CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75276

CORRESPONDENCE

ANDA 75-276

MAR 26 2003

Altana Inc.
Attention: Virginia Carman
60 Baylis Road
Melvile, NY 11747

Dear Madam:

This letter provides a correction to our February 28, 2003, Tentative Approval letter. Specifically, the last line of the last paragraph on page 2 has been changed to reflect the correct date of May 13, 2003. The tentative approval status of this application is unchanged.

This is in reference to your abbreviated new drug application (ANDA) dated December 18, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Betamethasone Dipropionate Gel, 0.05% (base) (Augmented).

Reference is also made to your amendments dated October 7, 2002, and February 14, and February 28, 2003.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Although we are unable to grant final approval at this time because the reference listed drug product (RLD) is subject to a period of patent protection as discussed below. Therefore, the application is **tentatively approved**. This tentative approval is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices of the facilities (cGMPs) used in the manufacture and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention.

The reference listed drug product (RLD) upon which you have based your application, Diprolene Gel of Schering Corp., is currently subject to a period of patent protection. As noted in

the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations, the Orange Book, U.S. Patent 4,489,070 (the '070 patent) is due to expire on May 13, 2003.. Your application contains a paragraph III certification to the '070 patent under Section 505(j)(2) (A)(vii)(III) of the Act. This certification states that you will not market this drug product prior to the expiration of the patent. Therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(B)(ii) of the Act until the '070 patent has expired, i.e., currently May 13, 2003.

In order to reactivate this application prior to final approval, please submit a MINOR AMENDMENT - FINAL APPROVAL REQUESTED. This amendment should be submitted 60 to 90 days prior to the date you believe the application will be eligible for final approval. The amendment should state the legal/regulatory basis for approval, and it should identify changes, if any, in the conditions under which the product was tentatively approved; i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. Note that this amendment should be submitted even if none of these changes were made.

In addition to this amendment, the agency may request at any time prior to the final date of approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to Agency review before final approval of the application will be made. Should you elect to amend this application to provide for such changes prior to final approval, we request that they be categorized as representing either "major" or "minor" changes. The amendment will be reviewed according to OGD policy in effect at the time of receipt.

This drug product may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the

Agency issues the final approval letter, this drug product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to May 13, 2003, you should amend your application accordingly.

For further information on the status of this application, or prior to submitting additional amendments, please contact Sarah Ho, R.Ph., Project Manager, (301) 827-5848.

Sincerely yours,

/S/

Gary Buehler 3/26/03
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-276
Division File
Field Copy
HFD-610/R. West
HFD-330
HFD-205

Endorsements:
HFD-600/N.Nashed/5/23/01
HFD-623/P.Schwartz/5/23/01
HFD-617/S.Ho/10/10/02
HFD-613/L.Golson/5/21/01
HFD-613/J.Grace/5/21/01
HGF-600/F.Holcombe/2/28/03

/S/ 3/26/2003

F/T by:gp/9/13/02

LETTER OUT - CORRECTION LETTER

ANDA 75-276

FEB 28 2003

Altana Inc.
Attention: Virginia Carman
60 Baylis Road
Melvile, NY 11747

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated December 18, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Betamethasone Dipropionate Gel, 0.05% (base) (Augmented).

Reference is also made to your amendments dated October 7, 2002, and February 14, and February 28, 2003.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Although we are unable to grant final approval at this time because the reference listed drug product (RLD) is subject to a period of patent protection as discussed below. Therefore, the application is **tentatively approved**. This tentative approval is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices of the facilities (cGMPs) used in the manufacture and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention.

The reference listed drug product (RLD) upon which you have based your application, Diprolene Gel of Schering Corp., is currently subject to a period of patent protection. As noted in the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations, the Orange Book, U.S. Patent 4,489,070 (the '070 patent) is due to expire on May 13, 2003. Your application contains a paragraph III certification to the '070 patent under Section 505(j)(2) (A)(vii)(III) of the Act. This certification states that you will not market this

drug product prior to the expiration of the patent. Therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(B)(ii) of the Act until the '070 patent has expired, i.e., currently May 13, 2003.

In order to reactivate this application prior to final approval, please submit a MINOR AMENDMENT - FINAL APPROVAL REQUESTED. This amendment should be submitted 60 to 90 days prior to the date you believe the application will be eligible for final approval. The amendment should state the legal/regulatory basis for approval, and it should identify changes, if any, in the conditions under which the product was tentatively approved; i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. Note that this amendment should be submitted even if none of these changes were made.

In addition to this amendment, the agency may request at any time prior to the final date of approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to Agency review before final approval of the application will be made. Should you elect to amend this application to provide for such changes prior to final approval, we request that they be categorized as representing either "major" or "minor" changes. The amendment will be reviewed according to OGD policy in effect at the time of receipt.

This drug product may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to May 14, 2004, you should amend your application accordingly.

For further information on the status of this application, or prior to submitting additional amendments, please contact Sarah Ho, R.Ph., Project Manager, (301) 827-5848.

Sincerely yours,

/S/

for

2/28/2003

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-276

FEB 11 1998

Altana, Inc.
Attention: Virginia Carman
60 Baylis Road
Melville, NY 11747

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to our "Refuse to File" letter dated January 21, 1998, and your amendment dated January 29, 1998.

