STATISTICAL ANALYSIS PLAN

An Open Label, Safety Study to Assess the Potential for Adrenal Suppression Following Maximal Use Treatment with Desoximetasone 0.25% shampoo (Taro Pharmaceuticals U.S.A., Inc.) in Patients with Scalp Psoriasis

Protocol Number: DSXS1538a
Novum Study Number: 71515011

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SAP FINAL VERSION APPROVALS

An Open Label, Safety Study to Assess the Potential for Adrenal Suppression Following Maximal Use Treatment with Desoximetasone 0.25% shampoo (Taro Pharmaceuticals U.S.A., Inc.) in Patients with Scalp Psoriasis

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Revision History

VERSION	DATE	DESCRIPTION OF REVISIONS	REVISED BY
Draft 1.0	March 8, 2017	New Document	Jianhua Liu
Final 1.0	March 13, 2017	Finalized SAP	Jianhua Liu
Final 2.0	April 18, 2017	1. Adding safety population to the SAP 2. Deleting the section on secondary outcome.	Jianhua Liu

List of Abbreviations and Definition of Terms

Abbreviation	Term
ADaM	Analysis Data Model
AE	Adverse Event
BP	Blood Pressure
C	Celsius
CRF	Case Report Form
CRO	Clinical Research Organization
CDISC	Clinical Data Interchange Standards Consortium
FDA	Food and Drug Administration
HR	Heart Rate
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IGA	Investigator's Global Assessment
IND	Investigational New Drug
ml	Milliliter
MedDRA	Medical Dictionary for Regulatory Activities
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SDTM	Study Data Tabulation Model

TABLE OF CONTENTS

1. INTRODUCTION

This Statistical Analysis Plan (SAP) is based on the final Clinical Study Protocol DSXS1538a (Study No. 71515011) Rev. 2 dated December 20, 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:

- Clinical Study Protocol DSXS1538a (Study No. 71515011) Rev. 2 dated December 20, 2016
- Case Report Form Booklet Version 1.0 for Study No. 71515011 (DSXS1538a)

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

The objectives of this study are to:

1. Evaluate the potential of desoximetasone 0.25% shampoo to suppress HPA axis function in patients with moderate to severe scalp psoriasis.
2. Evaluate the efficacy parameters and adverse event (AE) profiles of desoximetasone 0.25% shampoo administered to patients with moderate to severe scalp psoriasis.

3. OVERALL STUDY DESIGN

This open-label, safety study is designed to evaluate the potential for adrenal suppression after maximal use treatment with desoximetasone 0.25% shampoo (Taro Pharmaceuticals, U.S.A.), for the treatment of moderate to severe scalp psoriasis.

Up to 40 eligible patients with stable plaque psoriasis of the scalp that satisfy all eligibility criteria will be enrolled into the study at Visit 1 to obtain 20 evaluable patients. Patients must be overall in good health. They should have a current diagnosis of moderate to severe scalp psoriasis with IGA score of at least 3 or 4.

Up to 40 patients will be enrolled to obtain 20 evaluable patients with a confirmed diagnosis of moderate to severe scalp psoriasis.

Patients enrolled in the study will apply product once daily for 28 days, according to provided instructions. Each patient is expected to receive 28 doses of study product.

Patients will attend a total of 3 Clinic Visits and a telephone follow-up phone call (Visit 4) 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
- **Visit 4 (Day 42± 4)**: Follow-Up Telephone Phone Call

The primary endpoint is the proportion of patients in the study with HPA axis suppression following treatment with the study medication.

The safety profile of each treatment group will be evaluated by comparing adverse events.

Study Schematic

	Visit 1	**Visit 2**	**Visit 3**	**Visit 4**
Day	**1**	**14 ± 2**	**29 ± 2**	**42 ± 4**
Procedures	Screening/ 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	
HEENT Exam	X	X	X	
% Scalp Affected	X	X	X	
Investigator Global Assessment	X	X	X	
Concomitant Medication	X	X	X	X
Laboratory Evaluations	X		X	
Cortisol Response Test	X		X	
Confirm Inc/Exc Criteria	X			
Dispense Wristband	X			
Weigh and Dispense Study Product	X	X		
Collect and Weigh Study Product		X	X	
Dispense/Review Patient Diary	X	X	X	
Ocular Assessment		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. SAMPLE SIZE

The sample size of 20 evaluable patients was deemed appropriate to meet the objective of the study.

