Dated: May 13, 1999.

Sue E. Swenson,

Commissioner, Administration on Developmental Disabilities.

[FR Doc. 99-12699 Filed 5-19-99; 8:45 am]

BILLING CODE 4184-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98E-0754]

Determination of Regulatory Review Period for Purposes of Patent Extension; Omnicef® Tablets

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined the regulatory review period for Omnicef® Tablets and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of an application to the Commissioner of Patents and Trademarks, Department of Commerce, for the extension of a patent which claims that human drug product.

ADDRESSES: Written comments and petitions should be directed to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Brian J. Malkin, Office of Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-6620.

SUPPLEMENTARY INFORMATION: The Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) and the Generic Animal Drug and Patent Term Restoration Act (Pub. L. 100-670) generally provide that a patent may be extended for a period of up to 5 years so long as the patented item (human drug product, animal drug product, medical device, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under these acts, a product's regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period consists of two periods of time: A testing phase and an approval phase. For human drug products, the testing phase begins when the exemption to permit the clinical investigations of the drug becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human drug product and continues until FDA grants permission to market the drug product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Commissioner of Patents and Trademarks may award (for example, half the testing phase must be subtracted as well as any time that may have occurred before the patent was issued), FDA's determination of the length of a regulatory review period for a human drug product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA recently approved for marketing the human drug product Omnicef® Tablets (cefdinir). Omnicef® Tablets is indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of specific microorganisms in specified conditions. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for Omnicef® Tablets (U.S. Patent No. 4,559,334) from Warner-Lambert Co., and the Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated December 14, 1998, FDA advised the Patent and Trademark Office that this human drug product had undergone a regulatory review period and that the approval of Omnicef® Tablets represented the first permitted commercial marketing or use of the product. Shortly thereafter, the Patent and Trademark Office requested that FDA determine the product's regulatory review period.

FDA has determined that the applicable regulatory review period for Omnicef® Tablets is 2,745 days. Of this time, 2,288 days occurred during the testing phase of the regulatory review period, while 457 days occurred during the approval phase. These periods of time were derived from the following dates:

1. *The date an exemption under section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) became effective:* June 1, 1990. FDA has verified the applicant's claim that the date the investigational new drug application became effective was on June 1, 1990.

2. *The date the application was initially submitted with respect to the human drug product under section 505 of the act:* September 4, 1996. FDA has verified the applicant's claim that the new drug application (NDA) for Omnicef® Tablets (NDA 50-739) was initially submitted on September 4, 1996.

3. *The date the application was approved:* December 4, 1997. FDA has verified the applicant's claim that NDA 50-739 was approved on December 4, 1997.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the U.S. Patent and Trademark Office applies several statutory limitations in its calculations of the actual period for patent extension. In its application for patent extension, this applicant seeks 1,601 days of patent term extension.

Anyone with knowledge that any of the dates as published is incorrect may, on or before July 19, 1999, submit to the Dockets Management Branch (address above) written comments and ask for a redetermination. Furthermore, any interested person may petition FDA, on or before November 16, 1999, for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period. To meet its burden, the petition must contain sufficient facts to merit an FDA investigation. (See H. Rept. 857, part 1, 98th Cong., 2d sess., pp. 41-42, 1984.) Petitions should be in the format specified in 21 CFR 10.30.

Comments and petitions should be submitted to the Dockets Management Branch (address above) in three copies (except that individuals may submit single copies) and identified with the docket number found in brackets in the heading of this document. Comments and petitions may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 4, 1999.

Thomas J. McGinnis,

Deputy Associate Commissioner for Health Affairs.

[FR Doc. 99-12651 Filed 5-19-99; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98E-0474]

Determination of Regulatory Review Period for Purposes of Patent Extension; Tazorac®

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined

the regulatory review period for Tazorac® and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of an application to the Commissioner of Patents and Trademarks, Department of Commerce, for the extension of a patent which claims that human drug product.

ADDRESSES: Written comments and petitions should be directed to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Brian J. Malkin, Office of Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-6620.

SUPPLEMENTARY INFORMATION: The Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) and the Generic Animal Drug and Patent Term Restoration Act (Pub. L. 100-670) generally provide that a patent may be extended for a period of up to 5 years so long as the patented item (human drug product, animal drug product, medical device, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under these acts, a product's regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period consists of two periods of time: A testing phase and an approval phase. For human drug products, the testing phase begins when the exemption to permit the clinical investigations of the drug becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human drug product and continues until FDA grants permission to market the drug product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Commissioner of Patents and Trademarks may award (for example, half the testing phase must be subtracted as well as any time that may have occurred before the patent was issued), FDA's determination of the length of a regulatory review period for a human drug product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA recently approved for marketing the human drug product Tazorac® (tazarotene). Tazorac® is indicated for the topical treatment of patients with stable plaque psoriasis of up to 20 percent body surface area involvement and for the topical treatment of patients with facial acne vulgaris of mild to moderate severity. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for Tazorac® (U.S. Patent No. 5,089,509) from Allergan, Inc., and the Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated September 28, 1998, FDA advised the Patent and Trademark Office that this human drug product had undergone a regulatory review period and that the approval of Tazorac® represented the first permitted commercial marketing or use of the product. Shortly thereafter, the Patent and Trademark Office requested that FDA determine the product's regulatory review period.