NAME OF DRUG: Betamethasone Dipropionate Gel, 0.5%

DATE OF APPLICATION: December 18, 1997

DATE (RECEIVED) ACCEPTABLE FOR FILING: January 30, 1998

We will correspond with you further after we have had the opportunity to review your application.

Please identify any communications concerning this application with the number shown above.

Should you have questions concerning this application contact:

Joe Buccine
Project Manager
(301) 827-5848

Sincerely yours,

/S/

Jerry Phillips
Director,
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-276

Altana, Inc.
Attention: Virgina Carman
60 Baylis Road
Melville, NY 11747

JAN 21 1998

Dear Madam:

Please refer to your abbreviated new drug application (ANDA) dated December 18, 1997, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Betamethasone Dipropionate Gel, 0.5%.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

The application lacks a letter of authorization from designating the to act as their agent in granting access to the Drug Master File (DMF) for Betamethasone Dipropionate.

You have provided a letter from dated February 24, 1988, authorizing FDA to examine their DMF for Betamethasone Dipropionate. Please obtain a current DMF authorization from to access their DMF for Betamethasone Dipropionate.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

In addition, please submit a diskette in ASCII format containing pharmacokinetic data and the model codes used in statistical analyses. For each study, two separate files should be configured as follows:

(a) subj seq trt per AUC_{0-t} AUC_{inf} (Where applicable) C_{max} T_{max} K_{el} and $t_{1/2}$;...

(b) subj seq per trt C_1 C_2 C_3.....C_n,

where C is the concentration at various sampling times. Fields should be delimited by one blank space and each missing value should be denoted by a period (.).

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3)If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Saundra T. Middleton
Project Manager
(301) 827-5862

Sincerely yours,

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Pharma

ALTANA

March 7, 2003

ALTANA Inc
60 Baylis Road
Melville, NY 11747
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www.altanainc.com

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

ORIG AMENDMENT
N/AM

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
MINOR AMENDMENT- FINAL APPROVAL REQUESTED

Dear Mr. Buehler:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the FDA correspondence dated February 28, 2003 granting Tentative Approval of the above referenced application. As requested, Altana Inc. is submitting this Minor Amendment- Final Approval Requested in order to reactivate the Betamethasone Dipropionate Gel, 0.05% (Augmented) application for final approval consideration.

The Reference Listed Drug product (RLD) upon which the Altana application is based, Diprolene® Gel of Schering Corp., is currently subject to a period of patent protection. As noted in Approved Drug Products with Therapeutic Equivalence Evaluations, the Orange Book, U.S. Patent 4,489,070 (the '070 patent) is due to expire on May 13, 2003. In the application, Altana Inc. included a paragraph III certification to the '070 patent under Section 505 (j) (2) (A) (vii) (III) of the Act. The certification states that Altana Inc. will not market Betamethasone Dipropionate Gel, 0.05% (Augmented) prior to the expiration of the patent. Altana Inc. also acknowledges that final approval of this application may not be made effective pursuant to 21 U.S.C. 355 (j) (5) (B) (ii) of the Act until the '070 patent has expired, i.e., currently May 13, 2003.

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Altana respectively requests that this application be reactivated, as it is eligible for final approval. No changes to the Chemistry, Manufacturing and Controls have been made since receipt of the tentative approval on February 28, 2003. Final Printed Labeling has been included in Attachment I along with a side-by-side comparison with previously submitted labeling.

An identical copy of this Amendment has been provided to the New York District Office. A document certification is attached.

If you have any questions or require additional information, please contact me at (631) 454-7677 extension 2091. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

VC/JF

Pharma

ALTANA

ALTANA Inc
60 Baylis Road
Melville, NY 11747
USA
T +1 (631) 454-7677
www.altanainc.com

February 28, 2003

NC

Robert L. West
Deputy Director
Office of Generic Drugs (HFD-601)
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

VIA Telefax (301) 594-0183
and Federal Express

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
TELEPHONE Amendment

Dear Mr. West:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to the Altana Amendment most recently submitted on February 14, 2003.

This Telephone Amendment has been prepared in response to the teleconference discussion held this afternoon between Altana and FDA representatives. Altana has revised the Paragraph III Patent Certification in accordance with this discussion. A copy of this certification is included with this submission.

If you have any questions or require any additional information please contact Ms. Audrey Zaweski, Associate Director at (631) 454-7677 extension 3007. FAX communications may be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

Pharma

ALTANA

February 14, 2003

Frank O. Holcombe, Jr., Ph.D.
Associate Director
Division of Chemistry (HFD-600)
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AM

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VIA Telefax (301) 594-0183
and Federal Express

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
TELEPHONE Amendment

Dear Dr. Holcombe:

Reference is made to the Altana Inc. Abbreviated New Drug Applicati on submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to the Altana Amendment most recently submitted on October 7, 2002.

This Telephone Amendment has been prepared in response to the teleconference discussion held this morning between Altana and FDA representatives. Altana has revised the In-Process and Finished Product Assay Specification for Betamethasone Dipropionate in accordance with this discussion. The Stability Assay Specification remains unchanged. The Betamethasone Dipropionate Assay Specifications have been summarized below:

In-Process:	)%
Finished Product:	)%
Stability:	%

Copies of the In-Process, Finished Product and Stability Specifications have been included with this submission for ease of review.

