STATISTICAL ANALYSIS PLAN

A Randomized, Placebo-Controlled, Double-Blind, Parallel-Group, Multi-Site Phase 2b Clinical Study to Assess the Efficacy, Safety and Tolerability of 8-Week Regimens of Novexatin®, 10% Topical Solution (Taro Pharmaceuticals, USA, Inc.) in Patients with Mild to Moderate Onychomycosis

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Novum Study Number: 71442603

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SAP FINAL VERSION APPROVALS

A Randomized, Placebo-Controlled, Double-Blind, Parallel-Group, Multi-Site Phase 2b Clinical Study to Assess the Efficacy, Safety and Tolerability of 8-Week Regimens of Novexatin®, 10% Topical Solution (Taro Pharmaceuticals, USA, Inc.) in Patients with Mild to Moderate Onychomycosis

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Revision History

VERSION	DATE	DESCRIPTION OF REVISIONS	REVISED BY
Draft 1.0	March 20, 2017	New Document	Jianhua Liu
Draft 2.0	December 12, 2017	Incorporate Novum's comments	Jianhua Liu
Final 1.0	February 26, 2018	Add additional analyses, incorporate client comments and finalize SAP	Jianhua Liu
Final 2.0	March 1, 2018	Add summary table T14.3.10 Summary of Frequency of Evaluation of Toenail Condition/Appearance	Jianhua Liu
Final 3.0	March 21, 2018	Incorporate client's comments	Jianhua Liu

List of Abbreviations and Definition of Terms

ADaM	Analysis Data Model
AE	Adverse Event
ANCOVA	Analysis of Covariance
BP	Blood Pressure
C	Celsius
CRF	Case Report Form
CDISC	Clinical Data Interchange Standards Consortium
CRO	Contract Research Organization
F	Fahrenheit
FDA	Food and Drug Administration
HR	Heart Rate
Hg	Mercury
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IND	Investigational New Drug
ITT	Intent-to-Treat
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities
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

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1. INTRODUCTION

This Statistical Analysis Plan (SAP) is based on the final Clinical Study Protocol NVXT 1404 (Novum Study No. 71442603) Rev. 2 dated July 8, 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 NVXT 1404 (Novum Study No. 71442603) Rev. 2 dated July 8, 2016
- Casebook for Novum Study No. 71442603 dated 11/30/2017

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. Determine the rates of complete therapeutic cure of Novexatin® 10% topical solution (Taro Pharmaceuticals, USA) after daily dosing for one 8-week treatment period (Treatment Group A) and two 8-week treatment periods separated by a 32-week rest period (Treatment Group B), and Placebo (vehicle) topical solution (Taro Pharmaceuticals, USA) after two 8-week treatment periods separated by a 32-week rest period (Treatment Group C), at three test-of-cure visits (Day 141, Day 281 and Day 365) in patients with mild to moderate distal subungual onychomycosis of the target toenail.
2. Compare rates of complete therapeutic cure between Treatment Groups according to a hierarchical evaluation scheme detailed in the statistical sections.
3. Evaluate safety and tolerability of the two regimens of Novexatin® 10% topical solution (Treatment Groups A and B) in patients with mild to moderate distal subungual onychomycosis of the target toenail.

3. OVERALL STUDY DESIGN

This randomized, placebo-controlled, double-blind, parallel-group, multi-site study is designed to evaluate and compare the efficacy and safety of two dosing regimens of Novexatin® 10%

topical solution (Taro Pharmaceuticals USA) for the treatment of mild to moderate distal subungual onychomycosis of the target toenail. Additionally the active formulation in these regimens will be assessed for superiority to a placebo topical solution.

Up to 180 eligible patients with distal subungual onychomycosis who meet all the inclusion criteria and none of the exclusion criteria will be randomized into the study at Visit 2. Patients must be at least 18 years of age, in overall good health. They should have a current diagnosis of distal subungual onychomycosis of mild-moderate severity. Before any study-specific procedures are performed all patients will read and sign the IRB-approved informed consent form.

At least 60 qualified patients in each treatment group will receive randomized and blinded study product. The randomization scheme will be 1:1:1 (Active Treatment A: Active Treatment B: Placebo C). The study products are:

Test: Novexatin® 10% Topical Solution (Taro Pharmaceuticals, USA)

Placebo: Placebo (Vehicle) Topical Solution (Taro Pharmaceuticals, USA)

Patients will be assigned to one of the three treatment groups:

Treatment Group A: Test treatment for Days 1 – 56 and Placebo treatment for Days 281 – 336
Treatment Group B: Test treatment for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo treatment for Days 1 – 56 and Days 281 – 336

Treatment and study durations will be as follows:

Study Duration: 365 days (52 weeks)

Patients will undergo evaluation for clinical and mycological cure of onychomycosis at the 7 clinic visits as per study schematic. Randomized patients who withdraw from the study will not be replaced. The study will be conducted according to the following schedule:

Visit Schedule:

- **Visit 1**: Days -35 to -1 (Screening)
- **Visit 2**: Day 1 (Baseline and Randomization / 1st Treatment start)
- **Visit 3**: Day 57 ± 4 (1st Treatment completion)
- **Visit 4**: Day 141 ± 7 (Interim)
- **Visit 5**: Day 281 ± 14 (2nd Treatment start)
- **Visit 6**: Day 337 ± 14 (2nd Treatment completion)
- **Visit 7**: Day 365 ± 14 (4 weeks post – treatment)

Unscheduled visits will be allowed as deemed necessary by Investigator.

The primary efficacy endpoint is the proportion of patients in each treatment group with a complete therapeutic cure of onychomycosis of the target toenail assessed at each of the two test-of-cure visits (Day 141and Day 365). The safety profile of each treatment group will be evaluated by comparing adverse events, application site reactions, monitoring vital signs and changes in clinical laboratory results obtained throughout the study.

