STATISTICAL ANALYSIS PLAN

An Open Label, Safety Study to Assess the Potential for Adrenal Suppression Following Treatment with Desoximetasone 0.15% Topical Spray (Taro Pharmaceuticals U.S.A., Inc.) in Patients with Atopic Dermatitis

Protocol Number: DSXS 1502a
Novum Study Number: 71615002

Sponsor:
Taro Pharmaceuticals U.S.A., Inc.
3 Skyline Drive,
Hawthorne, NY 10532
USA

Contract Research Organization:
Novum Pharmaceutical Research Services
225 W. Station Square Drive, Suite 200
Pittsburgh, PA 15219

May 19, 2017

Final Version 1.0

SAP FINAL VERSION APPROVALS

An Open Label, Safety Study to Assess the Potential for Adrenal Suppression Following Treatment with Desoximetasone 0.15% Topical Spray (Taro Pharmaceuticals U.S.A., Inc.) in Patients with Atopic Dermatitis

Written By: Signature: _____ Jianhua Liu, MSc Senior Biostatistician Novum Pharmaceutical Research Services	Date: 06/13/2017
Reviewed By: Signature: _____ Pina D'Angelo, MSc Senior Director, Scientific Affairs (Biostatistics) Novum Pharmaceutical Research Services	Date: 06/13/2017
Approved By: Natalie Yantovskiy Signature: _____ Natalie Yantovskiy Senior Director, Clinical Research Taro Pharmaceuticals U.S.A., Inc.	Date: 9 June 2017

Digitally signed by Natalie Yantovskiy
Date: 2017.06.09 11:04:50 -04'00'

Revision History

VERSION	DATE	DESCRIPTION OF REVISIONS	REVISED BY
Draft 1.0	January 19, 2017	New Document	Jianhua Liu
Final 1.0	May 19, 2017	SAP finalization	Jianhua Liu

List of Abbreviations and Definition of Terms

ADaM	Analysis Data Model
AE	Adverse Event
BP	Blood Pressure
BSA	Body Surface Area
C	Celsius
CRF	Case Report Form
CDISC	Clinical Data Interchange Standards Consortium
CRO	Contract Research Organization
EASI	Eczema Area and Severity Index
F	Fahrenheit
FDA	Food and Drug Administration
HR	Heart Rate
Hg	Mercury
HPA	Hypothalamic Pituitary Adrenal
ICH	International Conference on Harmonisation
IGA	Investigator's Global Assessment
IND	Investigational New Drug
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities
ITT	Intent-to-Treat
LOCF	Last Observation Carried Forward
OGD	The Office of Generic Drugs
PP	Per-Protocol
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SDTM	Study Data Tabulation Model
USA	United States of America

TABLE OF CONTENTS

1. INTRODUCTION

This Statistical Analysis Plan (SAP) is based on the final Clinical Study Protocol DSXS 1502a (Novum Study No. 71615002) Rev. 2 dated 09/06/2016. The SAP provides details on the planned statistical methodology for the analysis of the study data. The SAP also outlines the statistical programming specifications for the tables, listings and figures.

This SAP describes the study endpoints, derived variables, anticipated data transformations and manipulations, and other details of the analyses not provided in the study protocol. This SAP therefore outlines in detail all other aspects pertaining to the planned analyses and presentations for this study.

The following documents were reviewed in preparation of this SAP:

- Final Clinical Study Protocol DSXS 1502a (Novum Study No. 71615002) Rev. 2 dated 09/06/2016
- Case Report Form Version 1.0 for Novum Study No. 71615002

The reader of this SAP is encouraged to also read the clinical protocol for details on the conduct of this study, and the operational aspects of clinical assessments and timing for completing a patient in this study.

2. OBJECTIVES

1. The objective of this study is to evaluate the potential of desoximetasone 0.15% topical spray to suppress HPA axis function in patients with moderate to severe atopic dermatitis.
2. The secondary objectives are to evaluate to evaluate the efficacy parameters and adverse event (AE) profiles of desoximetasone 0.15% topical spray administered to patients with moderate to severe atopic dermatitis.

3. OVERALL STUDY DESIGN

This open label, safety study is designed to evaluate the potential for adrenal suppression after treatment with desoximetasone 0.15% topical spray (Taro Pharmaceuticals, U.S.A.), for the treatment of moderate to severe atopic dermatitis.

Approximately 25 to 50 eligible patients with atopic dermatitis that satisfy all eligibility criteria will be enrolled into the study at Visit 1. Patients must be overall in good health. They should have a current diagnosis of moderate to severe atopic dermatitis with IGA score of at least 3 or 4.

Approximately twenty-four (25) to fifty (50) patients stratified by age with a confirmed

diagnosis of moderate to severe atopic dermatitis with:

Cohort 1 – 10 -20 patients age 12-17 years of age with 10-30% body surface area (BSA) affected

Cohort 2 – 5-10 patients age 6-11 years of age with 10-30% body surface area (BSA) affected

Cohort 3 – 5-10 patients age 2-5 years of age with 10-30% body surface area (BSA) affected

Cohort 4 – 5-10patients 6 months to 1 year of age with 10-30% body surface area (BSA) affected

Cohorts will be enrolled in sequential order. Each cohort will initiate enrollment once the previous cohort has reached the minimum number of patients and a safety analysis has been reviewed. Each cohort will be enrolled based on the availability of patients.

Each cohort will be reviewed for the potential of HPA axis suppression. If at least 50% of patients in a Cohort experience HPA axis suppression, enrollment for that cohort will be stopped and no further cohorts will be initiated. If at least 35% of patients have experienced HPA axis suppression across all cohorts combined during the study, enrollment will be discontinued and no other cohorts will be initiated. Cohort 2 will not begin until safety data has been reviewed for Cohort 1. The same process will be followed for each Cohort until the study is complete. The enrollment in the individual Cohort may not be required if the satisfactory safety data for the same age group was obtained in the study DSXS 1502.

Patients enrolled in the study will apply product twice a day, according to provided instructions, for a total of 28 days.