If you have any questions or require any additional information please contact Ms. Audrey Zaweski, Associate Director at (631) 454-7677 extension 3007. FAX communications may be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

RECEIVED
FEB 2 0 2003
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Pharma

ALTANA

October 7, 2002

Frank O. Holcombe, Jr., Ph.D.
Associate Director
Division of Chemistry (HFD-600)
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

DRUG AMENDMENT
N/AM

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www.altanainc.com

VIA Telefax and Federal Express

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
TELEPHONE Amendment

Dear Dr. Holcombe:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to the Altana Amendment most recently submitted on February 19, 2002.

Recent communications with FDA have indicated that an upper limit of)% would be more appropriate for the Finished Product Assay Specification for Betamethasone Dipropionate. Altana has prepared another batch of Betamethasone Dipropionate Gel, 0.05% (Augmented) Lot# J448 to obtain additional finished product assay data to evaluate this recommendation. Samples of both the 15-gram and 50-gram tube sizes were filled and tested by the current analytical method. The results obtained have been summarized below with the previously accumulated data from the three original exhibit batches.

Finished Product Assay Results Summary (%)				
	Lot#			
	9753	9754	A095	J448
15g Beg.				
15g End				
50g Beg.				
50g End				

As previously stated, the accumulated finished product data for the four lots presented above point toward a need to consider all data when evaluating appropriate Assay Specifications for the drug product. While the zero-time data for Lot# A095 does not appear to be consistent with the zero-time data obtained for Lot#s 9753 and 9754, there does not appear to be an appropriately identifiable cause to exclude the data. In addition, the finished product data for the most recent batch produced also included an assay result above the FDA proposed limit of %.

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Altana's proposed Finished Product Assay Specification of % represents an assay range of % for the drug product release. The United States Pharmacopeia (USP) provides at least ±5% but most typically sets a limit of ±10% as an assay range for its compendial products. In addition, the current USP monographs for Betamethasone Dipropionate Cream, Lotion and Ointment all permit ±10% as an assay range for the Betamethasone Dipropionate. Altana's proposed Finished Product specification for the Augmented Gel is clearly more rigorous.

Altana Inc. commits to periodic review of the Assay Specifications as additional data is collected from future production batches of the drug product. As more information is obtained and evaluated, subsequent revisions to the Assay Specifications may be warranted.

Altana is also willing to discuss the proposed Assay Specifications with FDA in a teleconference call. Please contact me at (631) 454-7677 extension 2091 to schedule a time for this week. FAX communications may be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Blaboski for

Virginia Carman
Associate Director, Regulatory Affairs

VC/ab

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

February 19, 2002

Frank O. Holcombe, Jr., Ph.D.
Associate Director
Division of Chemistry (HFD-600)
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

N/A un

ORIG AMENDMENT

VIA Telefax and Federal Express

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
TELEPHONE Amendment

Dear Dr. Holcombe:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to the Altana Amendment most recently submitted on September 17, 2001.

Reference is also made to the January 5, 2002 teleconference call held between Patricia Beersblock, FDA and Audrey Bialeski, Altana Inc. regarding the proposed specifications for the drug product. Ms. Beersblock indicated that Dr. Holcombe would prefer to see % as the upper limit for the assay specification. Ms. Beersblock also stated that Altana could submit additional information regarding the assay specifications in another Telephone Amendment.

Altana has conducted further evaluation of the accumulated data (in-process, finished product and stability) for the three submitted exhibit batches. While the zero-time data for Lot# A095 does not appear to be consistent with the zero-time data obtained for Lot#s 9753 and 9754, there does not appear to be an appropriately identifiable cause to exclude the data. This data must be considered when evaluating appropriate Assay Specifications for the drug product.

Based on the data summaries and the % overage of Betamethasone Dipropionate in the drug product formulation, Altana Inc. is proposing the following Assay Specifications to ensure an appropriate shelf life for the marketed product. Altana will tighten the Finished Product Assay Specifications to % and the Stability Assay specifications to %. The In-Process Assay Specifications will remain unchanged at %.

The accumulated data has been summarized in the tables presented below.

In-Process Testing (%)		
Lot #	Average Assay Result	Assay Range (n=6)
9753	112.1	
9754	113.5	
A095	113.4	

Finished Product Assay Results Summary (%)			
	Lot#		
	9753	9754	A095
15g Beginning			
15g End			
50g Beginning			
50g End			

Stability Assay Results Summary (%)							
Lot #	Zero-Time	3 months	6 months	9 months	12 months	18 months	24 months
9753 –15g							
50g							
9754 – 15g							
50g							
A095 –15g							
50g							

Altana Inc. commits to periodic review of the Assay Specifications as additional data is collected from future production batches of the drug product. As more information is obtained and evaluated, subsequent revisions to the Assay Specifications may be warranted.

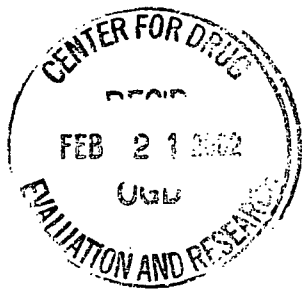
Please contact me at (631) 454-7677 extension 2091 if you require any additional information or clarification. FAX communications may be made to (631) 756-5114.

