

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER: 20-965

CHEMISTRY REVIEW(S)

DIVISION OF DERMATOLOGIC AND DENTAL DRUG PRODUCTS
HFD-540

JUN 16 1999

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-965 CHEM. REVIEW #: 1 REVIEW DATE: 10-JUN-1998

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	01-JUL-1998	03-JUL-1998	09-JUL-1998
AMENDMENT/BL	16-APR-1999	19-APR-1999	07-MAY-1999

NAME & ADDRESS OF APPLICANT: DUSA Pharmaceuticals, Inc. -
400 Columbus Avenue
Valhalla, NY 10595

Agent: Guidelines, Inc.
10320 USA Today Way
Miramar, FL 33025

DRUG PRODUCT NAME

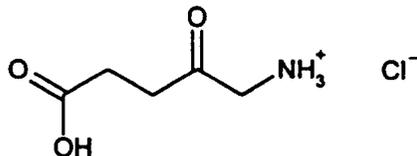
Proprietary: LEVULAN®
Nonproprietary/USAN: aminolevulinic acid hydrochloride
Code Names/ #'s: ALA, 5-ALA, 5-ALA HCl, S-
Chemical Type: amino acid salt
Therapeutic Class: 1 S

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

PHARMACOLOGICAL CATEGORY/INDICATION: Topical treatment of actinic
keratoses in conjunction with a
blue light illuminating device.

DOSAGE FORM: Solid for topical solution
STRENGTHS: 20%
ROUTE OF ADMINISTRATION: Topical
DISPENSED: Rx OTC

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



Chemical Name: 5-aminolevulinic acid hydrochloride
Mol. Formula: C₅H₉NO₃•HCl
Mol. Weight: 167.59
CAS No. [5451-09-2]
Melting Pt.: 151-156°C (decomp.)
pH (aq.): 1.77 (1:5 aqueous solution)
pK_a: 3.816
Solubilities: freely soluble in water; slightly soluble in methanol,
ethanol; practically insoluble in chloroform, hexane,
mineral oil.

SUPPORTING DOCUMENTS:

DMF Type II, authorized by
letter dated 29-JUN-1998; for the manufacture of 5-amino-levulinic
acid hydrochloride. This DMF has been reviewed in conjunction with
this NDA and found to be adequate. The sponsor provided all pertinent

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DUSA Pharmaceuticals
LEVULAN® KERASTICK™ for Topical Solution, 20%

chemistry, manufacturing and control data pertaining to the drug substance in the DMF.

DMF [redacted] Type III, [redacted] letter dated June 14, 1996, signed by [redacted] for the manufacture of tubular containers made from [redacted]

DMF [redacted] Type III, [redacted] authorized by letter dated 12-APR-1996, signed by [redacted] for the manufacture of [redacted] Low Density Polyethylene resin.

DMF [redacted] Type I, Guidelines Analytical Laboratories, Inc., authorized by letter dated 29-JUN-1998, signed by Sam Swetland; for the facilities, personnel and procedures used by this contract lab and agent.

RELATED DOCUMENTS:

Patents:

IND [redacted] for 5-ALA solution, 10%; active in HFD-540.

The following patents are claimed for the drug or method of use of the drug:

U.S. Patent No. 5,079,262, expiration date 28-JUL-2009, owned by Queens University at Kingston and assigned exclusively to DUSA Pharmaceuticals, Inc. for method of use of LEVULAN for topical treatment of actinic keratoses.

U.S. Patent No. 5,211,938, expiration date 18-MAY-2010, owned by Queens University at Kingston and assigned exclusively to DUSA Pharmaceuticals, Inc. for method of use of LEVULAN for topical treatment of actinic keratoses.

U.S. Patent No. 5,422,093, expiration date 28-JUL-2009, owned by Queens University at Kingston and assigned exclusively to DUSA Pharmaceuticals, Inc. for method of use of LEVULAN for topical treatment of actinic keratoses.

Appendices:

1. Manufacturing process flowchart, 7 pages.
2. [redacted] applicator tip schematic drawing, 1 page.
3. Microbiology consultation reviews, 11 pages.
4. Draft package insert incorporated changes, 17 pages.
5. Draft carton and applicator labels, 9 pages.
6. Stability program summary table, 2 pages.
7. Investigational formulation and clinical trial summary tables, 5 pages.
8. Report from Joint Pre-approval inspection, 15 pages.
9. Establishment Inspection Report, 2 pages.