Patients will attend a total of 3 Clinic Visits as follows:

- **Visit 1 (Day 1)**: Screening/Enrollment
- **Visit 2 (Day 14±2):** Interim Visit
- **Visit 3 (Day 29±2):** End of Study or Early Termination

Figure 1 Study Schematic

	Visit 1	Visit 2	Visit 3	Visit 4
Day	**1**	**14±2**	**29±2**	**42±4**
Procedures	Enrollment **Before 12 pm**	Interim Visit	End of Study/Early Termination **Before 12 pm**	Telephone Follow-Up Visit
Informed Consent	X			
Medical History and Demographics	X			
Vital Signs	X	X	X	
Pregnancy Test*	X	X	X	
Physical Exam	X		X	
% BSA Assessment	X	X	X	
IGA Score	X	X	X	
EASI Score	X	X	X	
Application Site Reactions	X	X	X	
Concomitant Medication	X	X	X	
Laboratory Evaluations	X		X	
Cortisol Response Test	X		X	
Confirm Inclusion/Exclusion Criteria	X			
Dispense Sunscreen and Wristband	X			
Weigh and Dispense Study Drug	X	X		
Collect and Weigh Study Drug		X	X	
Dispense/Review Patient Diary	X	X	X	
Adverse Events		X	X	X
Evaluation of Patient Compliance to the Protocol		X	X	

* Pregnancy test will be carried out for females of childbearing potential.

4. RANDOMIZATION AND BLINDING

Patients eligible for enrollment into the study will fall into one of four cohorts:

Cohort 1 – 10 -20 patients age 12-17 years of age with 10-30% body surface area (BSA) affected

Cohort 2 – 5-10 patients age 6-11 years of age with 10-30% body surface area (BSA) affected

Cohort 3 – 5-10 patients age 2-5 years of age with 10-30% body surface area (BSA) affected

Cohort 4 – 5-10 patients 6 months -1 year of age with 10-30% body surface area (BSA) affected

At Visit 1 eligible patients will be enrolled to the study and assigned a patient number.

Cohorts will be enrolled in sequential order. Each cohort will initiate enrollment once the previous cohort has reached the required number of patients and a safety analysis has been reviewed. Each cohort will be enrolled based on the availability of patients.

Each cohort will be reviewed for the potential of HPA axis suppression. If at least 50% of patients in each Cohort experience HPA axis suppression, enrollment for that cohort will be stopped and no further cohorts will be initiated. If at least 35% of patients have experienced HPA axis suppression across cohorts combined during the study, enrollment will be discontinued and no other cohorts will be initiated. Cohort 2 will not begin until safety data has been reviewed for Cohort 1. The same process will be followed for each Cohort until the study is complete.

The enrollment in the individual Cohort may not be required if the satisfactory safety data for the same age group was obtained in the study DSXS 1502.

5. SAMPLE SIZE

The sample size of 35 patients, stratified by age and % BSA, was determined to be sufficient.

6. STUDY ENDPOINTS

Primary Outcome Measures:

Hypothalamic Pituitary Adrenal (HPA) Axis Response to Cosyntropin demonstrating the absence or presence of adrenal suppression at the end of treatment

Secondary Outcome Measures:

Hypothalamic Pituitary Adrenal (HPA) Axis Response to Cosyntropin demonstrating the presence of adrenal suppression at the end of treatment with % BSA as a covariate.

7. STATISTICAL ANALYSIS METHODS

If not otherwise specified, statistical significance is defined as $p<0.05$ and is two-tailed. Data will be summarized with respect to demographic and baseline characteristics and safety variables.

For categorical variables, the number and percent of each category within a parameter will be calculated for non-missing data. For continuous variables, statistics will include n, mean, standard deviation, median, minimum and maximum values.

All statistical analyses will be conducted using SAS®, Version 9.4 or higher. Datasets will be prepared using headings from Clinical Data Interchange Consortium (CDISC) Study Data Tabulation Model (SDTM) implementation for human clinical trials and ADaM (Analysis Dataset Model).

7.1 Baseline Characteristics

7.1.1 Subject Disposition

The subject accountability and disposition information will be summarized by study cohort. The number of subjects enrolled, treated with study medication will be tabulated by study cohort. In addition, completion status and primary reason for withdrawal will be summarized by study cohort.

7.1.2 Demographic and Other Baseline Characteristics

The cohorts will be compared for basic demographics (age, gender, ethnicity and race), baseline IGA, baseline EASI and baseline total BSA.

Summary tables by cohort will be presented. Continuous variables will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum, maximum). Categorical variables will be summarized using frequencies and percentage.

Baseline comparability of the four cohorts will be presented using Chi-square test for the categorical variables, and Analysis of Variance for the continuous variables.

All data will be listed by cohort and patient.

7.1.3 Medical History

At Visit 1, patients will be questioned about medical history, including acute and chronic

medical history and medical history relevant to their atopic dermatitis.

Medical history data will be listed by cohort and patient.

7.1.4 Concomitant Medications

At Visits 1-3, patients will be questioned about current and concomitant medication over the past 12 weeks.

All prior and concomitant medications taken since screening until the end of the study will be listed by cohort and patient.

7.1.5 Pregnancy Test

Urine pregnancy tests on women of child-bearing potential will be performed at Visits 1, 2, and 3.

Positive pregnancy test results will be listed by cohort and patient.

7.2 Safety Analysis of Potential HPA Axis Suppression

Dosing will be twice a day for 28 days excluding the doses prior to the Cortisol Response Test (54 applications). All patients who are enrolled, use at least 42 doses of the study drug and have data from a post-treatment cortisol response test will be included in the analysis. Patients who have not used 42 doses of the study drug will be excluded from the primary analysis of HPA axis suppression.

The primary analysis of interest is the proportion of patients in each group who are considered to have demonstrated possible HPA axis suppression following treatment with the study medication. As a secondary analysis of the data a logistic regression of the proportion of patients in the study with HPA axis suppression may be performed with %BSA affected as a covariate. This will depend on the distribution of the %BSA data collected.

The study will be enrolled by Cohort starting with Cohort 1 and each cohort will be reviewed for the potential of HPA axis suppression. If at least 50% of patients in Cohort 1 experience HPA axis suppression once the minimum number of patients has been enrolled and completed the cohort, enrollment for that cohort will be stopped and no further cohorts will be initiated. If at least 35% of patients have experienced HPA axis suppression across cohorts combined during the study, enrollment will be discontinued and no other cohorts will be initiated. Cohort 2 will not begin until safety data has been reviewed for Cohort 1. The same process will be followed for each Cohort until the study is complete.