5. STUDY ENDPOINTS AND ANALYSIS POPULATIONS

Primary Outcome Measures:

Hypothalamic Pituitary Adrenal (HPA) Axis Response to Cosyntropin demonstrating the absence or presence of adrenal suppression at the end of treatment defined by the following criteria: 30 minute post Cortrosyn™ injection level cortisol level of ≤ 18 mcg/100ml during the Cortisol Response Test.

Safety Population:

Safety Population includes all patients who applied at least one dose of study drug.

6. 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, efficacy variables 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 number of observations, 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).

6.1 Baseline Characteristics

6.1.1 Demographics

Demographic information collected at baseline includes the following:

- Age (years)
- Gender (Male/Female)
- Ethnicity (Hispanic/non Hispanic)

- Race (White, Black/African American, Native Hawaiian or Other Pacific Islander, Asian, American Indian or Alaska Native, Other)

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

All data will be listed by patient.

6.1.2 Medical History

At Visit 1, patients will be questioned about medical history, including acute and chronic medical history and medical history relevant to their scalp psoriasis.

Medical history data will be listed by patient.

6.1.3 Physical Exam

A general physical exam will be conducted at Visit 1 and Visit 3. The physical exam must include a dermatological examination as a minimum.

Abnormal physical exam results will be listed by patient and visit.

6.1.4 Percent Scalp Affected

Patient's scalp will be examined by Investigator/designated clinician to determine the percent surface area affected with plaque psoriasis at all visits.

Descriptive summary (n, mean, standard deviation, median, minimum, maximum) will be presented for percent scalp affected by visit.

Percent scalp affected will be listed by patient and visit.

6.1.5 Pregnancy Test

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

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

6.1.6 Concomitant Medications

At Visits 1-3 and during the telephone follow-up phone call (Visit 4) patients will be questioned about current and concomitant medication use over the previous 12 weeks. At all Interim Visits patients will be questioned about ongoing or new concomitant medication use.

All prior and concomitant medications taken since screening will be listed by patient.

6.2 Statistical Analyses

6.2.1 Safety Analysis of Potential HPA Axis Suppression

Dosing will be once daily for 28 days. Patients who have normal adrenal function at baseline , use at least 21 doses of the study product and have data from a post-treatment cortisol response test will be included in the analysis.

The primary analysis of interest is to assess the proportion of patients considered to have demonstrated possible HPA axis suppression following treatment with the study medication.

A logistic regression of the proportion of patients in the study with HPA axis suppression may be performed as exploratory analysis with % scalp affected as a covariate. This will depend on the distribution of the % scalp data collected. See Appendix D for results from the cortisol response test considered indicative of potential HPA axis suppression.

6.2.2 Investigator Global Assessment

Patient will be examined to determine the severity of scalp psoriasis based on a global assessment of plaque elevation, scaling and erythema by the Investigator/designated clinician.

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

Investigator Global Assessment data will also be listed by patient and visit.

6.3 Safety Analysis

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

6.3.1 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. 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.

All AEs will be listed by patient.

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

6.3.2 Vital Signs

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

Vital sign data will be listed by patient and visit.

6.3.3 Laboratory Evaluation

At Visit 1 and Visit 3 a blood sample will be collected for hematology and clinical chemistry testing.

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 patient and visit.

6.3.4 Ocular Discomfort Assessment

At Visits 2 and 3 the patient will be asked to assess if any ocular discomfort was experienced, YES or NO, since the last clinic visit. If YES is reported, the patient will be asked to report the signs and symptoms experienced.

All data will be listed by patient and visit.

