A Multicenter Open Label Uncontrolled Study of the Long Term Safety and Efficacy of Calcitriol 3 mcg/g Ointment Applied Twice Daily for 26 Weeks in Pediatric Subjects (2 To 17 Years of Age) With Mild to Moderate Plaque Psoriasis

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A MULTICENTER OPEN LABEL UNCONTROLLED STUDY OF THE LONG TERM SAFETY AND EFFICACY OF CALCITRIOL 3 MCG/G OINTMENT APPLIED TWICE DAILY FOR 26 WEEKS IN PEDIATRIC SUBJECTS (2 TO 17 YEARS OF AGE) WITH MILD TO MODERATE PLAQUE PSORIASIS

STATISTICAL ANALYSIS PLAN

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This document is electronically approved and signed by: *Biometrics Manager*

Name	Reason for Signing	Date
[redacted]	Head of Department	30-May-2014

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Reviewer: [redacted]

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1 STUDY OBJECTIVES

The primary objective of this study is to evaluate the safety of up to 26 weeks of treatment with calcitriol 3 mcg/g ointment when used twice daily, without occlusion, to treat pediatric subjects (2 to 17 years of age) with mild to moderate plaque psoriasis.

Additional objective is to evaluate the long-term efficacy of up to 26 weeks of treatment with calcitriol 3 mcg/g ointment when used twice daily, without occlusion, to treat pediatric subjects (2 to 17 years of age) with mild to moderate plaque psoriasis.

2 STUDY DESIGN

This is an open-label, uncontrolled, multicenter long-term safety and efficacy study in pediatric subjects (age 2-17) with mild to moderate plaque psoriasis.

Approximately one hundred and forty (140) subjects will be enrolled into this study.

Qualified subjects will receive calcitriol 3 mcg/g ointment for a period of up to 26 weeks. The subject's parent/legal guardian or the subject under the responsibility of the parent/legal guardian will apply a thin film of study drug as needed to cover all involved areas twice daily, without exceeding a maximum of 0.5 g/kg of body weight or 28 g daily (whichever is the lower). If the subject experiences complete clearing of psoriasis per physician assessment (i.e. an IGA of 0), the subject should discontinue the study drug but continue to follow the visit schedule through the Week 26 visit. Treatment with study drug should be resumed if the IGA score is >0 and <4.

Subjects will be evaluated at screening, baseline and Weeks 4, 8, 12, 20, 26/Early Termination, and Follow-up visit Week 30.

3 EFFICACY AND SAFETY ASSESSMENT

Table 1 Schedule of Assessments

	Clinical Trial Assessments							
	Screening Period	Treatment Period[10]						Follow-up Period
	Screening *(Day -14)*[11, 15] *V1*	*Baseline (Week 0) V2*	Week 4[1] *V3*	Week 8[1] V4	Week 12[1] V5	Week 20[1] V6	Week 26 / ET[1, 5] V7	Week 30[1] V8
Informed Consent / Assent Form /HIPAA/PIPEDA	X							
Demographics	X							
Medical History	X							
Previous Therapies/Procedures[8]	X							
Physical examination and Vital signs[2]	X	X			X		X	
Inclusion/Exclusion Criteria	X	X[3]						
Urine Pregnancy Test (post menarcheal)	X	X	X	X	X	X	X	X
Record % Body Surface Area involved	X	X	X	X	X	X	X	X
Routine Blood Chemistry and Hematology	X		X		X	X	X	X
Urinalysis	X		X	X	X	X	X	X
Pharmacodynamic Serum[9]	X		X	X	X	X	X	X[12]
Pharmacodynamic Urine[9]	X				X[14]		X[14]	X[12]
25(OH)D & 1,25 (OH)2D	X				X		X	X[12]
IGA	X	X	X	X	X	X	X	X
Pruritus	X	X	X	X	X	X	X	X
Drug application		Twice a day from Baseline to V7[16]						
Study drug Dispensing (D) and Accountability (A)[4]		D	D/A	D/A	D/A	D/A	A	
Adverse Event information collection[7, 13]	X	X	X	X	X	X	X	X
Concomitant Therapies/Procedures[8]	X	X	X	X	X	X	X	X
Moisturizer and cleanser dispensed[6]		X	X	X	X	X	X	
Exit Form[5]								X

[1] Visit window of +/- 3 days.