FDA has determined that the applicable regulatory review period for Tazorac® is 2,684 days. Of this time, 1,958 days occurred during the testing phase of the regulatory review period, while 726 days occurred during the approval phase. These periods of time were derived from the following dates:

1. *The date an exemption under section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) became effective:* February 8, 1990. The applicant claims February 16, 1990, as the date the investigational new drug application (IND) became effective. However, FDA records indicate that the IND effective date was February 8, 1990, which was 30 days after FDA receipt of the IND.

2. *The date the application was initially submitted with respect to the human drug product under section 505 of the act:* June 19, 1995. FDA has verified the applicant's claim that the new drug application (NDA) for Tazorac® (NDA 20-600) was initially submitted on June 19, 1995.

3. *The date the application was approved:* June 13, 1997. FDA has verified the applicant's claim that NDA 20-600 was approved on June 13, 1997.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the U.S. Patent and Trademark Office applies several statutory limitations in its calculations of the actual period for patent extension. In its application for patent extension, this applicant seeks 845 days of patent term extension.

Anyone with knowledge that any of the dates as published is incorrect may, on or before July 19, 1999, submit to the Dockets Management Branch (address above) written comments and ask for a redetermination. Furthermore, any interested person may petition FDA, on or before November 16, 1999, for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period. To meet its burden, the petition must contain sufficient facts to merit an FDA investigation. (See H. Rept. 857, part 1, 98th Cong., 2d sess., pp. 41-42, 1984.) Petitions should be in the format specified in 21 CFR 10.30.

Comments and petitions should be submitted to the Dockets Management Branch (address above) in three copies (except that individuals may submit single copies) and identified with the docket number found in brackets in the heading of this document. Comments and petitions may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 4, 1999.

Thomas J. McGinnis,

Deputy Associate Commissioner for Health Affairs.

[FR Doc. 99-12652 Filed 5-19-99; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98E-0840]

Determination of Regulatory Review Period for Purposes of Patent Extension; Omnicef® Oral Suspension

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined the regulatory review period for Omnicef® Oral Suspension and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of an application to the Commissioner of Patents and Trademarks, Department of Commerce, for the extension of a patent which claims that human drug product.

ADDRESSES: Written comments and petitions should be directed to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Brian J. Malkin, Office of Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-6620.

SUPPLEMENTARY INFORMATION: The Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417)

EXCLUSIVITY SUMMARY for NDA # 21-184

Trade Name Tazorac® Cream 0.05%,0.1% Generic Name: tazaortene
Applicant Name ALLERGAN
Approval Date July 30, 2000

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. 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/_X_/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /__X/

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

   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.

2. 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 _____

NDA # _____ _____

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__/

APPEARS THIS WAY
ON ORIGINAL

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: <u>THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS</u>

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."

1. 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.

2. 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 /_X__/ NO /___/

(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: _____

APPEARS THIS WAY
ON ORIGINAL

(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 # 190168-024C; 190168-32C

Investigation #2, Study # 190168-029C; 190168-33C

Investigation #3, Study # 190168-31C; 190168-34C

3. 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 /___/

Investigation #2 YES /___/ NO /___/

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 /___/

Investigation #2 YES /___/ NO /___/

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 # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

4. 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.

(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 # _____ YES /___/	NO /___/ Explain: _____
	_____
	_____
Investigation #2	
IND # _____ YES /___/	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: _____

_____

_____

_____ 7-24-00

Signature of Preparer Date
Title: Kalyani Bhatt

/S/ 9/24/00

Signature of ~~Office of~~ Division Director Date

cc:
Archival NDA 21-184
HFD- 540/Division File
HFD- 540/Bhatt
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

21-184 Original NDA

HFD-540 Trade and generic names/dosage form: TRADENAME® TAZORAC (tazarotene) topical cream 0.05%, 0.1% Action:

Applicant ALLERGAN Therapeutic Class 3S

Indication(s) previously approved : NONE
Pediatric information in labeling of approved indication(s) is adequate __ inadequate X__ N/A
Proposed indication in this application: TREATMENT FOR PLAQUE PSORIASIS

