Official Title: **A Prospective, 16 Week, Phase IV Study to Evaluate Safety, Tolerability and Effectiveness in Patients With Severe Dementia of the Alzheimer's Type Exposed to Rivastigmine (Exelon)15cm2 Transdermal Patch**

NCT Number: NCT02989402

Document Date: Statistical Analysis Plan (Version 1.0): 01-December-2022

[redacted]

Statistical Analysis Plan

[redacted]

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STATISTICAL ANALYSIS PLAN

Study Title:	A prospective, 16 week, phase IV study to evaluate safety, tolerability and effectiveness in patients with severe dementia of the Alzheimer's type exposed to rivastigmine (Exelon) 15 cm^2 transdermal patch
Sponsor Identification:	CENA713DIN01
Phase:	Phase IV
Sponsor Study Number:	CENA713DIN01
[redacted]	[redacted]
Responsible Biostatistician:	[redacted]
Date of SAP:	01 Dec 2022
Version:	Final 1.0
Scope:	Final

[redacted]

2 Signatures

Sponsor:	Novartis
Protocol No./ [redacted]	CENA713DIN01 [redacted]
Protocol Version No./Date:	Final Version 02 (Original protocol) / 21-Dec-2016
Study Title:	A prospective, 16-week, phase IV study to evaluate safety, tolerability and effectiveness in patients with severe dementia of the Alzheimer's type exposed to rivastigmine (Exelon) 15 cm^2 transdermal patch
CRF Version No./Date:	Version 2.0/03 Apr 2018
SAP Version No./Date:	Final 1.0/ 01 Dec 2022

Prepared By [redacted]

DocuSigned by: [redacted]

01-Dec-2022 | 15:08 T

Date (DD-MMM-YYYY)

Reviewed By [redacted]

DocuSigned by: [redacted]

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Approved By

(Novartis)

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3 Document History

Version	Date	Change to previous version
Final 1.0	01 Dec 2022	Nil

4 Abbreviations

AE	Adverse Event
AD	Alzheimer's Disease
BMI	Body Mass Index
Cm	Centimeter
CMQ	Caregiver Medication Questionnaire
CRF	Case Report/Record Form
CRO	Contract Research Organization
CS	Clinically Significant
eCRF	Electronic Case Report Form
ENT	Ears, Nose and Throat
EOS	End of Study
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
ITT	Intent to Treat
IRB	Institutional Review Board
Kg	Kilogram
LOCF	Last observation Carry Forward
MMSE	Mini-Mental State Examination
NCS	Non Clinically Significant
[redacted]	[redacted]
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
UTI	Urinary Tract Infection

5 Introduction

This statistical analysis plan (SAP) provides the explicit guidance and describes the planned statistical and data handling methods to be followed during the final reporting and analyses. The intent of this document is to provide detailed information of the planned analysis of data related to safety and efficacy & to describe any applicable statistical procedures explicitly. It quotes the relevant statements directly from the protocol, for the applicable sections in this document (SAP). This SAP should be read in conjunction with the study protocol CENA713DIN01 version 02 (Original protocol) and dated 21-Dec-2016 and case report form (CRF) (version Final 2.0 dated 03 Apr 2018).

6 Study Objective(s)

6.1 Primary Objective

The primary objective of the study is:

1. To obtain safety data in patients with severe dementia of the Alzheimer's type treated with rivastigmine 27 mg -15 cm^2 transdermal patch for 16 weeks.

6.2 Secondary Objective(s)

The secondary objective of the study is:

1. To assess patient's compliance of rivastigmine 27 mg -15 cm^2 transdermal patch during 16 weeks treatment period
2. To assess the skin tolerability (irritation and adhesion) during 16 weeks treatment period
3. To assess the proportion of patients with UTI during 16 weeks treatment period
4. To evaluate treatment effect by rivastigmine 27 mg -15 cm^2 transdermal patch by assessing the changes in Mini-Mental State Examination (MMSE)
5. To evaluate treatment efficacy by rivastigmine 27 mg -15 cm^2 transdermal patch by assessing the changes in ADCS-Activities of Daily Living Inventory – Severe Impairment Version (ADCS-ADL SIV) Score.

7 Study Design

7.1 Overview

7.1.1 Study Design

This is a multicenter, prospective, phase IV study evaluating safety, tolerability and effectiveness of rivastigmine 27 mg -15 cm^2 transdermal patch prescribed in patients with severe dementia of the Alzheimer's type as per discretion of treating physician.

The prescription decision shall be independent of decision for inclusion in the study. Patients treated according to local routine clinical practice will be enrolled in the study upon signing an Informed Consent. Eligibility for study entry will be determined by the study investigator, in accordance with the selection criteria below. Signing of the Informed Consent defines the study entry visit. Routine urine examination shall

be done to detect any UTI. Compliance to treatment directions shall be reviewed by treating investigator at every visit.

After 8 week and at 16 week, it is expected for the physician to follow up as per routine practice in India. The treating physician will assess the safety, tolerability and effectiveness of the rivastigmine 27 mg -15 cm^2 transdermal patch and may consider continuing or changing the therapy.

Study Design Rationale

This is open label study to examine the safety, effectiveness, and tolerability of the treatment in routine clinical practice, to determine how the treatment works under ordinary and variable conditions, prescribed by clinicians with varying degrees of expertise and practicing across the spectrum of health care settings, to treat a heterogeneous group of patients.

The schedule of assessments will be as follows:

Examination	Baseline Visit 1 (Day 1)	Visit-2 (8 ± 2 weeks)	EOS Visit 3 (16 ± 2 weeks)
Informed consent	X		
Patient demographics (sex, age, etc)	X		
Relevant medical history	X		
Vitals	X	X	X
Physical examination*	X	X	X
Height** and weight	X	X	X
Inclusion/Exclusion criteria	X		
MMSE Score	X	X	X
ADCS-ADL SIV score	X		X
Concomitant medications		X	X
Treatment for AD	X	X	X
Urine examination	X	X	X
Skin irritation assessment		X	X
Patch adhesion assessment		X	X
Adverse Events (AEs)and Serious Adverse Events (SAEs) recording	X	X	X
Compliance assessment using caregiver questionnaire		X	X
EOS			X
EOS = End of Study X = Assessment to be recorded on CRF			
Physical examination includes examination of general appearance, skin, neck (including thyroid), eyes (excluding fundus), ears, nose, throat, lungs, heart, abdomen, back, lymph nodes, and extremities. In addition, a neurological exam consisting of cranial nerve, motor and sensory assessments as performed in routine clinical practice. It also includes recording of pulse and blood pressure as per routine clinical care.* * Height is assessed only at Visit 1*			

7.1.2 Treatment Regimen

The study will include the following open-label drug:

Exelon© patch: 15 cm^2 patch sizes loaded with 27 mg of rivastigmine.

7.2 Efficacy endpoints

Efficacy endpoints will be as follows:

1. Mini-Mental State Examination (MMSE):

Assessing the changes in Mini-Mental State Examination (MMSE): The MMSE is a brief, practical screening test for cognitive dysfunction (Folstein et al. 1975). The test consists of five sections (orientation, registration, attention-calculation, recall, and language & Praxis) and results in a total possible score of 30, with higher scores indicating better function. MMSE shall be recorded at the start and at each visit.