[2] Physical Examination to include: weight and review of systems: skin, cardiovascular, respiratory, abdomen, head and neck, musculoskeletal, neurological, lymph nodes and psychological. Height is to be evaluated at Screening visit only. Vital Signs to include: blood pressure, pulse rate

[3] Reconfirm that subject continues to meet inclusion/exclusion criteria.

[4] Total amount of Study Drug applied to involved skin should not to exceed 0.5 g/kg of body weight or 28g per day (whichever is the lower). First application to be made under the supervision of the investigator or designee. Record daily administration on dosing calendar. Dosing calendar to be checked at each visit after Baseline.

[5] Or at any time in case of early termination.

[6] The Cetaphil® Moisturizing Cream and Cetaphil® Gentle Skin Cleanser or equivalents will be provided by the Sponsor

[7] Events occurring after the Informed Consent Form and Assent Form (when applicable) have been signed should be recorded as Adverse Events in the eCRF

[8] Any therapy or medication other than study ointment will be noted on the Drugs/Therapies Form. Subjects that require a wash-out period of a prohibited therapy for >2 weeks, should be screen failed and may re-screen 1 time after completion of the washout period.

[9] PD Serum (non-fasting): calcium, phosphorus, albumin (in order to calculate the serum albumin-adjusted calcium) and PTH.

PD Urine: Urine calcium and creatinine on 24-hour urine specimen, when feasible or fasting (4 hours) urine sample in order to calculate Urine calcium: creatinine ratio. Subjects that are toilet-trained should be actively encouraged to complete 24-hour urine collection. A urine collection container/material will be given to the subject / subject's parent/legal guardian with the instruction to start collecting urine as of this visit and to bring the container back after the 24-hour/4-hour collection.

[10] Unscheduled visit: When necessary and exceptionally, because of either an AE needing a specific treatment, AE leading to withdrawal from the study, or other reason. An ongoing dialogue between subject, parent/legal guardian and investigators focusing on all aspects of the trial is encouraged. Any new information that arises in relation to the trial and that might affect the willingness of the subject and/or parent/legal guardian should be discussed. This brief discussion should be documented during each study visit.

[11] Subjects rolling over from SPR.18132 may omit the Screening Visit and proceed directly to the Baseline Visit after receipt of all required SPR.18132 Week 8 lab results and confirmation that the subject meets all inclusion and no exclusion criteria. Naïve subjects must complete the SPR.18131 Screening visit per Table.

[12] Lab assessment should only be done at Week 30 visit if results were abnormal at the Week 26/ET visit.

[13] Any subjects with suspected kidney stones are to be referred to the subject's PCP for treatment and the IDMC will be consulted on a case-by-case basis.

[14] The visit before: Distribute container and provide instructions for 24-hour urine collection to be started 1 day prior to Week 12 and Week 26/ET visits. The study site should contact the parent/legal guardian 48 hours prior to the visit to remind them to start the urine collection.

[15] Subjects may re-screen one time with written approval from the Sponsor prior to re-entry into the study.

[16] At Baseline, the study nurse show the subject's parents how to apply the drug.

3.1 Efficacy Assessment

3.1.1 Efficacy Measurements

IGA and Pruritus evaluations will be assessed at each visit on all treated areas.

3.1.1.1 IGA (as evaluated on all treated areas by a Board Certified Dermatologist)

The IGA will be evaluated at each visit on a 0 to 4 point scale. The following definitions will be used to score IGA:

0	**Clear**	No signs of psoriasis except for residual hypopigmentation / hyperpigmentation
1	**Almost Clear**	Just perceptible erythema, no induration, and no scaling
2	**Mild**	Mild erythema, no induration, and mild or no scaling
3	**Moderate**	Moderate erythema, mild induration, and mild or no scaling
4	**Severe**	Severe erythema, moderate to severe induration, and scaling of any degree

3.1.1.2 Pruritus (as evaluated on all treated areas)

Pruritus will be evaluated at each visit and scored on a 0 to 4 point scale. The following definitions will be used to score Pruritus:

Pruritus: an itching sensation.

