Please proceed to Section A.**
- ☐ **No: Please check all that apply: ____Partial Waiver ____Deferred ____Completed**
  NOTE: More than one may apply
  Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:**_____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Reason(s) for partial waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

tion D: Completed Studies

Age/weight range of completed studies:

Min _____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

_____
Regulatory Project Manager

cc: NDA
HFD-960/ Terrie Crescenzi
(revised 1-18-02)

OR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
-594-7337

REQUEST FOR WAIVER OF PEDIATRIC STUDIES

Allergan, Inc. is requesting a waiver of pediatric study requirements.

The condition for which this supplement is being filed,

does not occur in this prepubescent patient population (birth-17 years).

Bhatt, Kalyani

om: Walton_Thomas [Walton_Thomas@Allergan.com]
Sent: Tuesday, September 24, 2002 12:14 PM
To: Bhatt, Kalyani (e-mail)
Cc: Kresel_Peter; Walker_Patricia; Sefton_John; Garbe_David; Johnson_Steven(Legal)
Subject: Pediatric Waiver: NDA 21-184/S-002, AVAGE (tazarotene) Cream, 0.1%

Importance: High

Dear Ms Bhatt:

Allergan will be seeking a Full Waiver under 21 CFR § 314.55(c)(2)(i), which states that "the drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients and is not likely to be used in a substantial number of pediatric patients."

The indication for AVAGE Cream, as an adjunctive agent for the use in the mitigation (palliation) of facial fine wrinkling, mottled hyper- and hypopigmentation and benign facial lentigines in patients who use comprehensive skin care and sunlight avoidance programs, is not a condition that occurs in the pediatric population.

Please let me know if you have any questions or concerns.

Sincerely,

Thomas W. Walton
Pharmaceutical Regulatory Affairs
Allergan, Inc.
Tel: 714.246.4470
Fax: 714.246.4272
Walton_Thomas@Allergan.com

ALLERGAN

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

50 years
GROWTH & INNOVATION

16. DEBARMENT CERTIFICATION

Under Section 306(k) of the United States Food, Drug and Cosmetic Act, Allergan, Inc. has made a diligent effort to ensure that no individual group, corporation, partnership or association debarred under Sections 306 (a)-(b) of the Act, as referenced above, have provided any services in connection with this supplement.

Peter J. Kresel 6/1/01

Peter A. Kresel, MS, MBA — Date

Senior Vice President, Global Regulatory Affairs

Allergan, Inc.

DRAFT

Team Leader Memo for NDA 21-184 S002
Tradename and Labeling Discussion for Tazarotene cream 0.1%

September 20, 2002

The original tradename proposed by the Sponsor [redacted] was found to be not acceptable by Agency (see Division of Medications Errors and Technical Support or DMETS consult from March 28, 2002. This stemmed from DMETS discouraging the use of two proprietary names for the same active ingredient by the same application holder. DDDDP also had concerns regarding [redacted] due to the promotional nature of the name [redacted] However, after Dispute Resolution, a determination was made that a different name for the Tazarotene product may be acceptable.

The Sponsor proposed three additional proprietary tradenames ([redacted] AVAGE). These three additional proprietary tradenames were also forwarded to DMETS for review. While DMETS did not have name confusion concerns with [redacted] DDDDP had concerns regarding its possible promotional nature [redacted] and AVAGE were found not to be recommended by DMETS due to possible name confusion issues. The Sponsor subsequently submitted [redacted] which was thought to be acceptable by DMETS.

However, internal discussion regarding the Tradename issue found concern with having the [redacted] Further discussion regarding the AVAGE name was held with DMETS on September 20, 2002 via teleconference (in attendance were Jerry Phillips, Carol Holquist, Jonathan Wilkin, Markham Luke, and Victoria Lutwak). It was agreed that AVAGE would be acceptable if it was done in concert with a post-marketing commitment to do surveillance regarding name confusion. The prime candidates for name confusion were Amerge and Amaryl. However, both of those were pills, while AVAGE is a cream. Further, it was discussed that a Patient Package Insert would accompanying the AVAGE (Tazarotene) Cream product.

A labeling review was conducted on the revised PI and several changes were made to address concerns regarding the new indications regarding hypopigmentation and lentigenes.

/S/

Markham C. Luke, M.D., Ph.D.
Medical Officer/Clinical TL, Dermatology

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/s/

Markham Luke
9/20/02 03:34:55 PM
MEDICAL OFFICER
TL memo re: tradename and labeling for AVAGE Cream.

Jonathan Wilkin
9/29/02 01:58:59 PM
MEDICAL OFFICER

DRAFT

Medical Officer Review of NDA 21-184
Labeling Review for Submission of July 30, 2002

August 16, 2002

The Sponsor has submitted proposed revised labeling based on discussions held with the Agency after an Approvable action was taken for Tazarotene cream 0.1%. The Sponsor has proposed using the following description for their indication: [

Mottled hyperpigmentation – This entity has been recognized by Agency and the mitigation of it has been approved as an indication for two topical tretinoin products. Mottled hyperpigmentation was improved in both pivotal studies in white patients ($p<0.001$ for both), but only in one of the two pivotal studies in non-white patients ($p=0.012$ in study 033C and 0.266 in study 034C). Thus, the indication for mottled hyperpigmentation has only been demonstrated to be effective in patients that are characterized as being white. On further examination, it is noted that non-white patients did not achieve statistical significance in demonstrating benefit for the treatment of fine facial wrinkles in either study ($p = 0.099$ for study 033C and >0.999 in study 034C).
Lentigines – This entity would be a new indication. The Sponsor had designated this as a secondary endpoint and some efficacy is demonstrated. It is suggested that a potential hazard with this indication is that some facial pigmented lesions are not lentigines, but rather lentigo maligna, a type of melanoma. Such lesions should be carefully assessed by a dermatologist or other qualified physician before application of tazarotene.
[

It is suggested that the term mottled hypopigmentation may be more appropriate in this setting. Therefore, the suggested first paragraph for the Indications and Usage section would read:

"TRADENAME (tazarotene) Cream 0.1% is indicated 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.

The PRECAUTIONS section should state the following: "Some facial pigmented lesions are not lentigines, but rather lentigo maligna, a type of melanoma. Facial pigmented lesions of concern should be carefully assessed by a qualified physician (e.g. dermatologist) before application of TRADENAME (tazarotene) Cream. Lentigo maligna should not be treated with TRADENAME (tazarotene) Cream."

The Clinical Studies section should have a statement that addresses the fact that clinical studies did not include sufficient numbers of non-white patients to adequately assess for treatment effect of facial fine wrinkling, facial mottled hyper- and hypopigmentation or benign facial lentigines.

Phase 4 commitments

The Sponsor commented that it was not willing to complete the following recommendation for a Phase 4 commitment: "

for this indication."

