CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 73440

ADMINISTRATIVE DOCUMENTS

ANDA APPROVAL SUMMARY

ANDA:	CHEMIST:	DATE:
73-440	Naiqi Ya, Ph.D.	March 27, 1998

DRUG PRODUCT:
Desoximetasone

FIRM:
E. Fougera & Co., division of Altana Inc.

DOSAGE FORM:	STRENGTH:
Ointment	0.25%

cGMP:
EER was found acceptable on December 9, 1997.

BIO:
The Bio study was deemed satisfactory by Lin-whei Chuang on 6/10/96.

VALIDATION - *(Description of dosage form same as firm's):*
Not required - DS and DP are compendial.

STABILITY:
The containers in the stability studies are identical to those in the container section. The stability data support an expiration period of 15 months.

LABELING:
Container, carton, and insert labeling were approved by Angela Payne on 8/4/95.

STERILIZATION VALIDATION *(If applicable)*:
Not applicable.

SIZE OF BIO BATCH *(Firm's source of NDS ok?)*:
The bio batch size is and the drug substance was manufactured by

SIZE OF STABILITY BATCHES *(If different from bio batch, were they Manufactured via the same process?)*:
The size of the stability batch was The process for the stability batches differed from that for the Bio batch only in editorial ways.

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME?:
The proposed production batch sizes are . The manufacturing processes differed from that for the Bio batch only in editorial ways.

Signature of chemist:	Signature of supervisor:
3/27/98	3/27/98

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 73440

CORRESPONDENCE

fougera
Division of Altana Inc

505(j)(2)(A) ok
MBennett 11/16/89

November 8, 1989

Carl C. Peck, M.D.
Acting Director
Division of Generic Drugs
HFD-230, Room 17B-20
Office of Drug Standards
Center for Drug Evaluation & Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Re: INITIAL FILING
ABBREVIATED NEW DRUG APPLICATION
DESOXIMETASONE OINTMENT, USP 0.25%

Dear Dr. Peck:

E. Fougera & Co., a division of Altana Inc., hereby submits, in duplicate, this three volume Abbreviated New Drug Application pursuant to the provisions of Section 505(j)(2)(A) of the Federal Food, Drug and Cosmetic Act and Section 314.55 of Title 21 of the Code of Federal Regulations.

This submission is subdivided into five major sections as follows:

1. Labeling
2. Chemistry, Manufacturing and Controls
3. Environmental Impact Statement
4. Human Pharmacokinetics and Bioavailability
5. Methods Validation

Please note that a copy of labeling for the listed drug, Topicort Ointment 0.25% manufactured by Hoechst-Roussel Pharmaceuticals Inc., is included along with a Form 356H and original signature. In addition, our methods validation information is provided in triplicate and contains analytical methods and descriptive information needed to perform testing of the finished dosage form.

Sincerely,

E. FOUGERA & CO.
a division of Altana Inc.

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NOV 9 1989
GENERIC DRUGS

Andrew G. Clair, Ph.D.
Director
Regulatory Affairs

mac

fougera
Division of Altana Inc

AMENDMENT

March 21, 1990

Carl C. Peck, M.D.
Acting Director
Division of Generic Drugs
HFD-230, Room 17B-20
Office of Drug Standards
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Re: ANDA #73-440
Desoximetasone Ointment 0.025%

Dear Dr. Peck:

Reference is made to the subject application originally submitted to the Administration on November 8, 1989.

As per the Human Pharmacokinetics and Bioavailability section of the original application, we have enclosed the final report for an in-vivo randomized, double-blind controlled vasoconstriction study performed by The data shows no significant differences between the subject drug product and the innovator product (Topicort Ointment by Hoechst-Roussel).

Please add this information to the subject file.

Sincerely,

E. FOUGERA & CO.
division of Altana Inc.

Virginia Carman
Regulatory Affairs Associate

sbs
Enclosure

60 Baylis Road, Melville, N.Y. 11747 1-516-454-6996 Telex 144662

JUL 18 1990

ANDA 73-440

E. Fougera & Co.
Division of Altana, Inc.
Attention: Andrew G. Clair, Ph.D.
60 Baylis Road
Melville, NY 11747

Dear Sir:

Please refer to your abbreviated new drug application dated November 8, 1989, submitted pursuant to Section 505(j) of the Federal Food, and Drug and Cosmetic Act for Desoximetasone Ointment USP, 0.25%.