Sincerely,

ALTANA INC.

for Audrey Bialecki

Virginia Carman
Associate Director, Regulatory Affairs



VC/ab

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

September 17, 2001

Frank O. Holcombe, Jr., Ph.D.
Associate Director
Division of Chemistry (HFD-600)
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NDA AM

ORIG AMENDMENT

VIA Telefax and Federal Express

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
TELEPHONE Amendment

Dear Dr. Holcombe:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to the Altana Amendments most recently submitted on April 20, 25, 26 and 30, 2001.

Reference is also made to the teleconference call held between Frank Holcombe, Jr., FDA and Virginia Carman, Altana Inc. regarding the proposed specifications for the drug product.

Based on an evaluation of the drug product's formulation as well as the accumulated stability data, Altana Inc. has revised the Assay specification for the drug product In-Process and Finished Product Specifications. The drug product is formulated with a % overage of the Betamethasone Dipropionate. Altana is proposing to tighten the In-Process Assay Specification to % that is % of the formulated quantity of % for Betamethasone Dipropionate. The Finished Product Assay specifications have been revised to %. The Stability Assay specifications remain unchanged at %.

Please contact me at (631) 454-7677 extension 2091 if you require any additional information or clarification. FAX communications may be made to (631) 756-5114.

Sincerely,

ALTANA INC.

SEP 19 2001

Virginia Carman
Associate Director, Regulatory Affairs

VC/ab

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

April 30, 2001

Dr. Paul Schwartz
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

ORIG AMENDMENT

N1Am

RE: ANDA 75-276 **TELEPHONE AMENDMENT**
Betamethasone Dipropionate Gel, 0.05% (Augmented)

Dear Dr. Schwartz:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to our amendments of November 15, 1999, November 3, 2000, April 20, 2001, April 25, 2001 and April 26, 2001.

Reference is also made to a telephone conversation between members of the Office and Altana Inc. concerning our proposed specifications.

As discussed, please find enclosed revised in-process and finished product specifications.

This concludes Altana's response to this Telephone Amendment. If you have any questions, or require any additional clarifications, please contact me at (631) 454-4677 ext. 2091. Fax communication may be made to (631) 756-5114.

Sincerely,
ALTANA INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
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OGD

VC/cc

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

April 26, 2001

ORIG AMENDMENT

N/Am

Dr. Paul Schwartz
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

RE: ANDA 75-276 **TELEPHONE AMENDMENT**
Betamethasone Dipropionate Gel, 0.05% (Augmented)

Dear Dr. Schwartz:

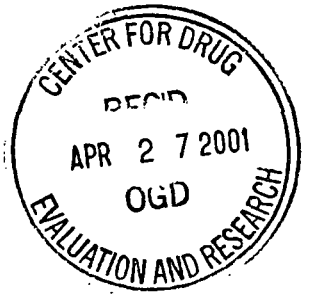
Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to our amendments of November 15, 1999, November 3, 2000, April 20, 2001 and April 25, 2001.

Reference is also made to a telephone conversation between members of the Office and Altana Inc. concerning Altana's proposed stability specifications.

As we explained to the office, we based our specification for "other degradation products" on the USP allowable limit for betamethasone dipropionate USP active drug substance.

USP 24/NFXVIII Supplement 2 revised the impurity limits for the active substance to "each not more than 1.0%, total not more than 2.0%". Altana has set the stability specification for each degradation product to "each not more than %". We've allowed a % limit over the full shelf life of the drug product.

Altana Inc., therefore, proposes to maintain the proposed degradation limit at "each not more than %" for "Other Degradation" products. This excludes the degradation products identified at



ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

April 20, 2001

Dr. Paul Schwartz
Office of Generic Drugs
Center of Drug Evaluation & Research
Food, Drug and Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ORIG AMENDMENT
N/Am

RE: ANDA 75-276 **TELEPHONE AMENDMENT**
Betamethasone Dipropionate Gel, 0.05% (Augmented)

Dear Dr. Schwartz:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel 0.05% (Augmented) in accordance with section 505(j) of the Federal Food Drug and Cosmetic Act. Reference is also made to our amendments of November 15, 1999 and November 3, 2000.

Reference is also made to telephone conversations of March 20, 2001, April 4, 2001 and April 19, 2001 between the Office and Altana. These discussions concerned analytical methods for the active substance, in-process and stability specifications, identification of peaks, and a commitment to assist the FDA laboratories in performing validation of our analytical methods.

We wish to address each item as follows:

In process and stability specifications:
The stability specifications submitted in the November 3, 2000 submission are not the current specifications. These were the originally submitted specifications and stability reports.

The stability and in-process specifications were revised in September 1999 and submitted as part of the November 15, 1999 amendment. The submitted specifications contained a revision in the pH from Additionally the degradant specifications were also revised. These specifications maybe found in Attachment 1.

Analytical methods for the active substance:
As previously stated, we use the USP method to test for "other impurities". The related substances test is based upon the USP method for chromatographic impurity. A verification study was performed to verify the assay methods and chromatographic purity. The conclusion is that the method is suitable for analyzing impurities and related substances at levels corresponding to % . These tests, i.e. other impurities, related substances, have since been replaced by chromatographic purity (see next paragraph).

We were additionally requested to see if we could lower our related substances limit. The USP 24 Amendment 2 has set limits of NMT 1.0% for each individual impurity. Our limits are currently at allowed by the USP. We are therefore requesting approval of new raw material specifications, which increase the individual limits to comply with the USP. We have also deleted as per USP, and replaced related substances with chromatographic purity. This report may be found in Attachment 2.