0	**None**	No-itching
1	**Mild**	Slight itching, not really bothersome
2	**Moderate**	Definite itching that is somewhat bothersome without loss of sleep
3	**Severe**	Intense itching that has caused pronounced discomfort, night rest interrupted
4	**Very Severe**	Very severe itching that has caused pronounced discomfort during the night and daily activities

3.1.1.3 Other Assessments:

Percent Body Surface Area (BSA) involved will be assessed using the methodology shown in Protocol, Section 13.3, Appendix 3 (Calculation of Percent Body Surface Area Involved).

3.2 Safety Assessment

A safety assessment will be conducted for all subjects at the screening visit (from the Informed consent signature) and every subsequent visit. The safety parameters are AEs, laboratory safety tests, physical examination, and vital signs.

3.2.1 Adverse Events (AE)

Adverse events (AEs) are to be monitored throughout the course of the clinical trial (from the subject signed the Informed Consent Form to the end of the subject's participation). All AEs are to be reported on the Adverse Event Form of the eCRF with complete information as required, including onset/end dates of AEs, severity of AEs, relationship to the study drug, serious AEs and AEs of special interested.

3.2.2 Laboratory Safety Tests

The following laboratory safety tests will be performed according to the Schedule of Assessments.

- Hematology:

White blood cell (WBC) count with differential, red blood cell (RBC) count, hemoglobin (Hb), hematocrit (hct), mean cell volume (MCV), and platelet count (Plt)

- Blood chemistry (non-fasting):

Total protein, alanine aminotransferase (ALT) (SGPT), aspartate aminotransferase (AST) (SGOT), alkaline phosphatase (ALP), blood urea nitrogen, creatinine, and bilirubin (total and conjugated).

- Urinalysis:

A semi-quantitative urinalysis will be performed. The following parameters will be evaluated: glucose, ketones, blood, proteins, leukocytes, and nitrites.

- Pharmacodynamic parameters:

Serum (non-fasting): calcium, phosphorus, albumin (in order to calculate the serum albumin-adjusted calcium), PTH

Urine: Calcium and creatinine (in order to calculate urine calcium:creatinine ratio) on 24-hour urine specimens, when feasible, or fasting (4 hours) urine samples

- Other Assessments
  - 1, 25(OH)2D
  - 25(OH)D

- Urine Pregnancy Test

Post menarcheal female subjects of childbearing potential will have a urine pregnancy test performed at all visits. For pre-menstrual subjects who begin menses after the Screening visit, pregnancy tests will be performed according to the Schedule of Assessments for females of childbearing potential (Baseline, Week 4, Week 8, Week 12, Week 20, Week 26/ET, and Week 30).

3.2.3 Physical Examination and Vital Signs

3.2.3.1 Physical examination

The following body systems should be evaluated as "normal" or "abnormal" by the Investigator, at the visits per the Schedule of Assessments:

- Skin
- Cardiovascular system
- Respiratory
- Abdomen
- Head and neck
- Musculoskeletal system
- Neurological function (mental status exam [level of consciousness, cognitive function], cranial nerve assessment, reflex testing, motor system assessment, sensory system assessment)
- Lymph nodes
- Psychological

Weight will be recorded every time a physical examination is performed and height will be evaluated at Screening Visit only.

The Investigator may choose to further investigate any other sign that he/she observes during the physical examination.

3.2.3.2 Vital signs

Systolic and diastolic blood pressures and pulse rate will be performed after 5 minutes rest in sitting position.