The Sponsor queried in an email dated August 14, 2002 as to whether other companies in the topical retinoid drug class have also been asked to provide this type of study.

There was an open-label extension of the original Renova 0.05% trials where therapy was continued for an additional 24 weeks. In addition, patients were discontinued and followed for signs of worsening.

The Renova 0.05% label states the following in the clinical studies section: "Most of the improvement in these signs was noted during the first 24 weeks of therapy. Thereafter, therapy primarily maintained the improvement realized during the first 24 weeks. A majority of patients will lose most mitigating effects of RENOVA 0.05% on fine wrinkles, mottled hyperpigmentation, and tactile roughness of facial skin with discontinuation of a comprehensive skin care and sun avoidance program including RENOVA 0.05%; however, the safety and effectiveness of using RENOVA 0.05% daily for greater than 48 weeks have not been established."

It is suggested that this may be approached via labeling to provide information to prescribers that no studies have been conducted to assess duration of the positive effects of treatment for this indication. This was discussed with the Sponsor via a telecon on the 15th of August, 2002. The Sponsor agreed that this would be acceptable.

With the new indication for lentigines, it is recommended that the following additional Phase 4 commitment be agreed to "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."

Additionally, labeling should address the unknown effect of applying topical tazarotene to lentigines beyond 1 year.

Markham C. Luke, M.D., Ph.D.
Medical Officer/Clinical TL, Dermatology

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

/s/

Markham Luke
9/20/02 01:23:05 PM
MEDICAL OFFICER
Labeling Review for new indication labeling for Tazarotene Cream 0.1%: pigmentation and lentigenes

Jonathan Wilkin
9/29/02 01:55:44 PM
MEDICAL OFFICER

MEMORANDUM OF MEETING MINUTES

Meeting Date: February 21, 2001 **Time:** 9:30 AM **Location:** N225 **Mtg. ID #:** 6590

Application: Pre-NDA Meeting for IND

Drug: Tradename (tazarotene) Cream, 0.1%

Indication:

Sponsor: Allergan

Meeting Chair: Jonathan Wilkin, M.D./Division Director

Meeting Recorder: Kalyani Bhatt/Project Manager

FDA Attendees, titles, and Office/Division:

Jonathan Wilkin, M.D., Division Director, DDDDP, HFD-540
William Timmer, Ph.D, Chemistry Reviewer, DNDCIII, HFD-830
James Vidra, Ph.D, Chemistry Acting Team Leader, DNDCIII, HFD-830
Amy Nostrandt, Ph.D., Pharmacology-Toxicology Reviewer, DDDDP, HFD-540
Tapash Ghosh, Ph.D., Biopharmaceutic Reviewer, DPEIII, HFD-880
Hon-Sum Ko, M.D., Medical Reviewer, DDDDP, HFD-540
Markam Luke, M.D., Ph.D, Acting Medical Team Leader, DDDDP, HFD-540
Mohamed Alosh, Ph.D., Biostatistics Team Leader, DBIII, HFD-725
Kalyani Bhatt, Project Manager, DDDDP, HFD-540

External Constituent Attendees and titles:

Trudy Rumbaugh, M.D. Director, Global Regulatory Affairs, Retinoids
Zhiling Yu, Ph.D., Principal Scientist, Pharmacokinetics and Drug Metabolism
Deborah Lew-Kaya, PharmD, Manager, Skin Care Clinical Research and Development
John Sefton, Ph.D., Director, Clinical Skin Therapeutics
Patricia Walker, Ph.D., M.D., Vice President, Skin Care Clinical Research and Development
Katherine Stern, MS, Principal Statistician, Biostatistics

Purpose:

The sponsor has submitted the studies that are completed to date in the briefing package dated January 23, 2001. To provide general guidance on the Clinical Efficacy Supplement/NDA submission plans. There are questions to be answered on pages 007-010 of the briefing package.

Chemistry, Manufacturing and Controls:

Sponsor's Question:

The active pharmaceutical ingredient and the finished dosage form are unchanged, including the container closure systems, manufacturing and controls, from those previously approved in NDAs 20-600 and 21-184. Therefore, Allergan plans to cross-reference these applications in the event, a full NDA is required. In the case of a Clinical Efficacy Supplement filing, no CMC data will be included. Does the FDA concur?

FDA's Response

As a clinical efficacy supplement will be submitted, no CMC information is required.

However, Allergan will need to submit the following information:

1) An updated EA.
2) A statement indicating that 'there were no CMC changes to the original approved NDAs 20-600 (Gel) and 21-184 (Cream).'
3) Notification if any new prior approval supplements are submitted to NDAs 20-600 and 21-184.

Pharmacology/Toxicology:

Sponsor's Question:

The sponsor proposes to cross-reference nonclinical study reports submitted to previous NDA's 20-600 and 21-184 in the event that a new NDA is submitted for this indication. If instead, an efficacy supplement is submitted, no Pharmacology/Toxicology data will be included. The sponsor requests concurrence on this plan.

FDA's Response:

This plan seems appropriate.

Biopharmaceutics:

Sponsor's Questions:

Clinical Pharmacokinetics: Allergan has completed one clinical pharmacokinetic study in male and female patients with photodamage. We also conducted therapeutic drug monitoring of tazarotenic acid, the major metabolite and pharmacologically active species of tazarotene, in male and female patients in one of the Phase 3 studies. We believe these studies, in addition to the extensive clinical pharmacokinetics studies completed for tazarotene gel (psoriasis/acne) and tazarotene cream (psoriasis/acne), are sufficient for filing. Does the FDA concur?

Biopharmaceutics: (cont.)

FDA's Response:

The sponsor conducted one clinical pharmacokinetics study (190168-038C) after a single dose and after repeat topical applications once daily to either the face only or to an exaggerated body surface area (15%) in male and female patients with photodamage facial skin. They also conducted therapeutic drug monitoring of tazarotenic acid, the major and pharmacologically active metabolite of tazarotene, in male and female patients with photodamage facial skin after application of the 0.1% cream once daily in a double-blind followed by an open-label study (190168-033C). These studies along with previous studies conducted with tazarotene creams and gels will be adequate to fulfill Biopharmaceutics requirements of the NDA submission.

Clinical:

Sponsor's Questions:

Regulatory Affairs:

1. Allergan believes that the Guidance document "Separate Marketing Applications and Clinical Data for Purposes of assessing User Fees Under the Prescription Drug User Fee Act of 1992"(Attachment E, Section II. B.3), we can submit a Clinical Efficacy Supplement for the use of tazarotene cream 0.1% for the [redacted] to NDA 21-184. This is further supported by the precedent of our Clinical Efficacy Supplement for the treatment of acne vulgaris submitted to this NDA on December 8, 2000.

