

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 50-756

CHEMISTRY REVIEW(S)

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

NDA #: 50-756

CHEM.REVIEW #: 2

REVIEW DATE: 21-Sep-00

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
NDA 50-756/000	09-APR-98	13-APR-98	Chem. Rev. #1
Amendment BC	29-Jun-00	30-Jun-00	05-Jul-00
Amendment BC	20-Sep-00	21-Sep-00	21-Oct-00

NAME & ADDRESS OF APPLICANT:

Dermik Laboratories, Inc.
500 Arcola Road
P.O. Box 1200
Collegeville, PA 19426-0107
ATTN: Edward J. Smith
Manager CMC
Regulatory Affairs
Telephone: (610) 454-8094
FAX: (610) 454-2283

OCT 25 2000

DRUG PRODUCT NAME

Proprietary:

Nonproprietary/USAN:

Code Names/#'s:

Chemical Type/

Therapeutic Classes:

BenzaClin Topical Gel
clindamycin phosphate &
benzoyl peroxide
DL-6021

4S

ANDA Suitability Petition/DESI/Patent Status:

Not applicable

PHARMACOLOGICAL CATEGORY/INDICATION:

Antibiotic (clindamycin phosphate)

Keratolytic (benzoyl peroxide)

Gel

Clindamycin phosphate, 1% USP

Benzoyl peroxide, 5% USP

Topical

Rx OTC

DOSAGE FORM:

STRENGTHS:

ROUTE OF ADMINISTRATION:

DISPENSED:

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

Clindamycin phosphate: Methyl-7-chloro-6,7,8-trideoxy-6-(1-methyl-trans-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-threo- α -D-galacto-octo-pyranoside-2-(dihydrogen phosphate).

Benzoyl peroxide: Dibenzoyl peroxide

Molecular Formula: clindamycin phosphate, $C_{18}H_{34}ClN_2O_8PS$

Benzoyl peroxide, $(C_6H_5CO)_2O_2$

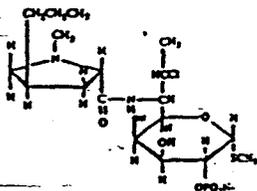
Molecular Weight: Clindamycin phosphate, 504.97

Benzoyl peroxide, 242.23

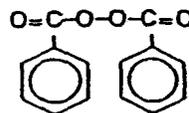
CAS No.: Clindamycin phosphate, 24729-96-2

Benzoyl peroxide, 96-36-0

Molecular Structures:



Clindamycin phosphate



benzoyl peroxide

SUPPORTING DOCUMENTS: NDA 50-756/000, the original Not Approvable NDA.
EER Summary Report dated 11-Feb-00.

CONSULTS:

Not applicable

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REMARKS/COMMENTS:

The original NDA 50-756/000 was found to be Not Approvable on April 1, 1999 because _____ the manufacturer, was found to be non-compliant with the Agency's Good Manufacturing Practice regulations. _____ used in the manufacture of the combination drug, BenzaClin Gel. Therefore the primary purpose of this major Information Amendment was to provide documentation that _____ was now GMP compliant, and secondarily, that clindamycin phosphate powder meet USP requirements. In addition, the applicant also submitted the following five CMC changes of new information for review:

1. Updated 24-month stability data extending the BenzaClin Gel's expiration date.
2. Revised drug product specifications.
3. Revised drug product labeling and proposed storage time _____
4. Discussion of plans _____
5. Revised _____

These seven CMC issues were reviewed and commented on in Chemistry Review #2. The results from this CMC review indicated the major CMC deficiency and single CMC Informational Request were corrected. All five NDA 50-756 changes and/or updates have been reviewed and all found acceptable.

CONCLUSIONS & RECOMMENDATIONS:

NDA 50-756/BC is recommended for an approval. This approval is based primarily on the reinspection and approval of the _____ manufacturing facilities and the acceptability of the CMC Informational Request. Five CMC updates and/or changes to this NDA are acceptable with a minor administrative Informational Request made on the fifth change.

The minor administrative change requested was to inform the DMF _____ Holder to submit a current listing of authorized companies and individuals to this DMF.

[/S/ 9/18/00]

James D. Vidra, Ph.D.
Review Chemist, HFD-830/HFD-540

Attachments (2)

APPEARS THIS WAY
ON ORIGINAL

- cc: Orig. NDA #50-756/BC
- HFD-540/Division File
- HFD-540/ProjMan/White
- HFD-540/Pharm/Mainigi
- HFD-540/MedOff/Huene
- HFD-540/ChemTL/DeCam

filename: N50756/BC

[/S/ 10/25/00]
[/S/ 10/27/00]