Also refer to your amendment dated March 21, 1990.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. described on pages 201-208 of the application should be provided. Also please provide complete lists of all equipment used to manufacture and test the drug product.

2. lot 02852 should be retested for and include a copy of the used to identify the drug substance as a third identification test, matching vs the USP standard), and add a test for degradation with proposed specifications for single and total degradation products.

3. A copy of the used to identify the drug substance supplied by must be included. In addition please provide a test for degradation products for the drug substance with proposed specifications for single and total degradation products.

4. Full in-house COAs using all the tests described in either the USP XXII or NF XVII monographs for White Petrolatum USP, Beeswax (called white wax in the NF) and Propylene Glycol USP should be submitted. Additional tests for Sorbitan Sesquiolate are identification, water, residue on ignition, iodine value, and assays of fatty acids and polyols. Additional tests that should be submitted for Fatty Acid Pentaerythritol Ester are: an identification test and a heavy metals test.

Finally, additional tests should be submitted for the identification of stearate and aluminum, moisture, heavy metals and an assay of Aluminum Stearate; and a complete up-to-date COA for Citric Acid USP (anhydrous).

5. A retesting protocol for active and inactive ingredients and containers as required under 21 CFR 211.87 of the regulations must be provided.

6. The sizes of the used to make lot PD8902 and the production batches should be specified. Was lot PD8902 made on pilot or production equipment? Please be specific.

7. A complete batch record from a batch made with Desoximetasone is needed. Please manufacture the batch using only full scale production equipment, and provide all in-process, yield and reconciliation data, a COA of the finished product, data from a cycle study, and three month accelerated stability data at 40°C, in both the 15 and 60 gm tubes are reguired. Please add to the COA of the finished product data and specifications for degradation. Since the product will be packaged in containers larger than 3.5 gm, it should be analyzed, while product is under stability, at the surface, middle and bottom of the container and sampled near the crimp. Please include tests and specifications for appearance, clarity, color, homogeneity, odor, pH, consistency, particle size distribution, degradation and strength. (See Guideline for Submitting Documentation for the Stability of Human Drugs & Biologics, page 17).

8. Data must be provided which shows both the caps and tubes pass USP's tests for Biological Tests - Plastics & other polymers. (page 1572 of USP XVII).

9. Engineering diagrams of the 15 and 60 gm container/ closure systems packaged with this product are needed.

10. An additional identification test of the finished product and a test for degradation should be included. Please propose specifications for single degradation products,

and total degradation products.

11. A commitment is needed to test all lots placed upon stability post approval at date of manufacture (initial) and at 3, 6, 9, 12, 18, 24 months and yearly thereafter to 5 years. Please modify SOPs 6.02.2 and 6.02.3 accordingly.

12. Room temperature stability data at the next test station for lot PD8902 should be submitted and include data for appearance, clarity, color, homogeneity, odor, pH consistency, particle size distribution, degradation and strength. Please also include the exact temperature when both the 15 and 60 gm tubes were removed for stability testing and the date they were sent to QA for testing after date of manufacture.

13. Data of a cycle study for lot PD8902 should be submitted.

14. Though the container and unit dose labels for both tube size are satisfactory, the package insert requires the following changes:

COMMENTS:

A. CLINICAL PHARMACOLOGY

Pharmacokinetics - Delete the final paragraph. This pharmacokinetic information is product specific and may be included only if your firm conducts an appropriate study.

B. PRECAUTIONS

1. Nursing Mothers, line 4 - Italicize (or underline) "not".

2. Pediatric Use - Italicize (or underline) paragraph 1.

C. ADVERSE REACTIONS - Delete paragraph 2, "In controlled studies..."

D. Beginning with the CLINICAL PHARMACOLOGY section, delete USP from the drug title. Retain "USP" in the HOW SUPPLIED section.

E. Precede the date of the insert with "Revised" of "Issued".

RECOMMENDATIONS:

Please revise your labels and labeling, then prepare and submit final printed copy of each.

