Clinical Study Protocol

An Open-Label, Observational Study Evaluating Topicort® Topical Spray 0.25% (desoximetasone) BID in Psoriasis Patients Being Treated with Biologic Agents

Testing Facility

Psoriasis Treatment Center of Central New Jersey

59 One Mile Road

East Windsor, NJ 08520

(609) 443-4500

Study Sponsor and Principal Investigator

Jerry Bagel, MD

Study Sub-Investigator(s)

David Nieves, MD

Brian Keegan, MD, PhD

Institutional Review Board

Western IRB

1019 39th Avenue SE Suite 120
Puyallup, WA 98374-2115

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PROTOCOL SYNOPSIS:

Study Title	Open Label, Observational Study, Evaluating Topicort® BID in Psoriasis Patients Being Treated with Biologic Agents.
Sponsors	Jerry Bagel, MD
Study Objectives	**Primary Objective:** To determine PGA x BSA improvement after 16 weeks of Topicort add-on therapy **Secondary Objectives:** BSA x PGA, patient satisfaction
Study Design	A two-phase, single center, observational study of 20 subjects to assess 4 weeks of add-on therapy of Topicort® BID and 12 weeks BID on two consecutive days a week to patients with ≤5% BSA who are receiving biologic therapy for at least 24 weeks
Study Centers	Psoriasis Treatment Center of Central New Jersey 59 One Mile Road, East Windsor, NJ 08520
Study Population	Adult male and female subjects with moderate to severe chronic plaque psoriasis
Main Inclusion Criteria	Subjects must meet the following criteria to be enrolled in this study: 1. Male or female adult ≥ 18 years of age; 2. Diagnosis of chronic plaque-type 3. Patient with ≤5% BSA 4. Patient has been treated with biologic for a minimum of 24 weeks 5. Able and willing to give written informed consent prior to performance of any study-related procedures.
Main Exclusion Criteria	Subjects who meet any of the following criteria will be excluded from participation in this study: 1. >5% BSA 2. Patient not receiving biologic agent, or receiving biologic agent <24weeks
Study Drug Dosage and Administration	All patients will receive Topicort® BID for 4 weeks. After week 4 patients will receive Topicort® BID on two consecutive days a week for 12 weeks
Study Visits	Visit 1 (Screening) Visit 2 (Baseline) Visit 3 (Week 4) Visit 4 (Week 8) Visit 5 (Week 16)
Study Endpoints	Primary Endpoints: PGA x BSA improvement after 4 weeks and 16 weeks Patient satisfaction at week 4 and week 16 Body Surface Area improvement at week 4 and week 16 Physician's Global Assessment improvement at week 4 and week 16 Frequency of local skin reactions AE/SAE

Study Duration	***16 weeks***

2 ETHICS AND REGULATORY OBLIGATIONS

2.1 Institutional Review Board (IRB)

Written IRB approval of this protocol must be obtained before the study is initiated. Compliance with Title 21 of the US Code of Federal Regulations (CFR), Part 56, is required in order to protect the rights and welfare of human subjects involved in this study.

2.2 Ethical Conduct of the Study

The study will be conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and its amendments. In addition, the study will be performed in compliance with Good Clinical Practices (GCP), including the archiving of essential documents.

2.3 Subject Information and Consent

The Informed Consent Form will be reviewed and approved by the IRB. The purpose, duration and possible risks and benefits will be explained to each potential subject. Consent in writing must be obtained from the subject before enrollment into the study. Consents will be signed and dated as required by Title 21 of CFR, Part 50. The consent will also comply with the requirements of the Health Insurance Portability and Accountability Act (HIPAA). The original, signed Informed Consent Form will be retained by the Investigator. A signed copy of the Informed Consent Form will be given to the subject. Each subject will be assigned a subject number that will be used in lieu of the subject's name on further research documentation.

3 INTRODUCTION

3.1 Overview of Psoriasis

Psoriasis is a chronic immunological disease characterized by infiltration of the skin with activated T cells and by abnormal keratinocyte proliferation and differentiation, resulting in marked inflammation and thickening of the epidermis. Psoriasis affects 1-3% of the world population, making it one of the most prevalent inflammatory immunological diseases.[1] There are several clinical subtypes of psoriasis: plaque, guttate, erythrodermic, inverse, and pustular. Plaque psoriasis is the most common type of psoriasis affecting 75-80% of psoriasis sufferers.[2] It

presents as raised silvery scale, which can cover large areas, with underlying erythema, itching, and discomfort.