Figure 1 Study Schematic

PROCEDURE	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7
	Screening	Randomization / Baseline / 1st treatment start	1st treatment Completion	Interim **Test of cure**	2nd treatment start **Test of cure**	2nd treatment completion	4 weeks post – treatment **Test of cure** or ET
Day	**-35 to -1**	**1**	**57 ± 4 (Week 8)**	**141 ± 7 (Week 20)**	**281 ± 14 (Week 40)**	**337 ± 14 (Week 48)**	**365 ± 14 (Week 52)**
Informed Consent	X						
Inclusion/ Exclusion Criteria Review	X	X					
Demographics	X						
Medical History	X						
Physical Examination	X						X
Vital Signs	X		X		X	X	X
KOH test	X			X			X
Fungal Culture collection	X			X			X
Clinical Lab Tests	X		X				X
Target Nail trimming (if needed) before nail involvement/appearance assessments		X	X	X	X	X	X
Target toenail involvement (assessed by visual assessment)*	X	X	X	X	X	X	X
Planimetry Assessment		X	X	X	X	X	X
Evaluation of toenail condition/appearance (by patient and investigator)		X	X	X	X	X	X
Investigator Clinical Assessment	X	X	X	X	X	X	X
Urine Pregnancy Test**	X	X	X	X	X	X	X
Dispense study product, supplies		X			X		
Dispense Diary/Instructions		X	X	X	X	X	
Application site reactions			X	X	X	X	X
Collect unused/empty bottle			X			X	
Collect and Review Patient Diary			X	X	X	X	X
Adverse Event Assessments		X	X	X	X	X	X
Concomitant Medication Review	X	X	X	X	X	X	X
Schedule next visit	X	X	X	X	X	X	

* At Visit 1, both toenails will be assessed if a bilateral infection of the big toenails are present.
** All women of childbearing potential

4. RANDOMIZATION AND BLINDING

The study product will be packaged and blinded by an independent clinical packaging company. The randomization will be generated in blocks of 3, containing the study products in three configurations:

A. bottles #1 & 2 – Test and bottles #3 & 4 – Placebo

B. bottles #1 & 2 – Test and bottles #3 & 4 – Test

C. bottles #1 & 2 – Placebo and bottles #3 & 4 – Placebo.

Three patients worth of study product bottles 1 & 2 will be packed into a larger box. This larger box will be designated "one block" of study product. The study product bottles 1 & 2 will be blinded, packaged and delivered to the study site in blocks at the beginning of the enrollment. Bottles 3 & 4 will be delivered to the study site before Visit 5 (2^{nd} treatment start).

At each Visit 2 and Visit 5 each patient will receive two 5 ml bottles of study product according to the randomization code. Patients will be randomized to a treatment regimen in a blinded fashion by assigning randomization numbers in ascending sequential order starting with the lowest available randomization number at each site. All patients randomized will be identified by initials, date of birth, and a unique six-digit patient number. The first two-digits will identify the Investigator site where the patient was enrolled and the last four will correspond with the randomization number of study product bottle assigned to the patient. A perforated or two-part label will be attached to each of the small sized boxes of study product supplies. Both pieces of the label will include the following information: Protocol number, randomization number, space for patient's initials, statement that the study product is for investigational use only, space for dispensing date and the Sponsor's name. In addition all patients will be provided with written instructions on how to use the study product. One part of the label shall remain attached to the box. The other part will be removed prior to dispensing and attached to the study product log.

The Investigator, staff at the study site, study monitors, and data analysis/management personnel will be blinded to the patient assignment.

At the end of the study, after all the clinical data has been entered and the study database has been locked, a copy of the randomization will be sent to the statistician.

5. SAMPLE SIZE

The primary statistical analysis of interest is a comparison of the rates of therapeutic cure (as defined by "clinical cure" AND "mycological cure") of Novexatin® 10% topical solution to the rate of therapeutic cure of placebo in the Intent-to-Treat Population (ITT). The rate of therapeutic cure for the Novexatin® 10% topical solution 8-week regimens is expected to be approximately

49%. The rate of therapeutic cure for placebo is expected to be approximately 21%. Approximately 46 patients in each treatment group in the ITT population will provide over 80% power to show a difference at $p < 0.05$ (two-sided Z test and a pooled response rate for the standard error of the difference in proportions) between each of the active treatment groups and the placebo group. To allow for a 23% drop-out rate, a total of 180 patients will be enrolled in the study, with up to 60 patients in each of the treatment groups.

6. STUDY ENDPOINTS

Primary Endpoint:

The proportion of patients in each treatment group with a complete therapeutic cure of onychomycosis of the target toenail assessed at each of the two test-of-cure visits (Day 141 and Day 365).

Secondary Endpoints:

1. The proportion of patients in each treatment group with a complete or almost complete therapeutic cure of onychomycosis of the target toenail assessed at each of the two test-of-cure visits (Day 141 and Day 365).
2. The proportion of patients in each treatment group with a mycological cure of the target toenail assessed at each of the two test-of-cure visits (Day 141 and Day 365).
3. The proportion of patients in each treatment group with a complete clinical cure of the target toenail assessed at each of three test-of-cure visits (Day 141, Day 281 and Day 365).
4. The proportion of patients in each treatment group with a satisfactory clinical cure of the target toenail assessed at each of three test-of-cure visits (Day 141, Day 281 and Day 365).

Complete therapeutic cure is defined as both complete clinical and mycological cure of the target toenail

Almost complete therapeutic cure is defined as both mycological and satisfactory clinical cure of the target toenail

Mycological cure is defined as a negative KOH test **and** a negative fungal culture.

Complete clinical cure is defined as 0% nail involvement.

Satisfactory clinical cure is defined as $\leq 5\%$ of the target toenail involvement.

7. STUDY POPULATIONS

Intent-to-Treat (ITT) Population

- All randomized patients who applied at least one dose of assigned study product
- Had a positive mycological culture screening (Visit 1)

The primary analyses will be conducted on the ITT population.

Patients who return randomized product bottles with evidence of intentional tampering or unblinding will be excluded from the ITT population and included in the Safety population.

Safety Population

All patients who were randomized and received study product will be included in the Safety population.

8. 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).

