

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

75014

CHEMISTRY REVIEW(S)

APPROVAL PACKAGE SUMMARY FOR 75-014

ANDA: 75-014

FIRM: Alpharma, U.S. Pharmaceutical Division

DRUG: Permethrin

DOSAGE: Lotion

STRENGTH: 1%

CGMP STATEMENT/EIR UPDATE STATUS: EER is acceptable 5/12/99

BIO STUDY/BIOEQUIVALENCE STATUS: Bio is satisfactory 9/29/99

METHODS VALIDATION: methods validation is acceptable 9/28/99

STABILITY: The firm has provided satisfactory 3 months accelerated stability data at 40°C/75%RH, 30°C/60%RH and 25°C/60%RH. The stability samples will be stored horizontal and upright.

LABELING REVIEW STATUS: Labeling is satisfactory 10/20/99

STERILIZATION VALIDATION: N/A

BATCH SIZES: The firm has provided the master formula and manufacturing procedure for intended production batch kg, and a copy of the exhibit batch lot #600/524-L565 for kg. The firm will use the same drug substance supplier, same manufacturing procedure, and same equipment.

COMMENTS: The Application is Approvable.

REVIEWER: Nashed E. Nashed, Ph.D.

DATE: 3/8/00

SUPERVISOR: Paul Schwartz, Ph.D.

3/16/00

ps 3/12/00

1. CHEMISTRY REVIEW NO. 1

2. ANDA # 75-014

3. NAME AND ADDRESS OF APPLICANT

Alpharma, U.S. Pharmaceutical Division
333 Cassell Dive, Suite 3500
Baltimore, MD 21224

4. LEGAL BASIS FOR SUBMISSION

The reference listed drug, Nix Crème Rinse (NDA #19-918) is entitled to a period of marketing exclusivity until November 1, 1999. Alpharma does not intend to introduce product into the marketplace prior to the expiration of this exclusive marketing period.

5. SUPPLEMENT(s)

Original 12/3/96

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Permethrin Lotion

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

Amendment 12/30/98

10. PHARMACOLOGICAL CATEGORY

Treatment of head lice

11. Rx or OTC

OTC

12. RELATED IND/NDA/DMF(s)

DMF's [

]

13. DOSAGE FORM

Lotion

14. POTENCY

1%

15. CHEMICAL NAME AND STRUCTURE

Generic name: Permethrin

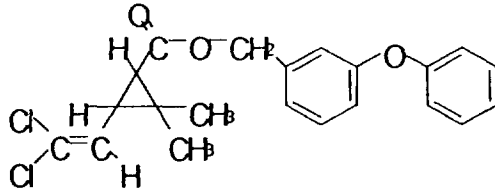
Chemical name: Cyclopropanecarboxylic acid, 3-(2,2-dichloroethyl)-2,2-dimethyl-, (3-phenoxyphenyl)methyl ester

Chemical formula: C₂₁H₂₀Cl₂O₃

Molecular weight: 391.29

CAS number: 52645-53-1

Chemical structure:



16. RECORDS AND REPORTS

17. COMMENTS

Please justify the reason for having % overage of the drug substance in your formulation.

Please revise your specifications for the drug substance to include test and specification for the residual solvents.

Please revise the bulk specifications to include limits for Viscosity and blend uniformity assay.

Please provide limit of quantitation and limit of detection for your method for determination of permethrin in permethrin crème rinse 1%.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER: DATE COMPLETED:

Nashed E. Nashed, Ph.D. 5/6/99

Supervisor: Paul Schwartz, Ph.D.

cc: ANDA 75-014
Division File
Field Copy

Endorsements:

HFD-627/NNashed/5/6/99, *5/24/99*
HFD-627/PSchwartz/5/19/99

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Chem #1

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 75-014

3. NAME AND ADDRESS OF APPLICANT

Alpharma, U.S. Pharmaceutical Division
333 Cassell Dive, Suite 3500
Baltimore, MD 21224

4. LEGAL BASIS FOR SUBMISSION

The reference listed drug, Nix Crème Rinse (NDA #19-918) is entitled to a period of marketing exclusivity until November 1, 1999. Alpharma does not intend to introduce product into the marketplace prior to the expiration of this exclusive marketing period.

