NDA 16-831/S-031

Betty C. Holland
Senior Manager
Drug Regulatory Affairs
Hoffmann-La Roche
Roche Dermatologics
340 Kingsland Street
Nutley, New Jersey 07110-1199

AUG 5 1993

Dear Ms. Holland:

Please refer to your supplemental New Drug Application (NDA) dated April 23, 1993, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Efudex (fluorouracil) Topical Solutions and Creams.

We also acknowledge receipt of your submission dated May 13, 1993.

The supplemental application provides for revisions and directions for testing for Efudex Topical Solution, 2% and 5%.

We have completed our review of this supplemental application, as amended, and it is approved effective as of the date of this letter.

This approval affects only those changes specifically submitted in this supplemental application. Other changes that may have been approved or are pending evaluation are not affected.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for an approved NDA.

Sincerely yours,

/S/ 8/3/93

Wilson H. De Camp, Ph.D.
Supervisory Chemist
Division of Anti-Infective Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc: Orig: NDA 16-831/S-031
HFD-520
HFD-520/Browder
HFD-520/Mokhtari-Rejali
td:7/19/93/n16831.s31

/S/ 8/3/93

HFD-130/JAllen
HFD-520/Lumpkin (reading file)
HFD-521/Cook
init. by SUPVCHEM/7/12/93
APPROVED

JUL 8 1993

NDA SUPPLEMENT REVIEW

CHEMIST'S REVIEW	1. **ORGANIZATION** DAIDP (HFD-520)	2. **NDA NUMBER** 16-831

3. **NAME & ADDRESS OF APPLICANT**
Hoffman-La Roche
Roche Dermatologics
340 Kingsland Street
Nutley, NJ 07110

4. **AF NUMBER**

5. **SUPPLEMENT(s) NUMBER(s) DATE(s)**
SCS-031
4/23/93

6. **NAME OF DRUG**
Efudex Topical Solution

7. **NONPROPRIETARY NAME**
5-Fluorouracil

8. **SUPPLEMENT(s) PROVIDES FOR:**
SCS-031, revised specifications and direction for Efudex topical solution, 2% & 5%, and revised stability testing.

9. **AMENDMENTS AND OTHER (REPORTS, etc.) DATES**
Amendment 5/13/93

10. **PHARMACOLOGICAL CATEGORY**
Chemotherapeutic

11. **HOW DISPENSED**
XXX
Rx OTC

12. **RELATED IND/NDA/DMF(s)**

13. **DOSAGE FORM(s)**
Topical Solution

14. **POTENCY(ies)**
2% & 5%

15. **CHEMICAL NAME AND STRUCTURE**
USP

	Yes	No

17. **COMMENTS** SPECIAL SUPPLEMENT--CHANGES BEING EFFECTED ON MAY 5, 1993. These revisions are similar to those described in SCS-030 for **Efudex Topical Cream, 5%** and revised stability testing for that product. The following revisions to the specifications and directions for testing for **Efudex Topical Solutions 2% and 5%** are provided:

stability protocol. The results of these tests will only be reported; no specific limits have been established.

Copies of the revised specifications and directions for testing and the revised methodology for Stability Testing for Efudex Topical Solution, 2% and 5% are provide, see Appendix I). Minor changes have being made; the specifications are acceptable. The microbiology purity and preservative effectiveness should be reviewed by Microbiologist. Thus, the approval letter should be concurrent with Micro. Review.

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18. **CONCLUSIONS AND RECOMMENDATIONS:**
Recommend approval letter should be handed by the CSO. For convince, a Draft is attached.

cc: Orig: NDA 16-831
HFD-520
HFD-520/MO/Sanders
HFD-520/Pharm/Browder
HFD-520/Micro/Sheldon
HFD-520/CSO/Cook
HFD-520/Mokhtari
HFD-520/WHDeCamp:R/D initialed /S/ 7/8/93

19.	REVIEWER	
NAME	**SIGNATURE**	**DATE COMPLETED**
Nahid Mokhtari-Rejali, Ph.D.	/S/	7/7/93

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MICROBIOLOGY REVIEW | **1. ORGANIZATION** DAIDP (HFD-520) | **2. NDA NUMBER** 16-831

3. NAME & ADDRESS OF APPLICANT
Roche Dermatologics
340 Kingsland Street
Nutley, New Jersey 07110

4. SUPPLEMENT(s) NUMBER(s) S-031 **DATE(s)** April 23, 1993

5. NAME OF DRUG Efudex

6. NONPROPRIETARY NAME Fluoroucil

7. SUPPLEMENT(s) PROVIDES FOR:

Revised Chemistry and Microbiology specifications and directions for testing 2% and 5% solutions and revised stability testing.

8. AMENDMENTS AND OTHER (REPORTS, etc.) DATES

11. PHARMACOLOGICAL CATEGORY
Antineoplastic

10. HOW DISPENSED
XXX
Rx OTC

11. RELATED IND/NDA/DMF(s)

12 DOSAGE FORM(s)
Topical solution

13. POTENCY(ies)
2% and 5%

14. CHEMICAL NAME AND STRUCTURE
CAS Registry No. 51-21-8

15. COMMENTS
This drug is the subject of a compendial monograph, USP XXII, pg. 583.

18. CONCLUSIONS AND RECOMMENDATIONS

The supplement provides for revised specifications for reporting the specific results of testing for *Pseudomonas aeruginosa* and *Staphylococcus aureus* in 2% and 5% test solutions. These revisions are similar to those described in the approved Supplement (SCM-030) for testing 5% cream preparation.

Considering the rationale provided by the applicant, I recommend approval of the supplement. Since there are numerous Chemistry issues to be reviewed, the Reviewing Chemist is to issue the approval letter.

cc: Orig: NDA 16-831/SCS-031
HFD-130/J Allen HFD-520
HFD-520/CH/Mokhtari-Rejali
HFD-520/CSO/Cook
HFD-520/MI/Soprey HFD-520/MO
HFD-520/PH/ HFD-520/ATS Init. 7/5/93

19. NAME Pandu R. Soprey, Ph.D.

REVIEWER SIGNATURE /S/

DATE COMPLETED June 28,1993