Commitment to assist with Methods Validation:
Altana Inc. hereby commits to assist the FDA's laboratories in validating our analytical methods.

Altana Inc. also confirms the methods validation samples have been submitted to the FDA laboratory.

This concludes Altana's response to this Telephone Amendment. If you have any questions or require additional clarifications, please contact me at (631) 454-7677 at extension 2091. Fax communication may be made to (631) 756-5114.

Sincerely,
ALTANA INC.

Virginia Carman
Associate Director, Regulatory Affairs

VC/cc

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

February 21, 2001

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

VIA FEDERAL EXPRESS

ORIG AMENDMENT
N/AM

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
MINOR Amendment

Dear Dr. Patel:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to the Altana Amendments submitted on November 3 and December 5, 2000.

Altana Inc. also acknowledges receipt of the FDA communication dated December 26, 2000 that provided chemistry comments regarding the submitted application. As requested, this correspondence has been identified as a MINOR Amendment and all comments have been addressed. Each item has been prepared in **comment/** response format.

The DMF is deficient. The DMF holder has been notified. Please do not respond until you have been notified by the DMF holder that the DMF deficiencies have been addressed.

Altana Inc. has received correspondence from the DMF holder that they have responded to the FDA deficiency letter dated December 11, 2000. Please refer to Attachment I.

This concludes Altana's response to this MINOR Amendment. Please contact me at (631) 454-7677 extension 2091 if you require any additional information or clarification. FAX communications may be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
FEB 23 2001
OGD

VC/ab

2/28/01

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

December 5, 2000

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
7500 Standish Place
Rockville, MD 20855

Via Federal Express

VIA ORIG AMENDMENT

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
TELEPHONE AMENDMENT

Dear Dr. Patel:

Reference is made to the Altana Inc. Abbreviated New Drug Application for Betamethasone Dipropionate Gel, 0.05% (Augmented) submitted December 18, 1997, pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to FDA correspondence dated June 22, 2000 and Altana's November 3, 2000 response.

Altana Inc. acknowledges receipt of FDA's December 5, 2000 Telephone Amendment. As requested this response has been appropriately identified as a TELEPHONE AMENDMENT.

As requested, Altana has revised the Post-Approval Stability Commitment and Protocol to remove

Once a sufficient database is established, data acquired from the first three production batches will be submitted with a as a Supplement to the application.

This concludes Altana's response to this Telephone Amendment. If you have any questions or require additional clarification please contact me at (631) 454-7677 extension 2091. Fax communications may be made to (631) 756-5114.

Sincerely,
Altana Inc.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
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DEC 06 2000
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VC:ab

Enclosures
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ALTANA

ana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

November 3, 2000

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
7500 Standish Place
Rockville, MD 20855

Via Federal Express

NDA ORIG AMENDMENT
N/Am

ANDA 75-276
Betamethasone Dipropionate Gel, 0.05% (Augmented)
MINOR AMENDMENT

Dear Dr. Patel:

Reference is made to the Altana Inc. Abbreviated New Drug Application for Betamethasone Dipropionate Gel, 0.05% (Augmented) submitted December 18, 1997, pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Altana Inc. acknowledges receipt of the following FDA correspondence dated June 22, 2000. As requested this response has been appropriately identified as a MINOR AMENDMENT.

Each item has been addressed in **comment**/response format.

CHEMISTRY DEFICIENCIES:

1. **DMF remains deficient. The DMF holder has been notified. Please do not respond to this amendment until you have been notified by the DMF holder that the new DMF deficiencies have been addressed.**

   Altana Inc. has received confirmation from the DMF holder that the new DMF deficiencies have been addressed. A copy of their correspondence has been included as Attachment I.

2. **Please explain the difference between the specifications on Specification No. and the specifications on the stability reports regarding the degradation products.**

   There is no difference between the specifications on Specification No. and the specifications on the stability reports. Both documents state the specifications as follows:

Betamethasone:	not more than	%
Others:	each not more than	%
Total:	not more than	%

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 516-454-7677 Fax: 516-756-5114 BYK GULDEN PHARMA GROUP

November 15, 1999

FPL AC

75-276

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 II, Room 286
7500 Standish Place
Rockville, Maryland 20855-2773

276

Re: ANDA 75-~~206~~ MAJOR AMENDMENT

Betamethasone Dipropionate Gel, 0.05%

Dear Dr. Patel:

Reference is made to our original Abbreviated New Drug Application submitted December 18, 1997 pursuant to Section 505(j) of the Act, as well as our amendment of January 29, 1998.

Reference is also made to the Agency's telefax of July 20, 1998 in which deficiencies in our application were noted.

We wish to respond to each of the Agency's concerns as follows:

A. Deficiencies

1. **Comment**

Please provide the particle size testing method for the drug substance of Betamethasone Dipropionate USP.

Response

The methodology for determining particle size for the active drug substance betamethasone dipropionate is included in Attachment 1.

2. **Comment**

Please establish an individual impurity limit for the drug substance of Betamethasone Dipropionate USP.

Response

Individual impurity limits have been established for the drug substance betamethasone dipropionate USP. Please see the revised specifications located in Attachment 2. Revised analytical procedures may be found in Attachment 3. Individual impurity and residual solvent testing was performed on the active substance lots used to manufacture the exhibit batches. Results of this testing may be found in Attachment 4.