   FDA's Response:

   Acceptable

2. Further, it is our intention that the labeling and tradename of tazarotene cream 0.1% for the treatment of photodamage will be separate and distinct from the labeling and tradename (TAZORAC ® for tazarotene cream 0.1% that will be marketed for psoriasis and acne. FDA has previously and recently approved such a supplement for NDA 18-936 for fluoxetine hydrochloride (Prozac ®/Serafem®). Does the FDA concur with the concept of having a separate tazarotene cream product, with a name other than TAZORAC®, which is appropriately labeled only for the [redacted]

   FDA's Response:

   The issue of tradenames has to be discussed with OPDRA. The case of fluoxetine is not comparable, as PROZAC® and SARAFEM® are different products containing different inactive ingredients. Justification for having two labels should be based on safety grounds with compelling public health arguments.

Clinical: (cont.)

3. Allergan is planning on submitting a fully electronic archival copy of the application in accordance with 21 CFR Part 11. We would like to submit all review copies of the Clinical Efficacy Supplement/NDA electronically as well. Does the FDA concur?

   FDA's Response:

   Concur for clinical portion of the electronic submission.
   The sponsor states that they will provide the CDs for back up.

Clinical Pharmacokinetics/Clinical Safety and Efficacy/Clinical Pharmacology:

1. This was answered earlier by the Biopharm Reviewer.

2. Adequate for filing. The indications will be a review issue. It should be noted that the ***primary*** hypothesis in the trials was with fine wrinkling and mottled hyperpigmentation. ***Secondary*** variables were lentigines and elastoses. Irregular depigmentation and pore sizes were "***other***" measures.

3. The Sponsor previously received comment on the histological study. In the protocol to that study, the term "histological safety profile" was not defined, and the Sponsor did not give a list of preplanned parameters to be evaluated. As such, this study might not necessarily have regulatory value. The parameters for histologic evaluation should have been delineated a priori, and the hypothesis clearly defined. The Sponsor is advised to provide documentation of their preplanned analytical methodology of this study, and reference to the pertinent IND submissions.

4. Information recommended by ICH E1A guideline should be submitted at the time of filing of the NDA. Material submitted at the time of filing would form the basis of the action on the application. Depending on the time of closure of the reviews, late information may or may not be included in labeling.

Biostatistics Question #2:

Concerning the analysis plans for the Integrated Summary of Safety (ISS) and Integrated Summary of Efficacy (ISE,), are the age categories for subgroup analyses acceptable to the agency (i.e., patients <40 years, patients 40 to 65 years, patients >65 years)?

FDA's Response:

This Medical Reviewer has no objections to the subdivisions for age analysis.

Biostatistics:

Sponsor's Question 1.

... Significant interactions were seen for some of the primary and secondary variables in both studies. If at least one center favored vehicle at study endpoint, then sensitivity analyses were performed, which excluded one center in each direction.

... If no centers favored vehicle, then the interaction was considered quantitative in nature and was not examined further. Is this acceptable to the FDA?

FDA's Response:

The sponsor's plan to conduct a sensitivity analysis when at least one center favors vehicle seems reasonable. In addition, a sensitivity analysis should be performed if some centers show extremely favorable results for the active test treatment. When deleting centers to check the robustness of the results, keep in mind that the sample sizes of the deleted centers can influence the conclusions.

Sponsor's Question 2.

...are the age categories for subgroup analyses acceptable to the agency (i.e., patients <40 years, patients 40 to 65 years, patients >65 years)?

FDA's Response:

This question was addressed by the medical reviewer.

Sponsor's Question 3.

Does the agency have any other questions or comments concerning the ISS and/or ISE analysis plans?

FDA's Response:

a) In addition to the analyses submitted by the sponsor where treatment success is defined as improvement from baseline by at least one grade, the sponsor should submit analyses based on the following definitions of treatment success:

   1) Success = achieving a severity score of 0 (none) at study endpoint.
   2) Success = achieving a severity score of 0 or 1 at study endpoint.
   3) Success = improvement from baseline by at least two grades.

b) The sponsor's submission should include the analysis results of Study 037C, which would be helpful for checking inter- and intra-rater reliability.

c) The sponsor's submission should include the planned random treatment allocation list, and a list of the subjects enrolled in the trial and time of enrollment.

d) Efficacy, Safety and Demographic data should be provided as SAS data sets export file.

e) The Integrated Summary of Efficacy Biostatistics Analysis Plan refers to "treatment-by-study" interaction (p 117). This reviewer assumes that the author intended to say "treatment-by-investigator," which is the phrase used in the Study Synopses of studies 033C and 034C (pp 22 and 27).

Administrative Comments:

1. Comments are based upon the briefing package, which is an unofficial briefing document submitted as information.

Pediatric Rule:

2. The Food and Drug Administration Modernization Act [FDAMA] of 1997, Section 111, Pediatric Studies of Drugs, effective April 1, 1999, requires the following:

For Pre-NDA applications:

1. Under 21 CFR, Section 312.47, the sponsor is required to inform the Agency about the status of on going or needed studies adequate to assess pediatric safety and effectiveness. The meeting package submitted for the Pre-NDA meeting must now include the status of needed or ongoing pediatric studies.

For NDA applications:

2. Under 21 CFR, Section 314.50. the NDA application is required to include the following: (d) (7) Pediatric Use Section. Requires that an NDA contain " a section describing the investigation of the drug for use in pediatric populations, including an integrated summary of the information (the clinical pharmacology studies, controlled clinical studies, or uncontrolled clinical studies, or data or information) that is relevant to the safety and effectiveness and benefits and risks of the drug in pediatric populations for the claimed indications, a reference to the full descriptions of such studies provided under paragraphs (3) and (5), and information required to be submitted under Section 314.55."

3. For additional information, please refer to the following CDER web site, www.fda.gov/cder/pediatric

4. **Financial Disclosure**
For applications submitted after February 2, 1999, the applicant is required either to certify to the absence of certain financial interests and arrangements of clinical investigators or to disclose those financial interests using Form 3454. For additional information, please refer to the following CDER web site, www.fda.gov/crdh/modact/fr112098a.html

5. **Labeling**
If you have an Information for Patients leaflet/labeling, please submit it with the NDA.

Chair Concurrence: /S/
Jonathan Wilkin, M.D./Division Director, DDDDP

Minutes Preparer: /S/
Kalyani Bhatt/Project Manager, DDDDP

/s/

Jonathan Wilkin
3/25/01 02:22:53 PM

MESSAGE CONFIRMATION

03/30/01 10:28

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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: 3-30-01 **Pages (including cover)** 8
TO: Trudy A. Cumbaugh, M.D.
COMPANY: Allergan
ADDRESS:
FAX PHONE#: 714-246-4272 **Our Fax # (301) 827-2075**
Voice # (301) 827-2020

MESSAGE:

Trudy,

Attach is the Pre NDA Meeting Minutes for IND Meeting date 2-21-01.

