CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
ANDA 077287

Name: Prednicarbate Cream
0.1% (Emollient)

Sponsor: Altana, Inc.

Approval Date: September 19, 2006

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 077287

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 077287

APPROVAL LETTER

ANDA 77-287

SEP 19 2006

ALTANA Inc
Attention: Robert J. Anderson
P.O.Box 2006
Melville, NY 11747

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated September 23, 2004, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Prednicarbate Cream, 0.1% (Emollient).

Reference is also made to your amendments dated January 27, and April 4, 2006.

We have completed the review of this ANDA and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved. The Division of Bioequivalence has determined your Prednicarbate Cream, 0.1% (Emollient) to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Dermatop of Sanofi Aventis US).

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications (HFD-42) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

Robert Lee Sest/ for
9/19/2006

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

cc: ANDA 77-287
Division File
Field Copy
HFD-610/R. West
HFD-205
HFD-610/Orange Book Staff

Approved Electronic Labeling Located at:
\\Cdsesubogd1\n77287\N_000\2005-07-28\Package Insert.pdf

Endorsements:
HFD-620/R.Murali/RM 4/5/06 4/5/06
HFD-623/J.Fan/
HFD-617/R.Adigun/RA 4/4/06
HFD-613/B.Weitzman/
HFD-613/J.Grace/

V:\FIRMSAM\ALTANA\LTRS&REV\77-287.ap.doc

F/T by

APPROVAL

P S 4/6/06
7/24/06

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 077287

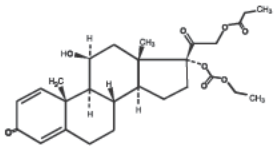
LABELING

fougera®

PREDNICARBATE CREAM 0.1% (EMOLLIENT)

FOR DERMATOLOGIC USE ONLY. **Rx only** **NOT FOR USE IN EYES.**

DESCRIPTION: Prednicarbate cream 0.1% (emollient) contains prednicarbate, a synthetic corticosteroid for topical dermatologic use. The chemical name of prednicarbate is 11β,17,21-trihydroxypregna-1,4-diene-3,20-dione 17-(ethyl carbonate) 21-propionate. Prednicarbate has the empirical formula $C_{27}H_{36}O_8$ and a molecular weight of 488.58. Topical corticosteroids constitute a class of primarily synthetic steroids used topically as anti-inflammatory and antipruritic agents. The CAS Registry Number is 73771-04-7. The chemical structure is:



Prednicarbate is a practically odorless white to yellow-white powder insoluble to practically insoluble in water and freely soluble in ethanol. Each gram of prednicarbate cream 0.1% (emollient) contains 1.0 mg of prednicarbate in a base consisting of white petrolatum, purified water, isopropyl myristate, lanolin alcohols, mineral oil, cetostearyl alcohol, aluminum stearate, edetate disodium, lactic acid, and magnesium stearate.

CLINICAL PHARMACOLOGY: In common with other topical corticosteroids, prednicarbate has anti-inflammatory, antipruritic, and vasoconstrictive properties. In general, the mechanism of the anti-inflammatory activity of topical steroids is unclear. However, corticosteroids are thought to act by the induction of phospholipase A_2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A_2.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Use of occlusive dressings with hydrocortisone for up to 24 hours have not been shown to increase penetration; however, occlusion of hydrocortisone for 96 hours does markedly enhance penetration. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Studies performed with prednicarbate cream 0.1% (emollient) indicate that the drug product is in the medium range of potency compared with other topical corticosteroids.

INDICATIONS AND USAGE: Prednicarbate cream 0.1% (emollient) is a medium-potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses. Prednicarbate cream 0.1% (emollient) may be used with caution in pediatric patients 1 year of age or older. The safety and efficacy of drug use for longer than 3 weeks in this population have not been established. Since safety and efficacy of prednicarbate cream 0.1% (emollient) have not been established in pediatric patients below 1 year of age, its use in this age group is not recommended.

CONTRAINDICATIONS: Prednicarbate cream 0.1% (emollient) is contraindicated in those patients with a history of hypersensitivity to any of the components in the preparations.

PRECAUTIONS: General: Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment. Patients applying a topical steroid to a large surface area or under occlusion should be evaluated periodically for evidence of HPA-axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free cortisol tests. Prednicarbate cream 0.1% (emollient) did not produce significant HPA-axis suppression when used at a dose of 30g/day for a week in 10 adult patients with extensive psoriasis or atopic dermatitis. Prednicarbate cream 0.1% (emollient) did not produce HPA-axis suppression in any of 59 pediatric patients with extensive atopic dermatitis when applied BID for 3 weeks to > 20% of the body surface. (See **PRECAUTIONS, Pediatric Use**). If HPA-axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of the application, or to substitute a less potent corticosteroid. Recovery of HPA-axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur, requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for those products. Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. (See **PRECAUTIONS, Pediatric Use**).

If irritation develops, prednicarbate cream 0.1% (emollient) should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing a failure to heal rather than noting a clinical exacerbation, as observed with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic patch testing. If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favorable response does not occur promptly, use of prednicarbate cream 0.1% (emollient) should be discontinued until the infection has been adequately controlled.

Information for Patients

Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged, otherwise covered or wrapped so as to be occlusive, unless directed by the physician.
4. Patients should report to their physician any signs of local adverse reactions.
5. Parents of pediatric patients should be advised not to use this medication in the treatment of diaper dermatitis. This medication should not be applied in the diaper area as diapers or plastic pants may constitute occlusive dressing (See **DOSAGE AND ADMINISTRATION**).
6. This medication should not be used on the face, underarms, or groin areas.

As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within two weeks, contact the physician.

Laboratory Tests: The following tests may be helpful in evaluating patients for HPA-axis suppression: ACTH stimulation test, AM plasma cortisol test, Urinary free cortisol test.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: In a study of the effect of prednicarbate on fertility, pregnancy, and postnatal development in rats, no effect was noted on the fertility or pregnancy of the parent animals or postnatal development of the offspring after administration of up to 0.80 mg/kg of prednicarbate subcutaneously. Prednicarbate has been evaluated in the Salmonella reversion test (Ames test) over a wide range of concentrations in the presence and absence of an S-9 liver microsomal fraction, and did not demonstrate mutagenic activity. Similarly, prednicarbate did not produce any significant changes in the numbers of micronuclei seen in erythrocytes when mice were given doses ranging from 1 to 160 mg/kg of the drug.

Pregnancy: Teratogenic Effects: Pregnancy Category C.: Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. Prednicarbate has been shown to be teratogenic and embryotoxic in Wistar rats and Himalayan rabbits when given subcutaneously during gestation at doses 1900 times and 45 times the recommended topical human dose, assuming a percutaneous absorption of approximately 3%. In the rats, slightly retarded fetal development and an incidence of thickened and wavy ribs higher than the spontaneous rate were noted. In rabbits, increased liver weights and slight increase in the fetal intrauterine death rate were observed. The fetuses that were delivered exhibited reduced placental weight, increased frequency of cleft palate, ossification disorders in the sternum, omphalocele, and anomalous posture of the forelimbs. There are no adequate and well-controlled studies in pregnant women on teratogenic effects of prednicarbate. Prednicarbate cream 0.1% (emollient) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when prednicarbate cream 0.1% (emollient) is administered to a nursing woman.

Pediatric Use: Prednicarbate cream 0.1% (emollient) may be used with caution in pediatric patients 1 year of age or older, although the safety and efficacy of drug use longer than 3 weeks have not been established. The use of prednicarbate cream 0.1% (emollient) is supported by results of a three week, uncontrolled study in 59 pediatric patients between the ages of 4 months and 12 years of age with atopic dermatitis. None of the 59 pediatric patients showed evidence of HPA-axis suppression. Safety and efficacy of prednicarbate cream 0.1% (emollient) in pediatric patients below 1 year of age have not been established, therefore use in this age group is not recommended. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA-axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment. In an uncontrolled study in pediatric patients with atopic dermatitis, the incidence of adverse reactions possibly or probably associated with the use of prednicarbate cream 0.1% (emollient) was limited. Mild signs of atrophy developed in 5 patients (5/59, 8%) during the clinical trial, with 2 patients exhibiting more than one sign. Two patients (2/59, 3%) developed shininess, and two patients (2/59, 3%) developed thinness. Three patients (3/59, 5%) were observed with mild telangiectasia. It is unknown whether prior use of topical corticosteroids was a contributing factor in the development of telangiectasia in 2 of the patients. Adverse effects including striae have also been reported with inappropriate use of topical corticosteroids in infants and children. Pediatric patients applying topical corticosteroids to greater than 20% of body surface are at higher risk for HPA-axis suppression. HPA-axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema. Prednicarbate cream 0.1% (emollient) should not be used in the treatment of diaper dermatitis.

ADVERSE REACTIONS: In controlled adult clinical studies, the incidence of adverse reactions probably or possibly associated with the use of prednicarbate cream 0.1% (emollient) was approximately 4%. Reported reactions included mild signs of skin atrophy in 1% of treated patients, as well as the following reactions which were reported in less than 1% of patients: pruritis, edema, paresthesia, urticaria, burning, allergic contact dermatitis and rash. In an uncontrolled study in pediatric patients with atopic dermatitis, the incidence of adverse reactions possibly or probably associated with the use of prednicarbate cream 0.1% (emollient) was limited. Mild signs of atrophy developed in 5 patients (5/59, 8%) during the clinical trial, with 2 patients exhibiting more than one sign. Two patients (2/59, 3%) developed shininess, and 2 patients (2/59, 3%) developed thinness. Three patients (3/59, 5%) were observed with mild telangiectasia. It is unknown whether prior use of topical corticosteroids was a contributing factor in the development of telangiectasia in 2 of the patients. (See **PRECAUTIONS, Pediatric Use**). The following additional local adverse reactions have been reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence: folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, secondary infection, striae and miliaria.

OVERDOSAGE: Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects. (See **PRECAUTIONS**).

DOSAGE AND ADMINISTRATION: Apply a thin film of prednicarbate cream 0.1% (emollient) to the affected skin areas twice daily. Rub in gently. Prednicarbate cream 0.1% (emollient) may be used in pediatric patients 1 year of age or older. Safety and efficacy of prednicarbate cream 0.1% (emollient) in pediatric patients for more than 3 weeks of use have not been established. Use in pediatric patients under 1 year of age is not recommended. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary. Prednicarbate cream 0.1% (emollient) should not be used with occlusive dressings unless directed by the physician. Prednicarbate cream 0.1% (emollient) should not be applied in the diaper area if the child still requires diapers or plastic pants as these garments may constitute occlusive dressing.

HOW SUPPLIED: Prednicarbate Cream 0.1% (Emollient) is supplied:

15 gram tube NDC 0168-0381-15
60 gram tube NDC 0168-0381-60

Store between 20°- 25°C (68°-77°F), with excursions permitted to 15°-30°C (59°-86°F).[see USP Controlled Room Temperature].

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747

I2381
R7/05
#108

NDC 0168-0381-15

fougera®

PREDNICARBATE CREAM 0.1% (EMOLLIENT)

Usual Dosage: Apply a thin film to the affected skin areas twice daily. Rub in gently. See package insert for full prescribing information.
Store between 20°- 25°C (68°-77°F), with excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].

WARNING: Keep out of reach of children.
TO OPEN: Use cap to puncture seal.
IMPORTANT: Do not use if seal has been punctured or is not visible.

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747

℞ only

FOR DERMATOLOGIC USE ONLY
NOT FOR USE IN EYES

NET WT 15 grams

Each gram of prednicarbate cream 0.1% (emollient) contains 1.0 mg of prednicarbate in a base consisting of white petrolatum, purified water, isopropyl myristate, lanolin alcohols, mineral oil, cetostearyl alcohol, aluminum stearate, edetate disodium, lactic acid, and magnesium stearate.

See crimp of tube for Lot Number and Expiration Date.

U5253 R7/05

N 3 0168-0381-15 2

#08

NDC 0168-0381-60

fougera®

PREDNICARBATE CREAM 0.1% (EMOLLIENT)

Usual Dosage: Apply a thin film to the affected skin areas twice daily. Rub in gently. See package insert for full prescribing information.
Store between 20°- 25°C (68°-77°F), with excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].
WARNING: Keep out of reach of children.