4 EFFICACY AND SAFETY VARIABLES

4.1 Efficacy Variables

- Percentage of subjects with an IGA Score of 0 (clear) or 1 (almost clear).
- Change from Baseline in Pruritus
- Change from Baseline in % BSA

4.2 Safety Variables

Key Safety variables are as follows:

- Key Laboratory Parameters:
  - Serum albumin-adjusted calcium
  - urine calcium : creatinine ratio,
  - phosphorus,
  - PTH.
- Adverse Events

5 POPULATIONS ANALYZED

5.1 Safety Population

The Safety Population is defined as all subjects who have applied the study drug at least once.

All statistical analyses will be performed based on the safety population.

Prior to the final database lock of the study, a data review will occur to assess the potential bias of any data issues for final statistical analyses. Subjects with major/minor protocol deviations will be identified in the data review meeting. No per protocol population will be defined.

6 SAMPLE SIZE CONSIDERATION

No formal sample size calculation has been performed. See Protocol Section 9.2 “Sample size determination”.

7 STATISTICAL METHODS AND DATA CONSIDERATIONS

SAS version 9.2 for windows will be used for all statistical analyses.

In general, the categorical variables will be summarized by frequency and percentage for each response category (N, %). The continuous variables will be summarized using means, medians, minimum, maximum, and standard deviations for the data collected at each visit.

7.1 Study Subjects

Subject disposition, demographics, baseline characteristics, previous and concomitant therapies, previous and concomitant procedures, and subjects with major protocol deviations will be summarized for the safety population.

7.1.1 Disposition of Subjects

The number of subjects and the number of subjects by site will be summarized in safety population.

The number and percentage of subjects who complete the study and subjects who discontinue from the study will be summarized as well as reasons for discontinuation. Discontinuation by site and by visit will be tabulated. The discontinued subjects will be listed with the reason for discontinuation, along with the relevant comments recorded on the CRF exit form.

7.1.2 Protocol Deviations

According to protocol deviation plan, protocol deviations will be tracked by Chiltern Insight System and reviewed periodically during regular study team meetings and prior to IDMC meeting (at least every 4 months). In the data review meeting prior to database lock, protocol deviations will be reviewed and be categorized to major / minor protocol deviations. The decisions of major or minor deviations will be based on the eligibility criteria, study conduct and/or the impact to the efficacy and safety results.

The major/minor protocol deviation will be detailed in evaluability criteria document prepared before data review meeting.

7.2 Efficacy Analysis

7.2.1 Data Sets Analyzed

All efficacy variables will be analyzed based on the Safety population.

7.2.2 Demographic and Baseline Characteristics

Demographic and Baseline characteristics will be summarized for the Safety population. Age will be summarized as a continuous variable. Gender, race, skin phototype, and age group (2-5 years, 6-12 years, 13-17 years) will be analyzed as categorical variables. Baseline IGA,

baseline pruritus, baseline percent body surface area involved and Maximum allowed Daily dose will be summarized as continuous variables.

Subjects rolling over from previous studies SPR.18132 and SPR.18102 will be tabulated (if needed) and listed with previous treatment and subject ID information.

7.2.3 Medical History, Previous and Concomitant Therapies/Procedures

Previous therapies are the therapies/medication with stop date at or prior to the first dose of study medication. Any therapy/medication usage post first dose of study medication are considered concomitant therapy.

Previous procedures are the procedures with stop date at or prior to the first dose of study medication. Any procedures post first dose of study medication are considered concomitant procedures.

Therapies/medication will be coded using WHODRUG dictionary (Version March 1, 2013). The number and percentage of subjects who take previous therapies and concomitant therapies will be summarized by ATC class and WHO DRUG in the Safety population, respectively.

Procedures will be coded using MedDRA dictionary (version 15.0). The number and percentage of subjects who take previous procedures and concomitant procedures will be summarized by System Organ Class and Preferred Term in the Safety population, respectively.

Medical history will be provided in a subject-by-subject listing.

7.2.4 Compliance

Compliance will be based on actual study drug exposure and expected study drug exposure. (Compliance = Actual study drug exposure /Expected study drug exposure). Compliance in days and compliance in doses are defined in Section 7.3.1.