The file is now closed. You are required to take an action described under 21 CFR 314.20 which will either amend or withdraw the application. Any amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a major amendment. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

7-17-90

Acting Director
Division of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #73-440
DUP/Division File
HFD-638/Poux
HFD-634/RPatel/SSherken/6-14-90
HFD-632/RPollock/RHassall/6-15-90
R/D initialed by SSherken
jmk/7-8-90/73440ltr.
F/T by jmk/7-13-90
Not Approvable

7/16/90

7-18-90

ANDA 73-440

JUL 18 1990

E. Fougera & Co.
Division of Altana, Inc.
Attention: Andrew G. Clair, Ph.D.
60 Baylis Road
Melville, NY 11747

Dear Sir:

Reference is made to your abbreviated new drug application dated November 8, 1989, submitted pursuant to Section 505(j) of the Federal Food, and Drug and Cosmetic Act for Desoximetasone Ointment USP, 0.25%.

In order for our laboratory to ascertain that your bulk drug conforms to USP (if not USP, then appropriate) requirements, send the following requirements, materials to the address below:

Materials to be sent:

1. Drug Substance — Manufacturer

   Desoximetasone
   Desoximetasone

   Send three times the amount needed to perform all USP testing. Package the material in a tight, moisture-free container sealed in an outer container. Identify the manufacturer, the manufacturer's address, DMF number and lot number of the bulk sent.

2. Certificates of Analysis (yours and the manufacturer's) for the lot sent.

3. Standards - Reference, Impurity, and Internal - Send three times the amount required by the USP. [If you do not send the standard and St. Louis doesn't have it, the analysis will be delayed].

4. Copies of representative chromatograms and/or spectra (if applicable.)

5. Copy of the method of analysis if the drug substance is not compendial.

6. A Material Safety Data Sheet (OSHA Form 174) or equivalent information.

Address:

FDA/Division of Drug Analysis
Attention: Chief, Drug Monitoring Branch
1114 Market Street, Room 1002
St. Louis, MO 63101

These materials must be sent within 30 days of receipt of this letter. If you cannot send these materials by this date, please notify the Drug Monitoring Branch by letter. If you fail to send the requested materials, or properly notify the Drug Monitoring Branch Chief of any delay, this submission should be withdrawn. Send copies of all correspondence regarding the samples requested to the ANDA.

We recommend that you send the samples by registered mail/return receipt requested.

Sincerely yours,

7-17-90

Acting Director
Division of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #73-440
DUP/Division File
HFD-638/Poux
HFD-634/RPatel/SSherken/6-14-90
HFD-632/RPollock/RHassall/6-15-90
R/D initialed by RHassall
jmk/7-8-90/73440ltr.chm
F/T by jmk/7-12-90
Samples to St. Louis

9/13/90

7/16/90

fougera
Division of Altana Inc.

ORIGINAL

Labeling in effect 3.2
Supplement
PR Label 9/4/95

1/C

May 9, 1995

Mr. Douglas Sporn
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

Re: ANDA 73-440
Desoximetasone Ointment USP, 0.25%

Dear Mr. Sporn:

Reference is made to a communication of July 18, 1990, from the Office of Generic Drugs, stating that our application was deficient and that additional information was necessary.

All comments have been answered. However, data from new batches were used to respond to several comments. Comment 7 requests that information on a of drug product manufactured using be submitted.

We acknowledge that our proposed scale up batch of We have, therefore, produced a material. This larger size will allow for a scale up to our proposed production sizes of

Information on three ots is included with this response.

Batch 2131 utilizing active drug substance is the bioequivalence batch. All responses concerning inactive raw materials refer to data from this batch.

Batches 5292 (utilizing drug substance) and 5293 (utilizing drug substance) are stability batches. All responses concerning additional stability

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MAY 10 1995
GENERIC DRUGS

5-22-95

60 Baylis Road, Melville, N.Y. 11747 1-516-454-6996 Fax: 516-420-1572

studies refer to data from these lots.

Full testing of all lots of active drug substance used to produce the three batches are included.

As a result of this scale up to ve have also performed another bioequivalence study. The complete study is included as Section B at the completion of our response to your letter. We, therefore, request that the bioequivalence study dated October 23, 1989, submitted in our original application of November 8, 1989, protocol number ALT 06/89F be withdrawn.

Please add this information to the subject file.

Sincerely,
E. Fougera & Co.
division of Altana Inc.

Virginia Carman
Associate Director,
Regulatory Affairs

VC/lae

encl.

c:\lisa\73-440

ANDA 73-440

E. Fougera & Co.
Division of Altana Inc.
Attention: Virginia Carman
60 Baylis Road
Melville, NY 11747

NOV 2 1995

Dear Madam:

This is in reference to your abbreviated new drug application dated November 8, 1989, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Desoximetasone Ointment USP, 0.25%.