5. SUPPLEMENT(s)

Original 12/3/96

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Permethrin Lotion

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

Amendment 12/30/98 - response to refuse to file
Amendment 7/16/99 - Fax amendment
Amendment 9/29/99 - Labeling amendment
Amendment 10/21/99 - Telephone amendment
Amendment 12/1/99

10. PHARMACOLOGICAL CATEGORY

Treatment of head lice

11. Rx or OTC

OTC

12. RELATED IND/NDA/DMF(s)

DMF's

13. DOSAGE FORM

Lotion

14. POTENCY

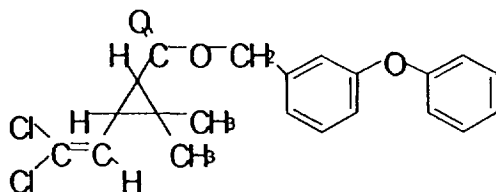
1%

15. CHEMICAL NAME AND STRUCTURE

Generic name: Permethrin
Chemical name: Cyclopropanecarboxylic acid, 3-(2,2-dichloroethyl)-2,2-dimethyl-, (3-phenoxyphenyl)methyl ester
Chemical formula: C₂₁H₂₀Cl₂O₃
Molecular weight: 391.29

CAS number: 52645-53-1

Chemical structure:



16. RECORDS AND REPORTS

17. COMMENTS

Based on your December 1, 1999 submission, it is apparent that the fluorination procedure results in a new uncharacterized resin containing organically bound fluorine. You have not provided evidence that this resin has been used in an approved drug product. Please follow the container closure systems for Packaging Human Drug and Biologics Guidance for industry for the information which should be submitted to qualify the new resin. Please also perform the USP (87) Biological Reactivity tests. Please also explain why recycled fluorinated HDPE can be reused as HDPE. Also demonstrate on at least 3 lots of bottles that a consistent resin is formed. Alternatively, you may wish to use an alternate container closure system.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER:

DATE COMPLETED:

Nashed E. Nashed, Ph.D.

12/7/99

Supervisor: Paul Schwartz, Ph.D.

cc: ANDA 75-014
Division File
Field Copy

Endorsements:

HFD-627/NNashed/12/7/99 ✓

HFD-627/PSchwartz/12/9/99 ✓

12/13/99
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Chem #2

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 75-014

3. NAME AND ADDRESS OF APPLICANT

Alpharma, U.S. Pharmaceutical Division
333 Cassell Dive, Suite 3500
Baltimore, MD 21224

4. LEGAL BASIS FOR SUBMISSION

The reference listed drug, Nix Crème Rinse (NDA #19-918) is entitled to a period of marketing exclusivity until November 1, 1999. Alpharma does not intend to introduce product into the marketplace prior to the expiration of this exclusive marketing period.

5. SUPPLEMENT(s)

Original 12/3/96

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Permethrin Lotion

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

Amendment 12/30/98 - response to refuse to file
Amendment 7/16/99 - Fax amendment
Amendment 9/29/99 - Labeling amendment
Amendment 10/21/99 - Telephone amendment
Amendment 12/1/99
Amendment 2/29/00 - Minor amendment

10. PHARMACOLOGICAL CATEGORY

Treatment of head lice

11. Rx or OTC

OTC

12. RELATED IND/NDA/DMF(s)

DMF's [

]

13. DOSAGE FORM

Lotion

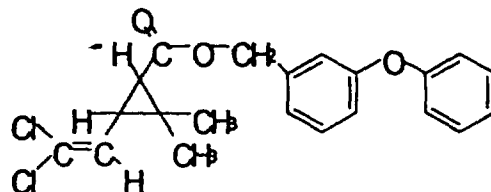
14. POTENCY

1%

15. CHEMICAL NAME AND STRUCTURE

Generic name: Permethrin
Chemical name: Cyclopropanecarboxylic acid, 3-(2,2-dichloroethyl)-2,2-dimethyl-, (3-phenoxyphenyl)methyl ester

Chemical formula: C₂₁H₂₀Cl₂O₃
Molecular weight: 391.29
CAS number: 52645-53-1
Chemical structure:



16. RECORDS AND REPORTS

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

The application is approvable.

19. REVIEWER:

DATE COMPLETED:

Nashed E. Nashed, Ph.D.

3/8/00

Supervisor: Paul Schwartz, Ph.D.

cc: ANDA 75-014

DUP

Field Copy

Division File

Endorsements:

HFD-627/NNashed/ *NN 3/26/00*
HFD-627/PSchwartz/3/16/00 *PS 3/22/00*

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