8.1 Baseline Characteristics

8.1.1 Patient Disposition

The patient disposition information will be summarized by treatment group. The number of patients randomized, treated with study medication will be tabulated by treatment group. In addition, completion status and primary reason for withdrawal will be summarized by treatment group.

8.1.2 Demographic and Other Baseline Characteristics

Baseline comparability of all treatment groups will be evaluated separately in the ITT and Safety populations.

The following baseline demographics (determined from their initial study visit) will be evaluated:

- 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 by treatment group 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 treatments 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 treatment group and patient.

8.1.3 Medical History

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

Medical history data will be listed by treatment group and patient.

8.1.4 Concomitant Medications

At Visit 1, patients will be questioned about current and concomitant medication use over the previous 6 months. At all other clinic visits, patients will be questioned about ongoing or new concomitant medication use.

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

8.2 Efficacy Analyses

8.2.1 Efficacy Analyses on Primary and Secondary Endpoints

The ITT population will be used to evaluate the efficacy of Novexatin® 10% topical solution for

the 8-week treatment regimens in Groups A, B and C.

Descriptive statistics will be summarized for the primary and secondary endpoints (including planimetry data) by study group. As this is a multi-centered study, results may also be presented by study site.

In order to preserve an overall type-I error (alpha) of 5% for evaluation of complete and almost complete therapeutic cure, complete and satisfactory clinical cure and mycologic cure, a hierarchical evaluation scheme will be employed for the primary and secondary endpoints. The four comparisons of interest for the primary endpoint and the secondary endpoints -1 and -2 are:

1. Group B versus Group C – at the test-of-cure visit at Day 365
2. Group A versus Group C – at the test-of-cure visit at Day 365
3. Group B versus Group A – at the test-of-cure visit at Day 365
4. (Group A + Group B) versus Group C – at the test-of-cure visit at day 141

The five comparisons of interest for the secondary endpoints -3 and -4 are:

1. Group B versus Group C – at the test-of-cure visit at Day 365
2. Group A versus Group C – at the test-of-cure visit at Day 365
3. Group B versus Group A – at the test-of-cure visit at Day 365
4. (Group A + Group B) versus Group C – at the test-of-cure visit at Day 281
5. (Group A + Group B) versus Group C – at the test-of-cure visit at Day 141

Statistical testing will begin with comparison 1. If statistical significance is attained with comparison 1 ($p < 0.05$), then a claim of superiority for comparison 1 can be made and the next comparison in the hierarchical evaluation scheme can be tested for statistical significance. If statistical significance is not attained for comparison 1 ($p \geq 0.05$), then testing of all subsequent comparisons is stopped. The hierarchical, conditional-stepwise evaluation scheme allows for each comparison to be evaluated at the 5% level, while preserving an overall type I error rate of no more than 5%. For the proportion of patients in each treatment group with a complete and almost complete therapeutic cure, complete and satisfactory clinical cure and mycological cure of onychomycosis of the target toenail, the statistical analysis for superiority will be conducted using a two-sided Cochran-Mantel-Haenszel (CMH) exact test, stratified by clinical site, at the 5% significance level. The primary and secondary analyses will be performed using an observed case (OC) analysis in the ITT population. Patients discontinued because of lack of treatment effect will be included in the primary analysis as treatment failures.

The following two sensitivity analyses will also be performed on the primary efficacy endpoint in the hierarchical, conditional-stepwise evaluation scheme:

1. Analysis will be performed also including patients without an assessment at Day 365 ± 14. Patients with missing data at Day 365 ± 14 will be considered therapeutic failures.
2. Analysis will be performed also including patients without an assessment at Day 365 ± 14. Patients in Group C with missing data at Day 365 ± 14 will be treated as therapeutic successes and patients from the Groups A and B with missing data at Day 365 ± 14 will be treated as therapeutic failures.

Similar sensitivity analyses will be conducted including patients without an assessment at Day 141 ± 7 for the 4th comparison in the hierarchical, conditional-stepwise evaluation scheme.

8.2.2 Treatment-by-Site Interaction and Pooling of Clinical Sites

As this is a multiple-site study, the interaction of treatment-by-site may be evaluated for superiority testing by the Cochran-Mantel-Haenszel test (stratified by site) using Breslow-Day test for the primary efficacy endpoint at the 5% significance level ($p < 0.05$, 2-sided) in the ITT population. A site(s) with a low enrollment rate(s) may be pooled with its geographically closest site, so as to avoid bias in the stratification of the sites in the CMH test and in the estimation of a treatment-by-site interaction effect. The pooling will be done for low enrolling sites that account for less than 4-7% of the total number of patients in the ITT population at the site with the highest enrolling rate. If no treatment-by-site interaction is identified with the primary endpoints then no adjustment will be made to any efficacy analysis.

8.2.3 Additional Analyses

In addition to the efficacy statistical analyses specified in the protocol, the analyses described in Section 8.2.1 above, including sensitivity analyses, will also be performed using the following endpoints:

1. Primary endpoint (complete therapeutic cure) with Canfield's evaluation for % toenail involvement.

2. Secondary endpoint #1 (complete or almost complete therapeutic cure) with Canfield's evaluation for % toenail involvement for complete cure in addition to the current evaluation for almost complete cure by Canfield's evaluation.

3. Secondary endpoint #3 (complete clinical cure) with Canfield's evaluation for % toenail involvement for complete cure.

Patients will only be included in analyses 1, 2 and 3 above if they meet inclusion criterion #6 (Mild to moderate severity at Visit 1 as defined by Investigator's estimation of approximately

10% to 35% toenail involvement) on the basis of Canfield's evaluation to define mild to moderate severity instead of by Investigator's estimation.

8.3 Safety Analysis

All study patients who are randomized to the active treatment period of the study, and received study product will be included in the comparative safety analysis. The safety profile of each treatment group will be evaluated by comparing adverse events, application site reactions, vital signs and changes in clinical laboratory results obtained throughout the study. Data will also be collected during the study to compare the results of the KOH stains to the mycological culture results observed during the study.

8.3.1 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 19.0 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.