6.4 Multiple Comparisons

No multiple comparison adjustment will be made in this study.

6.5 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.

6.6 Interim Analyses

There is no interim analysis planned in this study.

6.7 Changes to the Protocol Defined Statistical Analysis Plan

The protocol section 10.1.2 states that after completion of 20 patients an interim analysis will be performed and presented. This was an error in the protocol and no interim analysis will be performed.

7. 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 Patient Disposition

Patients	Total
Enrolled	xx
Completed Study	xx
Terminated Early	xx
Adverse event	xx
Enrolled in error	xx
Lack of efficacy	xx
Lost to follow-Up	xx
Non-compliance with study drug	xx
Non-compliance with study procedure	xx
Restricted medication used for the treatment of psoriasis	xx
Restricted medication used for reasons other than the treatment of psoriasis	xx
Significant worsening of scalp psoriasis required alternative or supplemental therapy	xx
Withdrawal by subject	xx
Other	xx

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Page 1 of N

T16.1.9.2 Summary of Protocol Deviations (Safety Population)

	Total
Total Patients with Protocol Deviations	xx
Total Deviations	xx
Assessment conducted out of window	xx
Enrolled in error	xx
Lost to follow-up	xx
Missed blood collection	xx
Missed visit	xx
Outside visit window	xx
Non-compliance with study drug	xx
Non-compliance with study procedure	xx
Restricted medication use	xx
Study product not applied approximately 24 hours before clinic visit	xx
Other	xx

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T16.1.9.3 Summary of Demographic Data (Safety Population)

		Total N=xx
Age (years)	n	xx
	Mean ± SD	xx.x ± xx.x
	Median	xx.x
	Range	xx.x – xx.x
Race	American Indian or Alaska Native	xx (xx.x%)
	Asian	xx (xx.x%)
	Black/African American	xx (xx.x%)
	Native Hawaiian or other Pacific Islander	xx (xx.x%)
	White	xx (xx.x%)
	Other	xx (xx.x%)
Ethnicity	Hispanic or Latino	xx (xx.x%)
	Not Hispanic or Latino	xx (xx.x%)
Gender	Female	xx (xx.x%)
	Male	xx (xx.x%)

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

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Page 1 of N

T16.1.9.4 Summary of Frequency of HPA Axis Suppression at the End of Treatment

HPA Axis Suppression	Total N=xx
Yes	xx (xx.x%)
No	xx (xx.x%)

N= number of patients included in HPA axis suppression analysis; % is based on N

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Page 1 of N

T16.1.9.5 Summary of Percent Scalp Affected with Plaque Psoriasis (Safety Population)

Visit	n	Mean	SD	Median	Min	Max
1	xx	xx.x	xx.x	xx.x	xx.x	xx.x
2	xx	xx.x	xx.x	xx.x	xx.x	xx.x
3	xx	xx.x	xx.x	xx.x	xx.x	xx.x

T16.1.9.6 Summary of Frequency of Investigator Global Assessment (IGA) (Safety Population)

Visit	0 (Clear)	1 (Minimal)	2 (Mild)	3 (Moderate)	4 (Severe)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

% is based on number of patients included in safety population.

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T16.1.9.7 Overall Summary of Adverse Events (Safety Population)

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

Related = Possible, Probable, Definite

T16.1.9.8.1 Summary of Frequency of All Adverse Events by Body System (Safety Population)

Body System	MedDRA Term	Events	Patients
Patients with at least one AE	Total	xx	xx (xx.x%)
Ear and labyrinth disorders	Ear pain	xx	xx (xx.x%)

% is based on number of patients included in safety population.

T16.1.9.8.2 Summary of Frequency of All Adverse Events in ≥ 2% of Patients by Body System (Safety Population)

T16.1.9.9 Summary of Frequency of All Adverse Events by Severity (Safety Population)

Body System	MedDRA Term	Mild	Moderate	Severe
Patients with at least one AE	Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ear and labyrinth disorders	Ear pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

% is based on number of patients included in safety population.