TO OPEN: Use cap to puncture seal.
IMPORTANT: Do not use if seal has been punctured or is not visible.

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747

℞ only

FOR DERMATOLOGIC USE ONLY
NOT FOR USE IN EYES

NET WT 60 grams

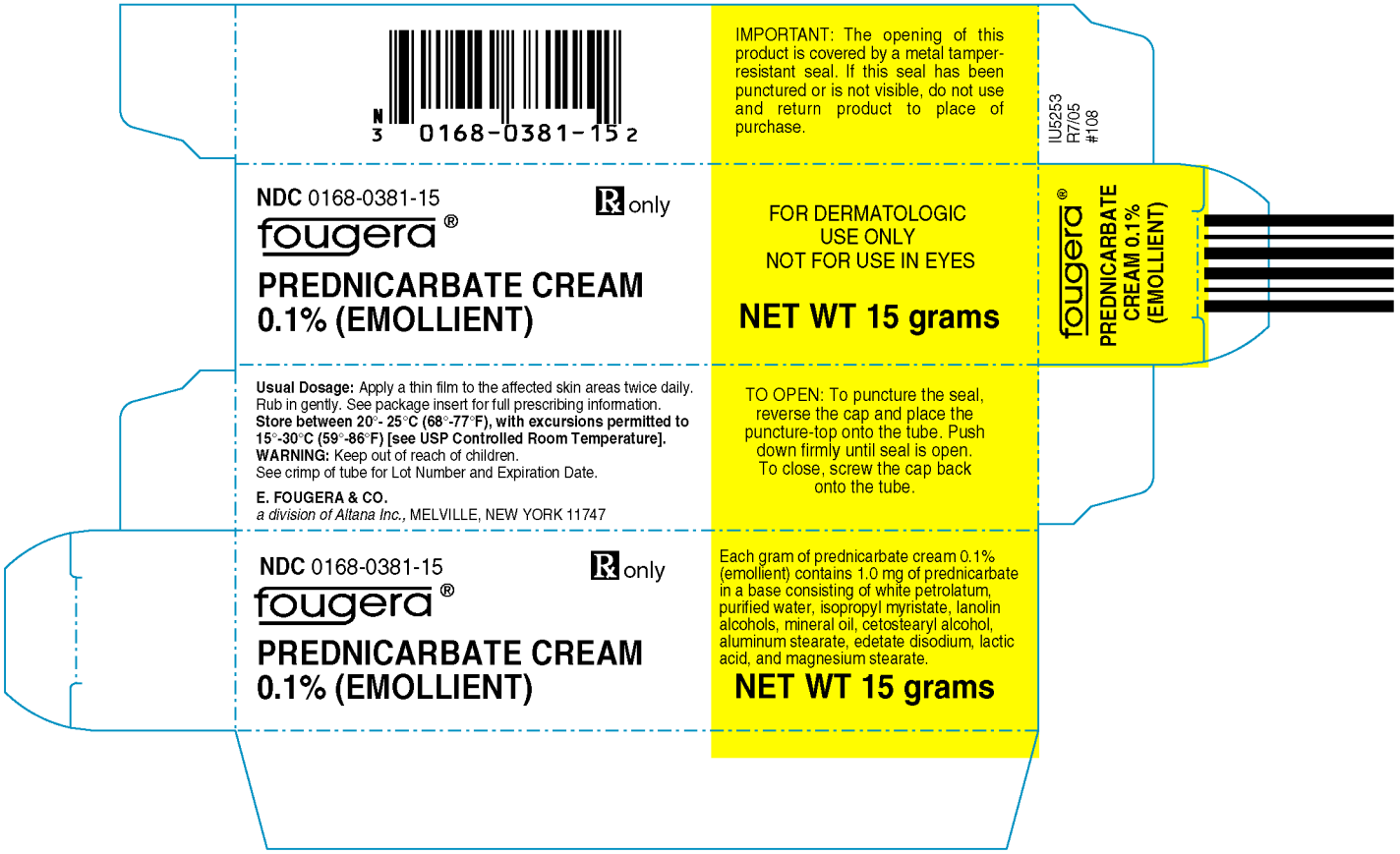
Each gram of prednicarbate cream 0.1% (emollient) contains 1.0 mg of prednicarbate in a base consisting of white petrolatum, purified water, isopropyl myristate, lanolin alcohols, mineral oil, cetostearyl alcohol, aluminum stearate, edetate disodium, lactic acid, and magnesium stearate.

See crimp of tube for Lot Number and Expiration Date.

H5254 R7/05

N 3 0168-0381-60 2

#12


N 3 0168-0381-15 2
IMPORTANT: The opening of this product is covered by a metal tamper-resistant seal. If this seal has been punctured or is not visible, do not use and return product to place of purchase.
IU5253
R7/05
#108
NDC 0168-0381-15
℞ only
fougera®
PREDNICARBATE CREAM 0.1% (EMOLLIENT)
FOR DERMATOLOGIC USE ONLY
NOT FOR USE IN EYES
NET WT 15 grams
fougera®
PREDNICARBATE CREAM 0.1% (EMOLLIENT)
Usual Dosage: Apply a thin film to the affected skin areas twice daily. Rub in gently. See package insert for full prescribing information.
Store between 20°- 25°C (68°-77°F), with excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].
WARNING: Keep out of reach of children.
See crimp of tube for Lot Number and Expiration Date.
E. FOUGERA & CO.
a division of Altana Inc., MELVILLE, NEW YORK 11747
TO OPEN: To puncture the seal, reverse the cap and place the puncture-top onto the tube. Push down firmly until seal is open. To close, screw the cap back onto the tube.
NDC 0168-0381-15
℞ only
fougera®
PREDNICARBATE CREAM 0.1% (EMOLLIENT)
Each gram of prednicarbate cream 0.1% (emollient) contains 1.0 mg of prednicarbate in a base consisting of white petrolatum, purified water, isopropyl myristate, lanolin alcohols, mineral oil, cetostearyl alcohol, aluminum stearate, edetate disodium, lactic acid, and magnesium stearate.
NET WT 15 grams

108

IMPORTANT: The opening of this product is covered by a metal tamper-resistant seal. If this seal has been punctured or is not visible, do not use and return product to place of purchase.

IH5254
R7/05
#112

NDC 0168-0381-60

fougera®

℞ only

PREDNICARBATE CREAM 0.1% (EMOLLIENT)

FOR DERMATOLOGIC USE ONLY
NOT FOR USE IN EYES

NET WT 60 grams

fougera®
PREDNICARBATE CREAM 0.1% (EMOLLIENT)

Usual Dosage: Apply a thin film to the affected skin areas twice daily. Rub in gently.
See package insert for full prescribing information.
Store between 20°- 25°C (68°-77°F), with excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].
WARNING: Keep out of reach of children.
See crimp of tube for Lot Number and Expiration Date.

E. FOUGERA & CO.
a division of Altana Inc., MELVILLE, NEW YORK 11747

TO OPEN: To puncture the seal, reverse the cap and place the puncture-top onto the tube. Push down firmly until seal is open.

To close, screw the cap back onto the tube.

NDC 0168-0381-60

fougera®

℞ only

PREDNICARBATE CREAM 0.1% (EMOLLIENT)

Each gram of prednicarbate cream 0.1% (emollient) contains 1.0 mg of prednicarbate in a base consisting of white petrolatum, purified water, isopropyl myristate, lanolin alcohols, mineral oil, cetostearyl alcohol, aluminum stearate, edetate disodium, lactic acid, and magnesium stearate.

NET WT 60 grams

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 077287

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 77-287

Date of Submission: December 2, 2004

Applicant's Name: Altana Inc.

Established Name: Prednicarbate Cream, 0.1% (Emollient)

Labeling Deficiencies:

1. **GENERAL COMMENT [ALL LABELING]**

   The established name of this product is Predinicarbate Cream, 0.1 %. Please revise your labels and labeling accordingly. If you prefer, you may include "Emollient" after the established name as follows: "Prednicarbate Cream (Emollient)" or after the established name and strength "Prednicarbate Cream 0.1% (Emollient)".

2. **CONTAINER:** ((b) (4) 15 gram, 60 gram tubes) - See general comment.
3. **CARTON:** (15 gram, 60 gram) – See general comment.
4. **INSERT:** See general comment

Please revise your labels and labeling, as instructed above, and submit each labeling piece in final print.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidance for industry regarding electronic submissions: Providing Regulatory Submissions in Electronic Format — ANDAs (Issued 6/2002) (http://www.fda.gov/cder/guidance/5004fnl.htm). The guidance specifies labeling to be submitted in pdf format. To assist in our review, we request that labeling also be submitted in MS Word format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -
http://www.fda.gov/cder/cdernew/listserv.html or
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24		X	
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	X		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X

Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			X
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			X
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			X
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			X
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

NOTES/QUESTIONS TO THE CHEMIST: The firm's recommended temperature range is Store between 20° and 25°C (68 - 77°F); excursions permitted to 15° – 30°C (59° – 86°F). [See USP Controlled Room Temperature]. The RLD storage recommendation is "Store between 5^0 C and 25^0 C (41^0 F and 77^0 F)" Can the **firm's use a more restrictive temperature range and does the stability data support this temperature range?**

FOR THE RECORD:

1. MODEL LABELING

Review based on the labeling for the reference listed drug, Dermatop Emollient Cream, 0.1% by Dermik Laboratories, (NDA 20-279/S-001): Approved May 3,1996; **Revised 2003.**

2. PATIENTS/EXCLUSIVTIES:

Patent Data – NDA 20-279

No	Expiration	Use Code	Use	File
		There are no unexpired patents for this product in the Orange Book database		NONE

Exclusivity Data For NDA 20-279

Code/sup	Expiration	Use Code	Description		Labeling Impact
			There is no unexpired exclusivity for this product		NONE

3. INACTIVE INGREDIENTS

There does not appear to be a discrepancy in inactives between the DESCRIPTION and the composition statement.

Name of the Ingredient	Prednicarbate Cream (Altana) (w/w%)	Reference Listed Drug (w/w%)	Pharmaceutical function
Prednicarbate	0.1	0.1	Active ingredient
White Petrolatum USP	(b) (4)		
Purified Water USP			
Isopropyl Myristate NF			
Lanolin Alcohols NF			
Mineral Oil USP			
Cetostearyl Alcohol NF			
Aluminum Stearate			
Edetate Disodium USP			
Lactic Acid (b) (4) USP			
Magnesium Stearate NF			

*The combined level of mineral oil and white petrolatum were determined by HPLC as (b) (4).

4. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

- USP: NONE
- RLD: "Store between 5° C and 25° C (41° F and 77° F)"
- ANDA: Store between 20° and 25°C (68 - 77°F); excursions permitted to 15° – 30°C (59° – 86°F). [See USP Controlled Room Temperature]

5. DISPENSING STATEMENT COMPARISON

- USP: None.
- RLD: None.
- ANDA: None.

6. PACKAGE CONFIGURATION

- RLD: Packaged in 15 g, (b) (4) and 60 g tubes.
- ANDA: Packaged in (b) (4), 15 g, and 60 g lined aluminum tubes.

7. CONTAINER/CLOSURE: Prednicarbate Cream 0.1% is packaged in (b) (4) 15g and 2 oz/60 g lined aluminum tubes.

Tubes

(b) (4)

(b) (4)

[redacted]

8. **FNISHED DOSAGE FORM**

- ANDA: A white to off-white, smooth and homogeneous cream.

9. **MANUFACTURING FACILITY OF FINISHED DOSAGE FORM**
Altana, Inc.
55 Cantiage Rock Road
Hicksville, NY 11802

Date of Review: **Date of Submission: December 2, 2004**

Primary Reviewer: B. Weitzman **Date:** 6/8/2005

Team Leader: John J. Grace **Date:** 6-10-05

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cc: ANDA 77-287
DUP/DIVISION FILE
HFD-613/Bweitzman/JGrace (no cc)
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Review

APPROVAL SUMMARY

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 77-287

Date of Submission: **July 28, 2005**

Applicant's Name: Altana Inc.