All AEs will be listed by treatment group and patient.

A summary table of the number and percent of patients with AEs by system organ class, preferred term, and treatment will be presented. Each patient will be counted only once within each preferred term. Other summaries may be added based on the obtained data.

A frequency summary table of the number of AEs by system organ class, preferred term, severity, and treatment 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 treatment 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 treatments using Fisher's exact test. If the global Fisher's exact test is statistically significant among the three treatment groups at the 5% alpha level (i.e., $p < 0.05$), then Fisher's exact test using only the Group A and Group B may be performed to identify any potential statistically significant differences that are clinically relevant between the two active treatment groups over the period from Day 1 to Day 141 ± 7 days (i.e., following completion of the first 8 weeks of treatment when both groups have the same test treatment regimen) and over the study duration from Day 1 to Day 365 ± 14 days.

8.3.2 Vital Signs

The patient's vital signs will be recorded (heart rate, blood pressure, temperature and respiration rate) at Visits 1, 3, 5, 6 and 7.

Descriptive summaries (number of observations, mean, standard deviation, minimum, median and maximum) will be provided by treatment group and visit.

8.3.3 Clinical Laboratory Results

Clinical laboratory results (hematology, chemistry and urinalysis) will be collected at Visits 1, 3 and 7.

Descriptive summaries (number of observations, mean, standard deviation, minimum, median and maximum) will be provided by treatment group and visit.

All data will be listed by treatment group and visit.

8.3.4 Application Site Reactions

At Visits 3, 4, 5, 6 and 7, the Investigator will examine the treatment area and complete the signs and symptoms of irritation assessment.

A frequency summary table comparing the application site reactions for each treatment group will be presented by visit.

All data will be listed by treatment group and patient.

8.3.5 Evaluation of Toenail Condition/Appearance:

The toenail, one of the two great toenails, that the investigator considers to be the most appropriate as the target toenail will be identified and designated as the "target toenail" at Visit 2 and used for evaluations.

The overall appearance of the target toenail over time will be monitored during the study:

1. Self-assessed by patients. The results of the self-assessment will be recorded by the patient before beginning therapy at Visit 2 and at all subsequent visits. Patients will use a 5-point scale (see Appendix A) for target toenail appearance.
2. Assessed by Investigator: Investigators will rate the status of the target toenail before beginning therapy at Visit 2 and at all subsequent visits. Nail condition/appearance by investigator will be evaluated after nail trimming to the distal groove and before further trimming, if required, for the mycological evaluation. Investigators will use a 5-point scale (see Appendix A) target toenail appearance.

A frequency summary table for each treatment group will be presented by visit.

All data will be listed by treatment group, patient, and evaluation day.

8.4 Multiple Comparisons

No multiple comparison adjustment will be made in this study other than the pre-defined hierarchical testing for the primary and secondary endpoints.

8.5 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.

The following rules and conventions will be used for patients who terminate from the study early or are dropped from the study because of protocol deviations.

Any patient who either requests to be dropped from the study because of lack of therapeutic efficacy or is dropped by the Investigator for lack of therapeutic efficacy will automatically be considered a "clinical failure" regardless of their target toenail assessment score at the termination visit.

Any patient who uses any protocol restricted medication specifically for the treatment of their infection will be discontinued from further participation in the study and automatically be considered a "clinical failure" regardless of their target toenail assessment score at the last visit.

Any patient who uses any protocol restricted medication NOT specifically for the treatment of their onychomycosis will be discontinued from further participation in the study. The patient will be considered a "clinical cure" or "clinical failure" based on the target toenail assessments at the termination visit.

Any patient who is dropped for any reason other than those covered above will be included in the ITT, provided they had a positive baseline culture and applied at least one dose of the study product. Examples would include: failure to use the study products as required by the protocol, patient withdraws consent for continued participation, patient fails to make study visits on a timely basis.

8.6 Interim Analyses

There is no interim analysis planned in this study.

8.7 Changes to the Protocol Defined Statistical Analysis Plan

The protocol states that the statistical analysis for superiority will be conducted using two-sided Z-Tests and a pooled response rate for the standard error of the difference in proportions for each comparison of interest. The CMH exact test stratified by clinical site is preferred for a multi-site study for which the randomization is intended to be balanced among treatments within each site (i.e., stratified by site), because it accounts for the variability in clinical site whereas the Z-test does not account for site variability in the model. During the analysis, the statistical analysis for superiority will be conducted using a two-sided Cochran-Mantel-Haenszel (CMH) exact test, stratified by clinical site, at the 5% significance level.

The wording in section 8.5 "Methods for Handling Missing Data" was updated to coincide with the ITT definition. The ITT states that patients will be included in the ITT as long as they have received one dose of assigned study product and had a positive mycological culture at Visit 1.

Additional analyses that were not delineated in the protocol were included in section 8.2.3 of the SAP.

9. TABLE, LISTING AND FIGURE SHELLS

The following shells 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

Tables for Report Body

Table I Number of Patients

Population	Total	Treatment Group A	Treatment Group B	Treatment Group C
Safety	xxx	xxx	xxx	xxx
ITT	xxx	xxx	xxx	xxx

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo treatment for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Appendix 16.2.3

Table II Summary of Patient Disposition

Patients	Treatment Group A	Treatment Group B	Treatment Group C	Total
Screened				xxx
Randomized	xxx	xxx	xxx	xxx
Completed Study	xxx	xxx	xxx	xxx
Terminated Early	xxx	xxx	xxx	xxx
Adverse event	xxx	xxx	xxx	xxx
Lack of efficacy	xxx	xxx	xxx	xxx
Lost to follow-up	xxx	xxx	xxx	xxx
etc.				
Other	xxx	xxx	xxx	xxx

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo treatment for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Appendix 16.2.1