3.2 Rationale for Treating Psoriasis with Biologic and Topical Therapy

Topical steroids play an in important role in the long term management of psoriasis. Data from the COBRA trial suggests that super potent topical corticosteroids are appropriate and well tolerated for use when added to existing therapeutic regimens.[3] After 4 weeks of treatment, 80.0% of subjects in the add-on therapy group were clear or almost clear, or had an improvement in severity from baseline by 2 grades.[4] Another study analyzing disease severity and patient treatment satisfaction revealed that patients with psoriasis are often dissatisfied with available treatments.[5] Patient preferences of topical treatments can greatly impact compliance rates. Recent evidence shows that spray is a patient's preferred vehicle more than 2 to 1 over creams, ointments, lotions, gel and foams.[6] By combining biologic and topical corticosteroid therapy, efficacy and patient satisfaction outcomes are expected to increase.

4. STUDY OBJECTIVE

To explore the effectiveness and safety of combining Biologic Agents and Topicort® for patients with plaque psoriasis.

5. INVESTIGATIONAL PLAN

5.1 Overall Study Design and Plan

20 subjects treated with a biologic agent for at least 24 weeks with a body surface area less than or equal to 5%, will receive Topicort® twice daily for 4 weeks followed by twice daily BID on two consecutive days a week (e.g. Saturday and Sunday) for 12 weeks.

5.2 Study Population Criteria

Males and females ≥ 18 years of age with moderate-to-severe chronic plaque psoriasis

5.2.1 Inclusion Criteria

Patients who meet all of the following criteria will be enrolled in the study:

1. Male or female adults ≥ 18 years of age.
2. Diagnosis of chronic plaque-type psoriasis.
3. Able to give written informed consent prior to performance of any study related procedures.
4. Treated with a biologic agent for a minimum of 24 weeks at baseline.
5. Plaque-type psoriasis as defined at screening and baseline by BSA ≤ 5%.
6. Females of childbearing potential (FCBP) must have a negative pregnancy test at Screening and Baseline. FCBP who engage in activity in which conception is possible

must use one of the approved contraceptive options: hormonal contraception; intrauterine device (IUD); tubal ligation; or partner's vasectomy; Male or female condom diaphragm with spermicide, cervical cap with spermicide, or contraceptive sponge with spermicide.

7. Subject must be in general good health (except for psoriasis) as judged by the Investigator, based on medical history, physical examination.

5.2.2 Exclusion Criteria

Patients will NOT be enrolled in this study if they meet any of the following criteria:

1. >5% Body Surface Area
2. Any condition, which would place the subject at unacceptable risk if he/she were to participate in the study.
3. Pregnant or breast feeding, or considering becoming pregnant during the study.
4. Malignancy or history of malignancy, except for:
   a. treated [ie, cured] basal cell or squamous cell in situ skin carcinomas;
   b. treated [ie, cured] malignancy with no evidence of recurrence within the previous 5 years.
5. Use of any investigational drug within 4 weeks prior to randomization, or within 5 pharmacokinetic/pharmacodynamic half lives, if known (whichever is longer).
6. Use of oral systemic medications for the treatment of psoriasis within 4 weeks (includes, but not limited to, oral corticosteroids, methotrexate, acitretin, apremilast and cyclosporine).
7. Patient used other topical therapies to treat within 2 weeks of the Baseline Visit (includes, but not limited to, topical corticosteroids, vitamin D analogs, or retinoids).
8. Patient received UVB phototherapy within 2 weeks of Baseline.
9. Patient received PUVA phototherapy within 4 weeks of Baseline.
10. Patient has a known hypersensitivity to the excipients of Topicort Spray® as stated in the label.

5.3 Source of Subjects and Recruitment Methods

The Investigator will manage the recruitment of subjects upon approval of the study by the Institutional Review Board. Subjects may be recruited from internal patient lists and outside IRB approved advertisements.