2. ADCS-ADL SIV SCORE:

This is a tool to assess the ability of patients with moderate to severe dementia to perform activities of daily living. ADCS-ADL SIV score is done at start and end of visit. This includes 19 questions and total score is 54. Administration instructions and Instruction card for the rater to use when administering the scale is separately provided

7.3 Safety Assessments

Safety endpoints will be as follows:

- Urine examination
- Skin reaction at patch
- Patch adhesion
- Adverse events.
- Compliance by Caregiver medication questionnaire

8 General Statistical Considerations

8.1 Descriptive Statistics

The following descriptive statistics will be calculated for continuous data and for ordered categorical data (ordinal data):

Summary statistics are displayed with the following digits:

Description	Characteristic	Number of decimal places
Count	n	0
Count corresponding to the number of patients for a group	N	0
Mean	Mean	As in source + 1
Standard Deviation	SD	Mean+1
Minimum	Min	As in source
Median	Median	As in source + 1
Maximum	Max	As in source
1st Quartile / 3rd Quartile	Q1/Q3	As in source + 1
Percentage relative to N #	%	1

Number of decimal places can be more than one, if necessary. All table percentages should be rounded to one decimal place if not stated otherwise.

All data will be presented in the patient data listings.

If either table or listing does not include any observation, then the following placeholder will be used: "NO DATA CONTRIBUTED TO THIS TABLE / LISTING".

8.2 Analysis Population

Two population will be considered for the analysis: The intend to treat (ITT) population and safety population. Analysis for all efficacy endpoints using the ITT population will be the primary approach for analysis. For safety endpoints, safety population will be used for analysis.

Analysis Population	Definition
Screened Population	All the subjects who screened in the study will be considered
Intend to treat Population	The intend to treat (ITT) set will include all patients having signed the Informed Consent, who have at least one post baseline assessment.
Safety population	The safety set will include all patients who provide Informed Consent to collect information and who were treated with at least one patch of rivastigmine 27 mg- 15 cm^2 transdermal patch during this study. Of note, the statement that a patient had no AE also constitutes a safety assessment

8.3 Definitions

In the following table, the definitions and calculation of derived variables are summarized

Variable / Term	Definition / Way of calculation
Age	Int ((informed consent date – Birth date +1)/365.25)
Baseline	The last valid value prior to the first dose of study treatment
BMI (kg/m2)	Weight (kg) / (Height (m) x Height (m))
Duration of exposure	Treatment end date- treatment start date + 1
Treatment Start Date	Date of dose administration on Day 1 in Investigational Product Log in the CRF
Treatment End Date	The last date from the 'Investigational Product Log' form to be considered as treatment end date
Treatment Emergent AE (TEAE)	An AE will be considered as treatment-emergent if the time of onset is on or after the time of the first dose or any AE that exist prior to first dose and if it increased in severity during the study.

8.4 Protocol Deviation

The relevant protocol deviations have to be defined by a systematic data review prior to database closure. For this purpose, protocol violations that occurred during the study such as violations of inclusion/exclusion criteria or forbidden concomitant medications or patient non-compliance will be assessed as 'major' or 'minor' depending on their potential to interfere with the objectives of the study. Listings will be prepared to show the eligibility of all patients. Comprehensive justification for the classification of a protocol violation/deviation as "major" will be given in the integrated clinical study report.

The protocol deviations (Major and Minor) will be summarized using frequency count and percentage and overall, using ITT Population.

The list of protocol deviations will be reviewed by the sponsor and finalized before locking the database.

8.5 Data Handling

8.5.1 Imputation of Missing data

LOCF (last observation carried forward) method will be used for missing values at week 16.

Safety

No imputation will be done on missing safety data, unless for partially incomplete dates for remote events such as AE, concomitant medication etc.

For partial start dates:

1. If the year is unknown, then do not impute the date but assign a missing value.
2. If the month is unknown, then:
    a. If the year matches the year of the dose date, then impute the month and day of the dose date.
3. If the day is unknown, then:
    a. If the month and year match the month and year of the first dose date, then impute the day of the dose date.

For partial end dates:

1. If the year is unknown, then do not impute the date but assign a missing value.
2. If the month is unknown, then do not impute the date and mark as ongoing for AE and Concomitant medication.
3. If the day is unknown, then assign the last day of the month.

After implementing the rules above, to determine whether AEs (or medications) with missing start or stop dates are pretreatment or on/after treatment, the following strategy will be used:

1. If the start date and stop date are both missing, then the most conservative approach is taken and the AE (or medication) is considered to be treatment-emergent (or concomitant medication).

2. If the start date is missing but the stop date is not missing and is on or after the day of first study dose administration, then the most conservative approach is taken and the AE (or medication) is considered to be treatment-emergent (or concomitant medication).

3. If the start date is missing but the stop date is not missing and is before the day of first study dose and after the date of signed informed consent, then the AE (or medication) is considered to be before treatment (or prior medication).

4. If the start date is not missing but the stop date is missing, then the most conservative approach is taken, and medication is considered to be concomitant while the AE is defined by the start date.
If the adverse event relationship flag is missing, the relationship for the adverse event will be imputed and will be considered as possibly related. If the Adverse Event Severity flag is missing, the severity will be imputed with the maximum severity as “Severe” and if the adverse event is flagged as Serious adverse event and the severity flag is missing then the maximum severity imputed will be “life-threatening”

8.6 Sample Size Calculation

Incidence of adverse event data of ACTION study (74.60%) for Rivastigmine patch per day over a 24-week study period in patients with severe AD.
The sample size is determined based on a precession approach considering normal approximation. A sample of 93 subjects will be able to estimate the incidence rate with a maximum error of 10% of the true population proportion with 90% of the cases. We assumed that the true population proportion is 0.746 (what is observed in US44)
Similarly, a sample of 41 subjects will be able to estimate the incidence rate with a maximum error of 10% of the true population proportion with 85% of the cases and sample of 23 subjects of the true population proportion with 80% of the cases.
Considering the drop out of 10% and the true population proportion with 90%, 102 patients shall be enrolled.

8.7 Interim Analysis

No interim analyses are planned.

8.8 Statistical Software

All statistical analyses will be performed with SAS®, Version 9.4 or later.

9 Statistical Analyses

9.1 Patient Disposition

Patient disposition will be tabulated with number and percentages of patient's enrolled, dosed, completed the study according to the protocol or discontinued the study prematurely. The patients who prematurely discontinued the study and the reasons for their discontinuation will be presented. The disposition table will be summarized using "screened population".

9.2 Demographic Data and Baseline Characteristics

- Age (year)
- Gender
- Height (cm)
- Weight (kg)
- BMI((kg/m^2)
- Baseline MMSE Total Score
- Baseline ADCS-ADL SIV Total score
- Diagnosed with AD

9.3 Medical History

All general medical history including complete review of all current and past conditions will be coded using MedDRA version 20.1. General medical history conditions will be summarized by system organ class, preferred term using SAF population. The version of the utilized dictionary will be presented as part of the provided tables and listings. Listing of medical history will be provided.

Patients will be counted only once at the preferred term (PT), only once at the system organ class (SOC), and only once at patient level for the counting of total number of patients with a medical history term. Listings of medical history events for patients in the safety population will be provided.

9.4 Prior and concomitant medication

Prior and concomitant medications will be assessed at screening and at each subsequent study visit. Medications will be coded using WHODDE+ HD DEC 2017 and will be summarized by ATC class (the highest available level), preferred name for the safety population. Patients taking the same medication multiple times will be counted once per medication.

Medication will be classified as prior, If the medication that start and stop prior to the date of received study medication. Medications that are ongoing or ended after the first use of the study medication will be classified as concomitant. If the end date of the medication is unknown, it will also be considered as concomitant. Handling of missing date explained in section (Imputation of missing data section 8.5.1).