For all patients the actual amount of desoximetasone (mg) applied during the study will be

calculated from recorded bottle weights and presented.

7.3 Safety Analysis

Safety analysis will be conducted on all patients who applied at least one dose of study drug.

7.3.1 Adverse Events

All the adverse events (AEs) reported throughout the study will be coded and classified according to the MedDRA (Medical Dictionary for Regulatory Activities) coding dictionary (Version 19 or higher). Each adverse event is to be evaluated for date of start and end, seriousness, severity, causal relationship with the study drugs, action taken and outcome.

A summary table of the number and percent of patients with AEs by system organ class, preferred term, and cohort will be presented. Each patient will be counted only once within each preferred term.

A frequency summary table of the number of AEs by system organ class, preferred term, severity, and cohort will be presented. Severity will be classified as "Mild", "Moderate", or "Severe".

Similarly, a frequency summary table of the number of AEs by system organ class, preferred term, and relationship to a study drug, and cohort will be presented. Relationship to a study drug will be classified as "Not Related" or "Related" where "Related" includes "Possible", "Probable", or "Definite".

Should sufficient data exist, adverse event frequencies will be compared between cohorts using Fisher's exact test.

All AEs will be listed by cohort and patient.

7.3.2 Vital Signs

The patient's vital signs will be recorded (heart rate, blood pressure, temperature and respiration rate) at Visit 1, 2, and 3.

Abnormal vital signs will be listed by cohort and patient.

7.3.3 Laboratory Evaluations

At Visit 1 and Visit 3 a blood sample will be collected for hematology and clinical chemistry testing. The testing panel should include as a minimum the following tests:

Hematology

- Hematocrit
- White blood cell count
- Platelets
- Hemoglobin
- Red blood cell count
- Differential white cell count

Chemistry

- Alkaline phosphatase
- Total bilirubin
- Alanine transaminase
- Creatinine
- Aspartate transaminase
- Glucose
- Blood urea nitrogen

Shift analysis using the categories; below, above and within the laboratory normal range will be performed to identify any specific laboratory parameter that shows a trend toward potentially clinically significant changes.

All data will be listed by cohort and patient.

7.3.4 Investigator Global Assessment

At each visit the Investigator will perform an Investigator Global Assessment (IGA).

Investigator Global Assessment will be summarized using frequency and percentage by cohort and visit.

Investigator Global Assessment will also be listed by cohort and patient.

7.3.5 Eczema Area and Severity Index Score (EASI)

Eczema Area and Severity Index Score will be assessed at each visit.

EASI will be summarized using frequency and percentage by cohort and visit. EASI will also be listed by cohort and patient.

7.3.6 Percent BSA Affected

The % BSA recorded at Visit 1, 2, and 3 will be summarized descriptively by cohort and visit.

All data will be listed by cohort and patient.

7.3.7 Application Site Reaction

A frequency summary table comparing application site reaction for each cohort will be presented by visit.

All data will be listed by cohort and patient.

7.3.8 Pruritus Assessment

A frequency summary table comparing the severity of pruritus for each cohort will be presented by visit.

All data will be listed by cohort and patient.

7.4 Multiple Comparisons

No multiple comparison adjustment will be made in this study.

7.5 Methods for Handling Missing Data

For demographic and baseline characteristics, each variable will be analyzed using all available data. Patients with missing data will be excluded only from analyses for which data are not available.

7.6 Interim Analyses

There is no interim analysis planned in this study.

7.7 Changes to the Planned Analyses

Protocol Section 10.1.3 states as a secondary analysis of the data a logistic regression of the proportion of patients in the study with HPA axis suppression will be performed with %BSA affected as a covariate. The following will be applied during the analyses.

As a secondary analysis of the data a logistic regression of the proportion of patients in the study with HPA axis suppression may be performed with %BSA affected as a covariate. This will depend on the distribution of the %BSA data collected.

8. TABLE, LISTING AND FIGURE SHELLS

The following shells are provided in order to provide a framework for the display of data from this study. These shells may not be reflective of every aspect of this study but are intended to show the general layout of the Tables, Listings and Figures that will be included in the final

clinical study report. Tables, Listings and Figures are numbered following the ICH structure. Table headers, variables names and footnotes will be modified as needed following data analyses. All descriptive and inferential statistical analyses will be performed using SAS® statistical software Version 9.4 or higher, unless otherwise noted.

TABLE, LISTING AND FIGURE SHELLS

T16.1.9.1 Summary of Enrolled Patients

Patients	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Total
Screened					xxx
Randomized	xxx	xxx	xxx	xxx	xxx
Completed Study	xxx	xxx	xxx	xxx	xxx
Terminated Early	xxx	xxx	xxx	xxx	xxx
Adverse Event	xxx	xxx	xxx	xxx	xxx
Enrolled in error	xxx	xxx	xxx	xxx	xxx
Lack of efficacy	xxx	xxx	xxx	xxx	xxx
Lost to follow-up	xxx	xxx	xxx	xxx	xxx
etc.					
Other	xxx	xxx	xxx	xxx	xxx

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.2 Summary of Protocol Deviations (Safety Population)

	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Total
Total Patients with Protocol Deviations	xxx	xxx	xxx	xxx	xxx
Total Deviations	xxx	xxx	xxx	xxx	xxx
Enrolled in Error	xxx	xxx	xxx	xxx	xxx
Lost to Follow-up	xxx	xxx	xxx	xxx	xxx
Missed Visit	xxx	xxx	xxx	xxx	xxx
Non-compliance with study drug	xxx	xxx	xxx	xxx	xxx
Outside Visit Window	xxx	xxx	xxx	xxx	xxx
Restricted Medication Use	xxx	xxx	xxx	xxx	xxx
etc					
Other	xxx	xxx	xxx	xxx	xxx

Created on: ddmmmyy hh:mm

T16.1.9.3 Summary of Demographic Data (Safety Population)