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.
IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? __Yes (Continue with questions) __No (Sign and return the form)
WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)
___Neonates (Birth-I month) _Infants (1 month-2yrs) _Children (2-12yrs) _ Adolescents(12-16yrs)

__ 1. PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS. Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

__ 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

___3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

c. The applicant has committed to doing such studies as will be required.
(1) Studies are ongoing,
(2) Protocols were submitted and approved.
(3) Protocols were submitted and are under review.
(4) If no protocol has been submitted, attach memo describing status of discussions.

d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

___4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

_X_ 5. **If none of the above apply,** attach an explanation, as necessary.
NOT DETERMINED AS YET. NEED JUSTIFICATION FROM SPONSOR

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? No
ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from Medical Officer :
The applicant is requesting a waiver for pediatric studies on neonates, infants and children, because plaque psoriasis is not prevalent in the population from bith to 11 years and tazarotene creams would not represent a substantial thereapeutic benefit over existing anti-psoriatic therapies. The applicant should address potential benefit of tazarotene creams in the treatment of plaques psoriasis in the adolescent pediatric population before a waiver can be recommended.

9/24/00

Signature of Preparer and Title Kalyani Bhatt, Project Manager, HFD-540 Date 7-26-00

cc: Orig NDA 21-184
HFD-540/Div File
NDA 21-184 Action Package
HFD-540/DIV DIR/Wilkin
HFD-540/DERM TL/Walker
HFD-540/MO/Ko
HFD-540/PM/Bhatt
HFD-006/Crescenzi

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, TERRIE CRESCENZI, HFD-104 (CRESCENZIT)

(revised 3/06/00)

ALLERGAN

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

1.6 DEBARMENT CERTIFICATION

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

Peter A. Kresel, MS, MBA

Aug 24, 1999
Date

Senior Vice President, Global Regulatory Affairs

Allergan, Inc.

APPEARS THIS WAY
ON ORIGINAL

1.8 REQUEST FOR WAIVER OF PEDIATRIC STUDIES

Allergan, Inc. is requesting a waiver of pediatric study requirements for neonates, infants and children as:

Tazorac® (tazarotene topical cream) 0.05%, 0.1% does not represent a substantial therapeutic benefit over existing anti-psoriatic treatments, and Tazorac® (tazarotene topical cream) 0.05%, 0.1% would not likely be used in a substantial number of these patients.

Further, plaque psoriasis is not prevalent in this patient population (birth-11 years).

ALLERGAN

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

1.5 CERTIFICATION FOR EXCLUSIVITY

Allergan is submitting information in support of a request for three (3) years of exclusivity per section 505 of the Federal Food, Drug and Cosmetic Act for NDA 21-184, Tazorac® (tazarotene topical cream) 0.05%, 0.1%. The results of the following two, controlled clinical studies demonstrate that Tazorac® (tazarotene topical cream) 0.05%, 0.1% are safe and efficacious in the treatment of plaque psoriasis. In the opinion of the sponsor, these studies are essential to the approval of the New Drug Application for Tazorac® (tazarotene topical cream) 0.05%, 0.1%. The applicant of this NDA is the sponsor of [redacted] under which these clinical studies were conducted.

Study 190168-016C: A multi-center, double-blind, randomized, vehicle-controlled study of the safety and efficacy of 0.05%, and 0.1% tazarotene creams applied once-daily for 12 weeks, with a 12 week follow up, in the treatment of plaque psoriasis.

Study 190168-017C: A multi-center, double-blind, randomized, vehicle-controlled study of the safety and efficacy of 0.05% and 0.1% tazarotene creams applied once-daily for 12 weeks in the treatment of plaque psoriasis.

Allergan hereby certifies that to the best of our knowledge, the clinical investigations listed herein have not formed part of the basis of a finding of substantial evidence of effectiveness for a previously approved drug application or supplement.

Furthermore, no other drug product containing all of the same ingredients with the same conditions of approval has been previously approved for human use. Allergan is the sole owner of the synthetic processes for the active pharmaceutical ingredient, tazarotene, and the holder of the use patents for tazarotene-containing formulations. Therefore, no clinical investigations have been conducted, other than those sponsored by Allergan, that support the approval of this new drug application for Tazorac® (tazarotene topical cream) 0.05%, 0.1%. Tazorac® cream is currently not approved for human use.

Peter A. Kresel Sept 23, 1999

Peter A. Kresel, MS, MBA Date
Senior Vice President, Global Regulatory Affairs
Allergan, Inc.