Listings will be presented for prior and concomitant medications.

9.5 Treatment exposure

Study drug patch administered during the course of the study will be recorded on the corresponding Dosage Administration Record CRF

Duration of treatment exposure will be summarized descriptively using safety population by visit.

9.6 Primary and Secondary Analysis

9.6.1 Primary Analyses

- To obtain safety data in patients with severe dementia of the Alzheimer's type treated with rivastigmine 27mg -15 cm2 transdermal patch for 16 weeks.

  The primary safety objective of this study will be assessed by collecting adverse events. Adverse events will be analysed using SAF Population.

9.6.2 Secondary Analysis

1) To assess patient's compliance of rivastigmine 27 mg -15 cm^2 transdermal patch during 16 weeks treatment period
   The Compliance by Caregiver medication questionnaire will be summarized descriptively by visit using ITT population.

2) To assess the skin tolerability (irritation and adhesion) during 16 weeks treatment period
   Skin tolerability will be summarized by the number and percentages of patients using safety population.

3) To assess the proportion of patients with UTI during 16 weeks treatment period

   Proportion of patients with UTI will be summarized by the number and percentages of patients using safety population.

4) To evaluate treatment effect by rivastigmine 27 mg -15 cm^2 transdermal patch by assessing the changes in Mini-Mental State Examination (MMSE)

   The change from baseline for Week 8 and Week 16 in MMSE total score will be summarized descriptively using the ITT population and treatment for the study

5) To evaluate treatment efficacy by rivastigmine 27 mg -15 cm^2 transdermal patch by assessing the changes in ADCS-Activities of Daily Living Inventory – Severe Impairment Version (ADCS-ADL SIV) Score

   The change from baseline in ADCS-ADL SIV score will be summarized descriptively and scores will also be presented by frequencies and percentages using the ITT population and treatment for the study.

9.7 Safety Analysis

9.7.1 Adverse Events

Adverse Events will be coded using the Medical Dictionary of Regulatory Activities (MedDRA version 20.1), the coded terms will be used for summarizing the AE(s). Only treatment emergent adverse events (TEAE) will be summarized in tables, while all events will be listed. Adverse events will be analyzed using safety population.

An AE will be considered as treatment-emergent if the time of onset is on or after the time of the first dose or any AE that exist prior to first dose and if it increased in severity during the study period. Handling of missing data for AE are explained in section 8.5.1 (Imputation of missing data).

An overall summary table which summarizes, the number and percentages of patients with adverse events, serious adverse events, adverse events leading to death, adverse events related to study drug and adverse events by severity categories will be provided. All the AE tables will be summarized based on TEAE,

Patients experiencing any treatment emerging adverse events will be summarized by Preferred Term (PT) and SOC. The number and percentage of patients with at least one TEAE, SAE, discontinuation of study treatment due to death and TEAEs of severe intensity will be summarized by system organ class, preferred. Furthermore, listings of AEs, SAEs and Deaths will be provided.

Furthermore, an overall Adverse event listing will be provided, and a separate listing will be provided for AE leading to death.

AEs tables by primary system organ class and preferred term will be sorted in descending order of counts.

Also an overall AE summary table which summarizes, the number and percentages of patients with adverse events, serious adverse events, permanently discontinued study treatment, adverse events leading to death, adverse events related to study drug and adverse events by severity categories will be provided for the SAF population.

A patient experiencing the same AE multiple times will be counted only once for that preferred term. Similarly, if a patient experiences multiple AEs within the same system organ class that patient will be counted only once in that system organ class. Maximum severity will be considered if a patient has multiple severity reported for same AE. In summaries by relationship, if a patient has the same AE on multiple occasions, the closest relationship to study drug, will be used for summary.

9.7.2 Physical Examination

Physical examination will be performed at Baseline Visit 1(Day 1), Visit-2 (8 ± 2 weeks), EOS Visit 3 (16 ± 2 weeks). Physical examination will include an examination of general appearance, skin, neck (including thyroid), eyes (Excluding fundus), ENT, lungs, heart, abdomen, back, lymph nodes, extremities, Cranial nerve, Motor assessment, Sensory assessment, Rectal, External Genitalia, Breast and Pelvic Exams.

Physical examination results will be summarized by number and percentages using SAF population. Listing will be provided for the Physical Examination.

9.7.3 Vital Signs

Vital signs will be measured at baseline Visit 1(Day 1), Visit2 (8 ± 2 weeks) , EOS Visit 3 (16 ± 2 weeks)
The vital signs parameters include:

- Systolic Blood Pressure (mmHg)
- Diastolic Blood Pressure (mmHg)
- Pulse Rate (bpm)
- Respiratory Rate (brpm)
- Temperature (°F)
- Height (centimeters)
- Body weight (kg)

The actual and change from baseline vital signs parameters will be summarized descriptively by visits.
In addition, number and percentage of patients reaching ‘Normal’, ‘Abnormal CS’ and ‘Abnormal NCS’ results for Clinical significance will be summarized by visits. Data listings will be presented for vital signs parameters using SAF population.

9.7.4 Patch adhesion assessment

Patch adhesion assessment will be measured at Visit-2 (8 ± 2 weeks), EOS Visit 3 (16 ± 2 weeks).
A summary of these findings will be presented by number and percentages of patients using SAF population.
Data listings will be presented for Patch adhesion assessment.

9.7.5 Urine examination

Urine examination will be measured at Baseline Visit 1(Day 1), Visit-2 (8 ± 2 weeks), EOS Visit 3 (16 ± 2 weeks.

A summary of these findings will be presented by number and percentages of patients using SAF population

9.8 Multicenter Studies

Yes.

9.9 Subgroup Analyses

Not Applicable

10 Deviation from the Study Protocol

The following are the deviation from the study protocol.

S.No	Topic	Protocol	Changes from the protocol
1	Screened Population	NA	Screened population has been added in the analysis set in order to provide the information regarding the patient disposition.
2	Analysis Population	All analyses will be carried out on the ITT set, while adverse event analyses will be conducted in the safety set	Analysis for all efficacy endpoints using the ITT population will be the primary approach for analysis. For safety endpoints, safety population will be used for analysis.

11 Database Lock and Unblinding

The SAP will be finalized prior to database lock. After the data cleaning process is finalized according to the data management plan (DMP) and the assignment of patients to the analysis sets is agreed and signed by the sponsor, the study database will be locked. Since the study is open label unblinding is not applicable.

12 References

Nil

Official Title: **A Prospective, 16 Week, Phase IV Study to Evaluate Safety, Tolerability and Effectiveness in Patients With Severe Dementia of the Alzheimer's Type Exposed to Rivastigmine (Exelon)15cm2 Transdermal Patch**

NCT Number: NCT02989402

Document Date: Catalogue of Tables, Listings and Figures (Version 1.0): 01-December-2022

[redacted]

Catalogue of Tables, Listings and Figures

Sponsor:	Novartis
Protocol No [redacted]	CENA713DIN01[redacted]
Protocol Version No./Date	Final 2.0/ 21 Dec 2016
Study Title	A prospective, 16-week, phase IV study to evaluate safety, tolerability and effectiveness in patients with severe dementia of the Alzheimer's type exposed to rivastigmine (Exelon) 15 cm^2 transdermal patch.
SAP Version No./Date:	Final 1.0 / 01 Dec 2022

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Introduction

This catalog includes examples of tables, figures and listings to support the analysis of a Statistical Analysis Plan (SAP).