Thank-you.

NOTE ...

eting Date: August 20, 1999 Time: 1300 Location: N225
eting ID# 4561

IND [redacted] Tazorac (tazarotene topical cream) Cream, 1%

Indication: [redacted]

Sponsor: Allergan, Inc.

End of Phase 2 Meeting

Meeting Chair: Jonathan K. Wilkin, M.D.

Meeting Recorder (CSO/Project Manager): Frank H. Cross, Jr., M.A., CDR

FDA Attendees, titles and offices:

Jonathan K. Wilkin, M.D., Division Director, DDDDP, HFD-540
Abby Jacobs, Ph.D., Pharmacologist/Toxicologist Team Leader, DDDDP, HFD-540
Sue-Chih Lee, Ph.D., Biopharmaceutist, DPEIII, HFD-880
Hon-Sum Ko, M.D., Medical Officer, DDDDP, HFD-540
Markham Luke, M.D., Ph.D., Medical Officer, DDDDP, HFD-540
R. Srinivasan, Ph.D., Biostatistics Team Leader, DOBIV, HFD-725
Steve Thomson, Biostatistician, DOBIV, HFD-725
Frank H. Cross, Jr., M.A., CDR, Senior Regulatory Management Officer, DDDDP, HFD-540

onsor Attendees, titles and offices:

Trudy Rumbaugh, M.D., Director, Global Regulatory Affairs, Retinoids
Thomas Walton, RA Specialist, Global Regulatory Affairs
John Sefton, Ph.D., Director, Skin Care Clinical Research and Development
Patricia Walker, M.D., Ph.D., Director, Medical Affairs
Thomas Lin, Ph.D., Manager, Biostatistics
Richard Matsumoto, Ph.D., Principal Scientist, Pharmacokinetics

Meeting Objectives:

End of Phase 2 Meeting

With reference to the Meeting Request submitted June 24, 1999, and to the Meeting Briefing Package submitted July 19, 1999, the following discussion took place:

Chemistry, Manufacturing and Controls:

The attached document was provided to the Sponsor during the meeting. No discussion ensued.

Pharmacology/Toxicology:

comments.

Biopharmaceutics:

The purpose of the pharmacokinetic study is to determine the maximal systemic absorption following topical applications. This data can then be used to assist in assessing risk/benefit ratio. Our comments regarding the Sponsor's pharmacokinetic study plan are as follows:

1. Dosing amount of 2 mg/cm^2 is acceptable if the Phase 3 studies are conducted such that the label will have language to prevent use of the cream at higher dosing levels.

2. In one group of patients, the cream will be applied to 10% of total body surface area. The application sites should be specified.

3. The Sponsor is encouraged to submit the protocol for review prior to study initiation.

Clinical:

1. Sponsor's Regulatory Question: NDA submission will be based on 24 weeks of treatment from two, Phase 3 studies; the final results from the 1-year study for safety will be submitted later, upon availability. Is this acceptable to FDA?

Agency:

information on a separate 1-year study is available. Details of this one-year study should be given by the Sponsor. ce submission may be acceptable if results are submitted by the 120-day Safety Update, but not later.

2. Sponsor's Clinical Question 1: Allergan believes that our proposed Phase 3 clinical plan is adequate to support the indication [redacted] " Does FDA concur?

Agency:

As stated before, treatment of photodamage has to be determined on the basis of reversal of the long term process, especially for such components like carcinogenesis. A trial that evaluates the manifestations arising from photodamage is essentially looking at surrogates but may not necessarily lead to a claim of treatment of photodamage. In addition, it may be difficult to dissect some of the effects of UV radiation vs. those of chronological aging.

3. Agency comments on protocols submitted:

   a. Protocol number 190168-033C:

      i. Comments on overall study design:

         - Is randomization, # of centers, blinding, acceptable? Yes.

         - How many arms in the trial, what are the comparisons being made, are they appropriate?

           Total of 400 patients, with tazarotene 0.1% and vehicle creams for 24 weeks, then tazarotene 0.1% open-label for additional 28 weeks for all. Appropriate.

ii. Comments on Inclusion/Exclusion criteria:

- Do these reflect the target population? Yes. The Sponsor is encouraged to have proper representation of all demographic groups in their proposed studies. Exclusion of Fitzpatrick Skin Types V and VI will not be a NDA fileability issue.

- Are there unjustified exclusions that may affect labeling? No.

- Are washout periods appropriate? Yes.

- Are the clinical criteria appropriate for the proposed indication?

  See above comment on "photodamage". The clinical signs can be acceptable as individual indications if the drug is shown to be effective for those particular signs.

iii. Comments on Endpoints:

- What is the appropriate primary efficacy variable(s)? Is the "success" category clearly stated?

  No known appropriate primary efficacy variable for "photodamage" is available at this point. The primary endpoint being used, "overall integrated assessment of photodamage", has been used in the Phase 2 trial. Evidence of validation has not been presented. The success category is clearly defined (one-grade point improvement in the OIA), but validity of this endpoint is not determined, espeically with the effects of the covariate of age. Since "photodamage" will not be an acceptable indication, this parameter should not be the primary endpoint. Clinical signs of photodamage should be the primary endpoints. The Sponsor should determine from the Phase 2 trial which signs they intend to select as primary; otherwise severe penalty may be incurred for multiplicity.

- What is the appropriate secondary efficacy variable(s)? See last question's answer.

- Are the scoring scales appropriate? Yes, however, it is recommended that the Sponsor reconsider having more narrow scales and provide consistency across centers by proper Investigator training. Reproducibility of scoring by the same Investigator should also be demonstrated.

- Is the Point of Cure very clearly identified in the protocol? Yes, Week 24.

iv. Comments on Safety:

- What are the criteria being used to evaluate safety? AE reporting, pregnancy tests

- Are these criteria adequate? Yes, clinical laboratory tests are not needed, as such safety data have been amply collected for the same formulation in psoriasis studies that involve usage over a much larger area of body surface.

b. Protocol number 190168-034C:

Almost identical to protocol 190168-033C, but without the open-label 28-week extension, biopsy, skin replica and therapeutic drug monitoring. Thus, comments are same as for 190168-033C.

3. Sponsor's Clinical Question 2: Allergan believes that the clinical pharmacokinetics plan is adequate to make a determination of Pregnancy Category C, should systemic absorption prove to be low. Does FDA concur?

Tazorac (tazarotene topical gel) 0.05% and 0.1%, currently has a Pregnancy Category X, which states that the drug is contraindicated in pregnancy. This involves a risk-benefit analysis. The Sponsor needs to explain why a teratogen can be justified in the treatment of a cosmetic indication in pregnancy in order to not incur Pregnancy Category X.