APPEARS THIS WAY
ON ORIGINAL

OFFICES OF DRUG EVALUATION
ORIGINAL NDA/NDA EFFICACY SUPPLEMENT
ACTION PACKAGE CHECKLIST

NDA # 21-184 Drug: TAZORAC Creme 0.05%, 0.1%

Applicant: ALLERGAN Chem/Ther/other Types: 3S

PM: K. Bhatt Phone: 7-2049 HFD- 540

USER FEE GOAL DATE: 7-29-00 DATE CHECKLIST COMPLETED: _____

Arrange package in the following order (include a completed copy of this CHECKLIST):	Check or Comment
1. ACTION LETTER with supervisory signatures Are there any Phase 4 commitments?	AP _____ AE _____ Yes _____ No ✓
2. Have all disciplines completed their reviews? If no, what review(s) is/are still in draft?	Yes _____ No _____
3. LABELING (package insert and carton and container labels). (If final or revised draft, include copy of previous version with ODE's comments and state where in action package the Division's review is located. If Rx-to-OTC switch, include current Rx Package insert and HFD-312 and HFD-560 reviews of OTC labeling.)	Draft _____ Revised Draft ✓ Final _____
4. PATENT INFORMATION	✓
5. EXCLUSIVITY CHECKLIST	✓
6. PEDIATRIC PAGE (all NDAs)	✓
7. DEBARMENT CERTIFICATION (Copy of applicant's certification for all NDAs submitted on or after June 1, 1992).	✓
8. Statement on status of DSI's AUDIT OF PIVOTAL CLINICAL STUDIES If AE or AP ltr, explain if not satisfactorily completed. Attach a COMIS printout of DSI status. If no audits were requested, include a memo expaining why.	included
9. REVIEWS & MEMORANDA:	
DIVISION DIRECTOR'S MEMO | If more than 1 review for any	
GROUP LEADER'S MEMO |1 discipline, separate reviews	
MEDICAL REVIEW | with a sheet of colored paper.	July 11, 2000
SAFETY UPDATE REVIEW |Any conflicts between reviews	
STATISTICAL REVIEW |must have resolution documented	5-15-00
BIOPHARMACEUTICS REVIEW	7-3-00
PHARMACOLOGY REVIEW (Include pertinent IND reviews)	6-13-00
Statistical Review of Carcinogenicity Study(ies)	
CAC Report/Minutes	
CHEMISTRY REVIEW	
Labeling and Nomenclature Committee Review Memorandum	
Date EER completed _____ (attach signed form or CIRTS printout)	
FUR needed ___ No _____ FUR requested __ N/A _____	
Have the methods been validated?	Yes (attach) _____ No _____
Environmental Assessment Review /FONSI	FONSI Yes ___
MICROBIOLOGY REVIEW	3-8-00
What is the status of the monograph?	_____ N/A _____
10. CORRESPONDENCE, MEMORANDA OF TELECONS, and FAXes	✓
11. MINUTES OF MEETINGS	
Date of End-of-Phase 2 Meeting:	_____
Date of pre-NDA Meeting:	6-14-99
12. ADVISORY COMMITTEE MEETING MINUTES	Minutes _____ Info Alert _____
or, if not available, 48-Hour Info Alert or pertinent portion of transcript	

OFFICES OF DRUG EVALUATION
ORIGINAL NDA/NDA EFFICACY SUPPLEMENT
ACTION PACKAGE CHECKLIST

14. If approval letter, has ADVERTISING MATERIAL been reviewed? **If no and this is an AP with draft labeling letter, has advertising material already been requested?**	Yes_____ No_____ Yes, documentation attached_____ No, included in AP ltr _____
15. INTEGRATED SUMMARY OF EFFECTIVENESS (from NDA)	✓
16. INTEGRATED SUMMARY OF SAFETY (from NDA)	✓

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. XXXX-XXXX
Expiration Date: XX/XX/XX

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigator	
List attached (exceptions noted)	

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Eric Brandt	Chief Financial Officer
FIRM/ORGANIZATION: Allergan, Inc.	
SIGNATURE: Eric Brandt	DATE: 9/23/99

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

Please DO NOT RETURN this form to this address.

FORM FDA 3454 (10/98)

BILLING CODE 4160-01-C

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. XXXX-XXXX
Expiration Date: XX/XX/XX

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning _____ (Name of clinical investigator), who participated as a clinical investigator in the submitted study 190168-016C (Name of clinical study), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

any proprietary interest in the product tested in the covered study held by the clinical investigator;

any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Eric Brandt	Chief Financial Officer
FIRM/ORGANIZATION: Allergan, Inc.	
SIGNATURE: Eric Brandt	DATE: 9/23/99

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

<--Please DO NOT RETURN this form to this address.