General Statistical Considerations

All statistical analyses will be performed with SAS®, Version 9.4 or later.

The following descriptive statistics will be calculated for continuous data and for ordered categorical data (ordinal data):

Summary statistics are displayed with the following digits:

Description	Characteristic	Number of decimal places
Count	n	0
Count corresponding to the number of patients for a group	N	0
Mean	Mean	As in source + 1
Standard Deviation	SD	Mean+1
Minimum	Min	As in source
Median	Median	As in source + 1
Maximum	Max	As in source
1st Quartile / 3rd Quartile	Q1/Q3	As in source + 1
Percentage relative to N #	%	1

Number of decimal places can be two, if necessary. All table percentages should be rounded to one decimal place if not stated otherwise.

The above-mentioned decimals are for informative purpose only and patient to change based on the study requirement.

AEs Tables by primary system organ class and preferred term will be sorted alphabetically if not stated otherwise.

All data will be presented in the patient data listings.

If either table or listing does not include any observation, then the following placeholder will be used: “NO DATA CONTRIBUTED TO THIS TABLE / LISTING”.

List of Tables

Tables will be numbered within their section in ascending order.

No.	Table	Population
14.1 Patient Disposition		
TABLE 14.1.1	Summary of Patient Disposition	Screened population
TABLE 14.1.2	Number of Patients in Analysis Sets	Screened population
TABLE 14.1.3	Number of Patients by Protocol Deviations	Safety population
TABLE 14.1.4	Number of Patients at Each Visit	Safety population
TABLE 14.1.5	Number of Patients Enrolled by Study Center	Safety population
TABLE 14.1.6	Summary of Patient Demographic Data and Baseline Characteristics	Safety population
TABLE 14.1.7	Summary of Medical History Classified by MedDRA by SOC and Preferred Term	Safety Population
TABLE 14.1.8	Summary of Prior and Current Medications by ATC Class and Preferred Term	Safety Population
TABLE 14.1.9	Summary of Concomitant Medication by ATC Class and Preferred Term	Safety Population
TABLE 14.1.10	Summary of Treatment Exposure	Safety Population
14.2 Efficacy Analysis		
TABLE 14.2.1	Summary of Mini-Mental State Examination	ITT Population
TABLE 14.2.2	Summary of ADCS ADL-Severe Dementia Version	ITT Population
TABLE 14.2.2.1	Summary and change from baseline of ADCS ADL-Severe Dementia Version total score	ITT Population
TABLE 14.2.3	Summary of Responses on the Caregiver Medication Questionnaire	ITT Population
14.3 Safety Analysis		
TABLE 14.3.1	Overall Summary of Adverse Events	Safety Population
TABLE 14.3.2	Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term During the Study	Safety Population
TABLE 14.3.3	Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term and Severity	Safety Population
TABLE 14.3.4	Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term and Relation to study drug	Safety Population
TABLE 14.3.5	Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term and Action Taken	Safety Population
TABLE 14.3.6	Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term and Outcome	Safety Population
TABLE 14.3.7	Number and Percentage of Patients with Serious Treatment Emergent Adverse Events Classified by System Organ Class and Preferred Term	Safety Population

No.	Table	Population
TABLE 14.3.8	Summary of Skin tolerability during 16 weeks treatment period	Safety Population
TABLE 14.3.9	Summary of proportion of patients with UTI during 16 weeks treatment period	Safety Population
TABLE 14.3.10	Summary and Change from Baseline of Lab parameters by Visit and Treatment	Safety Population
TABLE 14.3.11	Summary of Overall Interpretation of Laboratory Parameters by Visit and Treatment	Safety Population
TABLE 14.3.12	Summary of Actual and Change from Baseline for Vital Sign by Visit	Safety Population
TABLE 14.3.13	Summary of Overall interpretation of Vital Signs by Visit	Safety Population
TABLE 14.3.14	Summary of Overall Interpretation of Physical Examination by Visit	Safety Population

List of Figures

Not Applicable

List of Patient Data Listings

In general, patient data listings should include all patients with data.

A listing with all titles of patient data listings should be provided in accordance with the following structure

No.	Listing
16.2.1.1	Inclusion / Exclusion Criteria
16.2.1.2	Study Completion Details
16.2.1.3	Date of Visit
16.2.2	Protocol Deviations
16.2.3	Patients excluded from the analysis
16.2.4.1	Patient Demographic and Baseline Characteristics
16.2.4.2	Medical History
16.2.4.3	Prior and Current Medication
16.2.4.4	Concomitant Medication
16.2.4.5.1	Investigational Product Log
16.2.4.5.2	Treatment Exposure
16.2.6	Individual efficacy response data
16.2.6.1	Mini-Mental State Examination
16.2.6.2	Caregiver Medication Questionnaire
16.2.6.3	Patch Adhesion and Skin Reaction at Patch Site
16.2.6.4	ADCS ADL — Severe Dementia Version

16.2.7.1	Adverse Event by Patient
16.2.7.1.1	Serious Adverse Event by Patient
16.2.8.1	Lab Parameters – Urine Examination
16.2.8.2	Vital Signs
16.2.8.3	Physical Examination
16.2.8.4	Treatment of Alzheimer Disease

Mockups of Tables, Figures and patient data listings

Please note: Yellow resp. cursive texts are working advices.

In General:

- *Required margins: at least 0.75 cm on the upper and lower margin and at least 1.0 cm on the left and right sides. All tables and listings will be landscape and centered format. All figures will be landscape and centered format, unless portrait orientation suggests that the information presented is easier to interpret.*
  All output should have the following header at the upper left margin:
  <Sponsor>
  Protocol No.: <Protocol No.>
  and the following header at the upper right margin:
  <Draft/Final Version>, ddmmmyyyy
  Page n of N
- *Tables/appendices/listings should be internally paginated (i.e., page numbers should appear sequentially within each table). The name of the SAS program used to generate the output shall be displayed in the lower left corner. SAS Monospace, font size 8 will be used, although the mockup below would indicate differently.*
- *Tables of Contents will be generated separately for Tables and Listings, listing numbers and titles. A file separate from Tables and Listings output must be produced. TOC pages will bear the standard header.*

Tables in general:

- *All necessary footnotes should be given to understand the values*
- *Tables template should be as mentioned in SAP .*
- *Align numbers generally to decimal points (do not center numbers)*

Figures in general:

- *Figures should be made clear to interpret the data points plotted;*
- *Appropriate legends should be placed to refer the plotted points*

Data Listings in general:

- *All Listings should be - paged by site and labeled with site number and sorted by investigation site, patient and actual date and time.*

6.1 Tables

Table 14.1.1: Patient Disposition

Table 14.1.1
Summary of Patient Disposition
(Screened Population)

	Total n (%)
Number of patients screened	xxx
Number of patients screen failure	xxx (xx.x)
Reasons for screen failure:	
Reason 1	xx (xx.x)
……..	……..
Number of patients enrolled	xxx (xx.x)
Number of patients dosed	xxx (xx.x)
Number of patients completed the study	xx (xx.x)
Number of patients withdrawn	xx (xx.x)
Reasons for withdrawn:	
Reason 1	xx (xx.x)
Reason 2	xx (xx.x)
……..	……..

n: Total number of patients in a given category
Percentage for reasons of withdrawn was calculated based on the number of patients dosed
Percentages are based on the total number of patients under screened patients
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.1.2: Number of Patients Included from Analysis Sets

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Table 14.1.2
Number of Patients in Analysis Sets
(Screened Population)

	Total (N = xxx) n (%)
Safety (SAF) Population	xx (xx.x)
Intend to treat Population (ITT)	xx (xx.x)

N: Total number of patients Screened

n: Total number of patients in a given category

Percentages are based on the total number of patient's under safety population.