4. Sponsor's Clinical Question 3: How would the absence of positive histological changes affect the labeling?

Presence of histological changes per se will not result in a claim unless supported by pertinent clinical data. Absence of benefit shown histologically suggests that the treatment is not acting on the process of photodamage. Histologic findings may be reported in the mechanism of action under the CLINICAL PHARMACOLOGY Section of the Package Insert.

5. Sponsor Biostatistics' Question: Allergan believes that the proposed statistical analysis plan is sufficient for the FDA to make a determination of safety and efficacy for the desired indication. Does FDA concur?

To be answered by Biostatistics.

Biostatistics:

1. Specific signs would be more appropriate as separate indications. These could be dichotomized, by taking the proportion of subjects who appear at the end of the study to have minimal involvement in that response, or, by taking the proportion with minimal or mild involvement. Alternatively, the Sponsor could consider the proportion who achieve at least a one or two step improvement from baseline. Perhaps even the original 6-step response could be used. In any event, it would seem that some study of both intrarater and interrater reliability would be useful to help justify interpretation of these endpoints.

2. Appropriate attention to any multiple comparisons issues will need to be addressed. Also, the method of analysis should be specified prior to initiation of the study.

3. The Sponsor proposes to define the intent-to-treat group of patients as all randomized patients who receive at least one application of study medication, with at least one follow-up visit. The preferred DDDDP definition is all patients dispensed treatment.

5. The Sponsor's proposed methods of analysis seem quite appropriate. This reviewer was able to essentially reproduce the Sponsor's power calculations; however, they need to be addressed for each separate indication.

Divisional Comments:

Pediatric Rule:

The Food and Drug Administration Modernization Act [FDAMA] of 1997, Section 111, Pediatric Studies of Drugs, effective April 1, 1999, requires the following:

Per 21CFR 314.50(d)(7), NDA applications are required to contain "A section describing the investigation of the drug for use in pediatric populations, including an integrated summary of the information (the clinical pharmacology studies, controlled clinical studies, or uncontrolled clinical studies, or other data or information) that is relevant to the safety and effectiveness and benefits and risks of the drug in pediatric populations for the claimed indications, a reference to the full descriptions of such studies provided under paragraphs (d)(3) and (d)(5) of this section, and information required to be submitted under Section 314.55."

The Sponsor should request a waiver in accordance with 21CFR 314.55(c).

Decisions (agreements) reached:

Unresolved issues or issues requiring further discussion:

None.

ıature, minutes preparer: /S/

Concurrence Chair (or designated signatory): /S/ 8/20/99

Handout: Briefing Package, dated July 19, 1999

Attachment: End of Phase 2 Meeting CMC Comments for IND [redacted] Tazorac (tazarotene topical cream) Cream, 0.1%

Redacted 2

pages of trade

secret and/or

confidential

commercial

information

cc:

IND [redacted]
HFD-105/OFFICE DIR/DeLap
HFD-540 HFD-540/DIV DIR/Wilkin
HFD-830/DIV DIR/Chen
HFD-830/DEP DIV DIR/Dunn
HFD-540/CHEM TL/DeCamp
HFD-540/CHEM/Hathaway
HFD-540/CHEM/Timmer
HFD-540/PHARM TOX TL/Jacobs
HFD-540/PHARM TOX/Nostrandt
HFD-880/BIOPHARM TL/Bashaw
HFD-880/BIOPHARM/Lee/8.20.99
HFD-540/DERM TL/Walker
HFD-540/MO/Ko/8.20.99
HFD-725/BIOSTAT TL/Srinivasan/8.20.99
HFD-725/BIOSTAT/Thomson/8.20.99
HFD-540/PROJ MGR/Cross
Drafted by: fhc/August 20, 1999
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Initialed by:
nl:

EMORANDUM OF MEETING

TO: Tom Walton, Specialist, Regulatory Affairs
COMPANY: Allergan, Inc.
FAX #: 714-246-4272

MESSAGE: Minutes from today's End of Phase 2 Meeting for IND [redacted] Tazorac (tazarotene top. cream) Cream, 1%, are attached to this facsimile transmission.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

45 DAY MEETING CHECKLIST

On initial overview of the NDA application: (YES/NO for the following questions, if applicable)

CLINICAL:

1. On its face, is the clinical section of the NDA organized in a manner to allow substantive review to begin?
   YES

2. Is the clinical section of the NDA indexed and paginated in a manner to allow substantive review to begin?
   This submission is completely electronic. Index and document access are via links.

3. On its face, is the clinical section of the NDA legible so that substantive review can begin? **YES**

4. If needed, has the Applicant made an appropriate attempt to determine the most appropriate dosage and schedule for this product (i.e., appropriately designed dose-ranging studies)? **YES**

   Study Number: **190168-025C**
   Study Title: **A multi-center, investigator-masked, randomized, vehicle-controlled, parallel comparison of tazarotene 0.01%, 0.025%, 0.05%, 0.1% creams and tretinoin 0.05% emollient cream applied once daily for 24 weeks in patients with photodamaged facial skin**

   Sample Size: **349** Arms: **as in study title**
   NDA Volume: **N/A** Pages: **N/A**

5. On its face, does there appear to be the requisite number of adequate and well-controlled studies in the application? **YES**

   Application Type: 505 (b) (1) (**Y**/~~N~~)
   505 (b) (2) (~~Y~~/**N**) Reference drug: **N/A**

Identification of pivotal trials:
Pivotal Study #1: Protocol Number: **190168-033C**
Page Location in NDA: Protocol: **N/A** Study Report: **N/A**

Is this an adequate multi-centered trial? **YES**

Center/Patients Enrolled **15/563**

Study Title: **A multi-center, double-blind, randomized, vehicle-controlled, parallel-group comoparison of the safety and efficacy of tazarotene cream 0.1% applied once daily for 24 weeks followed by treatment with tazarotene cream 0.1% (open-label) for 28 weeks in patients with photodamaged facial skin**

Study design: Randomized (**Y**/~~N~~) Double Blind (**Y**/~~N~~) Placebo controlled (**Y**/~~N~~)
Multicentered (**Y**/~~N~~)

Indication: _____

Study arms (dosage, duration, treatment length for each arm):
Controlled phase: tazarotene 0.1%, qd for 24 weeks vs vehicle qd for 24 weeks
Open-label phase: tazarotene 0.1%, qd for 28 weeks

Efficacy endpoints (Primary and secondary):
Primary: fine wrinkling and mottled hyperpigmentation
Secondary: lentigines and elastosis

How measured: 5-point scales - 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe

Pivotal Study #2: Protocol Number: 190168-034C
Page Location in NDA: Protocol: N/A Study Report: N/A