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Page 1 of N

T16.1.9.10 Summary of Frequency of All Adverse Events by Relationship (Safety Population)

Body System	MedDRA Term	Related	Not Related
Patients with at least one AE	Total	xx (xx.x%)	xx (xx.x%)
Ear and labyrinth disorders	Ear pain	xx (xx.x%)	xx (xx.x%)

Related = Possible, Probable, Definite
% is based on number of patients included in safety population.

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Page 1 of N

T16.1.9.11 Summary of Frequency of Serious Adverse Events (Safety Population)

Body System	MedDRA Term	Total N=xx
Injury, poisoning and procedural complications	Alcohol poisoning	xx

T16.1.9.12 Shift Analysis of Clinical Chemistry Laboratory Results from Baseline to End of Treatment (Safety Population)

Alanine Aminotransferase (U/L)

Baseline-> Endpoint	Low	Normal	High
Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

% is based on number of patients included in safety population.

Table will continue for other lab parameters.

Similar table will be created for T16.1.9.13.

T16.1.9.13 Shift Analysis of Clinical Hematology Laboratory Results from Baseline to End of Treatment (Safety Population)

L16.2.1 Listing of Discontinued Patients

Patient Number	Date of Discontinuation	Discontinuation Reason
xx-xxxx	yyyy-mm-dd	Adverse event
xx-xxxx	yyyy-mm-dd	Lost to follow-up

L16.2.2 Listing of Protocol Deviations

Patient Number	Event Description
xx-xxxx	Outside Visit Window (Visit 3)

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Page 1 of N

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

Patient Number	Exclusion Reason
xx-xxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

L16.2.4.1 Listing of Demographic Data

Patient Number	Age	Gender	Ethnicity	Race
xx-xxxx	30	Female	Not Hispanic or Latino	Black or African American

L16.2.4.2 Listing of Medical History

Patient Number	System	Diagnosis or Surgical Procedure	Start Date	End Date	Ongoing
xx-xxxx	Gynecologic	Menopause	yyyy-mm-dd	yyyy-mm-dd	

L16.2.4.3 Listing of Concomitant Medication

Patient Number	Treatment Area	Medication	Dosage	Frequency	Route	Location	Start/End Date	Indication
xx-xxxx	No	Advil	2 TAB	QD	Oral	xxxxxxxxx	yyyy-mm-dd / yyyy-mm-dd	Cold

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Page 1 of N

L16.2.5.1 Listing of Drug Administration

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

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: 28 applications (28 days of once daily dosing);
for subjects who discontinued early: the minimum between 28 and [(Date of Discontinuation – Date of First Application)+1].

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Page 1 of N

L16.2.5.2 Listing of Study Medication Weight

Patient Number	Bottle 1		Bottle 2		Total Amount Applied (g)
	Weight Dispensed (g)	Weight Collected (g)	Weight Dispensed (g)	Weight Collected (g)	
xxxx	xx	xx	xx	xx	xxx

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Page 1 of N

L16.2.6.1 Listing of Cortisol Response Test Results

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?	HPA axis Suppression
xx-xxxx	1	Yes	yyyy-mm-dd	hh:mm	hh:mm	hh:mm	xxx	xxx	No	No
	3	Yes	yyyy-mm-dd	hh:mm	hh:mm	hh:mm	xxx	xxx	Yes	No
xx-xxxx	1	Yes	yyyy-mm-dd	hh:mm	hh:mm	hh:mm	xxx	xxx	No	No
	3	Yes	yyyy-mm-dd	hh:mm	hh:mm	hh:mm	xxx	xxx	Yes	Yes

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Page 1 of N

L16.2.6.2 Listing of HPA Axis Suppression Follow-Up

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

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Page 1 of N

L16.2.6.3 Listing of Investigator Global Assessment (IGA)

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

L16.2.6.4 Listing of Percent Scalp Affected with Plaque Psoriasis

Patient Number	Visit 1	Visit 2	Visit 3 / Early Termination
xx-xxxx	xxx	xxx	xxx

L16.2.7 Listing of Adverse Events

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?
xx-xxxx	Nervous system disorders / Headache / Headache	No	yyyy-mm-dd / yyyy-mm-dd	Mild	Not Related	Recovered	Dose Not Changed/ None	No