Established Name: Prednicarbate Cream, 0.1% (Emollient)

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have Final Printed Labels and Labeling? Yes

(b) (4)

2. **CONTAINER [15 g tube]** – Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\15g Container.pdf
3. **CONTAINER [60 g tube]** – Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\60g Container.pdf
4. **CARTON [15 g tube]** – Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\15g Carton.pdf
5. **CARTON [60 g tube]** – Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\60g Carton.pdf
7. **PACKAGE INSERT** - Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\Package Insert.pdf

BASIS OF APPROVAL:

- Was this approval based upon a petition? No
- What is the RLD on the 356(h) form: Dermatop Emollient Cream, 0.1%
- NDA Number: 19-568
- NDA Drug Name: Prednicarbate Cream, 0.1% (Emollient)
- NDA Firm: Bristol-Myers Squibb Company
- Date of Approval of NDA Insert: 20-279/S-001: Approved May 3, 1996; Revised 2003
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side-by-side comparison
- Basis of Approval for the Carton Labels: Side-by-side comparison
- Revisions needed post-approval: **NO**
- Patents/Exclusivities: Refer to chart below.

Patent Data – NDA 20-279

No	Expiration	Use Code	Use	File
		There are no unexpired patents for this product in the Orange Book database		NONE

Exclusivity Data For NDA 20-279

Code/sup	Expiration	Use Code	Description		Labeling Impact
			There is no unexpired exclusivity for this product		NONE

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24		X	
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	X		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the		X	

insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			X
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			X
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			X
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			X
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

NOTES/QUESTIONS TO THE CHEMIST: The firm's recommended temperature range is Store between 20° and 25°C (68 - 77°F); excursions permitted to 15° – 30°C (59° – 86°F). [See USP Controlled Room Temperature]. The RLD storage recommendation is "Store between 5^0 C and 25^0 C (41^0 F and 77^0 F)" Can the **firm's use a more restrictive temperature range and does the stability data support this temperature range?**

FOR THE RECORD:

1. MODEL LABELING

Review based on the labeling for the reference listed drug, Dermatop Emollient Cream, 0.1% by Dermik Laboratories, (NDA 20-279/S-001): Approved May 3,1996; **Revised 2003.**

2. PATIENTS/EXCLUSIVTIES:

Patent Data – NDA 20-279

No	Expiration	Use Code	Use	File
		There are no unexpired patents for this product in the Orange Book database		NONE

Exclusivity Data For NDA 20-279

Code/sup	Expiration	Use Code	Description		Labeling Impact
			There is no unexpired exclusivity for this product		NONE

3. INACTIVE INGREDIENTS

There does not appear to be a discrepancy in inactives between the DESCRIPTION and the composition statement.

Name of the Ingredient	Prednicarbate Cream (Altana) (w/w%)	Reference Listed Drug (w/w%)	Pharmaceutical function
Prednicarbate	0.1	0.1	Active ingredient
White Petrolatum USP			
Purified Water USP			
Isopropyl Myristate NF			
Lanolin Alcohols NF			
Mineral Oil USP			
Cetostearyl Alcohol NF			
Aluminum Stearate			
Edetate Disodium USP			
Lactic Acid (b) (4) USP			
Magnesium Stearate NF			

(b) (4)

*The combined level of mineral oil and white petrolatum were determined by HPLC as (b) (4)

4. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

- USP: NONE
- RLD: "Store between 5° C and 25° C (41° F and 77° F)"
- ANDA: Store between 20° and 25°C (68 - 77°F); excursions permitted to 15° – 30°C (59° – 86°F). [See USP Controlled Room Temperature]

5. DISPENSING STATEMENT COMPARISON

- USP: None.
- RLD: None.
- ANDA: None.

6. PACKAGE CONFIGURATION

- RLD: Packaged in 15 g, (b) (4) and 60 g tubes.
- ANDA: Packaged in (b) (4), 15 g, and 60 g lined aluminum tubes.

7. CONTAINER/CLOSURE: Prednicarbate Cream 0.1% is packaged in (b) (4) 15g and 2 oz/60 g lined aluminum tubes.

Tubes

(b) (4)

(b) (4)

8. **FNISHED DOSAGE FORM**

- ANDA: A white to off-white, smooth and homogeneous cream.

9. **MANUFACTURING FACILITY OF FINISHED DOSAGE FORM**

Altana, Inc.
55 Cantiage Rock Road
Hicksville, NY 11802

Date of Review: **Date of Submission: July 28, 2005**

Primary Reviewer: B Weitzman **Date:** 8/10/2005

Team Leader: **Date:** 8/10/05

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cc: ANDA 77-287
DUP/DIVISION FILE
HFD-613/Bweitzman/JGrace (no cc)
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Review

APPROVAL SUMMARY
(Supersedes AS dated 8/10/2005)

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 77-287

Date of Submission: **July 28, 2005 and January 27, 2006**

Applicant's Name: Altana Inc.

Established Name: Prednicarbate Cream, 0.1% (Emollient)

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have Final Printed Labels and Labeling? Yes

1. **CONTAINER [15 g tube]** – Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\15g Container.pdf
2. **CONTAINER [60 g tube]** – Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\60g Container.pdf
3. **CARTON [15 g tube]** – Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\15g Carton.pdf
4. **CARTON [60 g tube]** – Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\60g Carton.pdf
5. **PACKAGE INSERT** - Satisfactory in FPL as of July 28, 2005 electronic submission.
\\Cdsesubogd1\n77287\N_000\2005-07-28\Package Insert.pdf

BASIS OF APPROVAL:

- Was this approval based upon a petition? No
- What is the RLD on the 356(h) form: Dermatop Emollient Cream, 0.1%
- NDA Number: 20-279
- NDA Drug Name: Prednicarbate Cream, 0.1% (Emollient)
- NDA Firm: Sanofi Aventis US
- Date of Approval of NDA Insert: 20-279/S-001: Approved May 3, 1996; Revised 2003
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side-by-side comparison
- Basis of Approval for the Carton Labels: Side-by-side comparison
- Revisions needed post-approval: **NO**
- Patents/Exclusivities: Refer to chart below.

Patent Data – NDA 20-279

No	Expiration	Use Code	Use	File
		There are no unexpired patents for this product in the Orange Book database		NONE

Exclusivity Data For NDA 20-279

Code/sup	Expiration	Use Code	Description		Labeling Impact
			There is no unexpired exclusivity for this product		NONE

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24		X	
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	X		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINSTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation see ASHP guidelines)		X	
Labeling(continued)	**Yes**	**No**	**N.A.**
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	

Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			X
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			X
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been usedto protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			X
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDArecommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light restant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a noeffect? If so, was a food study done?			X
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

NOTES/QUESTIONS TO THE CHEMIST: The firm's recommended temperature range is Store between 20° and 25°C (68 - 77°F); excursions permitted to 15° – 30°C (59° – 86°F). [See USP Controlled Room Temperature]. The RLD storage recommendation is "Store between 5^0 C and 25^0 C (41^0 F and 77^0 F)" Can the **firm's use a more restrictive temperature range and does the stability data support this temperature range?**
9/15/2006 E-mailed PM to check if this was resolved.

FOR THE RECORD:

1. MODEL LABELING

Review based on the labeling for the reference listed drug, Dermatop Emollient Cream, 0.1% by Sanofi Aventis US, (NDA 20-279/S-001): Approved May 3,1996; **Revised 2003.**

2. PATIENTS/EXCLUSIVTIES:

Patent Data – NDA 20-279

No	Expiration	Use Code	Use	File
		There are no unexpired patents for this product in the Orange Book database		NONE

Exclusivity Data For NDA 20-279

Code/sup	Expiration	Use Code	Description		Labeling Impact
			There is no unexpired exclusivity for this product		NONE

3. INACTIVE INGREDIENTS

There does not appear to be a discrepancy in inactives between the DESCRIPTION and the composition statement.

Name of the Ingredient	Prednicarbate Cream (Altana) (w/w%)	Reference Listed Drug (w/w%)	Pharmaceutical function
Prednicarbate	0.1	0.1	Active ingredient
White Petrolatum USP	(b) (4)		
Purified Water USP			
Isopropyl Myristate NF			
Lanolin Alcohols NF			
Mineral Oil USP			
Cetostearyl Alcohol NF			
Aluminum Stearate			
Edetate Disodium USP			
Lactic Acid (b) (4) USP			
Magnesium Stearate NF			

*The combined level of mineral oil and white petrolatum were determined by HPLC as (b) (4)

4. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

- USP: NONE
- RLD: "Store between 5° C and 25° C (41° F and 77° F)"
- ANDA: Store between 20° and 25°C (68 - 77°F); excursions permitted to 15° – 30°C (59° – 86°F). [See USP Controlled Room Temperature]

5. DISPENSING STATEMENT COMPARISON

- USP: None.
- RLD: None.
- ANDA: None.

6. PACKAGE CONFIGURATION

- RLD: Packaged in 15 g, (b) (4) and 60 g tubes.
- ANDA: Packaged in (b) (4), 15 g, and 60 g lined aluminum tubes.

7. CONTAINER/CLOSURE: Prednicarbate Cream 0.1% is packaged in (b) (4) 15g and 2 oz/60 g lined aluminum tubes.

Tubes

(b) (4)

8. FNISHED DOSAGE FORM

- ANDA: A white to off-white, smooth and homogeneous cream.

9. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

Altana, Inc.
55 Cantiage Rock Road
Hicksville, NY 11802

10. The sponsor's 1/27/2006 amendment withdraws the (b) (4) package size. This approval summary updates the one dated 8/10/2005 by removing reference to the (b) (4) package size and in that it reflects the change in ownership and control of the RLD sponsor.

Date of Review: September 15, 2006 **Date of Submission:** July 28, 2005 and January 27, 2006

Primary Reviewer: **Date:** 9/15/2006

Team Leader: **Date:** 9-15-06

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cc: ANDA 77-287
DUP/DIVISION FILE
HFD-613/CHoppes/JGrace (no cc)
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Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 077287

CHEMISTRY REVIEWS

ANDA 77-287

Prednicarbate Cream, 0.1%

Altana, Inc.

Raman D. Murali, Ph.D.

Chemistry I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 77-287

2. REVIEW #: 1

3. REVIEW DATE: April 5, 2005

4. REVIEWER: Raman D. Murali, Ph.D.

5. PREVIOUS DOCUMENTS:
   N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original submission	September 23, 2004
Refuse to Receive	November 24, 2004
Amendment	December 2, 2004
Acceptable for filing	December 3, 2004

7. NAME & ADDRESS OF APPLICANT:

Name:	Altana, Inc.
Address:	60 Baylis Road Melville, NY 11747
Representative:	Audrey Zaweski
Telephone:	(631) 454-7677 Ext. 3007
Facsimile:	(631) 756-5114

8. DRUG PRODUCT NAME/CODE/TYPE:

   a) Proprietary Name: N/A
   b) Non-Proprietary Name (USAN): Prednicarbate Cream, 0.1%

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Dermatop® Emollient Cream (Prednicarbate Emollient Cream, 0.1%), NDA 20-279 held by Dermik Laboratories.
The applicant, Altana, certifies that to the best of its knowledge there are no unexpired patents or unexpired exclusivity for this drug product. A copy of the list of Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) is included in this section confirming the above statement.

10. PHARMACOL. CATEGORY:

Topical corticosteroid used as an anti-inflammatory and anti-pruritic agent.