Is this an adequate multi-centered trial? YES

Center/Patients Enrolled 15/568

Study Title: A multi-center, double-blind, randomized, vehicle-controlled, parallel-group comoparison of the safety and efficacy of tazarotene cream 0.1% applied once daily for 24 weeks in patients with photodamaged facial skin

Study design: Randomized (Y/~~N~~) Double Blind (Y/~~N~~) Placebo controlled (Y/~~N~~)
Multicentered (Y/~~N~~)

Indication: _____

Study arms (dosage, duration, treatment length for each arm):
tazarotene 0.1%, qd for 24 weeks vs vehicle qd for 24 weeks

Efficacy endpoints (Primary and secondary):
Primary: fine wrinkling and mottled hyperpigmentation
Secondary: lentigines and elastosis

How measured: 5-point scales - 0=none, 1=minimal, 2=mild, 3=moderate, 4=severe

6. Are the pivotal efficacy studies of appropriate design to meet basic requirements for approvability of this product based on proposed draft labeling? YES

Proposed indication from sponsor's draft labeling: TRADENAME™ 0.1% Cream is indicated for the

[redacted]

As designed, could endpoints in pivotal trial #1 support labeling? No

As designed, could endpoints in pivotal trial #2 support labeling? No

7. Are all data sets for pivotal efficacy studies complete for all indication(s) requested? (this is a stat question?)
to be answered by Biometrics Reviewer

8. Do all pivotal efficacy studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?

PreIND Mtg: (Y/~~N~~)
IND number/s: [redacted]
PreIND Mtg Date: 3/16/98
EP2 Meeting Date: 8/20/99
Agency response to Phase 3 protocols: Comments on IND [redacted] submission 006 conveyed by CSO
PreNDA meeting date: 2/21/01

Do endpoints as described by sponsor in pivotal Study 1 conform to previous agency commitments? (Y/~~N/No previous commitment~~)

Do endpoints as described by sponsor in pivotal Study 2 conform to previous agency commitments? (Y/~~N/No previous commitments~~)
Are the pivotal trials multi-centered? Y/~~N~~
Are there adequate numbers of patients enrolled? Y/~~N~~

9. Has the Applicant submitted line listings in a format to allow reasonable review of the patient data? Has the Applicant submitted line listings in the format agreed to previously by the Division? YES

10. Has the Application submitted a rationale for assuming the applicability of foreign data (disease specific microbiologic specific) in the submission to the US population? N/A

11. Has the Applicant submitted all additional required case record forms (beyond deaths and drop-outs) previously requested by the Division? None requested

12. Has the Applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously agreed to by the Division? YES

13. Has the Applicant presented a safety assessment based on all current world-wide knowledge regarding this product? YES

14. Has the Applicant submitted draft-labeling consistent with 21CFR 201.56 and 21CFR 201.57, current divisional policies, and the design of the development package? YES to the first 3. See below re: indication.

15. Has the Applicant submitted all special studies/data requested by the Division during pre-submission discussions with the Sponsor? YES, except for -

- Data from the 28-week open-label period of 190168-033C. The Applicant should supply these data as soon as possible, and
- For Study 190168-036C, the Applicant has been advised to provide documentation of their preplanned analytical methodology of this study, and reference to the pertinent IND submissions, including the hypothesis being tested, and information on a priori delineation of parameters for histologic evaluation.

16. Has the Applicant complied with the requirements of the Pediatric Rule? YES
a) Is this an indication that would be applicable to the pediatric population? NO
b) What pediatric ages are included in the protocol? N/A
c) Does the Applicant request pediatric labeling? What age groups? NO

17. Financial disclosure of investigator
a) Does the NDA contain the appropriate form to comply with the filing requirement for Financial Disclosure for Investigators? YES

18. From a clinical perspective, is this NDA fileable? If "no", please state below why it is not. YES

If certain claims are not fileable please state which claims they are and why they are not fileable. Although the submission is fileable, the broad indication [redacted] is questionable. This has been repeatedly brought to the attention of the Applicant in previous interactions. In this submission, the Applicant also presents a histologic study (190168-036C). Whether the broad claim is acceptable becomes a review issue and is not a factor affecting filing.

Hon-Sum Ko, M.D.

Reviewing Medical Officer

Susan Walker, M.D.

Dermatology Team Leader

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

/s/

Hon-Sum Ko
8/6/01 02:12:54 PM
MEDICAL OFFICER

Susan Walker
8/8/01 01:40:16 PM
MEDICAL OFFICER

Jonathan Wilkin
8/14/01 11:27:40 AM
MEDICAL OFFICER

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: 9/17/02 Pages (including cover) 15 pgs

TO: Tom Walton

COMPANY: ALLERGAN

ADDRESS:

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

Voice # (301) 827-2020

MESSAGE: DRAFT LABEL for NDA 21-184 S002

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: O BM.

TELEPHONE: 301-827-2020

********** -COMM. JOURNAL- ********** DATE SEP-17-2002 ***** TIME 13:54 *********

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FILE NO.=139

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-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: 9/17/02 Pages (including cover) 15 pages
TO: Tom Walton
COMPANY: ALLERGAN
ADDRESS:
FAX PHONE#: Our Fax # (301) 827-2075
Voice # (301) 827-2020

MESSAGE: DRAFT LABEL for NDA 21-845 S002

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:
TITLE: U MN.
TELEPHONE: 301-827-2020

15 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: 4/19/02 Pages (including cover) 19

TO: TOM WALTON.

COMPANY:

ADDRESS:

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

Voice # (301) 827-2020

MESSAGE:

TOM.

Here is the DRAFT LABEL for NDA 21-184 S002.

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: D.M.

TELEPHONE: 301-827-2020

*************** -COMM. JOURNAL- ******************** DATE APR-19-2002 ***** TIME 10:12 ********

MODE = MEMORY TRANSMISSION START=APR-19 10:04 END=APR-19 10:12

FILE NO.=197

STN NO.	COMM.	ONE-TOUCH/ ABBR NO.	STATION NAME/EMAIL ADDRESS/TELEPHONE NO.	PAGES	DURATION
001	OK	■	917142464272	019/019	00:07:57

-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: 4/19/02 Pages (including cover) 19

TO: TOM WALTON.

COMPANY:

ADDRESS:

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

Voice # (301) 827-2020

MESSAGE: Tom,
Here is the DRAFT LABEL for
NDA 21-184 S002.

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: P.M.

TELEPHONE: 301-827-2020

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

Bhatt, Kalyani

From: Walton_Thomas [Walton_Thomas@Allergan.com]
Sent: Tuesday, September 24, 2002 12:29 PM
To: Bhatt, Kalyani (e-mail)
Cc: Kresel_Peter; Sefton_John; Johnson_Steven(Legal); Walker_Patricia; Humphries_Bill; O'Brien_Kevin; Garbe_David
Subject: NDA 21-184/S-002, AVAGE (tazarotene) Cream, 0.1%; PHASE 4 COMMITMENTS

Importance: High

Dear Ms Bhatt:

Peter Kresel, Senior Vice President, Global Regulatory Affairs, has asked me to inform you that Allergan accepts the 2, Phase 4 Commitments received by fax this morning concerning the above-referenced NDA/Supplement.