		Cohort 1 N=xx	Cohort 2 N=xx	Cohort 3 N=xx	Cohort 4 N=xx	Total N=xx	P-value
Age (years)	n	xx	xx	xx	xx	xx	x.xxxx
	Mean ± SD	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	
	Range	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	
Age Groups	<=1	-	-	-	xx (xx.x%)	-	
	2 – 5	-	-	xx (xx.x%)	-	-	
	6 – 11	-	xx (xx.x%)	-	-	-	
	12 – 17	xx (xx.x%)	-	-	-	-	-
	18 – 40	-	-	-	-	-	
	41 – 64	-	-	-	-	-	
	65 – 75	-	-	-	-	-	
	> 75	-	-	-	-	-	
Race	American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	x.xxxx
	Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
	Black/African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
	Native Hawaiian or other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
	White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
	Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Ethnicity	Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	x.xxxx
	Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

N= number of patients in the cohort; n= number of patients with data available; % is based on N

Created on: ddmmmyy hh:mm

Page 1 of 1

T16.1.9.3 Summary of Demographic Data (Safety Population)

		Cohort 1 N=xx	Cohort 2 N=xx	Cohort 3 N=xx	Cohort 4 N=xx	Total N=xx	P-value
Baseline Total BSA	n	xx	xx	xx	xx	xx	x.xxxx
	Mean ± SD	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	
	Range	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	
Baseline IGA	Clear	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	x.xxxx
	Almost Clear	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
EASI	n	xx	xx	xx	xx	xx	x.xxxx
	Mean ± SD	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	xx.x ± x.x	
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	
	Range	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	

N= number of patients in the cohort; n= number of patients with data available; % is based on N

Created on: ddmmmyy hh:mm

T16.1.9.4 Summary of Patients Randomized, Included in Safety Analysis of Potential HPA Axis Suppression by Study Center

Site No.	PI Name	Total		Cohort 1		Cohort 2		Cohort 3		Cohort 4	
		Rando-mized	Included	Rando-mized	Included	Rando-mized	Included	Rando-mized	Included	Rando-mized	Included
All	-	xx	xx(xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)
xx	xxxx	xx	xx (xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)
xx	xxxx	xx	xx(xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)	xx	xx(xx.x%)

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.5 Summary of Frequency of HPA Axis Suppression at the End of Treatment (Day 28)

HPA Axis Suppression	All N=xx	Cohort 1 N=xx	Cohort 2 N=xx	Cohort 3 N=xx	Cohort 4 N=xx
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.5a Summary of Logistic Regression Analysis Results of HPA Axis Suppression at the End of Treatment (Day 28)

	Odds Ratio	95% Wald Confidence Limits	Wald Chi-Square	P-value
Cohort 1 vs. Cohort 2	x.xxxx	x.xxxx, x.xxxx	x.xxxx	x.xxxx
Cohort 1 vs. Cohort 3	x.xxxx	x.xxxx, x.xxxx	x.xxxx	x.xxxx
Cohort 1 vs. Cohort 4	x.xxxx	x.xxxx, x.xxxx	x.xxxx	x.xxxx
Cohort 2 vs. Cohort 3	x.xxxx	x.xxxx, x.xxxx	x.xxxx	x.xxxx
Cohort 2 vs. Cohort 4	x.xxxx	x.xxxx, x.xxxx	x.xxxx	x.xxxx
Cohort 3 vs. Cohort 4	x.xxxx	x.xxxx, x.xxxx	x.xxxx	x.xxxx
Baseline % BSA affected	x.xxxx	x.xxxx, x.xxxx	x.xxxx	x.xxxx

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.6 Summary of Percent BSA Affected with Atopic Dermatitis (Safety Population)

Visit	Statistic	Cohort 1 (N = xx)	Cohort 2 (N = xx)	Cohort 3 (N = xx)	Cohort 4 (N = xx)
1	n	xx	xx	xx	xx
	Mean ± SD	xxx.x ± xxx.x	xxx.x ± xxx.x	xxx.x ±x xx.x	xxx.x ± xxx.x
	Median	xxx.x	xxx.x	xxx.x	xxx.x
	Range	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x	xxx.x – xxx.x
2					
3					

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.7 Summary of Frequency of Investigator Global Assessment (IGA) (Safety Population)

Visit	Score	Cohort 1 (N = xx)	Cohort 2 (N = xx)	Cohort 3 (N = xx)	Cohort 4 (N = xx)
1	0 (Clear)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	1 (Almost Clear)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	2 (Mild Disease)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	3 (Moderate Disease)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	4 (Severe Disease)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	0 (Clear)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	1 (Almost Clear)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	2 (Mild Disease)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	3 (Moderate Disease)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	4 (Severe Disease)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3					

T16.1.9.8 Summary of Total Score - Eczema Area and Severity Index (EASI) (Safety Population)

Visit	Statistic	Cohort 1 (N = xx)	Cohort 2 (N = xx)	Cohort 3 (N = xx)	Cohort 4 (N = xx)
1	n	xx	xx	xx	xx
	Mean ± SD	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
	Median	xxx.x	xxx.x	xxx.x	xxx.x
	Range	xxx - xxx	xxx – xxx	xxx - xxx	xxx - xxx
2					
3					

Created on: ddmmmyy hh:mm

T16.1.9.9 Overall Summary of Adverse Events (Safety Population)

Description	Cohort 1 N=xx	Cohort 2 N=xx	Cohort 3 N=xx	Cohort 4 N=xx	Total N=xx
Patients Randomized	xxx	xxx	xxx	xxx	xxx
Patients with at least one AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Discontinued study drug due to above AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
AEs reported	xxx	xxx	xxx	xxx	xxx
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serious AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Related = Possible, Probable, Definite

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.10.1 Summary of Frequency of All Adverse Events by Body System (Safety Population)

Body System	MedDRA Term	Cohort	Events	Patients	Fisher's p-value
Patients with at least one AE	Total	Cohort 1 (N=xx)	xx	xx (xx.x%)	x.xxxx
		Cohort 2 (N=xx)	xx	xx (xx.x%)	
		Cohort 3 (N=xx)	xx	xx (xx.x%)	
		Cohort 4 (N=xx)	xx	xx (xx.x%)	
Ear and labyrinth disorders	Ear pain	Cohort 1 (N=xx)	xx	xx (xx.x%)	x.xxxx
		Cohort 2 (N=xx)	xx	xx (xx.x%)	
		Cohort 3 (N=xx)	xx	xx (xx.x%)	
		Cohort 4 (N=xx)	xx	xx (xx.x%)	

N = Total number of patient in each cohort; Percentage is based on total number of patients.