Table III Summary of Protocol Deviations

	Treatment Group A N=xxx	Treatment Group B N=xxx	Treatment Group C N=xxx	Total N=xxx
Total Patients with Protocol Deviations	xxx	xxx	xxx	xxx
Total Deviations	xxx	xxx	xxx	xxx
Lost to Follow-up	xxx	xxx	xxx	xxx
Missed Visit	xxx	xxx	xxx	xxx
Non-compliance with study drug	xxx	xxx	xxx	xxx
etc	xxx	xxx	xxx	xxx
Other	xxx	xxx	xxx	xxx

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo treatment for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Appendix 16.2.2

Table IV Summary of Patients Excluded from Efficacy Analysis

	Treatment Group A N=xxx	Treatment Group B N=xxx	Treatment Group C N=xxx	Total N=xxx
Safety Population	xxx	xxx	xxx	xxx
Excluded from Safety population	xxx	xxx	xxx	xxx
ITT Population	xxx	xxx	xxx	xxx
Excluded from ITT population	xxx	xxx	xxx	xxx
Inclusion/Exclusion criteria not met	xxx	xxx	xxx	xxx
etc.	xxx	xxx	xxx	xxx

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo treatment for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Appendix 16.2.3

Table V Summary of Superiority Analysis Results of Primary Efficacy Endpoint (Proportion of Patients with Complete Therapeutic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population – Observed Case Analysis)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Complete Therapeutic Cure (n)		Proportion of Patients with Complete Therapeutic Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population using observed case.
P-value will not be presented if the preceding one is >=0.05.
Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.1, adeff

Table VI Sensitivity Analysis #1: Superiority Analysis Results of Primary Efficacy Endpoint (Proportion of Patients with Complete Therapeutic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Complete Therapeutic Cure (n)		Proportion of Patients with Complete Therapeutic Cure (%)		Difference (%)	P-value[#]
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365*	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141**	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population.

P-value will not be presented if the preceding one is >=0.05.

*Patients with missing data at Day 365 ± 14 are considered therapeutic failures.

**Patients with missing data at Day 141 ± 7 are considered therapeutic failures.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.3, adeff

Table VII Sensitivity Analysis #2: Superiority Analysis Results of Primary Efficacy Endpoint (Proportion of Patients with Complete Therapeutic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Complete Therapeutic Cure (n)		Proportion of Patients with Complete Therapeutic Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365*	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141**	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population.

P-value will not be presented if the preceding one is >=0.05.

* Patients in Group C with missing data at Day 365 ± 14 are considered therapeutic successes and patients in Groups A and B with missing data at Day 365 ± 14 are considered therapeutic failures.

** Patients in Group C with missing data at Day 141 ± 7 are considered therapeutic successes and patients in Groups A and B with missing data at Day 141 ± 7 are considered therapeutic failures.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.3, adeff

Table VIII Summary of Adverse Events (Safety Population)

Description	Treatment Group A N=xxx	Treatment Group B N=xxx	Treatment Group C N=xxx	Total N=xxx
Patients with AEs				
Patients with at least one AE	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%)
AEs reported	xx	xx	xx	xx
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%)
Not Related	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%)
Death	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%)

Related includes "Possible", "Probable", or "Definite" related.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing 16.2.7.1

Tables for section 14

T14.1.1 Summary of Patients Included in Analysis Population by Study Center

Site No.	PI Name	Total Randomized	Safety				ITT			
			Group A	Group B	Group C	Total	Group A	Group B	Group C	Total
xx	xxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
xx	xxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.4.1, adsl
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T14.1.2.1 Summary of Demographic Data
(Safety Population)

		Treatment Group A N=xxx	Treatment Group B N=xxx	Treatment Group C N=xxx	Total N=xxx	P-value
Age (years)	n	xx	xx	xx	xx	x.xxxx
	Mean ± SD	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	
	Range	xx-xx	xx-xx	xx-xx	xx-xx	
Race	American Indian or Alaska Native	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%)	
	Black/African American	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%)	
	White	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%)	
Ethnicity	Hispanic or Latino	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%)	
Gender	Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	x.xxxx
	Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

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

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.4.1
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Similar tables will be created for T14.1.2.2

T14.1.2.2 Summary of Demographic Data (Intent-to-Treat Population)

T14.2.1 Summary of Superiority Analysis Results of Primary Efficacy Endpoint Using Canfield Evaluation (Proportion of Patients with Complete Therapeutic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population – Observed Case Analysis)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Complete Therapeutic Cure (n)		Proportion of Patients with Complete Therapeutic Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population using observed case.
P-value will not be presented if the preceding one is >=0.05.
Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.3, adeff
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T14.2.2 Sensitivity Analysis #1: Superiority Analysis Results of Primary Efficacy Endpoint Using Canfield Evaluation (Proportion of Patients with Complete Therapeutic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Complete Therapeutic Cure (n)		Proportion of Patients with Complete Therapeutic Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365*	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141**	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population.

P-value will not be presented if the preceding one is >=0.05.

*Patients with missing data at Day 365 ± 14 are considered therapeutic failures.

**Patients with missing data at Day 141 ± 7 are considered therapeutic failures.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.3, adeff
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T14.2.3 Sensitivity Analysis #2: Superiority Analysis Results of Primary Efficacy Endpoint Using Canfield Evaluation (Proportion of Patients with Complete Therapeutic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Complete Therapeutic Cure (n)		Proportion of Patients with Complete Therapeutic Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365*	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141**	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population.

P-value will not be presented if the preceding one is >=0.05.

* Patients in Group C with missing data at Day 365 ± 14 are considered therapeutic successes and patients in Groups A and B with missing data at Day 365 ± 14 are considered therapeutic failures.