11. DOSAGE FORM: Cream

12. STRENGTH/POTENCY: 0.1%

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: __x_Rx ___OTC

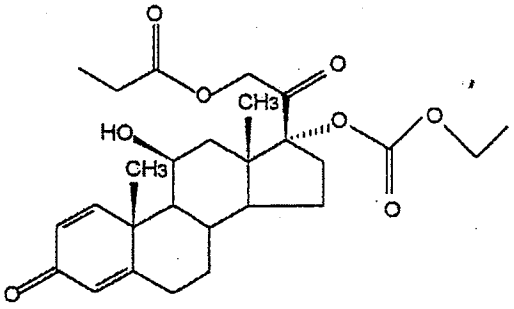
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

___x__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: 11β-Hydroxy-3,20-dioxopregna-1,4-diene-17,21-diyl 17-ethylcarbonate 21-propanoate
Molecular formula: $C_{27}H_{36}O_8$
Molecular weight: 488.6
CAS Number: 73771-04-7



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Holder	Item Referenced	Code[1]	Status[2]	Date Review Completed	Comments
(b) (4)	II	(b) (4)		1	Inadequate	May 19, 2005	Reviewed by R. Murali
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")
[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

Consults/ CMC Related Reviews	Recommendation	Date	Reviewer
Microbiology	N/A		
EES	Acceptable	1/28/05	
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. _X___ Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 77-287

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This ANDA is presently non-approvable. The minor chemistry deficiencies listed in the review should be addressed before the application can be approved. Labeling and Bioequivalency reviews are pending.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug product Prednicarbate cream is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.
Each gram of Prednicarbate cream contains 1.0 mg of Prednicarbate in a base of consisting of White Petrolatum USP, Purified Water USP, Isopropyl Myristate NF, Lanolin Alcohols NF, Mineral Oil USP, Cetostearyl Alcohol NF, Aluminum Stearate, Edetate Disodium USP, Lactic Acid (b) (4) USP and Magnesium Stearate NF.
The drug product is supplied in (b) (4) 15g and 60g lined aluminum tubes. It is to be stored in controlled room temperature, 15°C to 30 °C. The proposed expiration dating for the drug product is (b) (4) months.
The drug substance, Prednicarbate is a synthetic corticosteroid which is a class of primarily synthetic steroids used topically as an anti-inflammatory agent. The chemical name of Prednicarbate is 11β-Hydroxy-3,20-dioxopregna-l,4-diene-17,21-diyl 17-ethylcarbonate 21-propanoate.
Prednicarbate is not described in the USP Monograph. It is a white to off-white powder. Molecular formula is $C_{27}H_{36}O_8$ and molecular weight is 488.6.

B. Description of How the Drug Product is Intended to be Used

The drug product is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. The drug product did not produce significant hypothalamic-pituitary-adrenal (HPA) axis suppression when used at a dose of 30g/day for a week in patients with extensive

psoriasis or atopic dermatoses. The MDD is calculated to be 30 mg/day of the active. Prednicarbate cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

MDD = 30 mg/day

	IT	QT
DS	0.10%	0.15%
DP	0.2%	0.5%

C. Basis for Approvability or Not-Approval Recommendation

The ANDA is non-approvable due to minor deficiencies related to DMF deficiencies, drug substance specifications, container closure system and drug product in-process, release and stability testing.

III. Administrative

A. Reviewer's Signature

/R Murali

B. Endorsement Block

HFD-627/R. Murali/ RM 7/6/05
HFD-627/J. Fan/
HFD-617/A. Vu/ 7/6/05

V:\FIRMSAM\ALTANA\LTRS&REV\77287.RV1.DOC

C. CC Block

ANDA 77-287
ANDA DUP 77-287
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(b) (4)

[redacted]

30. MICROBIOLOGY

N/A

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS

N/A

32. LABELING

Review pending

33. ESTABLISHMENT INSPECTION

Acceptable 1/28/05

34. BIOEQUIVALENCE

Review pending

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

Altana is claiming a categorical exclusion from the requirement of an environmental impact analysis statement pursuant to 21 CFR 25.15 (d) and 25.31(a).

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-287 APPLICANT: Altana Inc.

DRUG PRODUCT: Prednicarbate Cream, 0.1%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

4.

5.

6.

7.

8.

9. (b) (4)

10.

11.

12.

13.

14.

15.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

The Bioequivalency and Labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you separately.

Sincerely yours,

7/6/05

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

cc: ANDA 77-287
ANDA DUP 77-287
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-627/R. Murali/5/2905 RM 7/6/05
HFD-627/J. Fan/ 7/3/05
HFD-617/A. Vu/ 7/6/05

F/T by: ard/7/5/05

V:\FIRMSAM\ALTANA \LTRS&REV\77287.RV1.DOC

TYPE OF LETTER: NOT APPROVABLE - MINOR

ANDA 77-287

Prednicarbate Emollient Cream, 0.1%

Altana, Inc.

Raman D. Murali, Ph.D.

Chemistry I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 77-287 (First Generic)

2. REVIEW #: 2

3. REVIEW DATE: September 2, 2005; Revised: December 19, 2005

4. REVIEWER: Raman D. Murali, Ph.D.

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original submission	September 23, 2004
Refuse to Receive	November 24, 2004
Amendment	December 2, 2004
Acceptable for filing	December 3, 2004

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	August 23, 2005
Amendment	October 19, 2005

7. NAME & ADDRESS OF APPLICANT:

Name: Altana, Inc.
Address: 60 Baylis Road
Melville, NY 11747
Representative: Audrey Zaweski
Telephone: (631) 454-7677 Ext. 3007
Facsimile: (631) 756-5114

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Prednicarbate Emollient Cream, 0.1%

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Dermatop® Emollient Cream (Prednicarbate Emollient Cream, 0.1%), NDA 20-279 held by Dermik Laboratories.
The applicant, Altana, certifies that to the best of its knowledge there are no unexpired patents or unexpired exclusivity for this drug product. A copy of the list of Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) is included in this section confirming the above statement.

10. PHARMACOL. CATEGORY:

Topical corticosteroid used as an anti-inflammatory and anti-pruritic agent.

11. DOSAGE FORM: Cream

12. STRENGTH/POTENCY: 0.1%

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: __x_Rx ___OTC

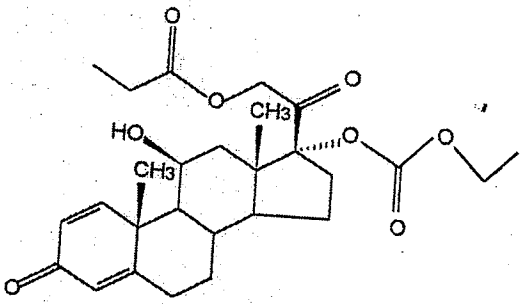
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

____x__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: 11β-Hydroxy-3,20-dioxopregna-1,4-diene-17,21-diyl 17-ethylcarbonate 21-propanoate
Molecular formula: $C_{27}H_{36}O_8$
Molecular weight: 488.6
CAS Number: 73771-04-7



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF # (b) (4)	Type	Holder	Item Referenced (b) (4)	Code[1]	Status[2]	Date Review Completed	Comments
	II			1	adequate	September 15, 2005	Reviewed by R. Murali
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")
[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

Consults/ CMC Related Reviews	Recommendation	Date	Reviewer
Microbiology	N/A		
EES	Acceptable	1/28/05	
Methods Validation	N/A		
Labeling	Acceptable	8/10/05	B. Weitzman
Bioequivalence	Acceptable	9/16/05	H. Nguyen
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. _X___ Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 77-287

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This ANDA is presently non-approvable. The minor chemistry deficiencies listed in the review should be addressed before the application can be approved.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug product Prednicarbate Emollient cream is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.
Each gram of Prednicarbate Emollient cream contains 1.0 mg of Prednicarbate in a base of consisting of White Petrolatum USP, Purified Water USP, Isopropyl Myristate NF, Lanolin Alcohols NF, Mineral Oil USP, Cetostearyl Alcohol NF, Aluminum Stearate, Edetate Disodium USP, Lactic Acid (b) (4) USP and Magnesium Stearate NF.
The drug product is supplied in (b) (4) 15g and 60g lined aluminum tubes. It is to be stored in controlled room temperature, 15°C to 30 °C. The proposed expiration dating for the drug product is (b) (4) months.
The drug substance, Prednicarbate is a synthetic corticosteroid which is a class of primarily synthetic steroids used topically as an anti-inflammatory agent. The chemical name of Prednicarbate is 11β-Hydroxy-3,20-dioxopregna-l,4-diene-17,21-diyl 17-ethylcarbonate 21-propanoate.
Prednicarbate is not described in the USP Monograph. It is a white to off-white powder. Molecular formula is $C_{27}H_{36}O_8$ and molecular weight is 488.6.

B. Description of How the Drug Product is Intended to be Used

The drug product is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. The drug product did not produce significant hypothalamic-pituitary-adrenal (HPA) axis suppression when used at a dose of 30g/day for a week in patients with extensive

psoriasis or atopic dermatoses. Prednicarbate cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

Maximum Daily Dose (MMD) Calculations:
The firm provided the following MDD calculation:
In order to calculate the Maximum Daily Dose (MMD), the reference article *The Finger-Tip Unit-A New Practical Measure* was used[1]. Based upon the article, the nominal weight of cream required for "whole-body treatment of an adult male was 20.1 g". Therefore, when applying a product twice daily[2] on two arms and the back of a patient's trunk (33% body coverage), a dose of 13.3 g (20.1 g x 33% x 2) is to be used per day. The percutaneous adsorption rate of prednicarbate is 3%[2]. Therefore, MDD, Identification Threshold (IT) and Qualification Threshold (QT) calculations are as follows:

MDD = 0.4 mg drug substance/day

	IT	QT
Drug Substance	0.10%	0.15%
Drug Product	1.0%	1.0%

[1]C.C. Long and A.Y. Finlay. *The Finger-Tip Unit-A New Practical Measure.* Clinical and Experimental Dermatology 1991; 16: 444-447.
[2]Based upon current package insert for Dermatop® Emollient Cream, last revised May 2003

C. Basis for Approvability or Not-Approval Recommendation

This ANDA is not approvable due to minor deficiencies related to drug substance release and drug product release and stability specifications.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

HFD-627/R. Murali/12/19/05 12/19/05
HFD-627/J. Fan/ 12/19/05 12/20/05
HFD-617/A. Vu/

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C. CC Block
ANDA 77-287
ANDA DUP 77-287
DIV FILE
Field Copy

Following this page, 17 pages withheld in full-(b)(4)

(b) (4)

30. MICROBIOLOGY

N/A

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS

N/A

32. LABELING

Acceptable 08/10/05 by B. Weitzman

33. ESTABLISHMENT INSPECTION

Acceptable 1/28/05

34. BIOEQUIVALENCE

Acceptable 09/16/05 by H. Nguyen

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

Altana is claiming a categorical exclusion from the requirement of an environmental impact analysis statement pursuant to 21 CFR 25.15 (d) and 25.31(a).

Chemistry Assessment Section

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-287 APPLICANT: Altana Inc.

DRUG PRODUCT: Prednicarbate Cream, 0.1%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. (b) (4)

2.

B. In addition to responding to the deficiency presented above, please note and acknowledge the following comment in your response:

Please provide all available long-term drug product stability data.

Sincerely yours,

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

cc: ANDA 77-287
ANDA DUP 77-287
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-627/R. Murali/12/19/05 RM 12/19/05
HFD-627/J. Fan/ 12/19/05 12/20/05
HFD-617/A. Vu/ 12/21/05

F/T by: ard/12/19/05

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TYPE OF LETTER: NOT APPROVABLE-MINOR

ANDA 77-287

Prednicarbate Emollient Cream, 0.1%

Altana, Inc.

Raman D. Murali, Ph.D.

Chemistry I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 77-287 (First Generic)

2. REVIEW #: 4

Chemistry Review #3 was not located. There appears to be a numbering error.

3. REVIEW DATE: June 28, 2006

4. REVIEWER: Raman D. Murali, Ph.D.

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original submission	September 23, 2004
Refuse to Receive	November 24, 2004
Amendment	December 2, 2004
Acceptable for filing	December 3, 2004
Amendment	August 23, 2005
Amendment	October 19, 2005
Amendment	January 27, 2006

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	April 4, 2006

7. NAME & ADDRESS OF APPLICANT:

Name:	Altana, Inc.
Address:	60 Baylis Road Melville, NY 11747
Representative:	Audrey Zaweski
Telephone:	(631) 454-7677 Ext. 3007
Facsimile:	(631) 756-5114

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A

b) Non-Proprietary Name (USAN): Prednicarbate Emollient Cream, 0.1%

9. LEGAL BASIS FOR SUBMISSION:

The Reference Listed Drug is Dermatop® Emollient Cream (Prednicarbate Emollient Cream, 0.1%), NDA 20-279 held by Dermik Laboratories.
The applicant, Altana, certifies that to the best of its knowledge there are no unexpired patents or unexpired exclusivity for this drug product. A copy of the list of Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) is included in this section confirming the above statement.