5.4 Subject Enrollment and Treatment Assignment

20 subjects of either gender with moderate-to severe plaque psoriasis will be enrolled to receive open-label Topicort® BID for 4 weeks followed by BID on two consecutive days a week for 12 weeks.

5.5 STUDY TREATMENT

5.5.1 Topicort® Topical Spray 0.25% (desoximetasone)

5.5.1.1 Topicort ® Description

Topicort ® Topical Spray is a Class I, super-potent corticosteroid indicated for the treatment of plaque psoriasis in patients 18 years or older. Each gram of Topicort® Topical Spray 0.25% contains 2.5mg of desoximetasone in a clear, colorless liquid.

5.5.1.2 Topicort® Dosing Schedule

Topicort® will be supplied by Taro Pharmaceuticals U.S.A. Inc. and applied approximately 12 hours apart twice daily for 4 weeks followed by twice daily two times a week (applied 2 consecutive days) for 12 weeks.

5.5.1.3 Topicort® Dispensing and Dosing Record

Topicort® will be dispensed to the study subjects by the authorized site personnel following instructions in Topicort® Label. Subjects will return all unused Topicort® to the study site. Site personnel will keep a record of Topicort® dispensed to and returned by each subject and note any missed doses.

5.5.1.4 Topicort Spray® Dosage Adjustments

If an SAE or an adverse event that is thought to be related to Topicort® and is not alleviated by symptomatic intervention, Topicort® will be discontinued. Subjects who permanently discontinue Topicort® therapy under this protocol should receive standard care of psoriasis treatment as prescribed by their physician.

5.5.2 Permitted Concomitant Therapy

The use of steroid-free topical emollients is allowed during the study. Appropriate interventions (e.g., prescribed medications) may be performed as the investigator deems necessary to treat concomitant illnesses and/or safeguard the subjects' wellbeing. No investigational product or device may be used during the study.

5.6 Study Procedures

5.6.1 Informed Consent

This Study will be conducted in compliance with CFR Title 21, Part 50 (Informed Consent of Human Subjects). Informed consent will be obtained from each subject in writing before participation in the Study. A signed copy of the Informed Consent Form will be provided to each subject. A provision to obtain a signed authorization to provide protected health information to the study sponsor, internal quality assurance agencies, health insurance agencies, and other parties as specified in the Federal Health Insurance Portability and Accountability Act (HIPAA) privacy regulation will be included in the Informed Consent Document. HIPAA authorization is voluntary. However, since the use and release of health information is critical to the conduct of the study, subjects who do not provide authorization to use and disclose their health information will not be enrolled into the study. Subjects who withdraw their authorization to use and release health information during study participation will be formally discontinued from the study. The investigator may use and release at any time all the information collected prior to a subject's withdrawal of the authorization to all authorized parties to satisfy scientific, regulatory, and financial concerns.

5.6.2 Inclusion and Exclusion Criteria

Subjects' eligibility to participate in the study will be determined according to the Inclusion and Exclusion Criteria during the screening period (0 – 30 days prior to the first dose of the study drug). Subjects who ultimately do not satisfy the eligibility criteria except changing treatments and undergoing a washout period, will not be enrolled into the study. Subjects who need to meet eligibility requirements will be asked to make the necessary changes. Subjects who agree and comply will be re-evaluated prior to Baseline. Screening and Baseline may occur on the same day if a washout is not required.

5.6.3 Demographics and Medical History

The following information will be obtained for each subject during screening: date of birth, sex, race/ ethnic origin, medical and surgical history, year of diagnosis of plaque psoriasis, current anti-psoriasis treatments, and previous anti-psoriasis treatments within the last 6 months. All current therapies for other medical conditions will be documented. Medical history will be reviewed and updated at the Baseline Visit to ensure that the patient remains eligible to participate in the study.

5.6.4 Urine Pregnancy Test

Pregnancy testing (urine β-human chorionic gonadotrophin [β-HCG]) will be conducted in all female subjects, except those without childbearing potential (e.g., one year post-menopause, post-hysterectomy, post-bilateral oophorectomy, etc) at Screening and Baseline Visit (Week 0)

prior to the first dose of Topicort®. An interim urine pregnancy test may be performed if there is reason to believe the subject may have become pregnant during the study. Subjects with a positive pregnancy test will not be eligible to participate or to continue to receive study treatment.