** Patients in Group C with missing data at Day 141 ± 7 are considered therapeutic successes and patients in Groups A and B with missing data at Day 141 ± 7 are considered therapeutic failures.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.3, adeff
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T14.2.4.1 Summary of Superiority Analysis Results of Secondary Efficacy Endpoint-1 (Proportion of Patients with Complete or Almost Complete Therapeutic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population – Observed Case Analysis)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Complete or Almost Complete Therapeutic Cure (n)		Proportion of Patients with Complete or Almost Complete Therapeutic Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population using observed case.
P-value will not be presented if the preceding one is >=0.05.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.1, adeff
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T14.2.4.2 Summary of Superiority Analysis Results of Secondary Efficacy Endpoint-1 Using Canfield Evaluation (Proportion of Patients with Complete or Almost Complete Therapeutic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population – Observed Case Analysis)

T14.2.5 Summary of Superiority Analysis Results of Secondary Efficacy Endpoint-2 (Proportion of Patients with Mycologic Cure at the Test-of-Cure Visits) (Intent-to-Treat Population – Observed Case Analysis)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Mycologic Cure (n)		Proportion of Patients with Mycologic Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population using observed case.
P-value will not be presented if the preceding one is >=0.05.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.1, adeff
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T14.2.6.1 Summary of Superiority Analysis Results of Secondary Efficacy Endpoint-3 (Proportion of Patients with Complete Clinical Cure at the Test-of-Cure Visits) (Intent-to-Treat Population – Observed Case Analysis)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Complete Clinical Cure (n)		Proportion of Patients with Complete Clinical Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 281	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population using observed case.
P-value will not be presented if the preceding one is >=0.05.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.1, adeff
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T14.2.6.2 Summary of Superiority Analysis Results of Secondary Efficacy Endpoint-3 Using Canfield Evaluation (Proportion of Patients with Complete Clinical Cure at the Test-of-Cure Visits) (Intent-to-Treat Population – Observed Case Analysis)

T14.2.7 Summary of Superiority Analysis Results of Secondary Efficacy Endpoint-4 (Proportion of Patients with Satisfactory Clinical Cure at the Test-of-Cure Visits) (Intent-to-Treat Population – Observed Case Analysis)

Test of Cure Visit	Treatment Comparison Group 1 versus Group 2	Number of Patients (N)		Number of Patients with Satisfactory Clinical Cure (n)		Proportion of Patients with Satisfactory Clinical Cure (%)		Difference (%)	P-value#
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
Day 365	Group B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0056
	Group A versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	0.0842
	Group B versus Group A	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 281	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA
Day 141	Group A+B versus Group C	xxx	xxx	xxx	xxx	xx.x	xx.x	xx.x	NA

Superiority testing was conducted at the 5% significance level ($p < 0.05$; using CMH exact test) in the ITT population using observed case.
P-value will not be presented if the preceding one is >=0.05.

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.5.1, adeff
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T14.3.1.1 Summary of Frequency of All Adverse Events by Body System: Day 1 to Day 141 ± 7 (Safety Population)

		Treatment Group A (N = xxx)		Treatment Group B (N = xxx)		Treatment Group C (N = xxx)		
Body System	MedDRA Term	Events	Patients n(%)	Events	Patients n(%)	Events	Patients n(%)	Fisher's p-value
Patients with at least one AE	Total	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	x.xxxx
Ear and labyrinth disorders	Ear pain	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	x.xxxx
	etc.							
etc.								

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.7.1
Created on: ddmmmyy hh:mm

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T14.3.1.2 Summary of Frequency of All Adverse Events by Body System: Day 1 to Day 365 ± 14 (Safety Population)

T14.3.2 Summary of Frequency of All Adverse Events by Relationship (Safety Population)

		Treatment Group A # of Events (N = xxx)		Treatment Group B # of Events (N = xxx)		Treatment Group C # of Events (N = xxx)	
Body System	MedDRA Term	Related n(%)	Not Related n(%)	Related n(%)	Not Related n(%)	Related n(%)	Not Related n(%)
Patients with at least one AE	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ear and labyrinth disorders	Ear pain	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	etc.						
etc.							

N = Total number of events in each treatment group; Percentage is based on total number of events.
Related includes "Possible", "Probable", or "Definite" related.
Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.7.1
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T14.3.3 Summary of Frequency of All Adverse Events by Severity (Safety Population)

Body System	MedDRA Term	Treatment Group A # of Events (N = xxx)			Treatment Group B # of Events (N = xxx)			Treatment Group C # of Events (N = xxx)		
		Mild n(%)	Moderate n(%)	Severe n(%)	Mild n(%)	Moderate n(%)	Severe n(%)	Mild n(%)	Moderate n(%)	Severe n(%)
Patients with at least one AE	Total	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)
Ear and labyrinth disorders	Ear pain	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)
	etc.									
etc.										

N = Total number of events in each treatment group; Percentage is based on total number of events.
Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.7.1
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T14.3.4 Summary of Frequency of Serious Adverse Events
(Safety Population)

Body System	MedDRA Term	Treatment Group A N=xx # of Events	Treatment Group B N=xx # of Events	Treatment Group C N=xx # of Events
Injury, poisoning and procedural complications	Alcohol poisoning		xx	xx

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.7.1
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T14.3.5 Summary of Vital Signs
(Safety Population)

Vital Sign (unit)	Visit	Statistic	Treatment Group A N=xx	Treatment Group B N=xx	Treatment Group C N=xx
Systolic Blood Pressure (mmHg)	1	n	xx	xx	xx
		Mean ± SD	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
		Median	xxx.x	xxx.x	xxx.x
		Range	xxx - xxx	xxx - xxx	xxx – xxx
	3				
	5				
	6				
	7				
Diastolic Blood Pressure (mmHg)					
Heart Rate (beats/min)					
Respiration Rate (breaths/min)					
Temperature (F)					

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.8.4
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T14.3.6 Summary of Clinical Laboratory Testing (Hematology)
(Safety Population)

Lab Test (unit)	Visit	Statistic	Treatment Group A N=xx	Treatment Group B N=xx	Treatment Group C N=xx
Hemoglobin (g/L)	1	n	xx	xx	xx
		Mean ± SD	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
		Median	xxx.x	xxx.x	xxx.x
		Range	xxx - xxx	xxx - xxx	xxx – xxx
	3				
	7				
Hematocrit (L/L)					
etc					

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.8.1
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T14.3.7 Summary of Clinical Laboratory Testing (Chemistry)
(Safety Population)

T14.3.8 Summary of Clinical Laboratory Testing (Urinalysis)
(Safety Population)

T14.3.9 Summary of Frequency of Application Site Reactions (Safety Population)