10. PHARMACOL. CATEGORY:

Topical corticosteroid used as an anti-inflammatory and anti-pruritic agent.

11. DOSAGE FORM: Cream

12. STRENGTH/POTENCY: 0.1%

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: __x_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

___x__Not a SPOTS product

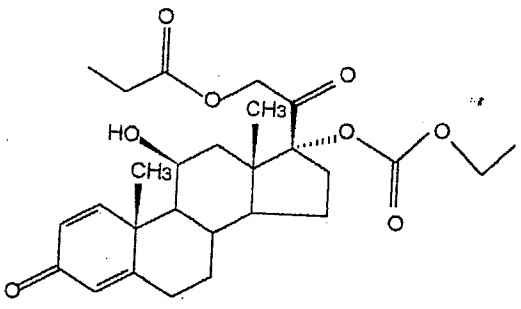
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: 11β-Hydroxy-3,20-dioxopregna-l,4-diene-17,21-diyl 17-ethylcarbonate 21-propanoate

Molecular formula: $C_{27}H_{36}O_8$

Molecular weight: 488.6

CAS Number: 73771-04-7



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Holder	Item Referenced	Code[1]	Status[2]	Date Review Completed	Comments
(b) (4)	II	(b) (4)		1	adequate	March 22, 2006	Reviewed by R. Murali
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")
[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

18. STATUS:

Consults/ CMC Related Reviews	Recommendation	Date	Reviewer
Microbiology	N/A		
EES	Acceptable	1/28/05	
Methods Validation	N/A		
Labeling	Acceptable	8/10/05	B. Weitzman
Bioequivalence	Acceptable	9/16/05	H. Nguyen
EA	Satisfactory (exclusion requested)		
Radiopharmaceutical	N/A		

The Chemistry Review for ANDA 77-287

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This ANDA is approvable.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug product Prednicarbate Emollient cream is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.
Each gram of Prednicarbate Emollient cream contains 1.0 mg of Prednicarbate in a base of consisting of White Petrolatum USP, Purified Water USP, Isopropyl Myristate NF, Lanolin Alcohols NF, Mineral Oil USP, Cetostearyl Alcohol NF, Aluminum Stearate, Edetate Disodium USP, Lactic Acid (b) (4) USP and Magnesium Stearate NF.
The drug product is supplied in (b) (4) 15g and 60g lined aluminum tubes. It is to be stored in controlled room temperature, 15°C to 30 °C. The proposed expiration dating for the drug product is 21 months.
The drug substance, Prednicarbate is a synthetic corticosteroid which is a class of primarily synthetic steroids used topically as an anti-inflammatory agent. The chemical name of Prednicarbate is 11β-Hydroxy-3,20-dioxopregna-1,4-diene-17,21-diyl 17-ethylcarbonate 21-propanoate.
Prednicarbate is not described in the USP Monograph. It is a white to off-white powder. Molecular formula is $C_{27}H_{36}O_8$ and molecular weight is 488.6.

B. Description of How the Drug Product is Intended to be Used

The drug product is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. The drug product did not produce significant hypothalamic-pituitary-adrenal (HPA) axis suppression when used at a dose of 30g/day for a week in patients with extensive psoriasis or atopic dermatoses. Prednicarbate cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

Following this page, 11 pages withheld in full (b)(4)

(b) (4)

30. MICROBIOLOGY

N/A

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS

N/A

32. LABELING

Acceptable 08/10/05 by B. Weitzman

33. ESTABLISHMENT INSPECTION

Acceptable 1/28/05

34. BIOEQUIVALENCE

Acceptable 09/16/05 by H. Nguyen

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

Altana is claiming a categorical exclusion from the requirement of an environmental impact analysis statement pursuant to 21 CFR 25.15 (d) and 25.31(a).

cc: ANDA 77-287
ANDA DUP 77-287
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-627/R. Murali/ RM 6/28/06
HFD-627/J. Fan/ 7/15/06
HFD-617/R. Adigun/ RA 7/20/06

F/T by:
V:\FIRMSAM\ALTANA \LTRS&REV\77287.RV4.DOC

TYPE OF LETTER: APPROVABLE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 077287

BIOEQUIVALENCE REVIEW

DIVISION OF BIOEQUIVALENCE REVIEW
(VASOCONSTRICTOR STUDIES)

ANDA No.	77-287
Drug Product Name	Prednicarbate Emollient Cream
Strength	0.1%
Applicant Name	Altana
Address	Melville, NY
Submission Date(s)	September 23, 2004
Reviewer	Hoainhon Nguyen
First Generic	Yes
File Location	v:\firmsam\altana\ltrs&rev\77287n0904.doc

I. Executive Summary

The firm has submitted a pilot dose-response- and a pivotal *in vivo* bioequivalence vasoconstriction study on its Prednicarbate Emollient Cream, 0.1%, referencing Dermik Labs' Dermatop® (prednicarbate) Emollient Cream, 0.1%. The pilot study used 20 female volunteers in determining an ED50 of 120 minutes to be used for the pivotal study. For the pivotal study 150 female volunteers were recruited for testing the vasoconstriction of the test product *vs.* Dermatop® Emollient Cream, 0.1% (Dermik Labs). For the pivotal study the firm selected 47 "evaluable" subjects from the 150 subjects completing the study. DBE also found and used 47 "evaluable" subjects. The study resulted in acceptable data (T/R ratio and 90% confidence interval calculated by Locke's method): 1.06 and 89.9-124.1. Both the pilot dose-response study and the pivotal pharmacodynamic bioequivalence study are acceptable.

The application is **complete** with no further bioequivalence deficiency at this time.

II. Table of Contents

III. Submission Summary

A. Drug Product Information

Test Product	Altana's Prednicarbate Emollient Cream, 0.1%
Reference Product	Dermatop® Emollient Cream (NDA #20-279, Dermik Labs, October 29, 1993)
Indication	Indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.
Potency	0.1%
Drug Specific Issue (If Any)	None
DBE History	This is the First Generic ANDA for Prednicarbate Emollient Cream product. To date, there has been no other ANDA or protocol submitted for the drug product. Control Document No. 01-531 ([(b) (4)] 10/23/01) addressed the inactive ingredient Lanolin Alcohol used in [(b) (4)] formulation ([(b) (4)]). The Program Support staff reviewed the CD and stated that *"Lanolin Alcohol has been used in previously approved application in amounts greater than the* [(b) (4)] *that they* [(b) (4)] *had proposed."*
Agency Guidance	Topical Dermatologic Corticosteroids: *In Vivo* Bioequivalence, June 2, 1995

B. Contents of Submission

Pilot Study	X	Yes
Pivotal Study	X	Yes
Chromameter Data	X	Yes
Visual Scores Data		No

C. Method Validation (Vol. C1.2, pp. 250-256)

Number of Operators	8
Number of Subjects per Validation	4
Number of Application Sites	4 per arm
Number of Readings	5 per site
Number of Validation Dates	5

Validation #1 (03/05/03):	Between Subject CV%	Between Site CV%	Within Site CV%
Operator #1	13.35	8.14	5.60
Operator #2	17.74	10.15	6.05

Validation #2 (06/19/03):	Between Subject CV%	Between Site CV%	Within Site CV%
Operator #2	12.71	8.88	4.47
Operator #3	13.60	8.28	6.65

Validation #3 (07/24/03):	Between Subject CV%	Between Site CV%	Within Site CV%
Operator #4	18.40	8.36	4.02
Operator #5	17.60	9.44	5.20
Validation #2 (10/17/03):	Between Subject CV%	Between Site CV%	Within Site CV%
Operator #4	23.22	7.73	4.17
Operator #6	23.99	7.65	3.19
Validation #3 (12/17/03):	Between Subject CV%	Between Site CV%	Within Site CV%
Operator #7	9.10	4.30	3.00
Operator #8	8.78	3.72	4.16

D. In Vivo Studies

1. PILOT DOSE RESPONSE STUDY

Study No. 10428210
Study Design 2-treatment, 1-period, randomized study
No. of subjects enrolled 20
No. of subjects completed 20
No. of subjects analyzed 20
Subjects
Sex(es) included (how many) Male None Female 14
Reference product Dermatop® Emollient Cream, 0.1%, Lot #L135, Exp. 08/05.
Strength tested 20 uL
Dose Durations 0.08, 0.50, 1, 2, 3, 4, 6 and 8 hours
Reading Times 0.50, 2, 4, 6, 8, 10, 12, 20 and 24 hours

Summary of Statistical Analysis: (Firm's analysis)

Parameter	Estimate	%CV
ED50	120.1	5.3
Emax	12.1	79.2

Summary of Statistical Analysis: (DBE's analysis) A sigmoidal function was fitted to the data of the pilot dose response study:

$$E = \frac{E_{max} \times Dose^{\gamma}}{ED_{50} + Dose^{\gamma}}$$

Where E_{max}, ED_{50} and γ (gamma) values are given below:

Parameter	Estimate	%CV
ED50	189.1	90.7
Emax	14.0	57.3
γ (gamma)	2.24	92.2

Although the firm used a curve linear function to fit the data, the ED50 value determined by the firm was less than the DBE's ED50 value and considered to be in the sensitive region of the curve. The pilot study is acceptable. The ED50 value of 120 minutes as selected for the pivotal study is acceptable.

2. PIVOTAL BIOEQUIVALENCE STUDY

Study No. 10428211
Study Design 2-treatment, 1-period, randomized study
No. of subjects enrolled 150
No. of subjects completed 150
No. of subjects with samples analyzed 47*
*NOTE: 47 of 55 met the qualifying criteria to be included in the statistical analysis.
Subjects
Sex(es) included (how many?) Male None Female 47
Test product Altana's Prednicarbate Emollient Cream, 0.1%, Lot No. N299, Manufacture Date 03/04
Reference product Dermatop® Emollient Cream, 0.1%, Lot No. L135, Expiration Date 08/05
Strength tested 20 uL of 0.1%
Dose Durations 120 minutes

Summary of Statistical Analysis (Locke's Method) as reanalyzed by the reviewer:

Parameter	Point Estimate	90% Confidence Interval
AUEC	1.06	89.9-124.1

The study is **acceptable**. The 90% confidence interval for AUEC is within the acceptable limit of 80.0-125.0.

E. Formulation

The test product formulation is shown in the review Appendix.

The inactive ingredients are within IIG limits. The formulation is acceptable.

F. Comments:

None.

G. Recommendations

The *in vivo* dose response study conducted by Altana on the reference product, Dermik Labs' Dermatop® Emollient Cream, 0.1%, Lot No. L135, and the *in vivo* pharmacodynamic bioequivalence study conducted by Altana on the test product, Prednicarbate Emollient Cream, 0.1%, lot # N299, comparing it with the reference product, Dermik Labs' Dermatop® Emollient Cream, 0.1%, lot # L135, have been found **acceptable** by the Division of Bioequivalence. The test product, Altana's Prednicarbate Emollient Cream, 0.1%, is bioequivalent to the reference product, Dermik Labs' Dermatop® Emollient Cream, 0.1%.