Analysis Dataset: XXXX

Source Listing: Listing xx.x.x

Table 14.1.3: Number of Patients by Protocol Deviations

Table 14.1.3
Number of Patients by Protocol Deviations
(Safety Population)

Protocol Deviation	Total (N=xx) n (%)
Number of patients with any protocol deviations (Major/Minor)	xx (xx.x)
Major Protocol Deviations	xx (xx.x)
Reason:	
Deviation 1	xx (xx.x)
Deviation 2	xx (xx.x)
.....	xx (xx.x)
Minor Protocol Deviations	xx (xx.x)
Reason:	
Deviation 1	xx (xx.x)
Deviation 2	xx (xx.x)
.....	xx (xx.x)

N = The total number of patients in the safety population
n = Number of patients with non-missing data within the specific category.
Percentages are based on the total number of patients in the safety population.
A patient may record more than one reason for a major/minor deviation. All reasons will be counted in the table.
Patients experiencing multiple deviation will be counted only once under the category of Major/Minor protocol deviations.
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.1.4: Number of Patients at Each Visit

Table 14.1.4
Number of Patients at Each Visit
(Safety Population)

Visit	Total (N = xx) n (%)
Baseline Visit	xx (xx.x)
Visit 2	xx (xx.x)
EOS	xx (xx.x)

N: Total number of patients in the safety population
n: Total number of patients in a given category
Percentages are based on the total number of patients under safety Population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.1.5: Number of Patients Enrolled by Study Center

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Table 14.1.5
Number of Patients Enrolled by Study Center
(Safety Population)

Center Number	Total (N = xx) n (%)
1	xx (xx.x)
2	xx (xx.x)
3	xx (xx.x)
4	xx (xx.x)
…	…….

N: Total number of patients in the safety population

n: Total number of patients in a given category

Percentages are based on the total number of patients under safety population

Analysis Dataset: XXXX

Source Listing: Listing xx.x.x

Table 14.1.6: Summary of Patient Demographic Characteristics

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Table 14.1.6
Summary of Patient Demographic Data and Baseline Characteristics
(Safety Population)

Variable	Statistics	Total (N = xxx)
Age (Years)	n	xxx
	Mean	xx.x
	SD	xx.x
	Min	xx.x
	Median	xx.x
	Max	x.x
Gender	Female	xx (xx.x)
	Male	xx (xx.x)
Height (cm)	n	xxx
	Mean	xx.x
	SD	xx.x
	Min	xx.x
	Median	xx.x
	Max	x.x
Weight (kg)	n	xxx
	Mean	xx.x
	SD	xx.x
	Min	xx.x
	Median	xx.x
	Max	x.x
BMI (kg/m^2)	n	xxx
	Mean	xx.x
	SD	xx.x
	Min	xx.x
	Median	xx.x
	Max	x.x

Variable	Statistics	Total (N = xxx)
Baseline MMSE Total Score	n	xxx
	Mean	xx.x
	SD	xx.x
	Min	xx.x
	Median	xx.x
	Max	x.x
Baseline ADCS-ADL SIV Total score	n	xxx
	Mean	xx.x
	SD	xx.x
	Min	xx.x
	Median	xx.x
	Max	x.x
Patient diagnosed for AD	Yes	xx (xx.x)
	No	xx (xx.x)

N: Total number of patients in the safety population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.1.7: Summary of Medical History Classified by MedDRA Preferred Term

Table 14.1.7
Summary of Medical History Classified by MedDRA by SOC and Preferred Term
(Safety Population)

System Organ Class / Preferred Term	(N = xx) n (%)
Number of patients with atleast one condition	xx (xx.x)
System Organ Class	xx (xx.x)
Preferred Term 1	xx (xx.x)
Preferred Term 2	xx (xx.x)
……	……

N: Total number of patients in the safety population
n: Total number of patients in a given category
Patients are counted only once within each SOC class and preferred term
Medical History Terms are coded using the Medical Dictionary of Regulatory Activities (MedDRA version 20.1)
Percentages are based on the total number of patients under safety population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.1.8: Summary of Prior Medications by ATC Class and Preferred Term

Table 14.1.8
Summary of Prior and Current Medications by ATC Class and Preferred Term
(Safety Population)

ATC Class Preferred Term	(N = xx) n (%)
Number of patients with at least one medication recorded	xx (xx.x)
ATC level	xx (xx.x)
Preferred Term 1	xx (xx.x)
Preferred Term 2	xx (xx.x)
……..	……

N = The total number of patients in the safety population
n = Number of patients with non-missing data within the specific category.
Percentages are based on the total number of patient's under safety population
Patients are counted only once within each ATC class and preferred term
Prior and current medications are coded using WHODDE+ HD DEC 2017
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.1.9
Summary of Concomitant Medication by ATC Class and Preferred Term
(Safety Population)

<Refer to table 14.1.8 for shell format>

Table 14.1.10: Summary of Treatment Exposure

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Table 14.1.10
Summary of Treatment Exposure
(Safety Population)

Variable	Statistics	Total (N = xxx)
Treatment Exposure (days)	n	xxx
	Mean	xx.x
	SD	xx.xx
	Min	xx.x
	Median	xx.x
	Max	x.x
Total Number of patches dispensed	n	xxx
	Mean	xx.x
	SD	xx.xx
	Min	xx.x
	Median	xx.x
	Max	x.x
Total Number of patches Returned	n	xxx
	Mean	xx.x
	SD	xx.xx
	Min	xx.x
	Median	xx.x
	Max	x.x

N: Total number of patient's in the safety population

Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.2.1: Summary of Mini-Mental State Examination

Table 14.2.1
Summary of Mini-Mental State Examination
(ITT Population)

Parameter	Visit	Statistics	Actual (N=xxx)	Change from baseline (N=xxx)
Orientation	Baseline	n	xx	
		Mean ± SD	xx.x ± xx.xx	
		Q_1	xx.x	
		Median	xx.x	
		Q_3	xx.x	
		(Min, Max)	(xx.x , xx.x)	
	Visit 2	n	xx	xx
		Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
		Q_1	xx.x	xx.x
		Median	xx.x	xx.x
		Q_3	xx.x	xx.x
		(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
	EOS	n	xx	xx
		Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
		Q_1	xx.x	xx.x
		Median	xx.x	xx.x
		Q_3	xx.x	xx.x
		(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
Registration	Baseline	n	xx	
		Mean ± SD	xx.x ± xx.xx	
		Q_1	xx.x	

Parameter	Visit	Statistics	Actual (N=xxx)	Change from baseline (N=xxx)
		Median	xx.x	
		Q_3	xx.x	
		(Min, Max)	(xx.x , xx.x)	
	Visit 2	n	xx	xx
		Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
		Q_1	xx.x	xx.x
		Median	xx.x	xx.x
		Q_3	xx.x	xx.x
		(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
	EOS	n	xx	xx
		Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
		Q_1	xx.x	xx.x
		Median	xx.x	xx.x
		Q_3	xx.x	xx.x
		(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
……	……	……..	……..	…….
Total	Baseline	n	xx	
		Mean ± SD	xx.x ± xx.xx	
		Q_1	xx.x	
		Median	xx.x	
		Q_3	xx.x	
		(Min, Max)	(xx.x , xx.x)	
	Visit 2	n	xx	xx
		Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx

Parameter	Visit	Statistics	Actual (N=xxx)	Change from baseline (N=xxx)
		Q_1	xx.x	xx.x
		Median	xx.x	xx.x
		Q_3	xx.x	xx.x
		(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
	EOS	n	xx	xx
		Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
		Q_1	xx.x	xx.x
		Median	xx.x	xx.x
		Q_3	xx.x	xx.x
		(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)

N: Total number of patient's in the ITT population
n: Total number of patients in a given category
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Programming note:

This table will consists of five sections (orientation, registration, attention-calculation, recall, and language & Praxis) and Total

Table 14.2.2: Summary of ADCS ADL-Severe Dementia Version

Table 14.2.2
Summary of ADCS ADL-Severe Dementia Version
(ITT Population)

ADCS ADL	(N=xx)
	n (%)
Eating,,	xx (xx.x)
Walking	xx (xx.x)
Bowel and Bladder	xx (xx.x)
Bathing,	xx (xx.x)
Grooming,	xx (xx.x)
---	---

N: Total number of patient's in the ITT population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.2.2.1: Summary and change from baseline of ADCS ADL-Severe Dementia Version total score

Table 14.2.2.1
Summary and change from baseline of ADCS ADL-Severe Dementia Version total score
(ITT Population)

Visit	Statistics	Actual (N=xxx)	Change from baseline (N=xxx)
Baseline	n	xx	
	Mean ± SD	xx.x ± xx.xx	
	Q_1	xx.x	
	Median	xx.x	
	Q_3	xx.x	
	(Min, Max)	(xx.x , xx.x)	
Visit 2	n	xx	xx
	Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
	Q_1	xx.x	xx.x
	Median	xx.x	xx.x
	Q_3	xx.x	xx.x
	(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
EOS	n	xx	xx
	Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
	Q_1	xx.x	xx.x
	Median	xx.x	xx.x
	Q_3	xx.x	xx.x
	(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
EOS	n	xx	xx
	Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
	Q_1	xx.x	xx.x
	Median	xx.x	xx.x

Visit	Statistics	Actual (N=xxx)	Change from baseline (N=xxx)
	Q_3	xx.x	xx.x
	(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)

N: Total number of patient's in the ITT population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.2.3: Summary of Responses on the Caregiver Medication Questionnaire

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Table 14.2.3
Summary of Responses on the Caregiver Medication Questionnaire Mean scores
(ITT Population)

Visit	Parameter	Category	Statistics	Total (N=xx) n (%)
Visit2	During the past 1 week	A patch ever skipped	Never	xx (xx.xx)
			1 day	xx (xx.xx)
			2 days	xx (xx.xx)
			3 days	xx (xx.xx)
			4 or more days	xx (xx.xx)
		The patch taken later than intended	Never	xx (xx.xx)
			1 day	xx (xx.xx)
			2 days	xx (xx.xx)
			3 days	xx (xx.xx)
			4 or more days	xx (xx.xx)
	Extent of agreement	I was concerned that my patient missed taking his / her patch medication	Always	
			Most of the time	

Visit	Parameter	Category	Statistics	Total (N=xx) n (%)
			Sometimes	
			Rarely	
			Never	
		I found it difficult to remember to administer the patch medication	Always	
			Most of the time	
			Sometimes	
			Rarely	
			Never	
	Overall compliance		n	xx
			Mean ± SD	xx.x ± xx.x
			Q1	xx.x
			Median	xx.x
			Q3	xx.x
			(Min, Max)	(xx.x , xx.x)
	satisfied or dissatisfied		n	xx
			Mean ± SD	xx.x ± xx.x
			Q1	xx.x
			Median	xx.x
			Q3	xx.x
			(Min, Max)	(xx.x , xx.x)

Visit	Parameter	Category	Statistics	Total (N=xx) n (%)
Visit3	---	---	--	--

N: Total number of patient's in the ITT population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Programming note:

This table will consist of mean scores of Visit-2 (8 + 2 weeks) and Visit-3 (16+ 2 weeks)

Table 14.3.1: Overall Summary of Adverse Events

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Table 14.3.1
Overall Summary of Adverse Events
(Safety Population)

	Total (N=xxx) n (%) E
Adverse Events	xx (xx.x) xx
Treatment Emergent Adverse Events	xx (xx.x) xx
Serious Adverse Events	xx (xx.x) xx
Adverse Event related to study drug	xx (xx.x) xx
Adverse Events Leading to Study Medication Discontinuation	xx (xx.x) xx
Adverse Events Leading to death	xx (xx.x) xx
AE's by maximum severity	
Mild	xx (xx.x) xx
Moderate	xx (xx.x) xx
Severe	xx (xx.x) xx

N = Total number of patients in the safety population
n: number of patients with atleast one AE in the specified field. E: Number of Events
This table includes only the treatment emergent adverse events
Percentages are based on the total number of patient's under Safety population
Adverse Events will be coded using the Medical Dictionary of Regulatory Activities (MedDRA version 20.1)
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.3.2: Summary of Patient's with Adverse Events Classified by System Organ Class, Preferred Term During the Study

Table 14.3.2

Summary of Patient's with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term During the Study
(Safety Population)

System Organ Class Preferred Term	Total (N=xxx) n (%) E
Number of patients with at least one AE	xx (xx.x) xx
SOC1	xx (xx.x) xx
PT 1	xx (xx.x) xx
….	Xx (xx.x) xx
SOC2	xx (xx.x) xx
PT 1	xx (xx.x) xx
PT 2	xx (xx.x) xx
…..	…..

N = Total number of patients in the safety population

n: number of patients with atleast one AE in the specified fiel . E: Number of Events

Patients are counted only once within each Preferred Term and System Organ Class

Percentages are based on the total number of patient's under Safety population

Adverse Events will be coded using the Medical Dictionary of Regulatory Activities (MedDRA version 20.1)

Analysis Dataset: XXXX

Source Listing: Listing xx.x.x

Programming Note:
Note 1: System organ class and preferred term are ordered alphabetically.
Note 2: Patients are counted only once within each Preferred Term and System Organ Class

Table 14.3.3: Summary of Patients with Adverse Events Classified by System Organ Class, Preferred Term and Severity

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Table 14.3.3
Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term and Severity
(Safety Population)

System Organ Class Preferred Term	Severity	Total (N=xxx) n (%) E
Number of patients with at least one AE	Mild	xx (xx.x) xx
	Moderate	xx (xx.x) xx
	Severe	xx (xx.x) xx
SOC 1	Mild	xx (xx.x) xx
	Moderate	xx (xx.x) xx
	Severe	xx (xx.x) xx
	Mild	xx (xx.x) xx
	Moderate	xx (xx.x) xx
PT 1	Severe	xx (xx.x) xx
	…….	
	.....	.....