Signs and Symptoms	Visit	Scale	Treatment Group A N=xx	Treatment Group B N=xx	Treatment Group C N=xx
Erythema (redness)	3	Absent	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Mild	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Moderate	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Severe	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	4				
	5				
	6				
	7				
Scaling/Dryness					
Stinging/Burning					
Erosion					
Edema (swelling)					
Pain					
Itching					

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.7.2
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T14.3.10 Summary of Frequency of Evaluation of Toenail Condition/Appearance (Safety Population)

Visit		Scale	Treatment Group A N=xx	Treatment Group B N=xx	Treatment Group C N=xx
Visit 2	Self-assessed by Patients	Very Poor	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Poor	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Normal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Good	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Very Good	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Assessed by Investigator	Very Poor	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Poor	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Normal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Good	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
		Very Good	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Visit 3					
Visit 4					
Visit 5					
Visit 6					
Visit 7					

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

Source: Listing L16.2.6.4
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L16.2.1 Listing of Discontinued Patients

Treatment	Patient Randomization Number	Discontinuation Reason	Population
Treatment Group A	xx-xxxx	Withdrawal by Patient	Per-Protocol
	xx-xxxx	Lost to Follow-up	Safety
Treatment Group B			
Treatment Group C			

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.2 Listing of Protocol Deviations

Treatment Group	Patient Randomization Number	Event Description	Population
Treatment Group A	xx-xxxx	Outside Visit Window (Visit 3)	Safety
Treatment Group B			
Treatment Group C			

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.3 Listing of Patients Excluded from the Analysis Population

Treatment Group	Patient Randomization Number	Included in Safety Population?	Reason. If Not Included in Safety Population	Included in ITT Population?	Reason. If Not Included in ITT Population
Treatment Group A	xx-xxxx	Yes		No	xxxxxxxxxx
Treatment Group B					
Treatment Group C					

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.4.1 Listing of Demographic Data

Treatment Group	Patient Randomization Number	Age	Gender	Ethnicity	Race
Treatment Group A	xx-xxxx	30	Female	Not Hispanic or Latino	Black or African American
Treatment Group B					
Treatment Group C					

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.4.2 Listing of Medical History

Treatment Group	Patient Randomization Number	System	Diagnosis or Surgical Procedure	Start Date	End Date	Ongoing
Treatment Group A	xx-xxxx	Gynecologic	Menopause	--/--/2012	yyyy-mm-dd	
Treatment Group B						
Treatment Group C						

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.4.3 Listing of Concomitant Medication

Treatment Group	Patient Randomization Number	Treatment Area	Medication	Dosage	Frequency*	Route	Start/End Date	Indication
Treatment Group A	xx-xxxx	No	Advil	2 TAB	QD	Oral	--/--/2017/ 08/12/2017	Cold
Treatment Group B								
Treatment Group C								

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

*PRN - As needed; QD – Daily (once per day); Q4H - Every 4 hours; Q8H - Every 8 hours; Q12H - Every 12 hours; BID - Twice per day; TID - 3 times per day; QID - 4 times per day; QOD - Every other day; QS - Every week; QM - Every month; Q3M - Every 3 months

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L16.2.5 Listing of Diary Entries and Study Compliance

Treatment Group	Patient Randomization Number	Period	Date of First Dose	Date of Last Dose	Total Doses Applied	Did the patient have between 75% - 125% dosing compliance?	Did the patient miss the scheduled applications for 4 or more consecutive days?
Treatment Group A	xxxx	Period 1	yyyy-mm-dd	yyyy-mm-dd	xx	No	No
		Period 2	yyyy-mm-dd	yyyy-mm-dd	xx	No	No
Treatment Group B							
Treatment Group C							

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.6.1 Listing of Investigator Clinical Assessment

Treatment Group	Patient Randomization Number	Visit	Exam Area	Result	Number of Toenails Infected	Nail Appearance	Target Toenail
Treatment Group A	xx-xxxx	1	Foot (Left)	Abnormal	2	xxxxxxxxx	Left big toe
		1	Foot (Right)	Normal			
		3 4 5 6 7					
Treatment Group B Treatment Group C							

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.6.2.1 Listing of Investigator Visual Assessment (Percent Nail Involvement of the Target Toenail)

Treatment Group	Patient Randomization Number	Visit1	Visit2	Visit3	Visit4	Visit5	Visit6	Visit7
Treatment Group A	xx-xxxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Treatment Group B								
Treatment Group C								

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.6.2.2 Listing of Canfield Assessment (Percent Nail Involvement of the Target Toenail)

L16.2.6.3 Listing of KOH Wet Mount & Mycological Culture

Treatment Group	Patient Randomization Number	Visit	Was the KOH Wet Mount sample taken from the designated Target Toenail?	KOH Wet Mount Result	Was the fungal culture sample taken from the designated Target Toenail?	Fungal Culture Result	Reason Not Done
Treatment Group A	xx-xxxx	1	Yes	Positive	Yes	Positive	
		4					
		5					
		7					
Treatment Group B							
Treatment Group C							

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.6.4 Listing of Investigator & Patient Evaluation Of Toenail Appearance & Condition

Treatment Group	Patient Randomization Number	Visit	Investigator Evaluation	Patient Evaluation
Treatment Group A	xxxx	2	1 Very Poor	2 Poor
		3	2 Poor	2 poor
		4		
		5		
		6		
		7		
Treatment Group B				
Treatment Group C				

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.6.5.1 Listing of Efficacy Endpoints (Observed Case)

Treatment Group	Patient Randomization Number	Test of Cure Visit	Secondary Endpoints: Mycological Cure	Secondary Endpoints: Complete Clinical Cure	Secondary Endpoints: Satisfactory Clinical Cure	Secondary Endpoints: Almost Complete Therapeutic Cure	Secondary Endpoints: Complete or Almost Complete Therapeutic Cure	Primary Endpoint: Complete Therapeutic Cure
Treatment Group A	xx-xxxx	Day 141	No	No	Yes	No	No	No
		Day 281	N/A	No	Yes	N/A	N/A	N/A
		Day 365	Yes	Yes	Yes	Yes	Yes	Yes
Treatment Group B								
Treatment Group C								