FORM FDA 3455 (10/98)

SF

August 13, 1999

Lauri Murphy
Allergan Skin Care
2525 Dupont Dr. Mailstop TL-1K
Irvine, CA 92612

RE: Protocol 190168-016C Financial Disclosure Form Exception

Dear Ms. Murphy:

In regards to you request for Financial Disclosure Forms for the aforementioned protocol, we have a exceptional circumstance that prevents our site from completing the questionnaire for [redacted] MD. [redacted] r was listed on the FDA Form 1572 as a sub-investigator. Unfortunately, [redacted]

Due to this medical condition, and in respect to his privacy, we will be unable to forward a completed form to you for this sub-investigator. If you need further assistance in this matter, please contact me at (206) 386-9500

Sincerely,

[redacted]

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

3 pages

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. XXXX-XXXX
Expiration Date: XX/XX/XX

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning _____ (Name of clinical investigator), who participated as a clinical investigator in the submitted study 190168-017C (Name of clinical study), is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
Eric Brandt	Chief Financial Officer
FIRM/ORGANIZATION: Allergan, Inc.	
SIGNATURE: Eric Brandt	DATE: 9/23/99

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

<--Please DO NOT RETURN this form to this address.

FORM FDA 3455 (10/98)

EF

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

3 pages

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

Form Approved: OMB No. 0910-0297
Expiration Date: November 30, 1996

USER FEE COVER SHEET

See Instructions on Reverse Before Completing This Form.

1. APPLICANT'S NAME AND ADDRESS

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

2. USER FEE BILLING NAME, ADDRESS AND CONTACT

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

Contact: Trudy Rumbaugh

3. TELEPHONE NUMBER (Include Area Code)

800-347-4500

4. PRODUCT NAME Tazorac® (tazarotene topical cream) 0.05%, 0.1%

5. DOES THIS APPLICATION CONTAIN CLINICAL DATA? ☒ YES ☐ NO

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

6. USER FEE I.D. NUMBER

3797

7. LICENSE NUMBER/NDA NUMBER

N021184

8. IT THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED BEFORE 9/1/92

☐ THE APPLICATION IS SUBMITTED UNDER 505(b)(2) *(See reverse before checking box.)*

☐ AN INSULIN PRODUCT SUBMITTED UNDER 506

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGIC PRODUCT LICENSED UNDER 351 OF THE PHS ACT

9.a. HAS THIS APPLICATION QUALIFIED FOR A SMALL BUSINESS EXCEPTION? ☐ YES ☒ NO

(See reverse if answered YES)

b. HAS A WAIVER OF APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☒ NO

(See reverse if answered YES)

This completed form must be signed and accompany each new drug or biologic product, original or supplement.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Trudy Rumbaugh	Trudy Rumbaugh Director Global Regulatory Affairs	9/30/99

FORM FDA 3397 (12/93)

Memorandum

Date: September 25, 2000

From: Hon-Sum Ko, M.D., Medical Officer

To: Kalyani Bhatt, Consumer Safety Officer

Re: NDA 21-184 Tazarotene Creams 0.05%, 0.1% in the Treatment of Plaque Psoriasis - Pediatric Studies.

A discussion was carried out on 9/25/00 between this Medical Officer, the Dermatology Team Leader and the Division Director regarding the request for waiver for pediatric studies from Allergan in NDA 21-184.

This waiver request covers pediatric patients from birth to age 11. Therefore, it is a request for partial waiver, which leaves out the age group between 12 to 17 (clinical studies in this NDA included patients aged 18 or older). The Applicant has not initiated studies on psoriasis to cover this age group (between 12 and 17), and has not stated plans to address this age group.

For pediatric use information, the regulations allow any of three approaches: required assessment, deferred submission, and waiver.

Our discussion came to the conclusion that psoriasis is not common before puberty, and therefore tazarotene creams are not likely to be used in the treatment of psoriasis in a substantial number of pre-pubertal patients. Although it may be possible to extrapolate efficacy from the adult population to pubertal and post-pubertal pediatric patients, safety information is needed for these patients, because tazarotene, a retinoid, has effects on epiphyses. The degree of systemic exposure in the treatment of plaque psoriasis in this pediatric age group may pose the potential of unwanted skeletal effects, as there is no upper limit of body surface area involvement in the use of tazarotene creams (for psoriasis). The surface area/volume ratio is not a critical issue in pubertal or post-pubertal adolescents, since this ratio should resemble that of adults in this age group.

Therefore, although a partial waiver (for pediatric patients from birth to age 11) has been requested and may be granted under 21 CFR 314.55(c)(4), safety information for the age group 12-17 is required under 21 CFR 314.55(a).