9/16/05
Hoaihon Nguyen, Review Branch I

9/16/2005
Shriniwas Nerurkar, Ph.D., Team Leader, Review Branch I

Barbara M Davit 9/16/05
Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs

HNguyen/09-06-05/v:\firmsam\altana\ltrs&rev\77287n0904.doc

IV. Appendix

A. Individual Study Reviews

1. Pilot Dose Response Study

Study Information

Study Number 10428210
Clinical Site Novum Pharmaceutical Research Services, Houston, TX
Investigators Mark Elliot Levine, M.D., Christopher H. Hendy, Ph.D., C.S.Pavelka, M.D., and Braulio Espino-Suarez.
Study/Dosing Date June 26, 2004
Statistician Novum Pharmaceutical Research Services, Houston, TX

Reference Product	Dermatop® Emollient Cream, 0.1%
Manufacturer	Dermik Labs
Batch/Lot No.	L135
Expiration Date	08/05
Strength	0.1%
Dosage Form	Cream

No. of Periods	1
No. of Groups	1
Randomization Scheme	Yes
Dose Durations	0.08, 0.50, 1, 2, 3, 4, 6 and 8 hours
Skin Blanching Reading Times	0, 0.50, 2, 4, 6, 8, 10, 12, 20 and 24 hours
IRB Approval	Yes
Informed Consent	Yes
Subject Screening	Yes
Length of Confinement	10 hours predose to 32 hours postdose
Safety Monitoring	Blood pressure (sitting), pulse rate, respiratory rate and oral temperature were measured during check-in.

Subject Demographics (N=20)

Age		Body Mass Index		Age Groups		Gender		Race	
				Range	%	Sex	%	Category	%
				<18	0.0			Caucasian	5.0
Mean	37.00	Mean	23.79	18-40	50.0	Male	0.0	Afr. Amer.	5.0
SD	12.20	SD	3.12	41-64	50.0	Female	100.0	Hispanic	75.0
Range	19	Range	18.9	65-75	0.0			Asian	15.0
	61		29.1	>75	0.0			Others	0.0

Study Results

Summary of Statistical Analysis: (Firm's analysis)

Parameter	Estimate	%CV
ED50	120.1	5.3
Emax	12.1	79.2

Summary of Statistical Analysis: (DBE's analysis) (See the analysis output in the review Appendix and Comments below)

Parameter	Estimate	%CV
ED50	189.1	90.7
Emax	14.0	57.3
γ (gamma)	2.24	92.2

The pilot study was acceptable.

Comments:

The DBE reanalyzed the data in consultation with a DBE senior scientist. A sigmoidal function was fitted to the data of the pilot dose response study in the following form:

$$E = \frac{E_{max} \times Dose^{\gamma}}{ED_{50} + Dose^{\gamma}}$$

where E_{max}, ED_{50} and γ (gamma) values are given below:

Parameter	Estimate	%CV
ED50	189.1	90.7
Emax	14.0	57.3
γ (gamma)	2.24	92.2

Although the firm used a curve linear function to fit the data, the ED50 value determined by the firm was less than the DBE's ED50 value and considered to be in the sensitive region of the curve. The pilot study is acceptable. The ED50 value of 120 minutes as selected for the pivotal study is acceptable.

2 Pivotal Bioequivalence Study

Study Information

Study Number 10428211
Clinical Site Novum Pharmaceutical Research Services, Houston, TX
Investigator Mark Elliot Levine, M.D., Christopher H. Hendy, Ph.D., C.S.Pavelka, M.D., and Braulio Espino-Suarez.

Study/Dosing Dates

Group 1	Subject Nos. 1-30	07/14/04
Group 2	Subject Nos. 31-60	07/17/04
Group 3	Subject Nos 61-90	07/24/04
Group 4	Subject Nos 91-120	07/31/04
Group 5	Subject Nos 121-150	08/21/04

Statistician Novum Pharmaceutical Research Services, Houston, TX

Treatment ID	Test	Reference
Test or Reference Product	Prednicarbate	Dermatop®
Manufacturer	Altana	Dermik Labs
Batch/Lot No.	N299	L135
Manufacture Date	03/04	
Expiration Date		08/05
Batch Size	(b) (4)	
Strength	0.1%	0.1%
Potency	99.1%	101.0%
Dosage Form	Cream	Cream
Formulation	See Appendix	

No. of Periods	1
No. of Groups	5
Randomization Scheme	Yes
Dose Duration	120 minutes (D1 = 60 minutes, D2=240 minutes)

Chromameter Reading Times	0, 0.5, 2, 4, 6, 8, 10, 12, 20 and 24 hours postdose
IRB Approval	Yes
Informed Consent	Yes
Subject Screening	Yes
Length of Confinement	Approximately 10 hours predose until 28 hours postdose.
Safety Monitoring	Blood pressure (sitting), pulse rate, respiratory rate and oral temperature were measured during check-in.

Subject Demographics (N=47)

Age		Body Mass Index		Age Groups		Gender		Race	
				Range	%	Sex	%	Category	%
				<18	0.0			Caucasian	15.8
Mean	31.97	Mean	24.23	18-40	76.3	Male	0.0	Afr. Amer.	7.9
SD	9.85	SD	2.99	41-64	23.7	Female	100.0	Hispanic	68.4
Range	18	Range	18.8	65-75	0.0			Asian	5.3
	49		29.9	>75	0.0			Others	2.6

Study Results

Number of Subjects Enrolled: 150
Number of Subjects Completing: 150
Number of Subjects Analyzed: 47
Number of Subjects with D2/D1 ≥ 1.25: 47 according to the firm's and reviewer's analysis.
Number of Subjects Analyzed by the Locke's Method: 47 according to the firm's and reviewer's analysis.

Adverse Events No adverse event was reported.

Protocol Deviations There was no significant protocol deviation that could have compromised the study outcome.

Statistical Analysis of Pharmacodynamic Data

Individual Subject D1 and D2	Attachment 2
Individual Subject AUEC	Attachment 2
90% Confidence Intervals (Locke's)	Attachment 3
Point Estimate	Attachment 3

Comments:

- The firm included all subjects with D2/D1≥ 1.25 except for the subjects with both negative D2 and D1 values. The reviewer agreed with the firm's selection of evaluable subjects.

Reviewer's Results: **Comparison between Test #1 and Reference**

Mean AUEC			**T/R%**	**Confidence Intervals**
N	Test	Reference		
47	9.82	9.26	106.0%	89.9-124.1

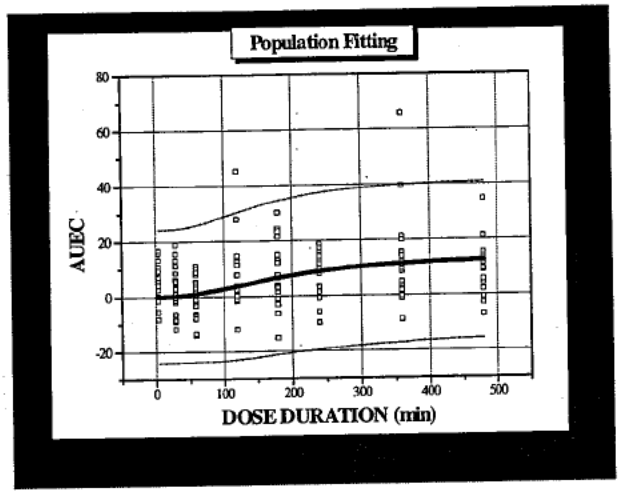
Firm's Results: **Comparison between Test #1 and Reference**

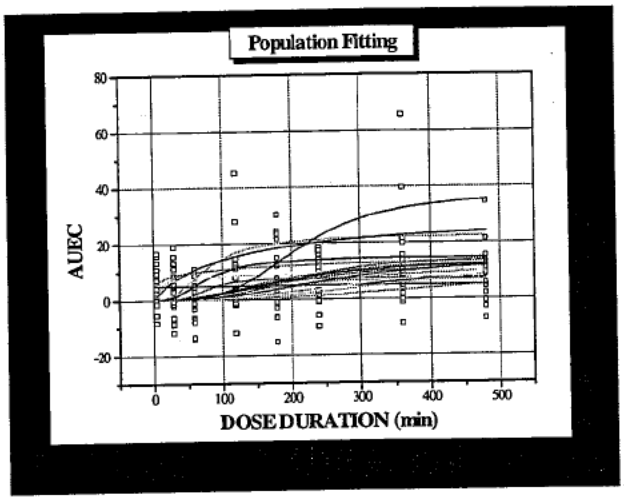
Mean AUEC			**T/R%**	**Confidence Intervals**
N	Test	Reference		
47	9.8	9.3	106.0%	89.9-124.0

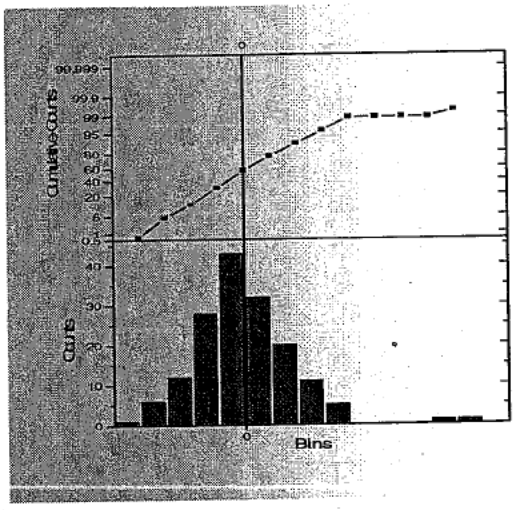
Conclusion: Based on the firm's analysis and the reviewer's reanalysis results above, the 90% confidence intervals for AUEC met the acceptable limit of 80.0-125.0. Therefore, the bioequivalence study is **acceptable**.

3. Attachments

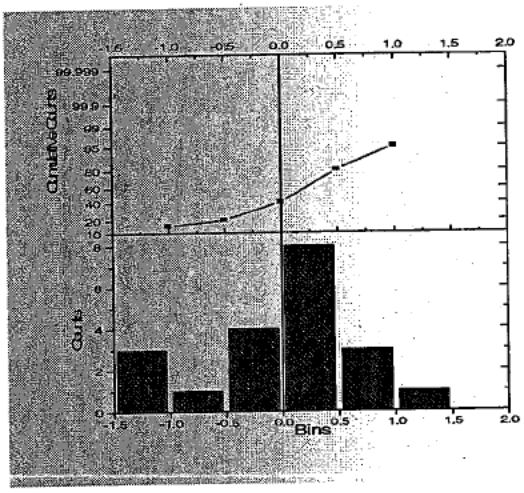
Attachment 1: ANDA #77-287 Prednicarbate Emollient Cream, 0.1% - Pilot Study - Analysis by the DBE







Residual Frequency Plot



ED50 Frequency Plot

Following this page, 6 pages withheld in full-(b)(4)

Attachment 4: Test Formulation

Name of the Ingredient	Prednicarbate Cream (Altana) (w/w%)	Pharmaceutical function
Prednicarbate	0.1	Active ingredient
White Petrolatum USP	(b) (4)	
Purified Water USP		
Isopropyl Myristate NF		
Lanolin Alcohols NF		
Mineral Oil USP		
Cetostearyl Alcohol NF		
Aluminum Stearate		
Edetate Disodium USP		
Lactic Acid (b) (4) USP		
Magnesium Stearate NF		

Comments: The inactive ingredients are within IIG limits. The formulation is acceptable.

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-287 APPLICANT: Altana Inc.