RECEIVED
SEP 24 2002
MEGA/CDER

Please call me if you have any questions or concerns.

Sincerely,

Thomas W. Walton
Pharmaceutical Regulatory Affairs
Allergan, Inc.
Tel: 714.246.4470
Fax: 714.246.4272
Walton_Thomas@Allergan.com

"WorldSecure Server <cder.fda.gov>" made the following
annotations on 09/24/02 12:27:50

[INFO] -- Access Manager:
This message was sent from Allergan across the internet in encrypted format and was successfully decrypted, unless otherwise noted.

Bhatt, Kalyani

ɔm: Walton_Thomas [Walton_Thomas@Allergan.com]
nt: Wednesday, September 18, 2002 7:38 PM
ıo: Bhatt, Kalyani (e-mail)
Subject: AVAGE (tazarotene) Cream, 0.1%

NDA 21-184
002 AVAGE Pac

Good morning Kalyani:

Here is the label. The draft label we received from you yesterday was nearly perfect, really. We had no major objection to anything. We found 2 areas where corrections for grammar and accuracy needed to be made and one where we felt rewording of a sentence made the study outcomes more clear. Our modifications are in red.

1: DESCRIPTION: We said AVAGE is also marketed "as" TAZORAC (grammar)

2: CLINICAL STUDIES: We modified the statement concerning the 2 secondary endpoints to "In the 24 week studies, efficacy was also demonstrated in mottled hypopigmentation and benign facial lentigines, which were secondary endpoints in those studies." (Made study outcomes more clear)

3: ADVERSE REACTIONS: We corrected the wording in the body of the second paragraph to bring it into agreement with the changes FDA made to the Table. (accuracy)

also incorporated your change of one word in the Patient Package Insert.

Other than these minor issues, the labeling is acceptable to Allergan.

Thank you for all your efforts on this supplement. Will call you tomorrow to confirm your receipt of this email.

<<NDA 21-184 SE1-002 AVAGE Package Insert 9-18-02.doc>>

Sincerely,

Tom

Thomas W. Walton
Pharmaceutical Regulatory Affairs
à Allergan, Inc.
Tel: 714.246.4470
Fax: 714.246.4272
Walton_Thomas@Allergan.com

==========
==========

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

********** -COMM. JOURNAL- ********** DATE SEP-17-2002 ***** TIME 13:54 *********

MODE = MEMORY TRANSMISSION START=SEP-17 13:49 END=SEP-17 13:54

FILE NO.=139

STN NO.	COMM.	ONE-TOUCH/ ABBR NO.	STATION NAME/EMAIL ADDRESS/TELEPHONE NO.	PAGES	DURATION
001	OK	#	917142464272	015/015	00:05:16

-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: 9/17/02 Pages (including cover) 15 pages
TO: Tom Walton
COMPANY: ALLERGAN
ADDRESS:
FAX PHONE#: Our Fax # (301) 827-2075
Voice # (301) 827-2020

MESSAGE: DRAFT LABEL for NDA 21-845002

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: CSO, RPM
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: 4/19/02 Pages (including cover) 19

TO: TOM WALTON.

COMPANY:

ADDRESS:

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

Voice # (301) 827-2020

MESSAGE: Tom.
Here is the DRAFT LABEL for NDA 21-184 S002.

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: D.M.

TELEPHONE: 301-827-2020

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

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

FAX COVER SHEET

TO:	Kalyani Bhatt	**FROM:**	Tom Waltm
FAX:	301 827 2091	**FAX:**	(714) 246-4272
TELEPHONE:	301 827 2056	**TELEPHONE:**	(714) 246- 4470
CC:		**DATE:**	4-15-02

Pages being sent including this cover page: 30

Message:

If you do not receive entire document, please call:

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ALLERGAN

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

April 15, 2002

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

REF: Tazarotene Cream, 0.1%
NDA 21-184/S-002
Proposed Tradename for Tazarotene Cream 0.1%

Dear Doctor Wilkin:

Following our electronic mail exchange and your teleconference with Peter Kresel on April 12, 2002, Allergan is supplying your Division with additional information concerning our application for a tradename and product labeling distinct from that approved for TAZORAC® (tazarotene) Cream 0.05%, 0.1%.

As you know, TAZORAC® (tazarotene) Cream 0.05%, 0.1% is currently approved for the treatment of acne vulgaris (0.1%) and plaque psoriasis (0.05%, 0.1%). S-002 seeks the approval for the use of Tazarotene Cream 0.1% in the . Our proposal is for Tazarotene Cream, 0.1% for this indication to be known as:

(tazarotene) Cream, 0.1%.

Also as you know, Allergan included in the filing of S-002 (as Attachment 3 to the Cover Letter) a rationale for the use of labeling and a tradename separate and distinct from TAZORAC® Cream. Today, new information has become available that supports our earlier tradename rationale and builds further on our rationale for differentiation.

++++++++++++++++++++++++++

Allergan, Inc. markets a broad spectra of prescription and OTC health care products intended to treat diseases and conditions across several disparate therapeutic areas. In the United States, Allergan, Inc.'s regulated products are reviewed by several FDA Centers: CDER (pharmaceuticals), CDRH (intraocular lenses, contact lens care) and CBER (BOTOX® botulinum toxin Type A).

Redacted 1

pages of trade

secret and/or

confidential

commercial

information

For your convenience, the following are attached:

-
-

We ask that this additional information be reviewed and filed to NDA 21-184/S-002 and that our proposed tradename [redacted] be approved for Tazarotene Cream 0.1% for the indication. Should you have any questions or require further information, please contact me at 714.246.4292 or Thomas Walton at 714.246.4470, Pacific Time.

Sincerely,

T. Rumbaugh M.D.

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

TR/tww

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

Bhatt, Kalyani

.om: Walton_Thomas [Walton_Thomas@Allergan.com]
Sent: Thursday, April 25, 2002 5:03 PM
To: 'Bhatt, Kalyani (e-mail)'
Subject: Draft Label


Response to Draft Label Wilkin...


NDA 21-184 SE1-002 FDA Label T...

Hi Kalyani. Sorry for the delay.

The official copy was sent by FedEx just now.