L16.2.8.1 Listing of Positive Pregnancy Test Results

Patient Number	Visit 1	Visit 2	Visit 3
xx-xxxx	Negative	Negative	Positive

L16.2.8.2 Listing of Vital Signs

Patient Number	Visit	Systolic BP (mmHg)	Diastolic BP (mmHg)	Heart Rate (beats/min)	Respiration Rate (breaths/min)	Temperature (F)
xx-xxxx	1	120	70	84	18	98.6
	2	140	80	74	18	97
	3	130	87	74	18	99.2

L16.2.8.3 Listing of Abnormal Physical Examination Results

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

L16.2.8.4 Listing of Clinical Hematology Laboratory Results

Patient Number	Visit	Hematocrit (L/L)	Basophils (10^9/L)	Platelets (10^9/L)	Hemoglobin (g/L)	etc.
xx-xxxx	1	xxx	xxx	xxx	xxx	xxx
	3	xxx	xxx	xxx	xxx (Low)	xxx

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L16.2.8.5 Listing of Clinical Chemistry Laboratory Results

Patient Number	Visit	Alkaline Phosphatase (U/L)	Alanine Transaminase (U/L)	Aspartate Transaminase (U/L)	Blood Urea Nitrogen (mmol/L)	etc.
xx-xxxx	1	xxx	xxx	xxx (High)	xxx	xxx
	3	xxx	xxx	xxx	xxx	xxx

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Page 1 of N

L16.2.8.6 Listing of Ocular Signs/Symptoms Assessment

Patient Number	Visit	Did the patient experience any ocular discomfort ?	Signs/Symptoms the patient experienced	Did the shampoo come into contact with the patient's eyes?	Patient's overall discomfort
xx-xxxx	2	Yes	Redness/Pain	Yes	Mild
	3	No			
xx-xxxx	2	Yes	Itching/Pain	Yes	None
	3	Yes	Itching/Pain	No	

8. APPENDICES

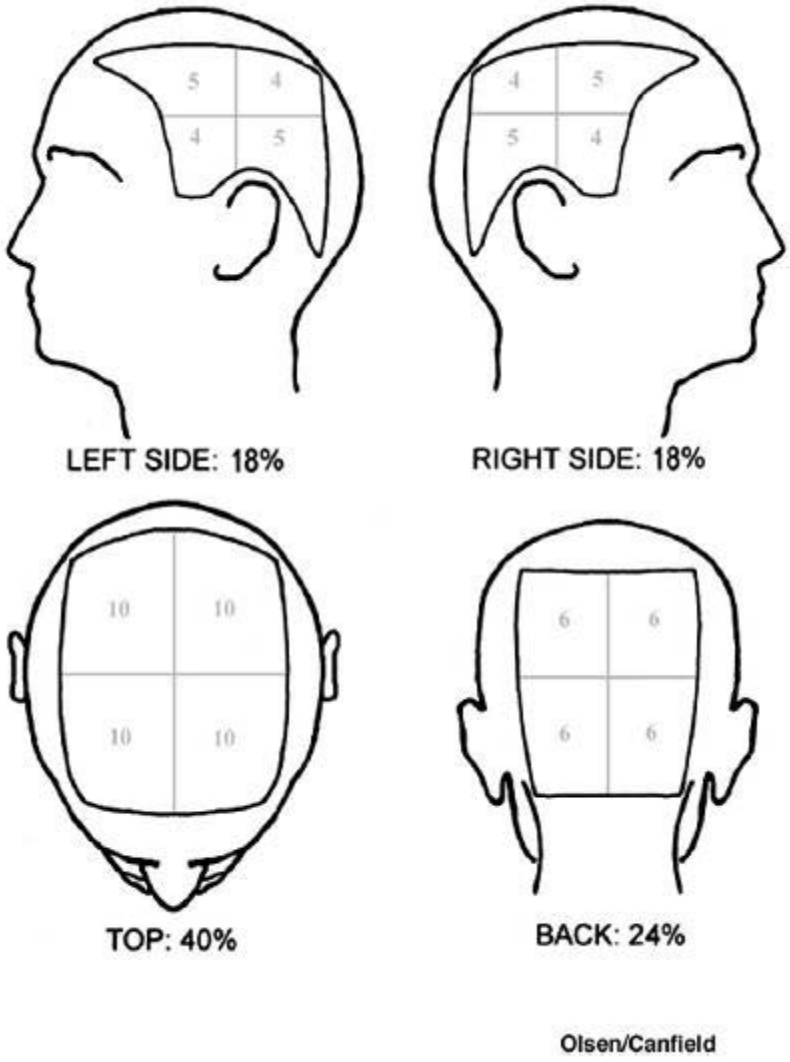
APPENDIX A: Investigator Global Assessment (IGA)