5.6.5 Physical Examination

A physical examination, including vital signs measurements, will be performed at each study visit. Any clinically significant abnormalities discovered during physical examinations after the Screening / Baseline visit should be documented and evaluated as potential adverse events.

5.6.6 Physician's Global Assessment (PGA)

PGA will be determined for all subjects throughout the study. PGA is a 5 point scale that records the overall disease severity at each clinical evaluation based on the average degree of erythema, induration, and scaling of areas affected by psoriasis. PGA uses a scale of 0 = Clear, 1 = Almost Clear, 2 = Mild, 3 = Moderate, and 4 = Severe. *See Appendix A*

5.6.7 Body Surface Area (BSA)

BSA will be determined for all subjects throughout the study. The subjects palm will be selected for the measuring unit of body surface area. The physician will equate the number of palms affected by psoriasis to derive the BSA total.

5.6.8 Patient Reported Outcomes

Subjects will complete the satisfaction questionnaire at weeks 4 and 16 and dermatology life quality index (DLQI) at weeks 0, 4, and 16. Questionnaires should be prior to medical procedures and clinical evaluations. *See Appendix B*

5.6.9 Localized Skin Reactions

Tolerability will be evaluated by the investigator using assessments of itching, dryness, burning/stinging, skin atrophy, striae, telangiectasia, and folliculitis. Any reaction requiring use of concomitant therapy will be recorded as an adverse event. *See Appendix C*

5.6.10 Early Discontinuation Procedures

Subjects will be prematurely discontinued from the study under the following conditions:

1. Subject requests to withdraw from the study.
2. Subject is noncompliant with protocol schedule, restrictions, and/or requirements.
3. Subject experiences an adverse event that makes it difficult or intolerable for the subject to continue treatment, or increases risk to the subject, or interferes with the investigator's ability to clinically evaluate the progress of the subject's treatment.
4. Subject begins an unapproved concomitant therapy for psoriasis or another medical condition that may increase risk to the subject if continuing study treatment.

5. Subject cannot be reached / lost to follow-up.
6. The study investigator suspends or terminates the study.
7. Other unanticipated reason.

Any subject who prematurely discontinues the study should complete the week 16 (End of Study) assessments. Any subject who withdraws consent to participate in the study will be removed from further treatment and/or study observation immediately upon the date of request.

6 Adverse Events

6.1 Adverse Events (AEs)

An adverse event (AE) is any untoward occurrence in a subject, whether or not related to the product. An AE does not necessarily have to have a causal relationship with the study treatment. AEs include events not present at baseline and events that worsened if present at baseline. Hospitalizations for pre-treatment conditions (e.g., elective cosmetic procedures) or surgeries that were planned prior to entry into the study are not considered adverse events.

Adverse events, regardless of causality, will be captured from the signing of the Informed Consent Form and for the duration of the subject's participation. Events will be captured as observations from investigator or events reported by subjects from the signing of the informed consent form.

6.2 Serious Adverse Events (SAEs)

A **serious adverse event** (SAE) is any untoward medical occurrence that meets one or more of the following criteria according to federal regulations:

a. results in death;
b. is life-threatening (the subject was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death if it were more severe);
c. results in persistent or significant disability or incapacity;
d. requires inpatient hospitalization or prolongation of existing hospitalization;
e. is a congenital anomaly or birth defect;
f. is considered an important medical event (may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the outcomes listed in the definition above).

6.2 .1 SAE Reporting

An **Adverse Event or Suspected Adverse Reaction** is considered ''serious'' if, in the view of either the investigator or sponsor, it results in any of the following outcomes:

- Death;
- A life threatening adverse event; (Note: the term "life-threatening" as used here

refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe);
- In-patient hospitalization or prolongation of existing hospitalization;
- A persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions);
- A congenital anomaly/birth defect;
- Any "other" important medical event.

Important medical events that may not result in death, be life-threatening or require hospitalization may be considered Serious Adverse Events when, based on appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Regardless of the above, any additional adverse events which the Principal Investigator considers significant should be immediately reported to Taro's Drug Safety Department.