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.10.2 Summary of Frequency of All Adverse Events in ≥ 2% of Patients by Body System (Safety Population)

T16.1.9.11 Summary of Frequency of All Adverse Events by Severity (Safety Population)

Body System	MedDRA Term	Cohort	Mild	Moderate	Severe
Patients with at least one AE	Total	Cohort 1 (N=xx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Cohort 2 (N=xx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Cohort 3 (N=xx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Cohort 4 (N=xx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ear and labyrinth disorders	Ear pain	Cohort 1 (N=xx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Cohort 2 (N=xx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Cohort 3 (N=xx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Cohort 4 (N=xx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = Total number of events in each cohort; Percentage is based on total number of events.

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.12 Summary of Frequency of All Adverse Events by Relationship (Safety Population)

Body System	MedDRA Term	Cohort	Related	Not Related
Patients with at least one AE	Total	Cohort 1 (N=xx)	xx (xx.x%)	xx (xx.x%)
		Cohort 2 (N=xx)	xx (xx.x%)	xx (xx.x%)
		Cohort 3 (N=xx)	xx (xx.x%)	xx (xx.x%)
		Cohort 4 (N=xx)	xx (xx.x%)	xx (xx.x%)
Ear and labyrinth disorders	Ear pain	Cohort 1 (N=xx)	xx (xx.x%)	xx (xx.x%)
		Cohort 2 (N=xx)	xx (xx.x%)	xx (xx.x%)
		Cohort 3 (N=xx)	xx (xx.x%)	xx (xx.x%)
		Cohort 4 (N=xx)	xx (xx.x%)	xx (xx.x%)

N = Total number of events in each cohort; Percentage is based on total number of events.
Related = Possible, Probable, Definite

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.13 Summary of Frequency of Serious Adverse Events (Safety Population)

Body System	MedDRA Term	Cohort 1 N=xx	Cohort 2 N=xx	Cohort 3 N=xx	Cohort 4 N=xx
Injury, poisoning and procedural complications	Alcohol poisoning	xx	xx	xx	xx

Created on: ddmmmyy hh:mm

Page 1 of N

T16.1.9.14 Summary of Shift Analysis of Clinical Laboratory Assessments (Chemistry) from Baseline to Day 28 (Safety Population)

Alanine Aminotransferase (U/L)

	Cohort 1 (N=xx)			Cohort 2 (N=xx)			Cohort 3 (N=xx)			Cohort 4 (N=xx)		
Baseline-> Endpoint	**Low**	**Normal**	**High**	**Low**	**Normal**	**High**	**Low**	**Normal**	**High**	**Low**	**Normal**	**High**
Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table will continue for other lab parameters.

Similar table will be created for T16.1.9.18.

T16.1.9.15 Summary of Shift Analysis of Clinical Laboratory Assessments (Hematology) from Baseline to Day 28 (Safety Population)

T16.1.9.16 Summary of Frequency of Pruritis Assessment (Safety Population)

Visit	Score	Cohort 1 (N = xx)	Cohort 2 (N = xx)	Cohort 3 (N = xx)	Cohort 4 (N = xx)
1	None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3					

T16.1.9.17 Summary of Application Site Reaction
(Safety Population)

Sign / Symptom	Visit	Statistic	Cohort 1 (N = xx)	Cohort 2 (N = xx)	Cohort 3 (N = xx)	Cohort 4 (N = xx)
Burning	1	Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	2					
	3					
Erosion						
Erosion						
Edema						
Pain						
Itching						
Dryness						

L16.2.1 Listing of Discontinued Patients

Cohort	Patient Number	Discontinuation Reason
Cohort 1	xx-xxxx	Withdrawal by Subject
	xx-xxxx	Lost to Follow-up
Cohort 2		
Cohort 3		
Cohort 4		

Created on: ddmmmyy hh:mm

L16.2.2 Listing of Protocol Deviations

Cohort	Patient Number	Event Description
Cohort 1	xx-xxxx	Outside Visit Window (Visit 3)
Cohort 2		
Cohort 3		
Cohort 4		

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.3 Patients Excluded from Safety Analysis of Potential HPA Axis Suppression

Cohort	Patient Number	Exclusion Reason
Cohort 1	xx-xxxx	Patient has not used 42 doses of the study drug
Cohort 2		
Cohort 3		
Cohort 4		

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.4.1 Listing of Demographic Data

Cohort	Patient Number	Age	Gender	Ethnicity	Race
Cohort 1	xx-xxxx	11	Female	Not Hispanic or Latino	Black or African American
Cohort 2					
Cohort 3					
Cohort 4					

Created on: ddmmmyy hh:mm

L16.2.4.2 Listing of Medical History

Cohort	Patient Number	System	Diagnosis or Surgical Procedure	Start Date	End Date	Ongoing
Cohort 1	xx-xxxx	Gynecologic	Menopause	yyyy-mm-dd	yyyy-mm-dd	
Cohort 2						
Cohort 3						
Cohort 4						

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.4.3 Listing of Concomitant Medication

Cohort	Patient Number	Treatment Area	Medication	Dosage	Frequency	Route	Start/End Date	Indication
Cohort 1	xx-xxxx	No	Lisinopril	20 MG	QD	PO	yyyy-mm-dd / yyyy-mm-dd	Hypertension
Cohort 2								
Cohort 3								
Cohort 4								

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.5.1 Listing of Drug Administration

Cohort	Patient Number	Date of First Dose	Date of Last Dose	Total Doses Applied	Compliance (%)
Cohort 1	xxxx	yyyy-mm-dd	yyyy-mm-dd	xx	xx.x
Cohort 2					
Cohort 3					
Cohort 4					

Note to programmer:
Compliance = [Total number of applications] / [Planned number of applications] * 100%, where Planned number of applications is determined as follows:
for subjects who completed the study successfully: 56 applications (28 days of twice daily dosing);
for subjects who discontinued early: the minimum between 56 and [(Date of Discontinuation – Date of First Application)].