3. **Comment**

Please clarify whether every batch of the drug substance and the inactive ingredients was tested in-house or not. If they are not, please provide the brief procedures for qualifying vendors.

Response

Every batch of active undergoes full USP testing in-house*. Inactive ingredients are qualified by doing full assays on three consecutive batches from each supplier. If all three batches meet USP specifications, the vendor is considered qualified. Additional batches of in actives will have "short" testing performed usually identification tests and assay. In addition, one incoming lot a year of each ingredient and supplier undergoes full testing.

If for some reason an ingredient from a particular vendor is not qualified, full testing is performed on all lots of this ingredient until three consecutive lots meet all USP/NF specifications.

*There are some tests such as OVI and Residual Solvent that we cannot perform in-house. This testing is sent to an outside laboratory : A cGMP letter was included in the application for however not for A letter stating compliance with cGMPs is enclosed in Attachment 5.

4. **Comment**

Please provide schedules and the tests for re-testing of the drug substance and inactive ingredients.

Response

As per SOP all raw materials not requiring microbial limits testing are re-tested at one-year intervals. If microbial limits testing is required, the substance is retest at six months. Therefore, all the substances used in the production of this drug product have a one year retest period. Retest specifications for all raw materials can be found in Attachment 6.

5. **Comment**

Please revise the manufacturing instructions for kg batch size to incorporate the changes at steps used in the three executed batches.

Response

The manufacturing instructions for both sizes have been revised to incorporate the changes at Steps used in the exhibit batches. The instructions for the kg batch size can be found in Attachment 7 and the kg batch size in Attachment 8.

6. **Comment**

Since the resins used to manufacture the caps for the 15g tubes are only described as in the standard tube specifications, please provide the name of manufacture/supplier and the part number/code.

Response

We wish to remove references to resin and These two resins were not used in the Manufacture of the caps. We apologize for this error. The 15g tube (manufactured by was manufactured with resin and

. (manufactured by utilizes resin and

Information on the resin and are already in the file. Please see Attachment 9 for information on the resin and

7. Comment

Please provide the tube specifications and drawing of the 15g tube, , manufactured by

Response

Attachment 10 contains updated specifications and drawing of the 15g tube

8. Comment

Please provide a container/closure testing commitment, which should include the protocol and schedule for initial release testing and re-testing.

Response

Please see Attachment 11 for the container closure testing commitment.

9. Comment

Please provide the sampling procedure for in-process testing and include a limit of relative standard deviation (RSD) in the assay specifications of the in-process controls since the assay tests included multiple samples at different positions

Response

The in-process specifications have been revised to include a specification stating that all in-process samples must have a relative standard deviation of not more than % and must fall within % of the labeled content of betamethasone dipropionate. Revised specifications may be found in Attachment 12.

As per SOP individuals collecting samples must be dressed appropriately to prevent contamination of the sample. A sampling thief is used to extract samples from the prior to the product being moved to storage containers or filling line. Two samples are taken from each sampling point. These samples are each placed in individual containers of an appropriate inert material (plastic, glass, etc.). The samples are not composited. One sample from each set is tested in the laboratory, while the second is retained as a backup sample. When microbiology testing is required, duplicate additional samples are taken.

10. Comment

Please reduce the Betamethasone Dipropionate assay upper limit in the in-process controls, finished products, and stability specifications from % of label claim to %, which is based on % overage in the formulation and % maximum allowable error in the assay method.

Response

Although % maximum error in the assay method is reasonable, additional range is needed for manufacturing variation. The need for tolerances and limits, which allow for variations arising from sources in addition to analytical error, is recognized by the USP. In the General Notices of USP 24 it states.

> "The tolerances and limits stated in the definitions in the monographs for Pharmacopoeia articles allow for such overages and for analytical error, for unavoidable variations in manufacturing and compounding, and for deterioration to an extent considered acceptable under practical conditions."

11. Comment

Specification of homogeneity is defined as all assays for Betamethasone Dipropionate fall within % of the mean in the finished product specifications. However, it is not clear how the mean is defined. Based on the stability data you provided, the mean is not calculated from the assays at top, middle and bottom of tube.

Response

The stability specification has been revised to clarify the homogeneity specification. It is defined as "the betamethasone dipropionate equivalent to betamethasone assay values for the beginning middle and end of the container are % of the mean of the three values. The mean of the three values falls within % of the labeled content for betamethasone dipropionate equivalent to betamethasone. Please see revised specifications in Attachment 13.

12. Comment

Please provide a justification, such as comparison between your product and the innovator product, for the high limits of degradation products in the finished product and stability specifications.

Response

As requested, studies were conducted to compare the levels of degradation products in Altana's Betamethasone Dipropionate Gel 0.05% with the levels in Schering's Diprolene Gel 0.055. The expiration date of Schering's lot 6RFH503 was 10/98; the full 18 month study at 25°C/60% R.H. was completed before this expiration date. The results of the various studies (4° -- 45° cycling, 40°C/75% RH and 25°C/60% R.H.) are presented in the tables located in Attached 14. The levels of degradation products were found to be comparable in the two gels.

13. Comment

The limits of degradation products in the certificates of analysis for the finished products, batch 9753, 9754, and A095, were different from the proposed specifications for finished product on pages 2416 and 2417. Please clarify.