Any Serious Adverse Event, whether deemed drug-related or not, must be reported by the Investigator to the Taro's Drug Safety Department by telephone **within 24 hours** after the Principal Investigator or Study Coordinator becomes aware of its occurrence. The Principal Investigator or the Principal Investigator's Designee must complete a Serious Adverse Event (SAE) Form and email it to Taro's Drug Safety Department, along with the patient's Adverse Events Log and Concomitant Medications Log **within 24 hours** of notification of the event. When appropriate, Taro's Drug Safety Department will notify the U.S. Food and Drug Administration (FDA) of drug related Serious Adverse Events.

Documentation of serious or unexpected adverse events and follow up information should be sent to Taro's Drug Safety Manager within 24 hours from reporting the event by the Investigator. Following is the contact information:

Taro Drug Safety Manager:
Margo Wyatt, RN, BSN,
Drug Safety Manager, Medical Affairs
Taro Pharmaceuticals U.S.A., Inc.
Tel: 914-345-9001 Ext. 6758
Email: margo.wyatt@taro.com **and** taropvus@taro.com

Taro's Drug Safety Department must notify FDA of fatal or life threatening adverse event as soon as possible but no later than 7 calendar days from reporting the event by the Investigator and within 15 calendar days for any other SAEs from the reporting of the event by Investigator.

The Sponsor-Investigator must inform all participating Investigators of any SAEs within 15 calendar days from reporting the event by the Investigator.

6.3 Pregnancy Reporting

The investigator will notify Taro Pharmaceuticals U.S.A. Inc. within 24 hours of discovery about any female subject who becomes pregnant after starting Topicort®. The investigator will follow the pregnancy and outcome. Any information gained will be shared with Taro Pharmaceuticals

U.S.A. Inc. Female subjects who become pregnant while using Topicort® will be discontinued from study treatment.

7 INVESTIGATIONAL PRODUCT HANDLING

7.1 Investigational Product Receipt

At study initiation and as needed thereafter, Topicort® will be shipped to a responsible person at the investigator's institution, who will check the amount and condition of the drug, and maintain a record of this information.

7.2 Topicort Spray® Storage

Investigational product will be stored per the storage conditions identified on drug label. At the study site, all IP will be stored in a locked, safe area to prevent unauthorized access.
Records of the actual storage conditions during the period of the study will be maintained.

8 RECORD RETENTION

The investigator must retain these documents according to local laws or requirements. Essential documents include, but are not limited to, the following:

- Signed informed consent documents for all subjects;
- Subject identification code list, screening log (if applicable), and enrollment log;
- Record of all communications between the Investigator and the IRB/EC
- List of Sub-investigators and other appropriately qualified persons to whom the Investigator has delegated significant study-related duties, together with their roles in the study, curriculum vitae, and their signatures;
- Copies of CRFs (if paper) and of documentation of corrections for all subjects;
- IP accountability records;
- All other source documents (subject records, hospital records, laboratory records, etc);
- All other documents as listed in Section 8 of the ICH consolidated guideline on GCP (Essential Documents for the Conduct of a Clinical Trial).

8.1 Study Monitoring

The investigator will self-monitor all study records for accuracy, completeness, and compliance with the protocol and GCPs and federal regulations. Study site facilities and study records will be made available to regulatory authorities' inspectors if an inspection takes place.

8.2 Statistics

It is desired to have approximately n=20 subjects at randomization. Analysis will be performed by the Investigator of PGA x BSA at weeks 4 and 16., PGA, BSA, and patient satisfaction at week 4 and 16. The Investigator will also analyze Frequency of local skin reactions and AE/SAE's.

8.2.1 Additional Statistical Considerations

Additional statistical procedures may be detailed in and performed according to a separate statistical plan at the discretion of sponsor-investigator.

9 REFERENCES

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7. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI). April 1992. Available from: www.dermatology.org.uk.