Currently there are no pediatric studies ongoing for tazarotene creams in the treatment of plaque psoriasis. Neither are there additional safety or effectiveness data anticipated after approval of the indication in adults. Thus, 21 CFR 314.55(b)(1) does not apply. Deferral of submission of required assessment, however, may be granted under 21 CFR 314.55(b)(2), which states:

"If FDA determines that there is an adequate justification for temporarily delaying the submission of assessment of pediatric safety and effectiveness, the drug product may be approved for use in adults subject to the requirement that the applicant submit the required assessments within a specified time."

This Reviewer believes that there is adequate justification for temporarily delaying the submission of required information in pediatric patients aged 12-17, as therapeutic benefit to adult patients with psoriasis should not be delayed simply because of the lack of pediatric information for the adolescent age group. Such information can be provided in phase 4.

Recommendations:

1. At the request of Allergan, a partial waiver for pediatric psoriasis studies may be granted for the age group from birth to 11 under 21 CFR 314.55(c)(4).
2. Deferred submission of information for the age group 12-17 may be permitted under 21 CFR 314.55(b)(2). Allergan should make a phase 4 commitment to provide safety information, including the effects on epiphyses, for tazarotene creams in the treatment of psoriasis in the age group 12-17 within a reasonable timeframe.

cc: NDA 21-184
HFD-540
HFD-540/CSO/Bhatt
HFD-540/CHEM/Timmer
HFD-540/PHARM/Nostrandt
HFD-880/BIOPHARM/Ghosh
HFD-540/MO/Walker/Ko
HFD-710/BIOMETRICS/Lawrence

Not in DFS

APPEARS THIS WAY
ON ORIGINAL

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

REQUEST FOR CONSULTATION

(Division/Office)		FROM:	
4FD-160 Peter Cooney		/S/	HFD-540
DATE: 11/15/99	IND NO.	NDA NO. 21-184	TYPE OF DOCUMENT	DATE OF DOCUMENT
NAME OF DRUG: Tazorac		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
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
- ☒ OTHER *(Specify below)*

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW	☐ CHEMISTRY
☐ END OF PHASE II MEETING	☐ PHARMACOLOGY
☐ CONTROLLED STUDIES	☐ BIOPHARMACEUTICS
☐ PROTOCOL REVIEW	☐ OTHER
☐ OTHER	

III. BIOPHARMACEUTICS

- ☐ SOLUTION
- ☐ BIOAVAILABILITY 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 ASSESSEMENT 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 *(Attach additional sheets if necessary)*

This is a New NDA 21-184. The Filability meeting is Nov. 22. 1999 @ 4:00

SIGNATURE OF REQUESTER	DATE	METHOD OF DELIVERY *(Check one)*
/S/	11/15/99	☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER

FORM FDA 3291 (7/83)

Teleconference Date: August 29, 2000 Time: 1500 Location: N225

NDA 21-184, Tazorac (tazarotene topical cream) Cream, 0.05%, 0.1%

Indications: Topical Treatment of Plaque Psoriasis

Sponsor: Allergan, Inc.

Purpose of Meeting: Guidance 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
Frank H. Cross, Jr., M.A., CDR, Senior Regulatory Management Officer, DDDDP, HFD-540

Sponsor Attendees, titles and offices:

Peter Kresel, Vice President, Regulatory Affairs
Trudy Rumbaugh, M.D., Director, Global Regulatory Affairs, Retinoids
Thomas Walton, Specialist, Regulatory Affairs

In response to the Applicant's request for feedback on progress of the NDA review, the Agency had the following discussion:

Agency:

The Agency reiterated to the Applicant the primary and secondary goal dates for the NDA. In addition, the Agency said that it would share its proposed labeling for this NDA as soon as possible. Finally, the Agency informed the Applicant that a Pregnancy Registry may be requested for this NDA.

Applicant:

The Applicant appreciated our feedback and looks forward to future interactions and discussions of the proposed labeling and the topic of a Pregnancy Registry for this drug.

The teleconference ended amicably.

Signature, minutes preparer: /S/

Concurrence Chair (or designated signatory): _____

cc:

NDA 21-184
HFD-540
HFD-540/DIV DIR/Wilkin
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
HFD-540/DERM TL/Walker
HFD-540/MO/Ko
HFD-725/ACT BIOSTAT TL/Al-Osh
HFD-880/BIOSTAT/Lee
HFD-540/PM/Cross
HFD-540/PM/Bhatt
Drafted by: fhc/September 21, 2000
c:\word\tazorac\nda21184\tconminb.doc
Initialed by:
final:

MEMORANDUM OF TELECONFERENCE

MEMORANDUM OF TELECONFERENCE

Meeting Date: August 1, 2000 **Time:** 4:00 PM **Location:** N225

Subject: NDA 21-184 Tazorac Cream 0.05% & —
Applicant: ALLERGAN

Meeting Chair: Dr. Jonathan Wilkin, Division Director, HFD-540
Meeting Recorder: Kalyani Bhatt, Project Management Staff, HFD-540

FDA Attendees:

Dr. Jonathan Wilkin, Division Director, HFD-540
Dr. Robert Delap, Office Director of ODE V
Dr. Jonca Bull, Deputy Office Director, ODE V
Dr. Hon-Sum Ko, Medical Reviewer , HFD-540
Dr. Amy Nostrandt, Pharm-Tox Reviewer, HFD-540
Dr. William Timmer, Chemistry Reviewer, HFD-540
Dr. Dennis Bashaw. Biopharmaceutics Team Leader, HFD-
Dr. Mohamed Al-Osh, Biostatistics Team Leader, HFD-540
Dr Sandra Kweder, Deputy Office Director, ODE IV
Dr. Allen Brinker, Epidemiologist, Office of Postmarketing Drug Risk Assessment II, HFD-430
Dr. Julie Beitz, M.D. Division Director, Office of Postmarketing Drug Risk Assessment II, HFD-430
Dr. Dianne Kennedy,
Dr. Anne Trontell,
Hollie Hamitlton
Patrick Guinn, Project Manger, HFD-
Mary-Jean Kozma-Fornaro,
Kalyani Bhatt, Project ManagerHFD-540

Purpose: To discuss the issues regarding the need — for topical tazarotene products and other topical retinoids

Background: The Division met with different members of the FDA to discuss —. This division consulted OPDRA for NDA 21-184, tazarotene creams, on —. Dr. Brinker, the OPDRA Reviewer, submitted his report on 7/24/00.

Discussion at the Meeting:
1. Dr. Brinker discussed that the strength of the animal studies would suggest initiation of a Tazarotene Exposure Cohort with — Since the data do not include actual human teratogenicity, it is ethically acceptable to discourage pregnancy during conduct of a Tazorac Exposure Cohort with —. He recommended that there could be 1) — 2) The sponsor may support a Tazorac

Pregnancy Prevention Program; this program could be similar to STEPS program. 3) Use of Teratogen Information Services (TIS).

2. It was noted that with Tazarotene Cream use, there have been no pregnancies reported, but with Tazarotene Gels, pregnancies were reported, and the information is in the label.

3. Dr. Kweder states that the aim of collection of human pregnancy data in such a case should be to evaluate that actual risk of birth defects associated with topical administration, so that the consumer can have better decision making upon inadventent esposure in pregnancy.

4. Dr. DeLap is concerned that collection of such data may run the risk of being exculpatory. Dr. Kweder points out that risks are often overestimated by the consumer, even when the language used is in an attempt to allay untoward fear.

5. Dr. Brinker asked whether human pregnancy data may be used to change pregnancy category. Such a change is not anticipated, even if clean pregnancy data may be available. Dr. Kweder notes that the pregnancy labeling rules will be changed.

6. The need to tie pregnancy registry in with approval of the NDA was discussed.

7. The need to address other topical retinoids was discussed. Dr. Kweder suggested the model of antiviral drugs. Another suggestion was to have a centralized Registry for all pharmaceutical companies that could pool all information. The Agency is actually considering such centralized registries, an issue being discussed with the CDC. Dr. DeLap wondered what may incentivize other firms to participate, and Dr. Kweder stated that incorporation of the data into the label would be a big incentive.

8. Dr. Wilkin summarized the actions to be taken:
a) talk to Allergan and
b) talk to other companies to decorate the teratogenic effects subsection with human pregnancy outcomes.

Signature, minutes preparer:_____

Concurrence Chair (or designated signatory):_____

cc:

NDA 21-184
HFD-540 Div File
HFD-540/Wilkin
HFD-540/Bhatt
Drafted: 8-2-00

MEMORANDUM OF MEETING

FILEABLE MEETING CHECKLIST

NDA 21-184

TAZORAC (tazarotene topical cream) 0.05% & 0.01%

November 22, 1999

Indication: Treatment of plaque psoriasis
Sponsor: Allergan, Inc
Type: 3S
Filing Date: November 29, 1999
Regulatory Due Date:
User Fee Date: 7-31-00 (10 month)

FILEABILITY

On initial overview of the NDA application:

PROJECT MANAGEMENT:

(1) Do any of the following apply to this application (i.e., if YES , the application MUST BE REFUSED TO FILE under 314.101 (e) and there is no filing over protest):

(a) Is the drug product already covered by an approved application?
NO.