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.5.2 Listing of Study Medication Weight

Cohort	Patient Number	Bottle 1		Bottle 2		Total Amount Applied (g)
		Date Dispensed	Weight Dispensed (g)	Date Collected	Weight Collected (g)	
Cohort 1	xxxx	yyyy-mm-dd	xx	yyyy-mm-dd	xx	xxx
Cohort 2						
Cohort 3						
Cohort 4						

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.6.1 Listing of Cortisol Response Test Results

Cohort 1

Patient Number	Visit	Was a Cortisol Response Test conducted?	Date	Basal Sample Draw Time	Injection Time	Post-Injection Draw Time	Basal Cortisol Concentration Level (mcg/100ml)	Post Injection Cortisol Concentration Level (mcg/100ml)	Have Abnormal Adrenal Function?	Have HPA Axis Suppression ?
xx-xxxx	1	Yes	yyyy-mm-dd	hh:mm	hh:mm	hh:mm	xxx	xxx	No	
	3	Yes	yyyy-mm-dd	hh:mm	hh:mm	hh:mm	xxx	xxx		No

Table will continue for other cohorts.

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.6.2 Listing of HPA Axis Suppression Follow-Up

Cohort 1

Patient Number	Is The Patient Showing Signs Or Symptoms Of HPA Axis Suppression?/ Was a Cortisol Response Test Conducted?	Follow-Up Test	Date/ Basal Sample Draw Time/ Injection Time/ Post-Injection Draw Time	Basal Cortisol Concentration Level (mcg/100ml)	Post Injection Cortisol Concentration Level (mcg/100ml)	Still Show Signs of HPA Axis Suppression?	Was the Patient Referred to an Endocrinologist
xx-xxxx	Yes/ Yes	Test 1	yyyy-mm-dd / hh:mm / hh:mm/ hh:mm	xxx	xxx	No	No

Table will continue for other cohorts.

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.6.3 Listing of Investigator Global Assessment (IGA)

Cohort	Patient Number	Visit 1	Visit 2	Visit 3 / Early Termination
Cohort 1	xx-xxxx	0	0	0
Cohort 2				
Cohort 3				
Cohort 4				

Created on: ddmmmyy hh:mm

L16.2.6.4 Listing of Percent BSA Affected with Atopic Dermatitis

Cohort	Patient Number	Visit 1	Visit 2	Visit 4 / Early Termination	Baseline Total BSA (m^2)
Cohort 1	xx-xxxx	xxx	xxx	xxx	x.xx
Cohort 2					
Cohort 3					
Cohort 4					

L16.2.6.5 Listing of Eczema Area and Severity Index (EASI)

Cohort	Patient Number	Visit	Location	Erythema	Induration, Papulation, Edema	Lichenification	Excoriation	Total Grade	Total EASI Score
Cohort 1	xx-xxxx	1	Head/Neck	0	0	0	0	0	xxxx
			Upper Limbs	0	0	0	0	0	
			Trunk	1	1	1	1	4	
			Lower Limbs	0	0	0	0	0	
		2							
		3							
Cohort 2									
Cohort 3									
Cohort 4									

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.6.6 Listing of Pruritis Assessment

Cohort	Patient Number	Visit 1	Visit 2	Visit 3/Early Termination
Cohort 1	xx-xxxx	0 (None)	1 (Mild)	1 (Mild)
Cohort 2				
Cohort 3				
Cohort 4				

Created on: ddmmmyy hh:mm

L16.2.6.7 Listing of Application Site Reaction

Cohort	Patient Number	Visit	Sign / Symptom					
			Burning	Erosion	Edema	Pain	Itching	Dryness
Cohort 1	xx-xxxx	1	0	0	0	1	0	0
		2	0	1	0	0	0	0
		3	0	0	0	1	0	0
Cohort 2								
Cohort 3								
Cohort 4								

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.7 Listing of Adverse Events by Cohort

Cohort	Patient Number	Body System / MedDRA Term / AE Term	Treatment Area	Start /End Date	Severity	Relationship to Study Drug	Outcome	Action Taken/ Other Action Taken	SAE?
Cohort 1	xx-xxxx	Nervous system disorders / Headache / Headache	No	yyyy-mm-dd / yyyy-mm-dd	Mild	Not Related	Recovered	Dose Not Changed/ None	No
Cohort 2									
Cohort 3									
Cohort 4									

Related = Possible, Probable, Definite

Created on: ddmmmyy hh:mm

Page 1 of N

L16.2.8.1 Listing of Positive Pregnancy Test Results

Cohort	Patient Number	Visit 1	Visit 2	Visit 3
Cohort 1	xx-xxxx	Negative	Negative	Negative
Cohort 2				
Cohort 3				
Cohort 4				

Created on: ddmmmyy hh:mm

L16.2.8.2 Listing of Abnormal Vital Signs

Cohort	Patient Number	Age	Visit	Vital Sign	Normal Range	Result
Cohort 1	xx-xxxx	xxx	1	Diastolic BP	xxx - xxx	xxx
			2			
			3			
Cohort 2						
Cohort 3						
Cohort 4						

Created on: ddmmmyy hh:mm

L16.2.8.3 Listing of Abnormal Physical Examination Results

Cohort	Patient Number	Visit	System	Results
Cohort 1	xx-xxxx	1	HEENT	Abnormal (Scar)
		2		
		3		
Cohort 2				
Cohort 3				
Cohort 4				

Created on: ddmmmyy hh:mm

L16.2.8.4 Listing of Clinical Hematology Laboratory Results

Cohort	Patient Number	Visit	Hematocrit (*unit*)	WBC (*unit*)	Platelets (*unit*)	Hemoglobin (*unit*)	etc.
Cohort 1	xx-xxxx	1	xxx	xxx	xxx	xxx	xxx
		3	xxx	xxx	xxx	xxx (Low)	xxx
Cohort 2							
Cohort 3							
Cohort 4							

L16.2.8.5 Listing of Clinical Chemistry Laboratory Results

Cohort	Patient Number	Visit	Alkaline Phosphatase (*unit*)	Alnine Transaminase (*unit*)	Aspartate Transaminase (*unit*)	Blood Urea Nitrogen (*unit*)	etc.
Cohort 1	xx-xxxx	1	xxx	xxx	xxx (High)	xxx	xxx
		3	xxx	xxx	xxx	xxx	xxx
Cohort 2							
Cohort 3							
Cohort 4							

Created on: ddmmmyy hh:mm

10. APPENDICES

APPENDIX A: Body Surface Area Calculation

Total Body Surface Area Calculation

To calculate the Total BSA the following procedure (Mosteller Formula[13]) should be followed.