DRUG PRODUCT: Prednicarbate Emollient Cream, 0.1%

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Barbara McDavit

Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

CC:ANDA 77-287
ANDA DUPLICATE
DIVISION FILE
FIELD COPY
HFD-652/ Bio Secretary - Bio Drug File
HFD-652/ HNguyen
HFD-652/ SNerurkar

Endorsements: (Final with Dates)
HFD-652/ HNguyen
HFD-652/ SNerurkar
HFD-651/ GJPSingh
HFD-617/ A. Sigler
HFD-650/ D. Conner BMD 9/16/05

9/16/05

V:\FIRMSAM\altana\ltrs&rev\77287n0904.doc
Printed in final on / /

Submission date: 09-23-04

BIOEQUIVALENCY - Acceptable

1. PILOT STUDY (STU)
   Clinical: Novum Pharm. Res. Services

   Strength: 0.1%
   Outcome: AC

2. PIVOTAL STUDY (STU)

   Clinical: Novum Pharm. Res. Services

   Strength: 0.1%
   Outcome: AC

OUTCOME DECISIONS: **IC** - Incomplete **UN** - Unacceptable (fatal flaw)
AC - Acceptable

WINBIO COMMENTS:

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #: 77-287 **SPONSOR:** Altana Inc.
DRUG & DOSAGE FORM: Prednicarbate Emollient Cream
STRENGTH(S): 0.1%
TYPES OF STUDIES: Dose Response Study & Pivotal PK/PD Vasocontrictor Study
CLINICAL STUDY SITE(S): Novum Pharm. Res. Services, Houston, TX
ANALYTICAL SITE(S): N/A
STUDY SUMMARY: Acceptable
DISSOLUTION: N/A

DSI INSPECTION STATUS

		Inspection status:	**Inspection results:**
Inspection needed:	NO		
First Generic	Yes		
New facility			
For cause			
Other			

Proposed Dissolution Method and Specifications from Original Submission Acceptable? N/A
Yes _____ No _____ (If no, project Manager should verify and sign below when acknowledgement amendment is received)

DBE Dissolution Method and Specifications acknowledged by firm? N/A Yes ____ No ____

AMENDMENT DATE: _____

PROJECT MANAGER: _____ **DATE:** _____

PRIMARY REVIEWER: Hoainhon Nguyen **BRANCH:** I
INITIAL: HNC DATE: 9/16/05

TEAM LEADER: Shriniwas Nerurkar, Ph.D. **BRANCH:** I
INITIAL: DATE: 9/16/2005

DIRECTOR, DIVISION OF BIOEQUIVALENCE: Dale P. Conner, Pharm.D.
INITIAL: DATE: 9/16/05

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 077287

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Pharma

ALTANA

September 23, 2004

ALTANA Inc
60 Baylis Road
P.O. Box 2006
Melville, NY 11747-0103
USA
T +1 (631) 454-7677
www.altanainc.com

77-287

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

VIA FEDERAL EXPRESS

Original Submission
Abbreviated New Drug Application
Prednicarbate Emollient Cream 0.1%

Dear Sir or Madam:

Pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act and in accordance with the provisions under 21 CFR §314.94, Altana Inc. is submitting this Abbreviated New Drug Application to market a new drug, **Prednicarbate Emollient Cream 0.1%.**

The Reference Listed Drug (RLD) that is the basis for this submission is Dermatop® **Emollient Cream** (prednicarbate emollient cream 0.1%), Manufactured by Dermik Laboratories, NDA 20-279. Included in this Seven (7) volume submission, along with Form FDA 356h, is the required Patent Status and Exclusivity Statements; Draft Labeling; Bioequivalence Study; full Components and Composition statements; Raw Materials Controls, description of the Manufacturing Facilities, Manufacturing and Processing Instructions, In-Process Controls, Filling and Packaging procedures; Container/Closure System; controls for the Finished Dosage Form, Analytical Methods; Stability of the Finished Dosage Form; Environmental Assessment and Certification Requirements of the Generic Drug Enforcement Act of 1992.

The Exhibit Batch, Batch #N299, included in this application was fully packaged utilizing the (b) (4) 15 and 60 gram fill presentations for which approval is currently requested. The number of units filled for each packaging size and the disposition of any remaining bulk product are reconciled in the exhibit batch record.

An electronic copy of the bioequivalence data is provided in the front cover of Volume 2 of the application. All study data is prepared on CD Rom in SAS transport files (Version 5). The CD Rom also includes the appropriate data definition file (description of each SAS file and its contents and definition of each dataset variable) prepared in Adobe Acrobat.

In addition, an electronic copy of the proposed labeling is provided in the front cover of volume 1 of the application. All files are provided in PDF format (version 5.0). Section 5 of the paper ANDA also includes draft labeling for the proposed product along with the RLD labeling. In addition, Section 5 contains annotated side-by-side comparisons as well as the labeling limitation statement.

Altana's Prednicarbate Emollient Cream 0.1% contains the same active ingredient and is identical in strength, dosage form and route of administration to the RLD. The proposed drug is qualitatively and quantitatively equivalent to the RLD. As discussed with the Office of Generic Drugs' Regulatory Support Branch on September 21, 2004, a justification for the proposed drug formulation has been included in Sections 4 and 7 of the application.

RECEIVED
SEP 2 4 2004
OGD/CDER

The information presented in this application supports the conclusion that the proposed drug is as safe and effective as the RLD for topical application in the treatment of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Altana Inc. commits to assist the FDA Laboratories in validating the analytical methods associated with Prednicarbate Emollient Cream 0.1%. We understand that this validation may be performed post approval.

All regulatory correspondence related to this Abbreviated New Drug Application should be addressed to the following:

Ms. Audrey Zaweski
Associate Director, Regulatory Affairs
Altana Inc.
60 Baylis Road
Melville, NY 11747
Telephone: (631) 454-7677 X 3007
Facsimile: (631) 756-5114

A certified copy of the technical section and a copy of the Methods Validation package, are being sent to the New York District Office under separate cover.

Please advise if you require any additional information.

Sincerely,
ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Senior Director, Scientific Affairs

RJA/ap

Enclosures

ANDA 77-287

NOV 24 2004

Altana Inc.
Attention: Robert J. Anderson
60 Baylis Road
Melville, NY 11747

Dear Sir:

Please refer to your abbreviated new drug application (ANDA) dated September 23, 2004 submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Prednicarbate Cream, 0.1%.

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 receive this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

> You have failed to provide stability data required to support a (b)(4) month expiration date. Please submit three months accelerated testing or twelve months long term testing. We refer you to the CDER Guideline for Submitting Documentation for the Stability of Human Drugs and Biologics.

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

In addition, your electronic labeling submission does not meet the requirements outlined in the guidance, *"Providing Regulatory Submissions in Electronic Format-ANDAs"*. Please send a corrected version as a amendment to the application.

Upon receipt of this communication, you may either amend your application to correct the deficiencies or withdraw your application under 21 CFR 314.99. If you have any questions please call:

Arianne Camphire
Project Manager
(301) 827-5862

Sincerely yours,

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 77-287
cc: DUP/Jackets
HFD-600/Division File
Field Copy
HFD-92

Endorsement: HFD-615/MShimer, Chief, RSB _____ date 23 Nov 2004
HFD-615/ACamphire, CSO _____ 11/23/04 date
Word File
V:/FIRMSAM/Altanta/LTRS&REV/77287.RTR
F/T File November 10, 2004
ANDA Refuse to Receive!

Pharma

ALTANA

505(j)(2)(A)(i)
ORIG AMENDMENT
N/AC

December 2, 2004

ALTANA Inc
60 Baylis Road
P.O. Box 2006
Melville, NY 11747-0103
USA
T +1 (631) 454-7677
www.altanainc.com

Wm Peter Rickman,
Director
Division of Labeling and Program Support
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

VIA FACIMILE (301) 594-1174/FEDERAL EXPRESS

ANDA 77-287
Prednicarbate Emollient Cream, 0.1%
AMENDMENT – RESPONSE TO REFUSE TO RECEIVE

Dear Mr. Rickman:

Reference is made to the Altana Inc. Abbreviated New Drug Application (ANDA) submitted on September 23, 2004 pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Prednicarbate Emollient Cream, 0.1%.

Reference is also made to the FDA "Refuse to Receive" correspondence dated November 24, 2004. As stated in this correspondence, FDA is refusing to receive this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

> **You have failed to provide stability data required to support a (b) (4) month expiration date. Please submit three months accelerated testing or twelve months long term testing. We refer you to the CDER Guideline for Submitting Documentation for the Stability of Human Drugs and Biologics.**

Altana Inc. has prepared this Amendment response in order to address the comments provided in the November 24, 2004 "Refuse to Receive" correspondence. Altana's ANDA should be sufficiently complete to merit a technical review.

STABILITY DATA

As requested, Altana Inc. is providing the three months accelerated stability reports for the exhibit batch (N299). Please refer to **Attachment I.**

At this time, the Altana ANDA should be received as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

RECEIVED
DEC 0 3 2004
OGD / CDER

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

Sincerely,

ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Senior Director, Scientific Affairs

RJA:sps

Attachment

ANDA 77-287

JAN 26 2005

Altana Inc.
Attention: Robert J. Anderson
60 Baylis Road
Melville, NY 11747

Dear Sir:

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 Receive" letter dated November 24, 2004 and your amendment dated December 2, 2004.

NAME OF DRUG: Prednicarbate Cream, 0.1%

DATE OF APPLICATION: September 23, 2004

DATE (RECEIVED) ACCEPTABLE FOR FILING: December 3, 2004

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:

Ann Vu
Project Manager
(301) 827-5848

Sincerely yours,

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 77-287

cc: DUP/Jackets
HFD-600/Division File
Field Copy
HFD-92

Endorsements: HFD-615/MShimer, RSB _____ date 26 JAN 2005
HFD-615/ACamphire, CSO _____ date 1/25/05
Word Document
V:\FIRMSAM\Altana\LTRS&REV\77287.ACK
F/T by AC January 14, 2005
ANDA Acknowledgment Letter!

MINOR AMENDMENT

ANDA 77-287

JUL 11 2005

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

APPLICANT: Altana, Inc.

TEL: 631-454-7677x 3007

ATTN: Audrey Zaweski

FAX: 631-756-5114

FROM: Thuyanh (Ann) Vu

PROJECT MANAGER: (301) 827-5754

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated September 23, 2004, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Prednicarbate Cream, 0.1%.

Reference is also made to your amendment dated December 2, 2004.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (✓ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

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 of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:
CMC comments enclosed

7/8/05

JUL 11 2005

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-287 APPLICANT: Altana Inc.

DRUG PRODUCT: Prednicarbate Cream, 0.1%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

4.

5.

6.

7.

8.

9. (b) (4)

10.

11.

12.

13.

14.

15.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

The Bioequivalency and Labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you separately.

Sincerely yours,

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

Pharma

ORIGINAL

ALTANA

July 28, 2005

ORIG AMENDMENT
N/A.F.

ALTANA Inc.
60 Baylis Road
P.O. Box 2006
Melville, NY 11747-0103
USA
T +1 (631) 454-7677
www.altanainc.com

Wm. Peter Rickman
Director
Division of Labeling and Program Support
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

VIA FEDERAL EXPRESS

ANDA 77-287
Prednicarbate Cream 0.1% (Emollient)
LABELING AMENDMENT

Dear Mr. Rickman:

Reference is made to the ALTANA Inc Abbreviated New Drug Application submitted on September 23, 2004 pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Prednicarbate Cream 0.1% (Emollient).

ALTANA acknowledges the FDA correspondence dated June 29, 2005 citing labeling deficiencies. Each item has been addressed in **comment** / response format.

1. **GENERAL COMMENT [ALL LABELING]**

   The established name of this product is Prednicarbate Cream, 0.1%. Please revise your labels and labeling accordingly. If you prefer, you may include "Emollient" after the established name as follows: "Prednicarbate Cream (Emollient)" or after the established name and strength "Prednicarbate Cream 0.1% (Emollient)".

   ALTANA has revised the labels and labeling to read "Prednicarbate Cream 0.1% (Emollient)".

2. **CONTAINER: ((b) (4) 15 gram, 60 gram tubes) – See general comment.**

   ALTANA has revised the container label for the (b) (4) 15 gram and 60 gram tube sizes to read "Prednicarbate Cream 0.1% (Emollient)". Twelve (12) copies of the final printed labeling are included as **Attachment I.**

3. **CARTON: (15 gram, 60 gram) - See general comment.**

   ALTANA has revised the carton label for the 15 gram and 60 gram tube sizes to read "Prednicarbate Cream 0.1% (Emollient)". Twelve (12) copies of the final printed labeling are included as **Attachment I.**

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4. INSERT: See general comment.

ALTANA has revised the package insert labeling to read "Prednicarbate Cream 0.1% (Emollient)". Twelve (12) copies of the final printed labeling are included as **Attachment I.**

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the guidance for industry regarding electronic submissions: Providing Regulatory Submissions in Electronic Format - ANDAs (issued 6/2002) (http://www.fda.gov/cder/guidance/5004fnl.htm). The guidance specifies labeling to be submitted in pdf format. To assist in our review, we request that labeling also be submitted in MS Word format.