(b) Does the submission purport to be an abbreviated application under 314.55; however the drug product is not one for which FDA has made a finding that an abbreviated application is acceptable under 314.55(b)?
NO.

(c) Is the drug product subject to licensing by FDA under the Public Service Act and Subchapter F of Chapter I of Title 21 of the CFR?
NO.

(2) Do any of the following apply to this application (i.e., if NO, the application MAY BE REFUSED TO FILE under 314.101(d) and there is the potential for filing over protest):

(a) Does the application contain a completed application form as required? under 314.50 or 314.55?
YES.

(b) On its face, does the application contain the sections of an application? required by regulation and Center guidelines?
YES. (Clinical, Biopharm, Statistics, Microbiology, Pharm/Tox, Chemistry)

(c) Has the applicant submitted a complete environmental assessment, which addresses each of the items specified in the applicable format under 25.31 or has the applicant submitted evidence to establish that the product is under 25.24 of the CFR? **THE APPLICANT IS REQUESTING CATAGORICAL EXCLUSION VOLUME 2, PAGE 074.**

(d) On its face, is the NDA formatted in compliance with Center guidelines including integrated efficacy and safety summaries?
YES. INTEGRATED SUMMARY OF EFFECTIVENESS IS LOCATED IN VOLUME 82, PAGE 91 AND THE INTEGRATED SUMMARY OF SAFETY IS LOCATED IN VOLUME 83, page 004 OF THE NDA.

(e) Is the NDA indexed and paginated?
YES.

(f) On its face, is the NDA legible?
YES.

(g) Has the applicant submitted all required copies of the submission and various sections of the submission?
NO. THERE WAS NO DESKCOPY FOR THE MICROBIOLOGY.

(h) Has the sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?
YES. THE STATEMENT IS THAT MOST STUDIES WERE CONDUCTED UNDER GLP's. THIS IS APPROPRIATE, AS NONCLINICAL PHARMACOLOGY AND ADME STUDIES DO NOT HAVE TO BE CONDUCTED UNDER GLP's.

(i) Does the application contain a statement that all nonclinical laboratory studies were conducted in compliance with the requirements set forth in Part 58 or a statement why a study was not conducted in compliance with those requirements?
YES. STATEMENT LOCATED IN APPENDIX B. BEGINNING OF EVERY FINAL STUDY

(j) If required, has the applicant submitted carcinogenicity studies?
NO. CARCOGENICITY STUDIES FOR THE DRUG SUBSTANCE HAVE BEEN REVIEWED WITH NDA 20-600 FOR TAZAROTENE GELS.

(k) On its face, does the application contain at least two adequate and well-controlled clinical trials? **YES, VOLUME 1 SECTION 5, 16 C STUDY VOLUME 18 PG 015, 17 C STUDY VOLUME 50 PAGE 136.**

(l) Does the application contain a statement that all clinical trials were conducted in accord with the IRB/Declaration of Helsinki provisions of the CFR?
YES. LOCATED IN VOLUME 18 PAGE 015 , FOR EACH CLINCAL STUDY REPORT THERE IS THE STATEMENT.

(m) Have all articles/study reports been submitted whether in English or translated into English?
YES. ALL OF THE ARTICLES HAVE BEEN SUBMITTED IN ENGLISH.

(n) Has the applicant submitted draft labeling in compliance with 210.56 and 210.57 of the CFR?
YES, LOCATED IN VOLUME 1.1 PAGE 168

(o) Has the applicant submitted the required DEBARMENT notice?
YES. LOCATED IN VOLUME 1, PAGE 139.

(p) Has the applicant submitted copies of all package inserts (or their equivalent) from all countries in which this product has been previously approved for marketing? Have all non-English package inserts been translated?
NOT APPLICABLE.

(q) Has the applicant stated that the integrated summary of safety includes all safety data for this product of which they are aware from all sources, domestic and foreign? What is the cut-off date for the preparation of the ISS?
AUGUST 18, 1999 IS THE CUT OFF DATE

(r) If this is a CANDA submission, has the applicant submitted a statement to the archival NDA that the text, tables, and data in the CANDA and the archival hardcopy NDA are identical? If they are not identical, is there a letter to the archival NDA that specifies distinctly ALL of the differences in the two submissions?
NO APPLICABLE.

- Pediatric Use Section: Has the sponsor requested Pediatric Exclusivity? No. If no, did the sponsor request a waiver? **YES, THE SPONSOR HAS REQUESTED A WAIVER FOR PEDIATRIC EXCLUSIVITY. VOLUME 1.1 PAGE 141**

- Financial Disclosure: Has the sponsor included form 3454 (3/99)
YES. VOLUME 1.1 PAGE 142

- Does the sponosr have a patient package insert? yes