N = Total number of patients in the safety population
n: number of patients with at least one AE in the specified field. E: Number of Events
Percentages are based on the total number of patient's under Safety population
Adverse Events will be coded using the Medical Dictionary of Regulatory Activities (MedDRA version 20.1)
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Programming Note:
Note 1: System organ class and preferred term are ordered alphabetically.
Note 2: Patients are counted only once within each Preferred Term and System Organ Class

Table 14.3.4: Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term and Relation to study drug

(Safety Population)

<Refer to table 14.3.3 for shell format>

Programming Note:
Note 1: System organ class and preferred term are ordered alphabetically.
Note 2: Patients are counted only once within each Preferred Term and System Organ Class

Table 14.3.5: Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term and Action Taken

(Safety Population)

<Refer to table 14.3.3 for shell format>

Programming Note:
Note 1: System organ class and preferred term are ordered alphabetically.
Note 2: Patients are counted only once within each Preferred Term and System Organ Class

Table 14.3.6: Summary of Patients with Treatment Emergent Adverse Events Classified by System Organ Class, Preferred Term and Outcome

(Safety Population)

<Refer to table 14.3.3 for shell format>

Programming Note:
Note 1: System organ class and preferred term are ordered alphabetically.
Note 2: Patients are counted only once within each Preferred Term and System Organ Class

Table 14.3.7: Number and Percentage of Patients with Treatment Emergent Serious Adverse Events Classified by System Organ Class and Preferred Term

(Safety Population)

<Refer to table 14.3.2 for shell format>

Programming Note:
Note 1: System organ class and preferred term are ordered alphabetically.
Note 2: Patients are counted only once within each Preferred Term and System Organ Class

Table 14.3.8: Summary of Skin tolerability during 16 weeks treatment period

Table 14.3.8
Summary of Skin tolerability during 16 weeks treatment period
(Safety Population)

Visit	Parameter	Category	Total (N=xx) n (%)
Visit 2	Score to capture comments relating to patch adhesion	0	xx (xx.x)
		1	xx (xx.x)
		2	xx (xx.x)
		3	xx (xx.x)
		4	xx (xx.x)
	Has patch skin reaction occurred?	Yes	xx (xx.x)
		No	xx (xx.x)
	Score to assess skin irritation (Dermal response)	0	xx (xx.x)
		1	xx (xx.x)
		2	xx (xx.x)
		3	xx (xx.x)
		4	xx (xx.x)
		5	xx (xx.x)
	Score to assess skin irritation (Other effects)	Yes	xx (xx.x)
		No	xx (xx.x)
	Other effects	O	xx (xx.x)
		P	xx (xx.x)

		V	xx (xx.x)
		B	xx (xx.x)
		Pu	xx (xx.x)
		H	xx (xx.x)
		W	xx (xx.x)
		S	xx (xx.x)
		A	xx (xx.x)
Visit 3	….	….	….

N: Total number of patient's in the safety population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.3.9: Summary of proportion of patients with UTI during 16 weeks treatment period

Table 14.3.9
Summary of proportion of patients with UTI during 16 weeks treatment period
(Safety Population)

	Total (N=xx) n (%)
Summary of patients with UTI	xx (xx.x)

N: Total number of patient's in the safety population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Table 14.3.10: Summary and Change from Baseline of Lab parameters by Visit and Treatment

Table 14.3.10

Summary and Change from Baseline of Lab parameters by Visit and Treatment

(Safety Population)

Lab Category	Parameters	Visit	Statistics*	Actual	Change from baseline
Chemical	Protein	Baseline	n	xx	
			Mean ± SD	xx.x ± xx.xx	
			Q_1	xx.x	
			Median	xx.x	
			Q_3	xx.x	
			(Min, Max)	(xx.x , xx.x)	
		Visit 2	n	xx	xx
			Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
			Q_1	xx.x	xx.x
			Median	xx.x	xx.x
			Q_3	xx.x	xx.x
			(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
……..	…….	.....	.....	.....	.....

N = Total number of patients in the safety population

Change from baseline = (Day X – baseline)

Analysis Dataset: XXXX

Source Listing: Listing xx.x.x

Programming note:

This table will consist of Physical (pH, Specific Gravity, Colour and Others), Chemical (Protein, Glucose, Ketones, Others) and Microscopy (Pus, RBC, Epithelial Cell, WBC and Others)

Table 14.3.11: Summary of Overall Interpretation of Laboratory Parameters by Visit and Treatment

Table 14.3.11
Summary of Overall Interpretation of Laboratory Parameters by Visit and Treatment
(Safety Population)

Lab Category	Lab Test	Visit	Categories	(N=xx)
				n (%)
Chemical	Protein	Baseline	Normal	xx (xx.x)
			Abnormal-NCS	xx (xx.x)
			Abnormal-CS	xx (xx.x)
		Visit 2	Normal	xx (xx.x)
			Abnormal-NCS	xx (xx.x)
			Abnormal-CS	xx (xx.x)
		…	…	…
	…	…	…	…

N = Total number of patients in the safety population
n: Total number of patient's in a given category
Percentages are based on the total number of patient's under safety population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Programming note:

This table will consist of Chemical (Protein, Glucose, Ketones and Others) and Microscopy (Pus RBC, Epithelial Cell WBC and Others) and Physical (pH, Specific Gravity, Colour and Others)

Table 14.3.12: Summary of Actual and Change from Baseline for Vital Signs by Visit

Table 14.3.12
Summary of Actual and Change from Baseline for Vital Sign by Visit
(Safety Population)

Lab Category	Visit	Statistics*	Actual	Change from baseline
Systolic Blood Pressure (mmHg)	Baseline	n	xx	
		Mean ± SD	xx.x ± xx.xx	
		Q_1	xx.x	
		Median	xx.x	
		Q_3	xx.x	
		(Min, Max)	(xx.x , xx.x)	
	Visit 2	n	xx	xx
		Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
		Q_1	xx.x	xx.x
		Median	xx.x	xx.x
		Q_3	xx.x	xx.x
		(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
	....	n	xx	xx
		Mean ± SD	xx.x ± xx.xx	xx.x ± xx.xx
		Q_1	xx.x	xx.x
		Median	xx.x	xx.x
		Q_3	xx.x	xx.x
		(Min, Max)	(xx.x , xx.x)	(xx.x , xx.x)
	.....	.....	.....	.....

N = Total number of patients in the safety population
Change from baseline = (Day X – baseline)
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

Programming note:

This table will consist of Respiration Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Pulse Rate and Body Temperature

Table 14.3.13: Summary of Overall interpretation for vital signs by Visit

Table 14.3.13

Summary of Overall interpretation for vital signs by Visit

(Safety Population)

Visit	Categories	Total (N=xxx) n (%)
Baseline	Normal	xx (xx.x)
	Abnormal-CS	xx (xx.x)
	Abnormal-NCS	xx (xx.x)
Visit 2	Normal	xx (xx.x)
	Abnormal-CS	xx (xx.x)
	Abnormal-NCS	xx (xx.x)
Visit 3	Normal	xx (xx.x)
	Abnormal-CS	xx (xx.x)
	Abnormal-NCS	xx (xx.x)

N = Total number of patients in the safety population

n: Total number of patient's in a given category

Percentages are based on the total number of patient's under safety population

Analysis Dataset: XXXX

Source Listing: Listing xx.x.x

Table 14.3.14: Summary of Overall Interpretation of Physical Examination by Visit

Table 14.3.14
Summary of Overall Interpretation of Physical Examination by Visit
(Safety Population)

Test	Visit	Categories	Total (N=xxx) n (%)
General Appearance	Baseline	Normal	xx (xx.x)
		Abnormal-CS	xx (xx.x)
		Abnormal-NCS	xx (xx.x)
	Visit 2	Normal	xx (xx.x)
		Abnormal-CS	xx (xx.x)
		Abnormal-NCS	xx (xx.x)
	Visit 3	Normal	xx (xx.x)
		Abnormal-CS	xx (xx.x)
		Abnormal-NCS	xx (xx.x)
	…	…	…
…	…	…	…

N = Total number of patients in the safety population
n: Total number of patient's in a given category
Percentages are based on the total number of patient's under safety population
Analysis Dataset: XXXX
Source Listing: Listing xx.x.x

6.2 Figures

Not Applicable

6.3 Patient Data Listings

All variables out of all available case report forms (CRFs) will be listed. Each patient data listing will be paged by site and treatment, if applicable. Patient ID will be the first column in each listing. The Patient Data Listing which is presented below after table of contents is only an example, it will be expanded according to study objectives and CRF.