Reference is also made to your amendment dated May 9, 1995.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

1. Desoximetasone is known to exist in at least two polymorphs, and polymorphism could affect bioavailability. Which polymorph are you using? Please present data supporting your answer.

   Do you plan to submit a method and limits for insuring that the same polymorph will always be used? Please justify your answer.

2. Page 155 of the original ANDA did not mention the use of any contract testing laboratories. However, pages 163-183, 197, and 210-228 of the amendment show results generated by

   Do you intend to employ as a contract testing laboratory for this product after the approval of ANDA 73-440?

3. The limits for homogeneity in the finished product and stability specifications should be of the mean rather than

4. The finished product specifications on page 789 and the analytical procedure on page 797 include the test for uniformity of dosage units, but the stability specifications on page 829 do not. Do you intend to market a container of this product smaller than 3.5 g in the future?

If no, you may delete this test from the finished product specifications and the analytical procedure.

If yes, you should add this test to the stability specifications.

5. The expression of limits for degradation products is misleading and unacceptable. On page 794, the quotient should be The limits should be revised accordingly.

Using the method we are proposing, the stability limit for the degradation product with and for total degradation products, would be ather than Similarly, the limit for other degradation products would be each rather than

We consider these limits to be too high. Please tighten your in-process, finished product, and stability specifications for degradation products and express the limits to one place past the decimal point.

6. The specifications for Microbial Limits for finished product and stability testing should include a limit for total microbial count. Please refer to USP 23 <1111>, fourth paragraph.

7. Please submit the stability report which is mentioned on pages 832 *et al*.

8. The in-process, finished product, and stability specifications should include (an) upper limit(s) for viscosity.

9. Please submit 18 month stability data for lots 5292 and 5293.

10. Please provide the protocol for the cycle study for which you have submitted results.

11. Please explain and justify the homogeneity results the end of the cycle study.

An addition to responding to these deficiencies, please note and acknowledge the following in your response:

1. Please include a Form FDA 356h with each ANDA, amendment, or supplement in the future.

2. The firms referenced in the application relative to the manufacture and testing of the product must be in compliance with current GMPs at the time of approval. We will request an evaluation from the Division of Manufacturing and Product Quality at the appropriate time.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MAJOR amendment and should be so designated in your cover letter. You will be notified in a separate letter of any deficiencies identified in the bioequivalence portion of your application. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

10/23/95

/s/ Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #73-440
ANDA #73-440/DUP/Division File
Field Copy
HFD-600/Reading File

Endorsements:

HFD-629/E.Schaefer/10-17-95
HFD-613/A.Payne/ 10/23/95
HFD-613/J.Phillips/ 10/25/95
HFD-629/P.Schwartz, Ph.D./10-17-95
HFD-617/AMWeikel, CSO/10-19-95
x:\new\firmsam\fougera\ltrs&rev\73440na2.d
F/T by MM 10-20-95
Not Approvable - Major

tougera
Division of Altana Inc.

Federal Express

March 1, 1996

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
HFD-630, Room 204
7500 Standish Place
Rockville, Maryland 20855-2773

AC

Re: ANDA 73-440
Desoximetasone Ointment USP, 0.25% (Major Amendment)

Dear Dr. Patel:

Reference is made to your communication of November 2, 1995 concerning deficiencies in our Abbreviated New Drug Application submitted pursuant to 505(j) of the Federal Food Drug and Cosmetic Act, and our amendment of May 9, 1995.

We wish to respond to each comment as follows:

Comment

1. Desoximetasone is known to exist in at least two polymorphs, and polymorphism could affect bioavailability. Which polymorph are you using? Please present data supporting your answer.

   Do you plan to submit a method and limits for insuring that the same polymorph will always be used? Please justify your answer.

Response

Polymorphism cannot affect the bioavailability of the ointment since the

60 Baylis Road, Melville, N.Y. 11747 1-516-454-6996 Fax: 516-420-1572

desoximetasone is dissolved in propylene glycol during the manufacturing process. When a substance is dissolved any differences in crystal structure are eliminated.

Comment

2. Page 155 of the original ANDA did not mention the use of any contract testing laboratories. However, pages 163-183, 197, and 210-228 of the amendment show results generated by

Do you intend to employ as a contract testing laboratory for this product after the approval of ANDA 73-440?