7.2.5 Efficacy Analysis

No formal inferential statistical analysis will be performed. All efficacy data will be summarized as observed based on analysis visit as well as additional analysis visit of Week 26 (LOCF, last observation carried forward). (Section 7.5). Analysis visit of Week 26 (LOCF) will be assigned as the last available data (excluding unscheduled visit) during treatment period. If there is no data available post baseline, the baseline visit will be used.

IGA and pruritus will be summarized over time by each category and by shift change.

Observed and changes from baseline of the IGA, Pruritus, and Percent BSA over time will be summarized as continuous variables. Additionally, change from baseline in efficacy data over time will be presented graphically.

In addition, IGA, pruritus, and Percent BSA will be summarized descriptively by gender, race, and age group (2-5 years, 6-12 years, 13-17 years).

7.2.6 Statistical and Analytical Issues

7.2.6.1 Adjustment for Covariates

Not applicable as there is no formal inferential statistical analysis will be performed.

7.2.6.2 Handling of Dropouts or Missing Data

All data will be summarized as observed based on analysis visit as well as additional analysis visit of Week 26 (LOCF, last observation carried forward) (Section 7.6). If there is missing baseline data, screening visit data will be used.

Week 26 (LOCF) will be assigned based on last available data during the treatment period, including baseline.

7.2.6.3 Interim Analyses and Data Monitoring

No interim analysis is planned for this study.

7.2.6.4 Multicenter Studies

This is an open-label, uncontrolled, multicenter long-term safety and efficacy study. No center effect will be examined.

7.2.6.5 Multiple Comparison/Multiplicity

Not applicable.

7.2.6.6 Use of an Efficacy Subset of Patients

The Per-Protocol population (PP) is not planned for this study. Subjects who have protocol deviations will be identified during the data review meeting prior to database lock.

7.2.6.7 Active-Control Studies Intended to Show Equivalence

Not applicable.

7.2.6.8 Examination of Subgroups

Descriptive summaries of IGA, pruritus, and percent BSA will be performed by gender, race, and age group (2-5 years, 6-12 years, 13-17 years).

7.3 Safety Analysis

7.3.1 Extent of Exposure

7.3.1.1 Study Duration

Study duration is calculated as the date of the last visit including follow up period minus the date of the baseline visit plus one. Study duration will be summarized by descriptive statistics.

7.3.1.2 Treatment Duration

Treatment duration is calculated as the date of the last application minus the date of the first application plus one. If the date of the last application is not available, the date of the last visit during treatment period will be used in calculation. If the date of the first application is not available, the baseline date will be used in calculation.

7.3.1.3 Study Drug Exposure

The study drug is applied twice daily. Temporary drug discontinuations and dose modifications is permitted in instances of out-of-range laboratory results, local tolerability issues, and clearing/worsening of disease. Subjects also have missed doses due to other unexpected reasons. Reason for missed doses (either temporary drug discontinuations or dose modification), incidence of temporary drug discontinuation and dose modification, and corresponding duration will be summarized and examined.

Actual study drug exposure and expected study drug exposure will be calculated in two definitions (in days and in doses). Missed doses due to complete clearing of psoriasis (IGA=0) will be excluded from the expected exposure. Any other missed dose due to non-safety or safety reason, even protocol allowed, will not be deducted from the expected study drug exposure.

Actual study drug exposure in days = Treatment duration (days) – number of days with no applications in both PM and AM (temporary drug discontinuations).

Actual study drug exposure in doses = Treatment duration *2 – number of missed doses.

Expected study drug exposure in days = Treatment duration (days) – number of days with no applications due to complete clearing of psoriasis (IGA=0) only.

Expected study drug exposure in doses = Treatment duration * 2 – number of missed doses due to complete clearing of psoriasis (IGA=0) only.

Compliance will be based on actual study drug exposure versus expected study drug exposure. Compliance will be a good index of data integrity rather than protocol deviations

Compliance (%) in days = Actual study drug exposure in days /expected study drug exposure in days.

Compliance (%) in doses = Actual study drug exposure in doses /expected study drug exposure in doses.

Actual study drug exposure, expected study drug exposure, and compliance in two definitions (in days or in doses) will be summarized.