Listing 16.2 Discontinued Patients

Novartis
[redacted]

ddmmmyyyy hh:mm
Page x of y

16.2 Discontinued Patients
Listing 16.2.1.1
Inclusion / Exclusion Criteria

Patient ID	Centre number	Category	S.No	Question	Status
xxxxx	xx	Inclusion/Exclusion	1	xxxx	Yes/No

Analysis Dataset: XXXX

Listing 16.2.1.2. Study Completion Details

Listing 16.2.1.2

Study Completion Details

Patient ID	Has subject completed the study?	If yes, date of study completion	If no, reason for discontinuation	if adverse event, or Serious Adverse Event please specify	Date of death	Other, please specify

Analysis Dataset: XXXX

Listing 16.2.1.3. Date of Visit

Novartis
[redacted]

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Page x of y

Listing 16.2.1.3

Date of Visit

Patient ID	Visit	Date of Visit

Analysis Dataset: XXXX

Listing 16.2.2. Protocol Deviations

Listing 16.2.2

Protocol Deviations

Patient ID	Protocol Deviation identified?	Deviation Description	Deviation Category	PD occurred in visit	PD start date and time	PD end date and Time

Analysis Dataset: XXXX

Listing 16.2.3. Patients excluded from the analysis

Listing 16.2.3

Patients excluded from the Analysis

Patient ID	Centre number	Patient excluded from the analysis?	Excluded analysis set	Reason for Exclusion

Analysis Dataset: XXXX

Listing 16.2.4.Demographic and baseline data

Listing 16.2.4 Demographic and baseline data

Listing 16.2.4.1

Patient Demographic and Baseline Characteristics

Patient ID	Center number	Date of Informed Consent	Date of Birth	Age (years)	Gender	Height (cm)	Weight (kg)	BMI (kg/m^2)

Analysis Dataset: XXXX

Listing 16.2.4.2. Medical History

Listing 16.2.4.2

Medical History

Patient ID	Disease / Condition	System Organ Class	Preferred Term	Date of diagnoses/surgery (partial dates allowed)	End Date of Disease/Condition/surgery (partial dates allowed)	is active problem at start of study drug?	Is subject receiving medication for this illness?

Medical History Terms are coded using the Medical Dictionary of Regulatory Activities (MedDRA version 20.1)
Analysis Dataset: XXXX

Listing 16.2.4.3. Prior Medication

Novartis
[redacted]

ddmmmyyyy hh:mm
Page x of y

Listing 16.2.4.3

Prior and current Medication

Patient ID	Medication Name	ATC Class	Preferred Term	Dose	Unit	Dosage form	Route	Frequency	Start Date	Ongoing (Yes/No)	Stop Date

Medications will be coded using WHODDE+ HD DEC 2017
Analysis Dataset: XXXX

Listing 16.2.4.4. Concomitant Medication

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[redacted]

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Page x of y

Listing 16.2.4.4

Concomitant Medication

Patient ID	Medication Or Therapy Name (Generic name)	Indication	ATC Class	Preferred Term	Dose (Units)	Dosage form	Frequency	Route	Visit	Medication started before screening?	Start Date	Stop Date/Ongoing

Medications will be coded using WHODDE+ HD DEC 2017
Analysis Dataset: XXXX

Listing 16.2.5. Compliance

Listing 16.2.5.1 Investigational Product Log

Patient ID	Investigational Product	Visit	Dose	Patches Dispensed Date	Total Number of patches dispensed	Patches Returned Date	Total Number of patches Returned	Comments, if any

Analysis Dataset: XXXX

Listing 16.2.5.2. Treatment Exposure

Listing 16.2.5.2

Treatment Exposure

Patient ID	Treatment Start Date	Treatment End Date	Treatment Exposure (Days)

Treatment exposure =Treatment end date – Treatment start date + 1

Analysis Dataset: XXXX

Listing 16.2.6. Individual efficacy response data

Listing 16.2.6 Individual efficacy response data

Listing 16.2.6.1

Mini-Mental State Examination

Patient ID	Visit	Test	Score	Change from baseline score
		Orientation		
		Registration		
		Attention-calculation		
		Recall		
		Language and Praxis		
		Total		

Change from baseline = (Day X – baseline)
Analysis Dataset: XXXX

Listing 16.2.6.2. Caregiver Medication Questionnaire

Listing 16.2.6.2

Caregiver Medication Questionnaire

Patient ID	Visit	Date performed	Question	Result

Analysis Dataset: XXXX

Listing 16.2.6.3. Patch Adhesion and Skin Reaction at Patch Site

Listing 16.2.6.3

Patch Adhesion and Skin Reaction at Patch Site

Patient ID	Visit	Question	Result

Analysis Dataset: XXXX

Listing 16.2.6.4. ADCS ADL — Severe Dementia Version

Listing 16.2.6.4

ADCS ADL — Severe Dementia Version

Patient ID	Visit	Question	Result

Analysis Dataset: XXXX

Listing 16.2.7. Adverse event

Listing 16.2.7 Adverse event

Listing 16.2.7.1

Adverse Event by Patient

Patient ID	Visit	Adverse Events	TEAE	System Organ Class	Preferred Term	Disorder Number	Start Date	End Date	Relation to study drug	Severity	Action Taken	Outcome	Serious AE	If SAE, Criteria / class of SAE
			Yes/No										Yes/No	

Adverse Events are coded using the Medical Dictionary of Regulatory Activities (MedDRA version 20.1)
Analysis Dataset: XXXX

Listing 16.2.7 .1.1. Serious Adverse Event by Patient

Listing 16.2.7.1.1

Serious Adverse Event by Patient

Patient ID	Visit	Adverse Events	TEAE	System Organ Class	Preferred Term	Disorder Number	Start Date	End Date	Relation to study drug	Severity	Action Taken	Outcome	SAE, Criteria / class of SAE
			Yes/No										

Adverse Events are coded using the Medical Dictionary of Regulatory Activities (MedDRA version 20.1)
Analysis Dataset: XXXX

Listing 16.2.8 Lab Parameters

Listing 16.2.8.1

Lab Parameters – Urine examination

Patient ID	Visit	Lab Category	Lab Parameter	Result	Unit	Interpretation	Comment, if Abnormal

Analysis Dataset: XXXX

Listing 16.2.8.2. Vital Signs

Listing 16.2.8.2

Vital Signs

Patient ID	Visit	Parameter Name	Result
		Respiration Rate (/min)	xxx
		SBP (mmHg)	
		DBP (mmHg)	
		Pulse Rate (bpm)	
		Body Temperature (°F)	
		Weight (kg)	
		Clinical Significance	

Analysis Dataset: XXXX

Listing 16.2.8.3. Physical Examination

Listing 16.2.8.3

Physical Examination

Patient ID	Visit	System	Interpretation	Describe Abnormality

Analysis Dataset: XXXX

Listing 16.2.8.4. Treatment of Alzheimer Disease

Listing 16.2.8.4

Treatment of Alzheimer Disease

Patient ID	Visit	Has a new AD medication added or changed from the previous visit?
		Yes/No

Analysis Dataset: XXXX