Response

At the time of original submission esting was not a requirement. Since then it has become a requirement for many of the USP substances. We will be utilizing as a contract testing laboratory for esting of the raw materials after ANDA 73-440 is approved. A copy of their GMP certification letter is included in Attachment 1.

Comment

3. The limits for homogeneity in the finished product and stability specifications should be of the mean rather than

Response

The limits for homogeneity in the finished product and stability specifications have been revised to require of the mean.

Attachments 5 and 6. (Response to comment 5)

Comment

4. The finished product specifications on page 789 and the analytical procedure on page 797 include the test for uniformity of dosage units, but the stability specifications on page 829 do not. Do you intend to market a container of this product smaller than 3.5 g in the future?

If no, you may delete this test from the finished product specifications and the analytical procedure.

If yes, you should add this test to the stability specifications.

Response

We do not intend to market a container of 3.5g or smaller. The test for uniformity of dosage units has been deleted from the finished product specifications and the analytical procedures, Attachments 5 and 7.

Comment

5. The expression of limits for degradation products is misleading and unacceptable. On page 794, the quotient should be multiplied by The limits should be revised accordingly.

Using the method we are proposing, the stability limit for the degradation product with and for total degradation products, would be
Similarly, the limit for other degradation products would be each

We consider these limits to be too high. Please tighten your in-process, finished product, and stability specifications for degradation products and express the limits to one place past the decimal point.

Response

The limits for degradation products have been revised as requested to reflect percentage of the active ingredient rather than % (w/w).

The test for foreign related substances in the desoximetasone raw material requires individual impurities to not exceed and the sum of all impurities to not exceed We have tightened our in-process and finished product specifications for the ointment to correspond to our previously set limits for the raw material.

Only one degradation product is actually found in the ointment. elative to desoximetasone of about assay. This degradation product is also found in the innovator product, Topicort® Ointment. See attachments 2 and 3 for chromatograms of our ointment and Topicort® Ointment which exhibit this compound. For a minimal expiration dating period of 18 months a stability specification limit of s necessary for this compound. Since only one degradation product is observed in the ointment the stability specification for other degradation products has been tightened to ne same limit used for the raw material, in-process and finished product specifications.

See Attachment 4 - in process specification
See Attachment 5 - finished product specification
See Attachment 6 - stability specification
See Attachment 7 - analytical procedures
See Attachment 8 - analytical validation

Comment

6. The specifications for Microbial Limits for finished product and stability testing should include a limit for total microbial count. Please refer to USP 23 <1111>, fourth paragraph.

Response

The finished product and stability testing specifications have been revised as requested. The total microbial count is limited to not more than

See attachments 5 and 6. (Response to comment 5)

Comment

7. Please submit the stability report which is mentioned on pages 832 *et al.*

Response

The stability reports mentioned on page 832 and elsewhere are presented in Attachment 9.

Comment

8. The in-process, finished product, and stability specifications should include (an) upper limit(s) for viscosity. We are concerned about Please justify your proposed in light of the suitability of the product for its intended use.

Response

The in-process, finished product and stability specifications have been revised to include an upper limit for viscosity. The lower limit for viscosity has also been tightened. The new specifications are

See attachments 4,5,6 and 7. (Response to comment 5)

The viscosity range for the ointment is well within the limits for acceptable

product performance. The ointment must have a high enough viscosity so that it does not flow excessively when applied to the skin, and it must be low enough so that it can be extruded from the tube and applied in a thin film.

Typically, ointments or creams for dermal application flow excessively at viscosities below about 20,000-30,000 cps (they become lotion-like). The practical upper limit for dermal products is so high it cannot be measured using a Brookfield viscometer. As an example, Burroughs Wellcome markets Zovirax® Ointment 5% (acyclovir); measurements in our laboratory indicate that the viscosity is greater than 5,000,000 cps. A marketed product similar in viscosity to desoximetasone ointment is our Lanolin Hydrous; a value of 490,000 cps was observed.

Studies of lots 5292 and 5293 showed that the ointment was easily extruded from both the 15g and 60g tubes. Extrusion from the 60g tubes seemed slightly easier than from the 15g tubes due to the larger tube opening. 200 mg aliquots from each lot and tube size were easily spread into 25 cm^2 thin films on human skin within 2 seconds.

