

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 20-985

CHEMISTRY REVIEW(S)

OCT 25 2000

DIVISION OF DERMATOLOGIC AND DENTAL DRUG PRODUCTS
HFD-540

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-985 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 25-OCT-2000

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	28-OCT-1999	29-OCT-1999	16-OCT-2000
AMENDMENT/BC	18-JAN-2000	20-JAN-2000	16-OCT-2000
AMENDMENT/BC	09-JUN-2000	12-JUN-2000	16-OCT-2000
AMENDMENT/BC	26-JUN-2000	27-JUN-2000	16-OCT-2000
AMENDMENT/BC	14-JUL-2000	26-JUN-2000	16-OCT-2000
AMENDMENT/BC	23-OCT-2000	24-OCT-2000	23-OCT-2000

NAME & ADDRESS OF APPLICANT:

Dermik Laboratories, Inc.
500 Arcola Road
P.O. Box 1200
Collegeville, PA 19426-0107

James P. Thompson,
Manager, Worldwide Regulatory Affairs

DRUG PRODUCT NAME

Proprietary:

Nonproprietary/USAN:

Code Names/ #'s:

Chemical Type/

Therapeutic Class:

Fluorouracil

Fluorinated nucleoside

Antimetabolite

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

PHARMACOLOGICAL CATEGORY/INDICATION:

DOSAGE FORM:

STRENGTHS:

ROUTE OF ADMINISTRATION:

DISPENSED:

Cream

0.5%

Topical

Rx OTC

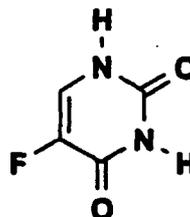
CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT.:

5-Fluoro-2,4(1H,3H)-pyrimidinedione

Molecular Formula: $C_4H_4FN_2O_2$

Molecular Weight: 130.08

CAS Number: [51-21-8]



SUPPORTING DOCUMENTS:

No. / Type	Subject	Holder	Status	Review Date	Letter Date
IND	Fluorouracil Cream	Dermik Labs., Inc.	Active	N/A	N/A
DMF			Adequate	01-MAR-2000	ADEQUATE
DMF			Adequate	24-OCT-2000	IR issued, 24-OCT-2000
DMF			Current	24-OCT-2000	ADEQUATE
DMF			Adequate	10-AUG-2000	ADEQUATE, IR Letter 16-AUG-2000
DMF			Current	Will not be reviewed.	N/A

CONSULTS:

The proposed trade name _____ was sent to the CDER OPDRA for evaluation 1/7/2000. This name was rejected, resulting in several subsequent submissions. As of the date of this review, no agreement has been reached on the trade name. If an approval action is issued, the new trade name should be submitted as a labeling supplement. See Labeling for additional details.

PATENTS:

None identified.

REMARKS/COMMENTS:

_____ (fluorouracil cream) Cream (DL-6025 cream; NDA 20-985) is used as antineoplastic, antimetabolite product for dermatological use. This product contains 0.5% 5-fluorouracil incorporated into Microsponge system, which is comprised of acrylate _____ and dimethicone.

The Microsponge™ system is a product designed by _____ which is also used for a similar product, _____ (NDA 20-475; Tretinoin microsponge gel, 0.1%).

DL-6025 Cream consists as both the 5-Fluorouracil, USP _____ and as 5-Fluorouracil in Acrylates _____, _____ in the formulation. The 5-fluorouracil Acrylates _____ consist of 5-Fluorouracil _____ w/w of the Microsponge) _____ in methyl methacrylate/ _____ glycol dimethacrylate _____ (Microsponge™) and _____ with dimethicone, as a _____ DL-6025 Cream is to be supplied in 30 g plastic tubes.

Adequate CMC information was submitted in support of the DL-6025 Cream, including 18 months stability data in support of the proposed _____ month expiration date. For a description of the CMCs, refer to Chemist Review Notes. The establishment evaluation report (EER) from the Office of Compliance found the firms responsible for the manufacturing of the finished drug acceptable for CGMPs (see EER dated 10/16/00).

The labeling was reviewed and found acceptable from a technical standpoint.

APPEARS THIS WAY
 ON ORIGINAL

NDA 20-985
TRADENAME (fluorouracil) Cream, 0.5%
Dermik Laboratories, Inc.

CONCLUSIONS & RECOMMENDATIONS:

The CMC sections for 5-Fluorouracil Cream, 0.5% are adequate. Therefore the NDA is approvable from a manufacturing and controls standpoint. The labeling was found acceptable from a technical standpoint, with the exception of the trade name issue.

[/S/] 10/25/00

Ernest G. Pappas
Review Chemist

Acknowledgments:

The Stability section was written by William C. Timmer, Ph.D.
The Investigational Formulations and Labeling sections were written by Wilson H. DeCamp, Ph.D.
DMFs were reviewed by Steve Hathaway.

cc: Orig. NDA 20-985
HFD-540/Division File
HFD-540/DivDir/JWilkin
HFD-540/ProjMgr/VLutwak
HFD-540/PharmTox/BHill
HFD-540/MedOffr/BVaughan
HFD-540/Chem/Pappas
HFD-540/Chem/Hathaway
HFD-540/ChemTeamLdr/WHDeCamp [S] 10/25/00

[/S/] 10/27/00

APPEARS THIS WAY
ON ORIGINAL

WITHHOLD 19 PAGE (S)