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

NDA #: 50-756 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 19-Jan-99

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
NDA 50-756/000	09-APR-98	13-APR-98	24-APR-98
BC	04-JUN-98	05-JUN-98	10-JUN-98
BC	01-Oct-98	02-Oct-98	21-Oct-98
BC	01-Oct-98	02-Oct-98	21-Oct-98
BC	01-Oct-98	05-Oct-98	21-Oct-98
BC	23-Oct-98	29-Oct-98	05-Nov-98
BC	09-Dec-98	11-Dec-98	24-Dec-98
BC	08-Jan-99	11-Jan-99	19-Jan-99
BL	20-Jan-99	26-Jan-99	29-Jan-99
BC	02-Feb-99		

TO BE REVIEWED AS SUPPLEMENT

NAME & ADDRESS OF APPLICANT:

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Worldwide Regulatory Affairs
Telephone: (610) 454-3026

DRUG PRODUCT NAME

Proprietary:

Nonproprietary/USAN:

clindamycin phosphate &
benzoyl peroxide

Code Names/#'s:

Chemical Type/

Therapeutic Classes:

4S

ANDA Suitability Petition/DESI/Patent Status: Not applicable

PHARMACOLOGICAL CATEGORY/INDICATION: Antibiotic (clindamycin phosphate)
Keratolytic (benzoyl peroxide)
Gel

DOSAGE FORM:

STRENGTHS:

Clindamycin phosphate, 1% USP
Benzoyl peroxide, 5% USP

ROUTE OF ADMINISTRATION:

Topical

DISPENSED:

X Rx OTC

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

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Benzoyl peroxide: Dibenzoyl peroxide

Molecular Formula: clindamycin phosphate, $C_{18}H_{34}ClN_2O_8PS$

benzoyl peroxide, $(C_6H_5CO)_2O_2$

Molecular Weight:

clindamycin phosphate, 504.97

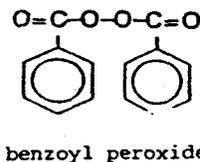
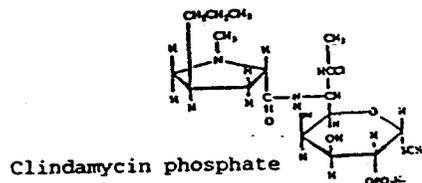
benzoyl peroxide, 242.23

CAS No.:

24729-96-2

96-36-0

Molecular Structures:



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clindamycin phosphate, 1% & benzoyl peroxide, 5%)

SUPPORTING DOCUMENTS:

CONSULTS:

Labeling & Nomenclature Committee requested on
9/22/98 (ATTACHMENT #5).
Establishment Inspection Results (ATTACHMENT #6).

REMARKS/COMMENTS:

NDA 50-756 has a 4S classification as the combination drug product,
 clindamycin 2-phosphate, 1% & benzoyl peroxide, 5%) Topical
Gel. Clindamycin 2-phosphate, USP, is a well-known antibiotic and
benzoyl peroxide, USP, an equally well-known keratolytic agent both
combined to topically treat acne vulgaris. This product is packaged in
two individual containers, e.g. a 25.0 gram polypropylene jar
containing benzoyl peroxide gel and a 10.3 ml polypropylene vial
containing clindamycin phosphate powder. The pharmacist adds five
milliliters of distilled water to the clindamycin powder mixing the two
until the antibiotic is completely dissolved. The compounder then adds
the solution to the gel and mixes thoroughly. is then
dispensed as a gel containing mg/gram as clindamycin phosphate
(labeled as 10 mg/g clindamycin or 1%) and mg/g hydrous benzoyl
peroxide (or 50.0 mg/g benzoyl peroxide or 5%). The total mixed
 gel formulation then consists of benzoyl peroxide, USP,
clindamycin phosphate, USP, carbomer NF, sodium hydroxide, NF,
dioctyl sodium sulfosuccinate, and purified water, NF.

The recommended shelf-life for the separate benzoyl peroxide gel is for
24 months at 25°C/60%RH, the for nine months at
25°C/60%RH and the combined mixture of gel and for up
to 16 weeks.

The following deficiencies and Informational Requests are recommended
for

Deficiencies:

1. The supplier,
received a WITHHOLD APPROVAL rating from OC on 8/19/98 for
multiple manufacturing deficiencies. A re-
inspection is scheduled for late March-early April.

Informational Requests:

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(clindamycin phosphate, 1% & benzoyl peroxide, 5%)



CONCLUSIONS & RECOMMENDATIONS:

NDA 50-756 is NOT RECOMMENDED FOR APPROVAL based upon the aforementioned deficiencies and informational requests.

IS/

2/10/99

James D. Vidra, Ph.D.
Review Chemist, HFD-830/HFD-540

- cc: Orig. NDA #50-756
- HFD-540/Division File
- HFD-540/ProjMan/White
- HFD-540/Pharm/Mainigi
- HFD-540/MedOff/Huene
- HFD-540/ChemSup/DeCamp
- HFD-830/ChemDir/Chen

[S/10/27/00]

filename: N50756/000

[S/10/27/00]

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