Tom

<<Response to Draft Label Wilkin.doc>>

<<NDA 21-184 SE1-002 FDA Label TRADENAME & all 3 indications.doc>>

Thomas W. Walton
Pharmaceutical Regulatory Affairs
å Allergan, Inc.
Tel: 714.246.4470
Fax: 714.246.4272
Walton_Thomas@Allergan.com <mailto:Walton_Thomas@Allergan.com>

Bhatt, Kalyani

From: Bhatt, Kalyani
Sent: Monday, April 22, 2002 12:08 PM
To: 'walton_thomas@allergan.com'
Subject: NDA 21-184 S002 Label

Tom here is the label in word. Also I just received the Biopharm comments that can be incorporated in the label. There is still internal discussion on the PI and PPI.
Thanks,
Kalyani


NDA 21-184 SE1-002 FDA Label 0...


Biopharm Label.doc

Bhatt, Kalyani

om: Walton_Thomas [Walton_Thomas@Allergan.com]
Sent: Friday, April 12, 2002 1:47 PM
To: 'Bhatt, Kalyani (e-mail)'
Cc: Rumbaugh_Trudy; Kresel_Peter
Subject: NDA 21-184/S-002 Taz Crm

Dear Ms Bhatt:

Thank you for speaking with Dr. Rumbaugh and me this morning.

As I mentioned in our telephone call, Allergan considers it absolutely imperative that we receive a trade name other than TAZORAC for the use of Tazarotene Cream 0.1% in the The product cannot be a commercial success without a different trade name due to the formulary/reimbursement issue The full rationale was submitted with our original supplement and subsequently amended.

The following issues are now in the forefront:

* The 10-month PDUFA action date is April 29, 2002

* The summer AAD is in June, 2002. We want to launch product at this votal meeting

* The product is made by Allergan in Waco, Texas and needs to get on the production schedule

* tubes have not been ordered yet due to the lack of trade name resolution

*

* Promotional materials must be submitted to DDMAC.

Therefore, unless Allergan can obtain a second trade name, Marketing/Legal at Allergan

Sincerely,

Bhatt, Kalyani

om: Walton_Thomas [Walton_Thomas@Allergan.com]
Sent: Friday, April 12, 2002 3:48 PM
To: 'Bhatt, Kalyani (e-mail)'
Subject: FW: trade1

trade1.pdf

Here's the first one.

Thomas W. Walton
Pharmaceutical Regulatory Affairs
å Allergan, Inc.
Tel: 714.246.4470
Fax: 714.246.4272
Walton_Thomas@Allergan.com

-----Original Message-----
From: HP9100C [mailto:HP9100C]
Sent: Wednesday, January 02, 1980 9:35 PM
To: WALTON_THOMAS
Subject: trade1

<<trade1.pdf>>

Please open the attached document.
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Sent by:	<HP9100C>
Number of pages:	5
Document type:	B/W Document
Attachment File Format:	Adobe PDF

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http://www.digitalsender.hp.com/reader-en

"WorldSecure Server <cder.fda.gov>" made the following annotations on 04/12/02 15:48:31

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Bhatt, Kalyani

From: Walton_Thomas [Walton_Thomas@Allergan.com]
Sent: Friday, April 12, 2002 3:52 PM
To: 'Bhatt, Kalyani (e-mail)'
Subject: FW: trade2

trade2.pdf

Here's the second one

Thomas W. Walton
Pharmaceutical Regulatory Affairs
Allergan, Inc.
Tel: 714.246.4470
Fax: 714.246.4272
Walton_Thomas@Allergan.com

-----Original Message-----
From: HP9100C [mailto:HP9100C]
Sent: Wednesday, January 02, 1980 9:40 PM
To: WALTON_THOMAS
Subject: trade2

<<trade2.pdf>>

---

ease open the attached document.
is document was sent to you using an HP Digital Sender.
Sent by: <HP9100C>
Number of pages: 2
Document type: B/W Document
Attachment File Format: Adobe PDF

To view this document you need to use the Adobe Acrobat Reader. For more
information on the HP Digital Sender, Adobe Circulate, or a free copy of the
Acrobat reader please visit:
http://www.digitalsender.hp.com/reader-en

"WorldSecure Server <cder.fda.gov>" made the following
annotations on 04/12/02 15:51:46

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==========

Thomas W. Walton
armaceutical Regulatory Affairs
Allergan, Inc.
Tel: 714.246.4470
Fax: 714.246.4272
Walton_Thomas@Allergan.com <mailto:Walton_Thomas@Allergan.com>

"WorldSecure Server <cder.fda.gov>" made the following
annotations on 04/12/02 13:50:43

[INFO] -- Access Manager:
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format and was successfully decrypted, unless otherwise noted.

==========

Bhatt, Kalyani

.om: Bhatt, Kalyani
Sent: Tuesday, April 09, 2002 10:55 AM
To: 'walton_thomas@allergan.com'
Subject: NDA 21-184 S-002 (Tazarotene) 0.01%/Photo Damage/Allergan

Tom,
What we are looking for is the 2 pivotal studies particularly 33c. Also if we could have the label in word before Wed if possible.
Thanks,
Kalyani

Bhatt, Kalyani

..om: Walton_Thomas [Walton_Thomas@Allergan.com]
Sent: Tuesday, April 09, 2002 11:51 AM
To: 'Bhatt, Kalyani'
Cc: Rumbaugh_Trudy
Subject: RE: NDA 21-184 S-002 (Tazarotene) 0.01%/Photo Damage/Allergan


TAZ Crm PI NonAnnot.doc


Taz Cream Acne FDA final versi...

Hi Kalyani:

Here are the two labels. First one is Photodamage and second one is Acne/Psoriasis

<<TAZ Crm PI NonAnnot.doc>> <<Taz Cream Acne FDA final version 10-11-01.doc>>

I will work on your other question concerning Appendix 3.

Tom

Thomas W. Walton
Pharmaceutical Regulatory Affairs
Allergan, Inc.
Tel: 714.246.4470
Fax: 714.246.4272
Walton_Thomas@Allergan.com

-----Original Message-----
From: Bhatt, Kalyani [mailto:BHATTK@cder.fda.gov]
Sent: Tuesday, April 09, 2002 7:55 AM
To: 'walton_thomas@allergan.com'
Subject: NDA 21-184 S-002 (Tazarotene) 0.01%/Photo Damage/Allergan

Tom,
What we are looking for is the 2 pivotal studies particularly 33c. Also if
we could have the label in word before Wed if possible.
Thanks,
Kalyani

"IRAPPS34 <allergan.com>" made the following
annotations on 04/09/02 08:04:03

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==========

APPEARS THIS WAY
ON ORIGINAL

Bhatt, Kalyani

rom: Bhatt, Kalyani
Sent: Monday, April 08, 2002 12:06 PM
To: 'walton_thomas@allergan.com'
Subject: FW: Tazorac

Tom could you address Dr. Huene' s request?

Please provide information on the adverse reactions of the skin and appendages that were considered to be severe in the two studies. The index for the electronic version states that these are in Appendix 3.0, but this Appendix is not provided.