10. APPENDICES

Appendix A

Physician's Global Assessment

Static Physician's Global Assessment (sPGA)

Score	Category	Description
0	Clear	**Plaque elevation** = 0 (no elevation over normal skin) **Scaling** = 0 (no evidence of scaling) **Erythema** = 0 (except for residual hyperpigmentation/ hypopigmentation)
1	Almost Clear	**Plaque elevation** = ± (possible but difficult to ascertain whether there is a slight elevation above normal skin) **Scaling** = ± (surface dryness with some desquamation) **Erythema** = ± (faint, diffuse pink or slight red coloration)
2	Mild	**Plaque elevation** = slight (slight but definite elevation, typically edges are indistinct or sloped) **Scaling** = fine (fine scale partially or mostly covering lesions) **Erythema** = mild (light red coloration)
3	Moderate	**Plaque elevation** = marked (marked definite elevation with rough or sloped edges) **Scaling** = coarser (coarser scale covering most or all of the lesions) **Erythema** = moderate (definite red coloration)
4	Severe	**Plaque elevation** = marked (marked elevation typically with hard or sharp edges) **Scaling** = coarser (coarse, non tenacious scale predominates covering most or all of the lesions) **Erythema** = severe (very bright red coloration)

Appendix B

Patient Reported Outcomes

DLQI

DERMATOLOGY LIFE QUALITY INDEX

Hospital No: Date:
Name: Score:
Address: Diagnosis:

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick ☑ one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	❒ ❒	Not relevant ❒
	If "No", over the last week how much has	A lot	❒	

	your skin been a problem at **work** or **studying**?	A little Not at all	❒ ❒	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒

Please check you have answered EVERY question. Thank you.

Treatment Satisfaction Questionnaire for Medication (TSQM) - 9

Instructions: Please take some time to think about your level of satisfaction or dissatisfaction with the medication you are taking in this clinical trial. We are interested in your evaluation of the effectiveness and convenience of the medication over the last two weeks, or since you last used it. For each question, please place a single check mark next to the response that most closely corresponds to your own experiences.

1. How satisfied or dissatisfied are you with the ability of the medication to prevent or treat your condition?
   - ☐1 Extremely Dissatisfied
   - ☐2 Very Dissatisfied
   - ☐3 Dissatisfied
   - ☐4 Somewhat Satisfied
   - ☐5 Satisfied
   - ☐6 Very Satisfied
   - ☐7 Extremely Satisfied

2. How satisfied or dissatisfied are you with the way the medication relieves your symptoms?
   - ☐1 Extremely Dissatisfied
   - ☐2 Very Dissatisfied
   - ☐3 Dissatisfied
   - ☐4 Somewhat Satisfied
   - ☐5 Satisfied
   - ☐6 Very Satisfied
   - ☐7 Extremely Satisfied

3. How satisfied or dissatisfied are you with the amount of time it takes the medication to start working?
   - ☐1 Extremely Dissatisfied
   - ☐2 Very Dissatisfied
   - ☐3 Dissatisfied
   - ☐4 Somewhat Satisfied
   - ☐5 Satisfied
   - ☐6 Very Satisfied
   - ☐7 Extremely Satisfied

4. How easy or difficult is it to use the medication in its current form?
   - ☐1 Extremely Difficult
   - ☐2 Very Difficult
   - ☐3 Difficult
   - ☐4 Somewhat Easy

☐5 Easy
☐6 Very Easy
☐7 Extremely Easy

5. How easy or difficult is it to plan when you will use the medication each time?
   ☐1 Extremely Difficult
   ☐2 Very Difficult
   ☐3 Difficult
   ☐4 Somewhat Easy
   ☐5 Easy
   ☐6 Very Easy
   ☐7 Extremely Easy

6. How convenient or inconvenient is it to take the medication as instructed?
   ☐1 Extremely Inconvenient
   ☐2 Very Inconvenient
   ☐3 Inconvenient
   ☐4 Somewhat Convenient
   ☐5 Convenient
   ☐6 Very Convenient
   ☐7 Extremely Convenient

7. Overall, how confident are you that taking this medication is a good thing for you?
   ☐1 Not at All Confident
   ☐2 A Little Confident
   ☐3 Somewhat Confident
   ☐4 Very Confident
   ☐5 Extremely Confident

8. How certain are you that the good things about your medication outweigh the bad things?
   ☐1 Not at All Certain
   ☐2 A Little Certain
   ☐3 Somewhat Certain
   ☐4 Very Certain
   ☐5 Extremely Certain