Response

The specifications used to release the material were the initial specifications written for this product Since that time analytical data have become available which have allowed us to better define the specifications. In this case the degradations limits for other compounds

were able to be reduced form "each not more than %" to "each not more than , and total degradation products from "not more than %" to "not more than %". The finished product specifications for pH and homogeneity have further been revised. Please see finished product specifications in Attachment 15.

14. Comment

In the Betamethasone Dipropionate assay method . NMT % difference between the area obtained for the final injection of the standard and the mean of the areas obtained for the first five injections of the standard is inconsistent with the conclusions of sample solution stability in the method validation Please justify.

Response

The analytical procedure has been revised. The revised procedure has specified in the system suitability section, "that the area of the last standard injection is to be within % of the mean of the areas of the first five standard injections. Please see revised analytical method in Attachment 16.

15. Comment

Please add a note in the sample preparation section of the Betamethasone Dipropionate assay method to indicate that a sample solution should be analyzed within 24 hours since a sample preparation is stable for 24 hours as the method validation reported.

Response

A note has been added to the revised analytical procedure to indicate that a sample solution should be analyzed within 24 hours. Please see revised analytical procedures in Attachment 16.

16. Comment

Two testing alert reports in the application reported that the assay results of the batch 9753 and A095 are out of the upper limit of assay specification without any assignable lab causes found. It is against the principle of GMP to repeat the test and average the results to pass a specification if the initial tests and results were found to be valid. Please comment.

Response

The laboratory followed SOP 'Analytical Test Decision Procedure" to determine the usability of the initial and retest data.

The testing was repeated by the chemist who performed the original assay. In this case the results were passing. Testing was performed again by a second chemist whose results confirmed the passing results of the first chemist.

Since the results of the initial testing could not be invalidated, the results were averaged in. This SOP has been reviewed by the local district office in conjunction with a preapproval inspection with no adverse comments.

A copy of the "decision tree" from SOP and it's reverse page with FDA's signature is included in Attachment 17.

17. Comment

Since significant upward trends for the degradants were observed in the accelerated and long-term stability data of all three batches, please note that complete long-term stability data are required to approve your proposed expiration data.

Response

Attachment 18 contains updated 24-month room temperature stability data. Based on these data we request an eighteen-month expiry date.

18. Comment

The DMF is currently inadequate. The DMF holder, has been notified.

Response

We acknowledge your comments concerning the referenced DMF. We have been informed that the DMF deficiencies have been addressed. A copy of the correspondence from is included in Attachment 19. As per the Office's request we also acknowledge that samples of the finished dosage form will be requested by the district office for methods validation. We will submit samples promptly when requested.

Labeling Deficiencies:

1. **General comments**

   a. The established name of this product is Betamethasone Dipropionate Gel. Throughout your labeling, please refer to your drug product as betamethasone dipropionate gel (augmented).

   b. Please note that USAN names are common nouns and should be treated as such in the text of labeling (i.e., lower case). Upper case may be used when the USAN name stands alone as on labels or on the title of the package insert.

   c. Replace the ' statement with the symbol "Rx only" or "R only". We refer you to the Guidance For Industry, "Implementation of Section 126, Elimination of Certain Labeling Requirements....", at the Internet site, http://www.fda.gov/cder/guidance/index.htm.

2. **Container (15g and 50g)**

   a. Please ensure that the established name and strength appears as the most prominent information on your label. For example:

   BETAMETHASONE DIPROPIONATE GEL, 0.05% (AUGMENTED)

   b. See General comments

   Response

   Container labeling has been revised to incorporate the Agency's General comments as well as the specific request for the product name to be the most prominent information on the label.

   We acknowledge the FDA-s request for draft labeling and further comments regarding possible changes to Final Printed labeling (FPL) based upon later review of FPL prior to approval. We are submitting FPL, which we believe, has incorporated the Agency's current requests. We believe

that reviewing our proposed FPL now will facilitate approval of the FPL in that, if correct, it may remove one labeling review cycle. Please see revised container labeling in Attachment 20.

3. CARTON (15g and 50g)

a. See GENERAL comments.

b. See CONTAINER comments.

Response

Revised carton labeling incorporating the Agency's requested changes is included in Attachment 21.

4. INSERT

a. GENERAL COMMENTS

Revised to delete the strength, "0.05%", appearing with the established name of your product throughout the text except the product title and HOW SUPPLIED section.

b. DESCRIPTION

Revised the first sentence of the second paragraph to read, ...molecular formula...rather than ...empirical formula...

c. PRECAUTIONS

i. General

Revised the first sentence of the eighth paragraph to read, ...antifungal...(delete dash)

ii. Carcinogenesis, Mutagenesis, and Impairment of Fertility

(A) revise to delete " form the subsection heading.

(B) Revised to delete the use of the terminal zero (i.e., "1" rather than ' and "2" rather than

iii. Pregnancy

Revised the first sentence of the third paragraph to read, ...pregnant women.

Response

Revised insert labeling incorporating the Agency's requested changes is included in Attachment 22.

We have included side-by-side comparisons of our proposed labeling with the previously submitted labeling as follows:

Container	Attachment 23
Carton	Attachment 24
Insert	Attachment 25

We also acknowledge that the Agency reserves the right to request further changes in our labels/labeling based upon changes in the approved labeling of the listed drug or upon further review of the application.