7.3.2 Adverse Events

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary (version 15.0).

Treatment-emergent adverse events (TEAEs) is defined as an AE with an onset date on or after the first application of the study drug. TEAEs will be tabulated in frequency tables by System Organ Class and Preferred Term for whole study and by period (Day 1 to Day 90, Day 91 to End of Treatment, Follow-up period). Additional summary tables will be provided for TEAEs that are considered serious (SAEs), related to the study drug(s), severe, and possibly related to Calcium Metabolism from predefined SOCs/HLGT . TEAEs of special interested and TEAEs leading to discontinuation will also be summarized. For a given TEAE, a subject will be counted once even if he/she has experienced multiple episodes of that particular TEAE. Subgroup summaries of TEAEs will be provided based on gender, race, and age group (2-5 years, 6-12 years, 13-17 years) when appropriate.

7.3.3 Laboratory Parameters

Analysis visit will be applied for the laboratory parameter summaries.

Descriptive statistics for each laboratory parameter will be provided for scheduled visit and for the changes from Screening at each post-baseline visit. “Final” visit (Week 26 (Final)) will be defined as the last post-baseline available observation during the treatment period.

A shift table for the laboratory data at Screening versus Final will be constructed for laboratory parameters for which numeric reference ranges are available. The number of subjects below, within, and above the laboratory reference ranges at Screening versus Final will be summarized.

For each laboratory test, a complete data listing will be provided for subjects who have any laboratory results outside the reference ranges, and for subjects who have any laboratory results with clinical significance.

Plot of mean change from screening and spaghetti plot (all-subjects-in-one figure or selective individual subject figure) will be used to explore the trend of laboratory data change over the study, especially for serum albumin-adjusted calcium, urine calcium/creatinine ratio, phosphorus, PTH. Box-and-Whisker plots for PTH and Calcium/Creatinine ratio by visit will be constructed for data exploration.

7.4 Vital Signs and Physical Exam

Descriptive statistics for vital signs parameter will be provided for scheduled visit and for the changes from Baseline at Week 12 and Week 26. “Final” visit (Week 26 (Final)) will be defined as the last post-baseline available observation during the treatment period. Nominal eCRF visit will be used as analysis visit.

Physical exam will be provided in a subject-by-subject listing.

7.5 Analysis Visit Definition

All efficacy variables, vital signs, and laboratory data will be summarized by analysis visit.

Analysis visit will be assigned according to the following algorithm to summarize the efficacy data by proper visit window interval. Study day is calculated as visit date minus the date of first application plus 1. Visit during treatment period will be used for analysis visits of Baseline to Week 26 assignment. Week 30 Follow-up will be the post-treatment/follow-up visit.

If multiple measurements are taken in the same interval, the one closest to the target study day will be used for the analysis. If two measurements are taken with equal differences in timing compared with the target date, the nominal visit number (recorded on the CRF page) will used.

Table 2 Analysis Visit for Efficacy Data Summaries

Analysis Visit	Analysis Visit Number in Derived Dataset	Target Study Day	Visit Window for IGA, Pruritus, % BSA(Study Day)
Screening	-1	-	[< 1]
Baseline	1	1	[<= 1]
Week 4	2	29	[2 – 42]
Week 8	3	57	[43 – 70]
Week 12	4	85	[71 – 112]
Week 20	5	141	[113 – 161]
Week 26	6	183	[162- 196]
Week 26(LOCF)	6.999	-	Last available data during treatment period, including Baseline.
Week 30 Follow-up	7	-	Last available data during Follow-up data.

For efficacy data, screening visit will be assigned to analysis visit of screening as recorded on CRF page. If multiple measurements of screening due to rescreening or other unexpected reasons, the screening visit closest to date of first application will be chosen. If there is missing measurement at Baseline, Screening data will be used to impute the missing baseline data, if necessary, i.e. Baseline will be the last available data prior to first application. Only scheduled visit will be assigned into appropriate analysis visit; unscheduled visit will not be assigned to analysis visit, therefore, not in the summary.