9. Taking all things into account, how satisfied or dissatisfied are you with this medication?
   ☐1 Extremely Dissatisfied
   ☐2 Very Dissatisfied
   ☐3 Dissatisfied

Appendix C

Local Skin Reactions Evaluation

Burning/Stinging and Itching are reported by the subject. Dryness, Skin Atrophy, Striae, Telangiectasia, and Folliculitis are observed by the evaluating Investigator.
Mark **one score** for each evaluation:

Grade	**Itching** (as reported by Subject within the last 24 hours)	**Mark Score**	**Dryness** (as observed by the Investigator)	**Mark Score**	**Burning/Stinging** (as reported by Subject within the last 24 hours)	**Mark Score**
None	No itching	☐ 0	No dryness	☐ 0	No burning/stinging	☐ 0
Mild	Slight itching, not really bothersome	☐ 1	Slight, but definite roughness	☐ 1	Slight burning sensation; not really bothersome	☐ 1
Moderate	Definite itching that is somewhat bothersome	☐ 2	Definite roughness	☐ 2	Definite warm, burning that is somewhat bothersome	☐ 2
Severe	Intense itching that may interrupt daily activities and/or sleep	☐ 3	Marked roughness	☐ 3	Hot burning sensation that causes definite discomfort and may interrupt daily activities and sleep	☐ 3

Please assess the **Presence and Absence** of the following:

Skin Atrophy	☐ not present	☐ present; specify location:
Striae	☐ not present	☐ present; specify location:
Telangiectasia	☐ not present	☐ present; specify location:
Folliculitis	☐ not present	☐ present; specify location:

Appendix D

Schedule of Assessments

Procedure	Screening	Enrollment / Baseline	Week 4	Week 8	Week 16
Informed Consent	X				
Demographics/Medical History	X				
Inclusion/Exclusion	X	X			
Adverse Events	X	X	X	X	X
Concomitant Medications	X	X	X	X	X
Investigator Assessments	X	X	X	X	X
Urine Pregnancy Test	X	X			
Local Skin Reaction		X	X	X	X
Investigational Product compliance/Diary Review		X	X	X	X
Patient Satisfaction			X		X
Dermatology Life Quality Index		X	X	X	X
IP dispense/accountability		X	X	X	X

Appendix E
Subject Diaries

	Date (MMM/DD)	Dose (Circle One)	Time (HH:MM)	Remark
Ex	Jan/01	AM / PM	0800	
	Jan/01	AM / PM	1030	
1		AM / PM		
		AM / PM		
2		AM / PM		
		AM / PM		
3		AM / PM		
		AM / PM		
4		AM / PM		
		AM / PM		
5		AM / PM		
		AM / PM		
6		AM / PM		
		AM / PM		
7		AM / PM		
		AM / PM		
8		AM / PM		
		AM / PM		
9		AM / PM		
		AM / PM		
10		AM / PM		
		AM / PM		
11		AM / PM		
		AM / PM		
12		AM / PM		
		AM / PM		
13		AM / PM		
		AM / PM		
14		AM / PM		
		AM / PM		

	Date (MMM/DD)	Dose (Circle One)	Time (HH:MM)	Remark
15		AM / PM		
		AM / PM		
16		AM / PM		
		AM / PM		
17		AM / PM		
		AM / PM		
18		AM / PM		
		AM / PM		
19		AM / PM		
		AM / PM		
20		AM / PM		
		AM / PM		
21		AM / PM		
		AM / PM		
22		AM / PM		
		AM / PM		
23		AM / PM		
		AM / PM		
24		AM / PM		
		AM / PM		
25		AM / PM		
		AM / PM		
26		AM / PM		
		AM / PM		
27		AM / PM		
		AM / PM		
28		AM / PM		
		AM / PM		

Extension (if needed)

	Date (MMM/DD)	Dose (Circle One)	Time (HH:MM)
29		AM / PM	
		AM / PM	
30		AM / PM	
		AM / PM	
31		AM / PM	
		AM / PM	
32		AM / PM	
		AM / PM	

Subject #_____ Initials:_____

Storage
- Keep study medication at room temperature.
- Keep out of reach of children

Dosing
- Administer twice daily (approximately 12 hours apart).
- Do not apply on face, underarms or groin
- Avoid heat, flames or smoking when applying.
- Do not bandage, cover, or wrap the treated area
- Spray only enough to cover affected area and rub in.
- Avoid bathing, showering or swimming right after applying the study medication.