To be eligible for inclusion in the study the IGA must be 3 or 4 at baseline. Patients will be considered to have shown improvement in disease severity if the IGA score decreases by at least one unit from the baseline score, and will be considered a treatment success if the IGA score decreases at least 2 units from the baseline score.

Score	Category	Description
0	Clear	Plaque elevation: no evidence of plaque elevation above normal skin level Scaling: no evidence of scaling Erythema: no redness
1	Minimal	Plaque elevation: very slight elevation above normal skin level, easier felt than seen Scaling: limited amount of very fine scales partially covers some of the plaques Erythema: very few of the plaques are light red
2	Mild	Plaque elevation: slight but definite elevation above the normal skin level, typically with edges that are indistinct or sloped on some of the plaques Scaling: mainly fine scales, some plaques are partially covered Erythema: some plaques are light red
3	Moderate	Plaque elevation: moderate elevation with rounded or sloped edges on most of the plaques Scaling: somewhat coarser scales; most plaques are partially covered Erythema: most plaques are red
4	Severe	Plaque elevation: marked to very marked elevation, with hard to very hard sharp edges on virtually all or all of the plaques Scaling: coarse, thick scales; virtually all or all plaques are covered; rough surface Erythema: virtually all or all plaques are bright to dusky red

APPENDIX B: Percent Scalp Affected

Investigators will use the following chart to identify areas and estimate scalp surface area affected by psoriasis plaques.[16]



APPENDIX C: Ocular Discomfort Assessment

At Visits 2 and 3 the patient will be asked to assess if any ocular discomfort was experienced, YES or NO, since the last clinic visit.

If YES is reported, the patient will be asked to report the signs and symptoms that apply from the list below or indicate any OTHER signs and symptoms experienced:

Redness	Stinging
Itching	Blur (decrease in vision)
Pain	Increased sensitivity
Swelling	Watery eyes
Burning	Spots, flashes and floaters
Eye Discharge	Foreign body sensation

In addition, the patient will be asked to indicate if the shampoo came into contact with their eye, YES or NO, since the last clinic visit. If YES is reported, the patient will be asked to rate the discomfort at the time of contact as None, Mild, Moderate or Severe.

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.

   The resulting blood samples should be sent to ACM Global Laboratory for immediate testing.

   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. If the Visit 1 Cortisol Response Test shows signs of HPA axis suppression as defined above the patient will be contacted and instructed to discontinue the use of study product, not to iniate any new steroid therapy, topical or otherwise and an End of Study Visit will be scheduled to conduct a Cortisol Response Test at least 28 days after the initial Cortisol Response Test at Visit 1 to assess for HPA axis suppression. At Visit 3 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 they 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 they 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

APPENDIX F: Clinical Laboratory Testing

As part of the Screening Procedures and at Visit 3 (or early termination for randomized patients only) patients will have a blood sample taken 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

Clinical Laboratory Testing will be performed at a Central Laboratory

ACM Medical Lab, Inc.

160 Elmgrove Park

Rochester, NY 14624, USA