Comment

9. Please submit 18 month stability data for lots 5292 and 5293.

Response

Updated stability data for lots 5292 and 5293 may be found in Attachments 10 and 11.

Comment

10. Please provide the protocol for the cycle study for which you have submitted results.

Response

For the cycling study the tubes were stored at 4°C for one week followed by storage at 45°C for one week. This was repeated three more times for a total of eight weeks of storage.

Comment

11. Please explain and justify the homogeneity results which were out of specifications at the end of the cycle study.

Response

Petrolatum-based ointments typically begin to melt at about 40°C. Melting can lead to separation of the ointment, with the active ingredient preferentially partitioning into one of the phases.

Labeling for this product requires storage at controlled room temperature (15°-30°C).

Additionally, we acknowledge:

1. That a Form FDA 356h should be included with each ANDA amendment, or supplement, and

2. That the firms referenced in the application relative to the manufacture and testing of the product must be in compliance with current GMPs at the time of approval.

We also acknowledge that this is a MAJOR amendment.

If there are any questions, please contact us at (516)454-7677.

Sincerely,
E. Fougera & Co.
division of Altana, Inc.

Virginia Carman
Associate Director,
Regulatory Affairs

VC/lae

encl.

C:\MISC\73-440.DEF

fougera®
a division of Altana Inc.

NDA ORIG AMENDMENT N/Pc

Federal Express

November 1, 1996

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

Attn: Paul Schwartz, Ph.D.

Re: ANDA 73-440 (Fax amendment)
Desoximetasone Ointment USP, 0.25%

Dear Dr. Schwartz:

Reference is made to our telephone conference of last week concerning the degradation rate of E. Fougera & Co.'s Desoximetasone Ointment vs Topicort (desoximetasone) Ointment (Hoechst-Roussel).

As requested, results of our comparison studies are included. As Mr. Pearce indicated, the degradation profile of both products is the same. It also appears that when stored under similar conditions, the degradation rate of the E. Fougera & Co. product is less than that of Topicort.

If there are any questions, please contact me at 516 454-7677 ext 2091.

Sincerely,
E. Fougera & Co.
division of Altana Inc.

Virginia Carman

Virginia Carman
Associate Director
Regulatory Affairs

60 Baylis Road, Melville, N.Y. 11747 1-516-454-6996 Fax: 516-756-7017

ANDA 73-440

E. Fougera & Co.
Division of Altana Inc.
Attention: Virginia Carman
60 Baylis Road
Melville, NY 11747

NOV 20 1996

Dear Madam:

This is in reference to your abbreviated new drug application dated November 8, 1989, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Desoximetasone Ointment USP, 0.25%.

Reference is also made to your amendment dated March 1, 1996, and telephone conversations with representatives of this office on October 24, November 8, and November 12, 1996.

In those conversations, you were informed that the application is deficient and, therefore, not approvable under Section 505 of the Act for the following reason:

> To justify your proposed degradant limit of please assay Topicort Ointment by Hoechst-Roussel at or near expiry after storage at room temperature. Report the levels of desoximetasone and the main degradant.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MINOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

11/19/96

cc: Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

fougera®
a division of Altana Inc.

FEDERAL EXPRESS

January 8, 1998

NDA [illegible]

N / AM

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs (HFD-600)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North 2, Room 286
7500 Standish Place
Rockville, MD 20855-2773

RE: ANDA 73-440 MINOR AMENDMENT
Desoximetasone Ointment USP, 025%

Dear Dr. Patel:

Reference is made to our original ANDA of November 8, 1989 submitted pursuant to Section 505(j) of the FD&C Act for the drug product Desoximetasone Ointment USP, 0.25%.

Reference is also made to our amendment of March 1, 1996 and subsequent telephone conversations with representatives of the Office on Oct. 24, Nov. 8, and Nov. 12, 1996, at which times we were informed that our proposed degradant limit of was . We also refer to your correspondence of Nov. 20, 1996 in which we were requested to justify this limit by assaying Topicort Ointment at or near the expiry after storage at room temperature, and report the levels of Desoximetasone and the main degradant.

We have performed the requested stability analysis of Topicort Ointment (Hoechst-Roussel). The degradation profile of the innovator's product is similar to our own after one year. Please see the attached summary report (Attachment 1) stability data (E. Fougera & Co. product) (Attachment 2), and analytical reports for Topicort (Attachment 3).