Dosing Diary
- Record all doses on the diary as soon as possible.
- Return diary and medication to all of your appointments.
- Record any comments or information in "remarks" section for missed dose, adverse event, or change in medication.
- Please make recordings clear and legible.

	Date (MMM/DD)	Dose (Circle One)	Time (HH:MM)	Remark
Ex	JAN/01	AM / PM	08:30	
	JAN/01	AM / PM	08:00	
Ex	JAN/02	AM / PM	09:00	
	JAN/02	AM / PM	09:30	
Week 4 Day 1		AM / PM		
		AM / PM		
Week 4 Day 2		AM / PM		
		AM / PM		
Week 5 Day 1		AM / PM		
		AM / PM		
Week 5 Day 2		AM / PM		
		AM / PM		
Week 6 Day 1		AM / PM		
		AM / PM		
Week 6 Day 2		AM / PM		
		AM / PM		
Week 7 Day 1		AM / PM		
		AM / PM		
Week 7 Day 2		AM / PM		
		AM / PM		

Week 8 Day 1		AM / PM	
		AM / PM	
Week 8 Day 2		AM / PM	
		AM / PM	
EXT 1		AM / PM	
		AM / PM	
EXT 1		AM / PM	
		AM / PM	
EXT 2		AM / PM	
		AM / PM	
EXT 2		AM / PM	
		AM / PM	
EXT 3		AM / PM	
		AM / PM	
EXT 3		AM / PM	
		AM / PM	

Subject # _____ Initials: _____

APPLY TWO CONSECUTIVE DAYS A WEEK

Storage
- Keep study medication at room temperature.
- Keep out of reach of children

Dosing
- Administer twice daily on two consecutive days a week (e.g. Saturday and Sunday).
- Do not apply on face, underarms or groin
- Avoid heat, flames or smoking when applying.
- Do not bandage, cover, or wrap the treated area
- Spray only enough to cover affected area and rub in.
- Avoid bathing, showering or swimming right after applying the study medication.

Dosing Diary
- Record all doses on the diary as soon as possible.
- Return diary and medication to all of your appointments.
- Record any comments or information in "remarks" section for missed dose, adverse event, or change in medication.
- Please make recordings clear and legible.

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Ex	JAN/01	AM / PM	08:30	
	JAN/01	AM / PM	08:00	
Ex	JAN/02	AM / PM	09:00	
	JAN/02	AM / PM	09:30	
Week 8 Day 1		AM / PM		
		AM / PM		
Week 8 Day 2		AM / PM		
		AM / PM		
Week 9 Day 1		AM / PM		
		AM / PM		
Week 9 Day 2		AM / PM		
		AM / PM		
Week 10 Day 1		AM / PM		
		AM / PM		
Week 10 Day 2		AM / PM		
		AM / PM		
Week 11 Day 1		AM / PM		
		AM / PM		
Week 11 Day 2		AM / PM		
		AM / PM		
Week 12 Day 1		AM / PM		
		AM / PM		
Week 12 Day 2		AM / PM		
		AM / PM		
Week 13 Day 1		AM / PM		
		AM / PM		
Week 13 Day 2		AM / PM		
		AM / PM		
Week 14 Day 1		AM / PM		
		AM / PM		
Week 14 Day 2		AM / PM		
		AM / PM		
Week 15 Day 1		AM / PM		
		AM / PM		
Week 15 Day 2		AM / PM		
		AM / PM		
Week 16 Day 1		AM / PM		
		AM / PM		
Week 16 Day 2		AM / PM		
		AM / PM		

Subject # _____ Initials: _____

APPLY TWO CONSECUTIVE DAYS A WEEK

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- Keep study medication at room temperature.
- Keep out of reach of children

Dosing
- Administer twice daily on two consecutive days a week (e.g. Saturday and Sunday).
- Do not apply on face, underarms or groin
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- Please make recordings clear and legible.