CONSULTS:

The proposed trade name "LEVULAN KERASTICK" was submitted to the Labeling and Nomenclature Committee (LNC) on 04-JUN-1999 through Chairman Dan Boring, Ph.D. (HFD-530).

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LEVULAN® KERASTICK™ for Topical Solution, 20%

CONCLUSIONS & RECOMMENDATIONS:

NOT APPROVABLE

Based on the review of the chemistry, manufacturing and controls information presented in the NDA, and the inspections of the manufacturing facilities, a recommendation of "Not Approvable" is made.

JS 6/14/99
J.S. Hathaway, Ph.D.
Review Chemist

cc: Orig. NDA 20-965 (with all appendices)
HFD-540/DivisionFile (with all appendices)

cc: With Appendices 1 and 2 only:

HFD-540/Chem/JSHathaway

HFD-540/ChemTeamLdr/WHDeCamp

HFD-540/DivDir/JWilkin

HFD-830/DivDir/CWChen

HFD-540/MedOffr/MOKun

HFD-540/PharmTox/LReidd

HFD-540/ProjMgr/OCintron

HFD-805/Micro/PCooney

HFD-805/Micro/BRiley

HFD-/BioPharm/DBashaw

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JS 6/17/99

APPEARS THIS WAY
ON ORIGINAL

DIVISION OF DERMATOLOGIC AND DENTAL DRUG PRODUCTS DEC 2 1999

HFD-540

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-965 **CHEM. REVIEW #:** 2 **REVIEW DATE:** 02-DEC-1999

<u>SUBMISSION/TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	01-JUL-1998	03-JUL-1998	Review #1
AMENDMENT/BL	16-APR-1999	19-APR-1999	Review #1
AMENDMENT/NC	28-JUL-1999	29-JUL-1999	08-AUG-1999
AMENDMENT/AZ	01-OCT-1999	04-OCT-1999	14-OCT-1999
AMENDMENT/BC	11-OCT-1999	15-OCT-1999	22-OCT-1999
AMENDMENT/BL	11-NOV-1999	12-NOV-1999	22-NOV-1999

NAME & ADDRESS OF APPLICANT: DUSA Pharmaceuticals, Inc.
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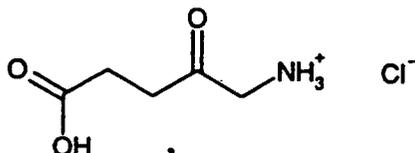
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<u>Nonproprietary/USAN:</u>	aminolevulinic acid hydrochloride
<u>Code Names/#'s:</u>	ALA, 5-ALA, 5-ALA HCl, S-
<u>Chemical Type/</u>	amino acid salt
<u>Therapeutic Class:</u>	1 S

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

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<u>DISPENSED:</u>	<input checked="" type="checkbox"/> Rx <input type="checkbox"/> OTC

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LEVULAN® KERASTICK™ for Topical Solution, 20%

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pK_a: 3.816

SUPPORTING DOCUMENTS:

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REMARKS

Amendments and correspondence covered in this review were received as follows:
7/29/99: Comparison of USP and EP specifications for Purified Water
10/4/99: Complete response to 6/27/99 action letter
10/15/99: Amendment of DMF [redacted]
11/12/99: Revision of package insert

CONCLUSIONS & RECOMMENDATIONS:

APPROVAL

Based on the review of the chemistry, manufacturing and controls information presented in the NDA and the subsequent amendments listed above, a recommendation of "Approval" is made.

[redacted] /S/ 12/2/99

J. S. Hathaway, Ph.D.
Review Chemist

cc: Orig. NDA 20-965
HFD-540/DivisionFile
HFD-540/Chem/JS Hathaway
HFD-540/ChemTeamLdr/WHDeCamp
HFD-540/DivDir/JWilkin
HFD-830/DivDir/CWChen
HFD-540/MedOffr/MOkun
HFD-540/PharmTox/LReid
HFD-540/ProjMgr/OCintron
HFD-805/Micro/PCooney
HFD-805/Micro/BRiley
HFD-/BioPharm/DBashaw

[redacted] /S/ 12/2/99
[redacted] /S/ 12/2/99

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