CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-748

CHEMISTRY REVIEW(S)

U.S. Food and Drug Administration — Office of New Drug Chemistry

DIVISION OF DERMATOLOGIC AND DENTAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

JAN 19 2000

NDA #: 20-748 CHEM.REVIEW #: 2 REVIEW DATE: January 10, 2000

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	16-JUL-97	18-JUL-97	20-JUL-97
AMENDMENT/BC	19-SEP-97	23-SEP-97	24-SEP-97
AMENDMENT/BC	20-OCT-97	21-OCT-97	21-OCT-97
AMENDMENT/BC	05-NOV-97	06-NOV-97	07-NOV-97
AMENDMENT/AZ	07-SEP-99	08-SEP-99	09-SEP-99

NAME & ADDRESS OF APPLICANT:

Galderma Laboratories, Inc.
3000 Alta Mesa Blvd.
Suite 300
Fort Worth, TX 76133

Christine Shank
Sr. Director, Regulatory Submissions
(817) 263-2676

DRUG PRODUCT NAME

Proprietary: Differin
Nonproprietary/USAN: Adapalene
Code Names/#'s: C.I.R.D. Galderma: CD 271

Chemical Type: 3
Therapeutic Class: S

PHARMACOLOGICAL INDICATION: acne vulgaris

DOSAGE FORM: cream
STRENGTHS: 0.1% (1 mg/g)
ROUTE OF ADMINISTRATION: topical
DISPENSED: X R_x _____ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

- 6-[3-(1-Admantyl)-4-methoxyphenyl]]-2-naphthoic acid

CONSULTS: None, no tradename needed; marketed product.

REMARKS/COMMENTS: None

CONCLUSIONS & RECOMMENDATIONS:

The application is recommended for an APPROVAL under section 505 of the FFD&C Act.

/S/

William C. Timmer, Ph.D.

cc: Orig. NDA 20-748
HFD-540/Division File
HFD-540/WTimmer/January 19, 2000
HFD-540/ChemTmLdr/WHDeCamp
HFD-540/MO/PHuene
HFD-540/MO-TL/SWalker
HFD-540/PharmTox/DMainigi
HFD-540/PharmToxTL/AJacobs
HFD-540/CSO/OCintron
HFD-160/Micro/VGreenman
HFD-160/MicroTL/PCooney

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DIVISION OF DERMATOLOGIC AND DENTAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

MAY [illegible]

NDA #: 20-748 CHEM.REVIEW #: 1 REVIEW DATE: 04-MAY-98

SUBMISSION/TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	16-JUL-97	18-JUL-97	20-JUL-97
AMENDMENT/BC	19-SEP-97	23-SEP-97	24-SEP-97
~~AMENDMENT/BC~~	~~05-OCT-97~~	~~05-OCT-97~~	~~03-OCT-97~~ WCT.
AMENDMENT/BC	20-OCT-97	21-OCT-97	21-OCT-97
AMENDMENT/BC	05-NOV-97	06-NOV-97	07-NOV-97

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Therapeutic Class: S

ANDA Suitability Petition/DESI/Patent Status: N/A

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- [illegible]

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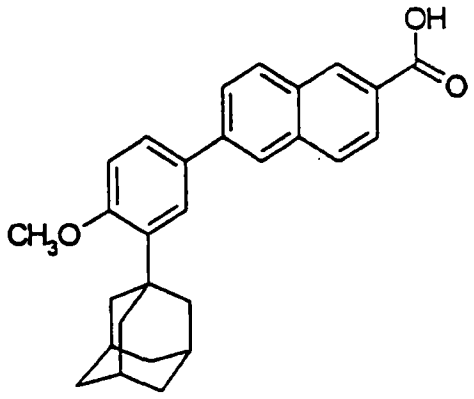

Molecular Formula: $C_{28}H_{28}O_3$

Molecular Weight: 412.53 g/mol

CAS Number: 106685-40-9

REMARKS/COMMENTS: None

CONCLUSIONS & RECOMMENDATIONS:

The application is recommended for an APPROVAL action under section 505 of the FFD&C Act.

Specific information requests are:

- **Regarding the Drug Substance**: The sponsor should develop and report impurity specifications; that is, impurity specifications should be part of *both* the analytical testing program and the stability program for the drug substance.
- **Regarding the Drug Product Components/Composition:**
- **Regarding Specifications and Analytical Methods:** Not all
- **Regarding In-Process Controls and Tests:**

- **Regarding Regulatory Specifications and Tests**: The applicant should develop a test for content uniformity, with s [redacted] A test for content uniformity of the drug product, with [redacted] should be developed.

- **Regarding Stability**: The applicant has not specified the humidity at which the current stability data was obtained. Relative humidity should be included in all future stability submissions. In addition, a test should be developed to measure content unforminity at all stability time points.

/S/

William C. Timmer, Ph.D.

cc: Orig. NDA 20-748
HFD-540/Division File
HFD-540/WTimmer/15-Nov-97
HFD-540/ChemTmLdr/WHDeCamp
HFD-540/MO/PHuene
HFD-540/Pharm/DMainigi
HFD-540/CSO/OCintron
HFD-160/Micro/VGreenman

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