60 Baylis Road, Melville, N.Y. 11747 1-516-454-6996 Fax: 516-756-7017

Based on these data, we request that our proposed degradation limit be revaluated and accepted, and that our application for Desoximetasone Ointment USP, 0.25% be approved.

Thank you for consideration of our request.

If there are any further questions, please contact me at (516) 454-7677 ext. 2091.

Sincerely,
E. Fougera & Co.
division of Altana Inc.
Virginia Carman
Virginia Carman
Associate Director
Regulatory Affairs

VC/lb

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fougera®
a division of Altana Inc.

March 13, 1998

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry 1
Office of Generic Drugs (HFD-600)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North 2 Room 286
7500 Standish Place
Rockville, MD 20855-2773

ORIG AMENDMENT
N/A

Re: ANDA 73-440 Telephone Amendment
Desoximetasone Ointment USP, 0.025%

Dear Dr. Patel:

Reference is made to our original application of November 8, 1989 submitted pursuant to Section 505 (j) of the FD&C Act.

Reference is also made to a telephone conversation held with the Office on March 13, 1998 at which time we were requested to a source of the active drug substance.

As requested, E. Fougera & Co., division of Altana Inc., is hereby upplier of the drug substance desoximetasone.

If we plan to in the future we will supplement the application post approval.

If there are any questions, please call me at (516) 454-7677 ext. 2091.

Sincerely,

Virginia Carman

VC:ar

Virginia Carman
Associate Director
Regulatory Affairs

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MAR 17 1998
GENERIC DRUGS

60 Baylis Road, Melville, N.Y. 11747 1-516-454-6996 Fax: 516-756-7017

RECORD OF TELEPHONE CONVERSATION/MEETING

Dr. Rudman indicated that the major degradation limit should be tighten to ' as based on the RLD (Topicort) testing data.

The applicant agreed to reduce the degradation limit to and set an appropriate expiration date based on this new limit.

The applicant also mentioned that they will start to test their product along with the RLD. They may file a supplemental application to increase the degradation limit if a similar level of degradation observed in both products at 18 months.

Ms. Carman will fax this telephone amendment and followed by a hard copy to the file.

DATE:
March 20, 1998

ANDA NUMBER:
73-440

IND NUMBER:
N/A

TELECON

INITIATED BY:
☐ APPLICANT/SPONSOR
■ FDA

MADE:
■ BY TELEPHONE
☐ IN PERSON

PRODUCT NAME:
Desoximetasone Ointment 0.25%

FIRM NAME:
E. Fougera & Co.

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:
Virginia Carman, RA
David Pearce, R&D

TELEPHONE NUMBER:
(516) 454-7677

SIGNATURE:

3/20/98

3/20/98

fougera
Division of Altana Inc.

March 24, 1998

NDA CMC AMENDMENT

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs (HFD-620)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North 2 Room 286
7500 Standish Place
Rockville, Md. 20855-2773

Re: ANDA 73-440
Desoximetasone Ointment USP, 0.025%

Dear Dr. Patel:

Reference is made to our original Abbreviated New Drug Application submitted, August 20, 1987 as well as our telefax amendment of February 4 1998.

Reference is also made to a telephone conference between representatives of the Office and E. Fougera & Co. concerning our proposed stability degradation limits, and expiry date for our Desoximetasone Ointment drug product.

Dr. Paul Schwartz of the Office indicated that the Office could not justify a specification for the degradation products, and that we would be allowed a maximum. We were also requested to assign a new expiry date based upon the "new" degradation product limits.

As requested, we have revised our stability specifications to lower the limit of degradation products to (Attachment 1)

We have also determined that our stability data can justify a fifteen (15) month expiry date for the proposed drug product. Our calculations are included. (Attachment 2)

Finally, as the new expiry date is fifteen (15) months, our Stability Protocol for this product has been revised to add a fifteen (15) month test station. (Attachment 3)

We understand that if further data are collected, that justify an increased expiry date, we may with the Office's concurrence be able to do so.

If there are any further questions, please contact me at (516) 454-7677, ext. 2091.

Sincerely,

Virginia Carman

Virginia Carman
Associate Director
Regulatory Affairs

RECEIVED
MAR 25 1998
GENERIC DRUGS

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30 Burt Drive, Melville, N.Y. 11747 1-516-454-6996 Telex 144662