Total Body Surface Area (BSA) in meters squared

m^2 = ((height (cm) x weight (kg)) /3600)^{½}

It is preferable that the patient's height and weight be measured in cm and kg however if needed:

To convert inches (in) to centimeters (cm) the following conversion should be used

1 inch = 2.54 cm

To convert pounds (lbs) to kilograms (kg) the following conversion should be used

1 lb = 0.45 kg

The patient's height and weight should be reported to the nearest cm and nearest 0.5 kg. The BSA should be reported to the nearest second decimal place.

For example a patient who is 68 inches tall and weighs 180 lbs will have a reported BSA of:

68 in x 2.54 = 173 cm

180 lb x 0.45 = 81.0 kg

BSA = SQRT ((173 x 81.0)/3600)

= 1.97 m^2

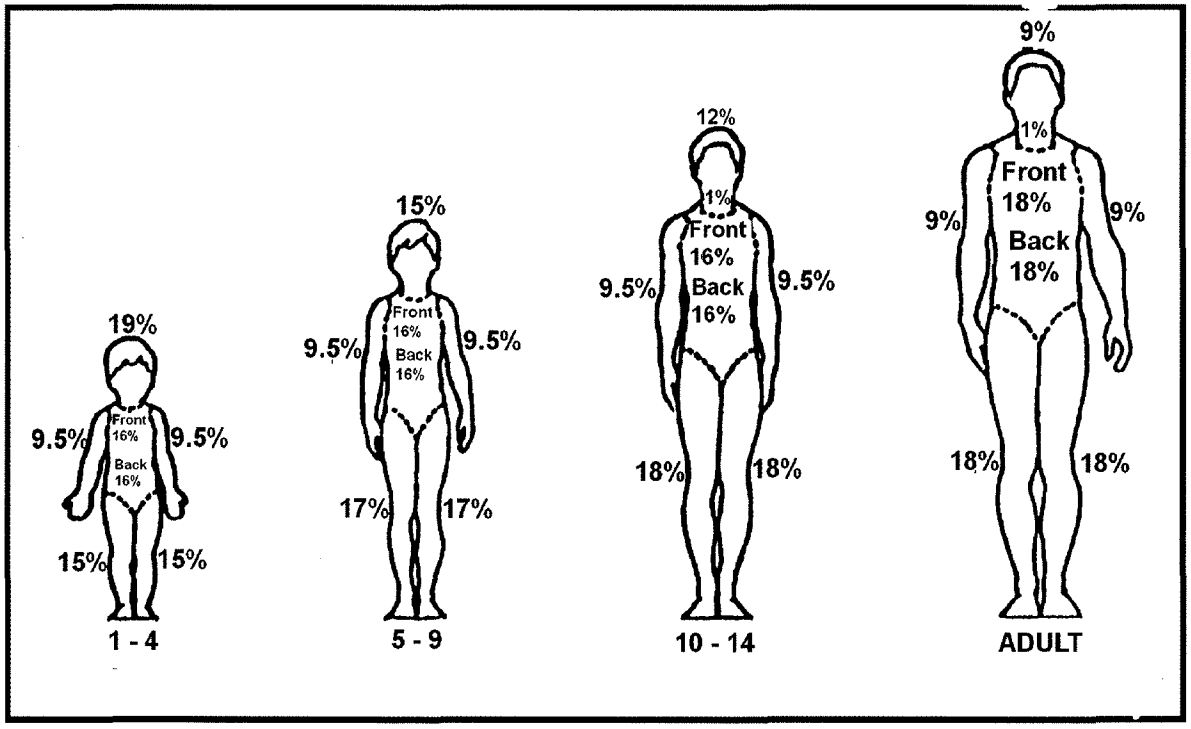
%BSA Affected

To estimate the % BSA Affected, the Investigator should use the method of approximation:

The "Rule of Nines" provides a general estimation of total BSA for several anatomic areas (each arm = 9%, each leg = 18%, back = 18%, chest and abdomen = 18%, head =

9%, groin = 1%). The Investigator may then visually estimate the proportion of the involved skin within each anatomic area and calculate the total percentage of BSA affected. In children, hips and legs are smaller and the head, neck and shoulders are larger, as a result, a modified "Rule of Nines" is used (see diagram below).

Part	1-4 year child body % of total	5-9 year child body % of total	10-14 year child body % of total	Adult body % of total
Arm	9.5%	9.5%	9.5%	9%
Head	19%	15%	12%	9%
Neck			1%	1%
Leg	15%	17%	18%	18%
Anterior trunk	16%	16%	16%	18%
Posterior trunk	16%	16%	16%	18%



APPENDIX B: Eczema Area and Severity Index Score (EASI)

The EASI is a composite score based on the severity of four different signs of atopic dermatitis in four different areas of the body multiplied by the percent of that specific body area affected multiplied by a weighting factor.

Erythema

0 = Clear	No evidence of erythema
1 = Mild	Definite light red coloration
2 = Moderate	Moderate redness, but not dark
3 = Severe	Dark red coloration

Induration/papulation/edema

0 = Clear	No evidence of any induration/papulation/edema
1 = Mild	Barely perceptible elevation
2 = Moderate	Clearly perceptible elevation
3 = Severe	Marked and extensive elevation

Lichenification

0 = Clear	No evidence of lichenification
1 = Mild	Slight thickening of skin discerible only by touch and with skin markings minimally exaggerated
2 = Moderate	Definite thickening of skin with skin marking exaggerated so at they form a visible criss-cross or ridged pattern
3 = Severe	Thickened skin with skin markings visibly portraying an exaggerated criss-cross or ridged pattern

Excoriation

0 = Clear	No evidence of excoriation
1 = Mild	Scant evidence of excoriation with no signs of deepers skin damage (absence of erosion or crusts)
2 = Moderate	Several linear marks of skin with some showing evidence of deeper skin injury (erosion, crust visible)
3 = Severe	Many erosive or crusty lesions present

The patient will be required to rate the severity of their pruritis (itching/scratching/discomfort) over the previous 24 hours using the following scale:

Pruritis

0 = None	None
1 = Mild	Occasional slight itching or scratching
2 = Moderate	Constant or intermittent itching/scratching/discomfort which is not disturbing sleep

3 = Severe	Bothersome itching/scratching/discomfort which is disturbing sleep

Eczema, induration, excoriation and lichenification are part of the EASI score but pruritis is not.