In accordance with the electronic labeling rule, ALTANA has provided the labeling content in electronic format. The labeling pieces have been provided in pdf format. To assist in FDA's review, the package insert labeling has also been provided in MS Word format. Please refer to the CD-ROM provided in the front cover of the Archival copy of the submission.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address –

http://www.fda.gov/cder/cdernew/listserv.html or
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

ALTANA acknowledges that prior to approval it may be necessary to further revise the labeling subsequent to approved changes for the reference listed drug. Altana will routinely monitor the following website for any approved changes-

http://www.fda.gov/cder/ogd/rld/labelingreviewbranch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

To facilitate review of this amendment and in accordance with 21 CFR 314.94(a)(8)(iv), a side-by-side comparison is provided with all the differences annotated and explained. See **Attachment II.**

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

Sincerely,

ALTANA INC

Audrey Zaweski for

Robert J. Anderson. Esq.
Vice President, Scientific Affairs

RJA:dt

Pharma

ALTANA

ORIG AMENDMENT

August 23, 2005

ALTANA Inc.
60 Baylis Road
P.O. Box 2006
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T +1 (631) 454-7677
www.altanainc.com

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, Room 150
Rockville, MD 20855

VIA FEDERAL EXPRESS

ANDA 77-287
Prednicarbate Cream 0.1% (Emollient)
MINOR AMENDMENT-RESPONSE TO CHEMISTRY DEFICIENCIES

Dear Dr. Patel:

Reference is made to the ALTANA Inc Abbreviated New Drug Application dated September 23, 2004 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Prednicarbate Cream 0.1% (Emollient).

ALTANA Inc acknowledges the FDA correspondence dated July 8, 2005, citing Chemistry Deficiencies.

This correspondence has been identified as a MINOR AMENDMENT. Each item has been addressed in **comment** / response format.

A. Deficiencies:

1. (b) (4)

2.

Following this page, 3 pages withheld in full-(b)(4)

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14. (b) (4)

15.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

The Bioequivalency and Labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you separately.

ALTANA acknowledges that the Bioequivalency and Labeling information provided are pending review and that any deficiencies found will be communicated to ALTANA separately.

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

Sincerely,

ALTANA INC

Audrey Zaweski for

Robert J. Anderson, Esq.
Vice President, Scientific Affairs

RJA:dt

RECORD OF TELEPHONE CONVERSATION

The call initiated in reference to the firm's Minor Amendment dated September 2, 2005. The Agency requested for additional long term stability data in support of their proposed expiration dating. The firm was asked to fax the request to the attention of James Fan at (301)540-0180 followed by hard copy in the mail. The firm agreed to the request.	**DATE:** 9/26/05
	ANDA NUMBER 77-287
	TELECON INITIATED BY **FDA**
	PRODUCT NAME: Prednicarbate Cream, 0.1%
	FIRM NAME: Altana
	FIRM REPRESENTATIVES: Amy Byron
	TELEPHONE NUMBER: (631) 454-7677
	FDA REPRESENTATIVES James Fan, Raman Murali
	SIGNATURES: RM 11/21/05 11/22/05

Orig: ANDA 77-287
Cc: Division File
Chem. I Telecon Binder
v:\firmsam\altana\telecons.doc

Pharma

ALTANA

October 19, 2005

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, Room 150
Rockville, MD 20855

ORIG AMENDMENT

ALTANA Inc
60 Baylis Road
P.O. Box 2006
Melville, NY 11747-0103
USA
T +1 (631) 454-7677
www.altanainc.com

VIA TELEFAX AND FEDERAL EXPRESS

ANDA 77-287
Prednicarbate Cream 0.1% (Emollient)
TELEPHONE AMENDMENT-RESPONSE TO CHEMISTRY DEFICIENCIES

Dear Dr. Patel:

Reference is made to the ALTANA Inc Abbreviated New Drug Application dated September 23, 2004 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Prednicarbate Cream 0.1% (Emollient).

Reference is also made to the teleconference held on September 26, 2005 between FDA and ALTANA representatives, where FDA cited the following chemistry deficiencies. This TELEPHONE AMENDMENT is being submitted in **comment** / response format.

1. **Please provide additional long-term stability data for Prednicarbate Cream 0.1% (Emollient) to support the proposed (b) (4) month expiry dating.**

   Updated long-term stability data are provided as **Attachment I**. All data are within specification and support an (b) (4) month expiry period for Prednicarbate Cream 0.1% (Emollient).

   ALTANA will submit (b) (4) month long-term stability to FDA immediately upon availability accompanied by a request for extension of the expiration date to (b) (4) months in a Changes Being Effected (CBE-0) supplemental application.

If you require additional information, please contact Ms. Audrey Zaweski, *Director*, Regulatory Affairs, at (631) 454-7677 ext. 3007. Fax communications may be made to (631) 756-5114.

Sincerely,
ALTANA Inc

Amy Boyson / for
Robert J. Anderson, Esq.
Vice President, Scientific Affairs

RJA:dt

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OCT 2 0 2005
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MINOR AMENDMENT

ANDA 77-287

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

DEC 22 2005

APPLICANT: Altana, Inc.

TEL: 631-454-7677x 3007

ATTN: Audrey Zaweski

FAX: 631-756-5114

FROM: Thuyanh (Ann) Vu

PROJECT MANAGER: (301) 827-5754

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated September 23, 2004, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Prednicarbate Emollient Cream, 0.1%.

Reference is also made to your amendments dated August 23 and October 19, 2005.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (__1__ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

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 of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:
CMC comments enclosed

12/22/05

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-287 APPLICANT: Altana Inc.

DRUG PRODUCT: Prednicarbate Cream, 0.1%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. (b) (4)

2.

B. In addition to responding to the deficiency presented above, please note and acknowledge the following comment in your response:

Please provide all available long-term drug product stability data.

Sincerely yours,

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

Pharma

ORIG AMENDMENT

ALTANA

January 27, 2006

Rashmikant M. Patel, Ph.D.
Director
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Metro Park North II
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VIA FEDERAL EXPRESS

ANDA 77-287
Prednicarbate Cream 0.1% (Emollient)
MINOR AMENDMENT-RESPONSE TO CHEMISTRY DEFICIENCIES

Dear Dr. Patel:

Reference is made to the ALTANA Inc Abbreviated New Drug Application dated September 23, 2004 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Prednicarbate Cream 0.1% (Emollient).

ALTANA Inc acknowledges the FDA correspondence dated December 22, 2005, citing Chemistry Deficiencies.

This correspondence has been identified as a MINOR AMENDMENT. Each item has been addressed in **comment** / response format.

A. Deficiencies:

1. [redacted] (b) (4)

2.

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(b) (4)

[redacted]

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

Please provide all available long-term drug product stability data.

Available Long-term Controlled Room Temperature Stability data are provided as **Attachment IV**. These data support a 21-month expiry period for the 15 gram and 60 gram tubes sizes. ALTANA is withdrawing the (b) (4) [redacted] tube size from consideration for approval with this application.

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

Sincerely,

ALTANA INC

Audrey Zaweski for/

Robert J. Anderson, Esq.
Vice President, Scientific Affairs

RJA:dt

Pharma

ALTANA

April 4, 2006

ORIG AMENDMENT

N/AM

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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, Room 150
Rockville, MD 20855

VIA TELEFAX (301)594-0180 AND FEDERAL EXPRESS

ANDA 77-287
Prednicarbate Cream 0.1% (Emollient)
CHEMISTRY AMENDMENT – REVISION TO POST APPROVAL STABILITY PROTOCOL

Dear Dr. Patel:

Reference is made to the ALTANA Inc Abbreviated New Drug Application dated September 23, 2004 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Prednicarbate Cream 0.1% (Emollient). Reference is also made to ALTANA's Minor Amendment submitted on January 27, 2006. To support the 21-month expiry period proposed in the January 27 Amendment, ALTANA is submitting a revised Post Approval Stability Protocol, which includes a 21-month stability test interval. A copy of the revised Post Approval Protocol is provided as **Attachment I**.

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

Sincerely,

ALTANA INC

Audrey Zaweski for

Robert J. Anderson, Esq.
Vice President, Scientific Affairs

RJA:dt

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OGD APPROVAL ROUTING SUMMARY

ANDA # 77-287 Applicant Altana, Inc.
Drug Prednicarbate Cream Strength(s) 0.1%

APPROVAL ☑ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐ OTHER ☐

REVIEWER:

1. Martin Shimer
Chief, Reg. Support Branch

DRAFT Package
Date 15 Nov 2005
Initials MAS

FINAL Package
Date
Initials

Contains GDEA certification: (Yes) No
(required if sub after 6/1/92)

Determ. of Involvement? Yes No
Pediatric Exclusivity System
RLD = NDA#
Date Checked
Nothing Submitted
Written request issued
Study Submitted

Patent/Exclusivity Certification: (Yes) No
If Para. IV Certification- did applicant
Notify patent holder/NDA holder Yes No
Was applicant sued w/in 45 days: Yes No
Has case been settled: Yes No Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes No
Date of latest Labeling Review/Approval Summary 8/10/2005
Any filing status changes requiring addition Labeling Review Yes ☐ No ☑
Type of Letter:
Comments: No Patents/exclusivities is eligible for Full Approval

2. Project Manager, Rosalyn Adigun Team 3
Review Support Branch

Date 11/25/05
Initials RA

Date
Initials

Original Rec'd date 9/23/04
Date Acceptable for Filing 12/3/04
Patent Certification (type)
Date Patent/Exclus.expires
Citizens' Petition/Legal Case Yes (No)
(If YES, attach email from PM to CP coord)
First Generic Yes (No)

EER Status Pending (Acceptable) OAI
Date of EER Status 01/28/2005
Date of Office Bio Review 9/16/05
Date of Labeling Approv. Sum 08/10/05
Labeling Acceptable Email Rec'd Yes ☑ No ☐
Labeling Acceptable Email filed Yes ☑ No ☐
Date of Sterility Assur. App. n/a
Methods Val. Samples Pending Yes No
MV Commitment Rcd. from Firm Yes No

Acceptable Bio reviews tabbed (Yes) No
Suitability Petition/Pediatric Waiver
Pediatric Waiver Request Accepted Rejected Pending
Previously reviewed and tentatively approved Date
Previously reviewed and CGMP def. /NA Minor issued Date
Comments:

Modified-release dosage form: Yes (No)
Interim Dissol. Specs in AP Ltr: Yes

3. David Read **(PP IVs Only)** Pre-MMA Language included
OGD Regulatory Counsel, Post-MMA Language Included
Comments:

Date
Initials

4. Div. Dir./Deputy Dir.
Chemistry Div. I II OR III
Comments:

Date 4/6/06
Initials GS

CMC Summary

REVIEWER:

FINAL ACTION

5. Frank Holcombe — **First Generics Only**
Assoc. Dir. For Chemistry
Comments: (First generic drug review) For Frank,

Date 9/18/06
Initials RR

CMC Dr. Radhika Rajagopalan
I am not sure of Paul's signature date. Amelia came down date July '06.

6. Vacant
Deputy Dir., DLPS

Date _____
Initials _____

7. Peter Rickman
Director, DLPS
Para.IV Patent Cert: Yes No X; Pending Legal Action: Yes No X; Petition: Yes No X
Comments:

Date 9/19/06
Initials PR

No patents No exclusivity
Labeling acceptable 9/15/2006 per AP Summary
Bio acceptable per Bio AP Summary 9/16/2005 (Dose Response Study, PK/PD Vasoconstrictor Study)
EER email acceptable 1/28/2005
Okay for Full Approval

OR

8. Robert L. West
Deputy Director, OGD
Para.IV Patent Cert: Yes No ; Pending Legal Action: Yes No ; Petition: Yes No
Comments:

Date _____
Initials _____

9. Gary Buehler
Director, OGD
Comments:
First Generic Approval PD or Clinical for BE Special Scientific or Reg. Issue

Date 9/19/06 for
Initials GB

10. Project Manager, Team 3
Review Support Branch
_____ Date PETS checked for first generic drug (just prior to notification to firm)
Applicant notification:
11.05 am Time notified of approval by phone 11.19 am Time approval letter faxed
FDA Notification:
9/19/06 Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
9/19/06 Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

Date 09/19/06
Initials RVA

File V:/division/dlps/approvrou9.doc