When assigning the analysis visits for vital signs, no visit window will be applied; Nominal eCRF visit will be used as analysis visit for summaries.

When assigning the analysis visits for laboratory data, no visit window will be applied, however, the following rules will be applied:

1. If sample date/time is prior to date/time of first application, the data will be considered as screening visit. If multiple measurements of screening due to rescreening, retest or other unexpected reasons, the data closest to date of first application will be chosen.

2. Lab data from scheduled visit will be considered first when assigning analysis visit of each scheduled visit. If there is no data from scheduled visit available within the visit window, the last of those corresponding unscheduled visit will be considered for assignment of analysis visits.

3. When assigning Final visit, the lab data from the last post-baseline scheduled visit during treatment period will be considered first. If the last scheduled visit during treatment period have missing lab data due to any reason and there are subsequent unscheduled lab data available, the last of those corresponding unscheduled lab data will be assigned as Final visit. Otherwise, the previous visit lab data will be considered in the same manner.

8 CHANGES FROM THE PROTOCOL ANALYSIS PLAN

No change from protocol analysis plan.

9 TABLE SHELLS AND REPORTING OUTPUT (GENERAL FEATURES)

The tentative list of tables to be produced in the reporting of this study is shown below. All eCRF data will also be available as subject listings and the eCRF data will be available in CDISC compliant data set. A separate document will be prepared for list of tables/figures/listing.

All summaries are based on Safety population.

9.1 Demographic and Baseline Characteristics Tables

Summary of Subject Enrollment

Summary of Subject Enrollment by Site within Country/Region

Summary of Subject Disposition

Summary of Subject Disposition by Site within Country/Region

Summary of Subjects with Major Protocol Deviations

Summary of Subject Demographics and Baseline Characteristics

Summary of Previous Therapies

Summary of Concomitant Therapies

Summary of Previous Procedure / Non-Drug Therapy

Summary of Procedure / Non-Drug Therapy

Summary of Compliance

9.2 Efficacy Tables

Efficacy results will be summarized descriptively and graphically versus time for all subjects and by subgroup.

Summary of IGA (including Percentage of Subjects with an IGA Score of 0 (Clear) or 1 (Almost Clear))

Summary of Pruritus (including Change from baseline in Pruritus)

Summary of Percent BSA (including Change from Baseline in %BSA)

Summary of IGA by Gender, Race, and Age Group

Summary of Pruritus by Gender, Race, and Age Group

Summary of Percent BSA by Gender, Race, and Age Group

9.3 Safety Tables

Summary of Study Duration

Summary of Treatment Duration

Summary of Medication Exposure

Overall Adverse Events

Adverse Events by System Organ Class and Preferred Term

Adverse Events by Preferred TermAdverse Events by System Organ Class and Preferred Term and by Maximum Severity

Adverse Events by System Organ Class and Preferred Term and by Period

Serious Adverse Events by System Organ Class and Preferred Term

Listing of Serious Adverse Events

Adverse Events Leading to Discontinuation by System Organ Class and Preferred Term

Listing of Adverse Events Leading to Discontinuation

Adverse Events Possibly related to Calcium Metabolism by System Organ Class and Preferred Term

Listing of Adverse Events Possibly Related Calcium Metabolism

Adverse Events Related to Study Drug by System Organ Class and Preferred Term

Adverse Events Related to Study Drug by Preferred Term

Listing of Adverse Events Related to Study Drug

Severe Adverse Events by System Organ Class and Preferred Term

Listing of Severe Adverse Events

Adverse Events of Special Interest by System Organ Class and Preferred Term

Listing of Adverse Events of Special Interest

Summary of Laboratory Data (Descriptive Statistics and graph)

Shift table of Laboratory Data

Listing of subjects with Laboratory Data out of reference range (and individual subjects spaghetti plots for key lab parameters)

Listing of subjects with Clinical Significant Laboratory Data

Listing of subjects with Positive Urine Pregnancy Test Results

Summary of Vital Signs

Overall Adverse Events by Gender, Race, and Age Group

Adverse Events by System Organ Class and Preferred Term by Gender, Race, and Age Group