

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number NDA 50-769

CHEMISTRY REVIEW(S)

NOV 27 2000

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

NDA #: 50-769/000

CHEM.REVIEW #: 1

REVIEW DATE: 01-Nov-00

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Original	26-Jan-00	28-Jan-00	31-Jan-00
Amendment BL	25-Jul-0	27-Jul-00	01-Aug-00
Amendment BC	06-Oct-00	10-Oct-00	16-Oct-00
Amendment BC	13-Oct-00	17-Oct-00	30-Oct-00
Fax on Telecon Minutes	24-Oct-00	24-Oct-00	NA
Amendment BC	27-Oct-00	30-Oct-00	30-Oct-00

NAME & ADDRESS OF APPLICANT:

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Worldwide Regulatory Affairs
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DRUG PRODUCT NAME

Proprietary:

Benzamycin Pak

Nonproprietary/USAN:

Erythromycin & Hydrous Benzoyl
Peroxide

Code Names/#'s:

DL-6026

Chemical Type/

CAS# 94-36-0, Hydrous Benzoyl Peroxide

CAS# 114-07-8, Erythromycin Base

Therapeutic Classes:

3S

ANDA Suitability Petition/DESI/Patent Status: NOT APPLICABLE!

PHARMACOLOGICAL CATEGORY/INDICATION: Topical treatment of acne vulgaris.

DOSE FORM:

Intranasal Spray Gel

STRENGTHS:

3% Erythromycin, USP

5% Benzoyl Peroxide, USP

ROUTE OF ADMINISTRATION:

Nasal

DISPENSED:

Rx OTC

CHEMICAL NAMES, STRUCTURAL FORMULA, MOLECULAR FORMULA,

MOL.WT:

Erythromycin[(3R,4S,5S,6R,7R,9R,11R,12R,13S,14R)-4-[(2,6-dideoxy-3-C-methyl-3-O-methyl-a-L-ribo-hexopyranosyl)-oxy]-14-ethyl-7,12,13-trihydroxy-3,5,7,9,11,13-hexa-methyl-6-[[3,4,6-trideoxy-3-(dimethylamino)-b-D-xylo-hexopyranosyl]oxy]oxacyclotetradecane-2,10-dione].

Benzoyl peroxide

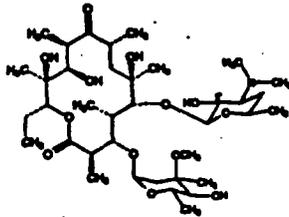
Benzamycin Pak® (erythromycin, 3%, & benzoyl peroxide, 5%) Gel

MOLECULAR FORMULAS:

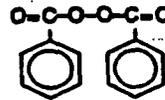
Erythromycin,	$C_{37}H_{67}NO_{13}$
Benzoyl peroxide.	$C_{14}H_{10}O_4$

MOLECULAR WEIGHTS:

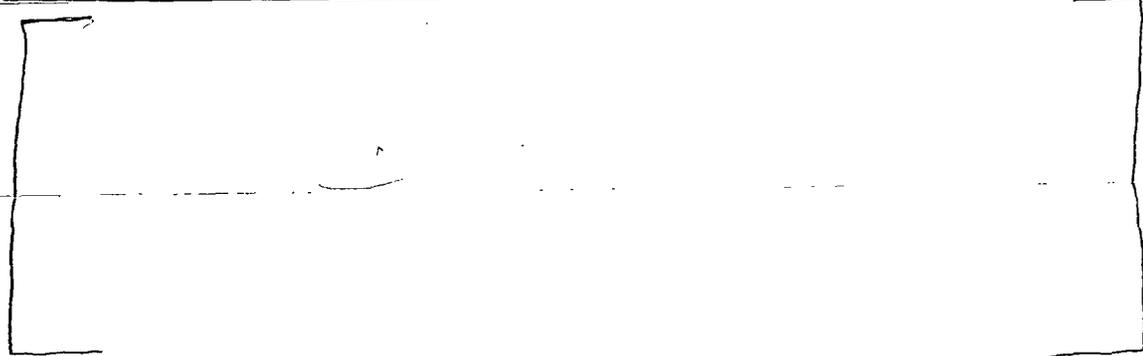
Erythromycin,	733.94
Benzoyl peroxide,	242.23

STRUCTURAL FORMULATIONS:

Erythromycin A



Benzoyl Peroxide

SUPPORTING DOCUMENTS:**REMARKS/COMMENTS:**

_____ was developed as a line extension to Benzamycin Topical Gel (NDA 50-557) therefore the applicant's strategy was to retain as much of the formulation as possible while converting the product into a two component product. The two components are _____ erythromycin gel and _____ benzoyl peroxide gel. Both drug substances are USP therefore Benzamycin Pak is a combination drug product. The Erythromycin, USP, is manufactured by the _____ while benzoyl peroxide is made by the _____. The drug product manufacturer was the _____.

Each component was packaged individually into a single use, dual dispensing, laminate pouch to achieve long-term stability thus stability and packaging became the major issues in this review. The primary stability issue was the _____ erythromycin gel. A number of erythromycin formulations were developed until _____ was identified that was stable for _____.

**APPEARS THIS WAY
ON ORIGINAL**

Benzamycin Pak® (erythromycin, 3%, & benzoyl peroxide, 5%) Gel

The container closure system was novel due to its dual dispensing, foil laminated, multi-layer designed pouch. Each chamber houses 0.425 grams of either the erythromycin or benzoyl peroxide gel for a total weight of 0.85 grams with the two chambers filled and available in a 60 count carton. The combined Benzamycin Pak drug product is stable for 18 months at 25°C/60%RH. The erythromycin in its gel component became unstable beyond 18 months in its current formulation. Therefore unless a new more stable formula is developed, no extension to this expiration date is possible.

Minor Information Requests were telephoned to the applicant on specifications and in-process controls with the requests granted.

A Phase IV CMC commitment requested a Flash Point or Flammability Study to be conducted on the — erythromycin gel containing — alcohol.

CONCLUSIONS & RECOMMENDATIONS:

The original NDA 50-769/000 for the Benzamycin Pak is RECOMMENDED FOR APPROVAL with the qualification that a Phase IV commitment be made to conduct a FlashPoint Study on the — Erythromycin Gel.

James D. Vidra, Ph.D.
Review Chemist

**APPEARS THIS WAY
ON ORIGINAL**

cc: Orig. NDA# 50-769
HFD-540/Division File
HFD-540/DivDir/Wilkin
HFD-540/ProjMan/Cross
HFD-540/MedOff/Vaughn
HFD-540/PharmTox/Brown
HFD-540/Chem/Vidra
HFD-540/TeamLdr/DeCamp — 11/27/00
HFD-830/DivDir/Chen

filename: N50769.000

11/27/00