We trust the submitted information will clarify any issues the Agency has concerning our application and that we will receive a tentative approval of the application.

If there are any further questions; please contact me at (631) 454-7677, extension 2091.

For your information our new fax number is (631) 756-5114.

Sincerely,
Altana Inc.

Virginia Carman
Associate Director
Regulatory Affairs

Enclosures

VC/et

BIOAVAILABILITY

ALTANA

tana Inc. 60 Baylis Road, Melville, N.Y. 11747 516-454-7677 Fax: 516-454-6389 BYK GULDEN PHARMA GROUP

June 11, 1998

Mr. Douglas Sporn, Director
Office of Generic Drugs
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD. 20855

ONG AMENDMENT
N/A B

RE: ANDA 75-276 **Bioequivalence Telephone Amendment**
Betamethasone Dipropionate Gel, 0.05%

Dear Mr. Sporn:

Reference is made to our Abbreviated New Drug Application of December 18, 1997.

Reference is also made to a telephone request from the Division of Bioequivalence for the analytical results for the test product (Betamethasone Dipropionate Gel, 0.05% manufactured by Altana, Inc.)

The submitted assay report lists two assay results for "beginning" and "end" samples. These two results are for samples taken at the beginning of the packaging run and end of the packaging run. This is done for each packaging size.

For release purposes both results must be within specifications. For reporting purposes the two results are averaged. Therefore, the assay results for Betamethasone Dipropionate Gel, 0.05% lot number 9753 are %.

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

Sincerely,

Altana Inc.

Virginia Carman

Virginia Carman
Associate Director
Regulatory Affairs

VC:pj

RECEIVED
JUN 16 1998
GENERIC DRUGS

ok to file
S. Middleton 2/4/98

BIOAVAILABILITY

ALTANA

ana Inc. 60 Baylis Road, Melville, N.Y. 11747 516-454-7677 Fax: 516-454-6389 BYK GULDEN PHARMA GROUP

FEDERAL EXPRESS

ORIG AMENDMENT

N/RE

January 29, 1998

Mr. Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Food and Drug Administration
Metro Park North 2
7500 Standish Place
Rockville, MD 20855-2773

RE: ANDA 75-276
Betamethasone Dipropionate Gel 0.05%

Dear Mr. Phillips

Reference is made to our Abbreviated New Drug Application of December 18, 1997 as well as your refusal file correspondence of January 21, 1998.

In your letter you requested a letter from designating the to act as their agent. Secondly, you requested an updated DMF letter from allowing us to reference their DMF.

As requested, please find enclosed letters from both,

Additionally, we've included a diskette which contains the data files for our vasoconstrictor bioequivalence study.

With the inclusion of this additional information, we trust that our application warrants a complete technical review.

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

Sincerely,
Altana Inc.

Virginia Carman

Virginia Carman
Associate Director
Regulatory Affairs

Enclosure

C:\GINGER\1998\LETTERS\ANDA7527.WPD

RECEIVED

JAN 30 1998

GENERIC DRUGS

Not OK File S. Middleton 1-9-98

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 516-454-7677 Fax: 516-454-6389 BYK GULDEN PHARMA GROUP

FEDERAL EXPRESS

December 18, 1997

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

RE: Original Submission
Abbreviated New Drug Application
Betamethasone Dipropionate Gel, 0.05%

Dear Sir or Madam:

Pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act and in accordance with the provisions of the Regulations contained in 21 CFR §314.94, Altana Inc., is submitting this Abbreviated New Drug Application to market a new drug, Betamethasone Dipropionate Gel, 0.05%.

The reference listed drug that is the basis for this submission is Diprolene® (Augmented Betamethasone Dipropionate) Gel, 0.05% (NDA 19-408), manufactured by Schering. The proposed drug, Betamethasone Dipropionate Gel, 0.05%, contains the same active ingredient in the same strength and dosage form, has the same indications and usage, and route of administration as the reference listed drug.

The exhibit batches (9753, 9754, A095) included in this application were fully packaged utilizing the 15 gram and 50 gram packages, two of which approval is currently requested. The number of units filled of each package size and the disposition of any remaining bulk product are reconciled in the exhibit batch record.

Included in the five (5) volume submission, along with Form FDA 356h, is the required Patent Certification and Exclusivity statements, draft Labeling, Bioequivalence Study, full Components and Composition statements, Raw Materials Control, Description of the Manufacturing Facilities, Manufacturing and Processing instructions, In-process Controls, Filling and Packaging procedures, information on the Container Closure System, controls for the Finished Dosage Form, Analytical Methods, Finished Dosage Form Stability, Environmental Impact Analysis statement, Certification Requirements of the Generic Drug Enforcement Act of 1992, and the Methods validation package.

All regulatory correspondences related to this Abbreviated New Drug Application should be addressed to:

Virginia Carman
Associate Director
Regulatory Affairs
Altana Inc.
60 Baylis Road
Melville, New York 11747
Tel. No. (516) 454-7677, Ext. 2091
Fax No. (516) 454-6389

A certified copy of this application (consisting of volumes 1.1, 1.4 & 1.5 and a copy of the Methods Validation package) is being sent to the New York District Office under separate cover.

We trust that this submission will meet with your approval. Please advise us if you require any additional information.

Sincerely,
Altana Inc.

Virginia Carman

Virginia Carman
Associate Director
Regulatory Affairs

VC/kmb

Enclosures

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