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.6.5.2 Listing of Efficacy Endpoints Using Canfield Evaluation

L16.2.6.5.4 Listing of Primary Efficacy Endpoints (Sensitivity Analysis)

			Sensitivity Analysis 1		Sensitivity Analysis 2	
Treatment Group	Patient Randomization Number	Test of Cure Visit	Per-Protocol Evaluation	Canfield Evaluation	Per-Protocol Evaluation	Canfield Evaluation
Treatment Group A	xx-xxxx	Day 141	No	No	No	No
		Day 281	Yes	Yes	Yes	Yes
		Day 365	Yes	Yes	Yes	Yes
Treatment Group B						
Treatment Group C						

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.7.1 Listing of Adverse Events by treatment group

Treatment Group	Patient Randomization Number	Body System / MedDRA Term / AE Term	Treatment Area	Start /End Date	Severity	Relationship to Study Drug	Outcome	Action Taken	Other Action Taken	SAE?
Treatment Group A	xx-xxxx	Nervous system disorders / Headache / Headache	No	yyyy-mm-dd / yyyy-mm-dd	Mild	Possible	Recovered	Dose Not Changed	None	No
Treatment Group B										
Treatment Group C										

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.7.2 Listing of Application Site Reactions

Treatment Group	Patient Randomization Number	Visit	Signs and Symptoms*						
			Erythema	Scaling/ Dryness	Stinging/ Burning	Erosion	Edema (swelling)	Pain	Itching
Treatment Group A	xxxx	3	0	0	0	1	0	0	0
		4	0	1	0	0	0	0	0
		5	0	0	0	1	0	0	0
		6	0	0	0	1	0	2	2
		7	0	0	0	1	0	2	2
Treatment Group B									
Treatment Group C									

*Signs and symptoms: 0 = Absent; 1 = Mild; 2 = Moderate; 3 = Severe

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336

Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336

Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.7.3 Listing of Abnormal Physical Examination Results

Treatment Group	Patient Randomization Number	Visit	System	Result	If Abnormal, provide comment
Treatment Group A	xx-xxxx	Visit 4	Cardiovascular	Abnormal (NCS)	xxxxxxxxxxxxxxxx
Treatment Group B					
Treatment Group C					

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.7.4 Listing of Positive Pregnancy Test Results

Treatment Group	Patient Randomization Number	Visit	Results
Treatment Group A	xx-xxxx	Visit 4	Positive
Treatment Group B			
Treatment Group C			

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.8.1 Listing of Clinical Laboratory Testing Results (Hematology)

Treatment Group	Patient Randomization Number	Visit	Date	Lab Test	SI Results	SI Unit	Normal Range
Treatment Group A	xx-xxxx	1	yyyy-mm-dd	Hemoglobin	xxx	g/L	xxx, xxx
		3	yyyy-mm-dd	Hemoglobin	xxx	g/L	xxx, xxx
		7	yyyy-mm-dd	Hemoglobin	xxx	g/L	xxx, xxx
Treatment Group B							
Treatment Group C							

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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L16.2.8.2 Listing of Clinical Laboratory Testing Results (Chemistry)

L16.2.8.3 Listing of Clinical Laboratory Testing Results (Urinalysis)

L16.2.8.4 Listing of Vital Signs

Treatment Group	Patient Randomization Number	Visit	Systolic BP (mmHg)	Diastolic BP (mmHg)	Heart Rate (beats/min)	Respiration Rate (breath/min)	Temperature (F)
Treatment Group A	xx-xxxx	1	120	70	84	18	98.6
		3	140	80	74	18	97.0
		5					
		6					
		7					
Treatment Group B							
Treatment Group C							

Treatment Group A: Novexatin® 10% Topical Solution for Days 1 – 56 and Placebo (Vehicle) Topical Solution for Days 281 – 336
Treatment Group B: Novexatin® 10% Topical Solution for Days 1 – 56 and Days 281 – 336
Treatment Group C: Placebo (Vehicle) Topical Solution for Days 1 – 56 and Days 281 – 336

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10. APPENDICES

Appendix A: Evaluation of Toenail Condition/appearance

The number of toenails infected should be counted. The toenail, one of the two great toenails, that the investigator considers to be the most appropriate as the target toenail will be identified at Visit 2 and designated as the "target toenail" and used for all further evaluations.

Evaluation of Toenail condition/appearance

The overall appearance of the target toenail over time will be monitored during the study:

Self-assessed by patients. The results of the self-assessment will be recorded by the patient before beginning therapy at Visit 2 and at all subsequent visits.. Patients will use a 5-point scale for target toenail appearance:

1. Very Poor
2. Poor
3. Normal/acceptable
4. Good
5. Very good

Assessed by Investigator. Investigators will rate the status of the target toenail before patient begins therapy at Visit 2 and at all subsequent clinic visits. Nail condition/appearance by investigator will be evaluated after nail trimming to the distal groove and before further trimming, if required, for the mycological evaluation. Investigators will use a 5-point scale target toenail appearance:

1. Very Poor
2. Poor
3. Normal/acceptable
4. Good
5. Very good

Appendix B: Application Site Reactions

Monitoring of local tolerability (inflammation) will be based upon established methods including observation of the area of administration and response scoring by the study personnel. Upon the visits to the clinical study site, each patient will be examined for signs of local inflammation and irritation that may be associated with the study products. If any such signs are identified, the response will be graded as follows:

Signs and Symptoms:

Erythema (redness)

Scaling/Dryness

Stinging/Burning

Erosion

Edema (swelling)

Pain

Itching

Grading Scale:

Absent 0

Mild 1 (slight, barely perceptible)

Moderate 2 (distinct presence)

Severe 3 (marked, intense)

Application site reactions will not be separately recorded as AEs since they are being captured at each visit for erythema, burning/stinging, erosion, edema, pain, itching or dryness unless the Investigator feels it is appropriate to do so.