EASI Score

The EASI score is calculated as follows:
Head/neck (E + I + X + L) x Area x 0.1 (in children ages 0-7, x 0.2)
Upper Limbs (E + I + X + L) x Area x 0.2
Trunk (E + I + X + L) x Area x 0.3
Lower Limbs (E + I + X + L) x Area x 0.4 (in children ages 0-7, x 0.3)
EASI SCORE = SUM OF ABOVE 4 REGIONS

E: Erythema,
I: Induration/papulation/edema
X: Excoriation
L: Lichenification

Severity is based on the Investigator's assessment of individual signs and symptoms 0 = none, 1 = mild, 2 = moderate, 3 = severe using the definitions above

The % of each body region affected is scored as the variable Area above in the EASI formula. For the 4 body regions (head/neck, upper limbs, trunk and lower limbs) if the:

Area = 0 if % affected is 0%
Area = 1 if % affected is 1 to 9%
Area = 2 if % affected is 10 to 29%
Area = 3 if % affected is 30 to 49%
Area = 4 if % affected is 50 to 69%
Area = 5 if % affected is 70 to 89%
Area = 6 if % affected is 90 to 100%

EASI Score can be presented to the nearest whole number (no decimals and all numbers should be rounded, 0.5 should be rounded up to the nearest whole number)

The minimum score would be 0 and the Maximum Score would be 72. To be eligible for participation in this study a patient must have an EASI of at least 15 at baseline.

APPENDIX C: Investigator Global Assessment (IGA)

To be eligible for inclusion in the study the IGA must be 3 or 4 at baseline. To be considered a Clinical Success the patient must score a 0, 1 at Visit 4.

0	Clear	Minor, residual discoloration, no erythema or induration/papulation, no oozing/crusting
1	Almost Clear	Just perceptible erythema, with almost no induration/papulation and no oozing/crusting
2	Mild Disease	Definite pink erythema with mild induration/papulation and no oozing/crusting
3	Moderate Disease	Red erythema with moderate induration/papulation and there may be some oozing/crusting
4	Severe Disease	Dark/bright red erythema with severe induration/papulation with oozing/crusting

APPENDIX D: Cortisol Response Test

This cortisol release test is modified from the procedure of Wood et al as described in the Product Label for Cortrosyn™ (cosyntropin) for injection (Amphstar Pharmaceuticals, Inc.).

The procedure is as follows:

1. A single 5 ml blood sample should be taken as the basal sample.
2. 0.25 mg (a single vial) of Cortrosyn™ (cosyntropin) should be reconstituted with 1.0ml of 0.9% sodium chloride injection USP injected intramuscularly. In patients under 3 years of age, 0.125mg of Cortrosyn™ will be used.
3. 30 minutes after the IM injection a second 5 ml blood sample should be obtained. The resulting two serum samples (at least 1 ml of serum in each) should be processed and labeled according to the instructions provided and sent the same day to ACM Global Laboratory for analysis of basal and post stimulated serum cortisol concentration.

At Visit 1 and Visit 4 all patients will have a cortisol response test performed. The resulting blood sample should be sent to ACM Global Laboratory for immediate testing.

Visit 1 Test

The results of the cortisol response test must be obtained prior to study drug being dispensed at Visit 2. Only patients with normal baseline (Visit 1) cortisol and adrenal function (see criteria below) should be enrolled in the study.

Visit 4 Test

The test at the End of Study visit should not be performed if the patient dosed within 12 hours.

A patient will be considered to have normal basal cortisol level and adrenal function if they meet all three criteria listed below under Normal. Failure to meet any of these criteria is indicative of abnormal adrenal function or potential HPA axis suppression.

	Cortisol Results	
	Normal	Abnormal
Basal (pre Cortrosyn™ injection)	≥ 5 mcg/100ml	< 5 mcg/100ml
30 minutes post Cortrosyn™ injection	≥ basal value + 7	< basal value + 7
	> 18 mcg/100ml	≤ 18 mcg/100ml

HPA Axis suppression will be defined as a 30 minute post Cortrosyn™ injection level cortisol level of ≤ 18 mcg/100ml. As the study treatment period will be over, any patients with results of

HPA axis suppression will be advised not to initiate any new steroid therapy, topical or otherwise, and to return to the site in 28 days at which time they will be assessed for HPA axis suppression.

Any patient presenting with symptoms of HPA axis suppression, such as nausea, headache, myalgia, fatigue or loose stool, will be referred to an endocrinologist. As an additional safety precaution, wristbands identifying the patient as someone suffering from adrenal suppression secondary to steroid withdrawal will be provided to alert medical personnel should any emergencies arise before adrenal function returns to normal.

If the results of the cortisol response test still show signs of HPA axis suppression 28 days after discontinuing therapy the patient will be asked to return in 28 days (56 days after discontinuing steroid therapy) for another follow-up test. If the patient is still showing signs of HPA axis suppression 56 days after discontinuing steroid therapy and presents with related symptoms, the patient will be referred to an endocrinologist.

If HPA axis suppression persists for 56 days after discontinuing steroid therapy, but the patient has no symptoms they will be asked to return in 28 days (84 days after discontinuing steroid therapy) for another follow-up test. If HPA axis suppression persists for 84 days after discontinuing steroid therapy patients will be referred to an endocrinologist regardless of symptoms.

Patients should not be subjected to Cortrosyn™ testing, or any other challenge to their adrenal response, any sooner than 4 weeks from their last Cortrosyn™ test.

Follow-Up Schedule for Patients showing signs of HPA Axis Suppression

Days after d/c	HPA Results	Symptoms	Patient Course
28	Normal	N/A	Study over
28	Abnormal	Yes	Refer to endocrinologist
28	Abnormal	No	Repeat test in 28 days
56	Normal	N/A	Study over
56	Abnormal	Yes	Refer to endocrinologist
56	Abnormal	No	Repeat test in 28 days
84	Normal	N/A	Study over
84	Abnormal	Yes or No	Refer to an endocrinologist