Statistical Analysis Plan

A Randomized Open-label Four-way Crossover Study to Compare the Pharmacokinetics, Safety, and Tolerability of Three Different Formulations of M207 3.8 mg (Administered as two 1.9 mg patches) on the Upper arm for 30 Minutes with Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers

Protocol No: CP-2019-002
Final Protocol Date: 15 April 2019
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Protocol Clarification Letter 2: 23 May 2019
Compound Name: M207 (Zolmitriptan Microneedle System)

Celerion Project CA27752
Final Version
Date: 04 July 2019

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Statistical Analysis Plan Signature Page

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Issue Date: 04 July 2019

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Table of Contents

1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the data from this study. The SAP may change due to unforeseen circumstances. Any changes made from the planned analysis within the protocol, after the locking of the database will be documented in the clinical study report CSR. The section referred to as Table Shells within this SAP describes the traceability of the tables, figures, and listings (TFLs) back to the data. Note that the header for this page will be the one used for the main body of the CSR.

Any additional exploratory analyses not addressed within this statistical analysis plan (SAP) and/or driven by the data, or requested by Zosano Pharma Corporation, will be considered out of scope and must be described in the CSR.

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

- To compare the pharmacokinetics (PK), safety and tolerability of M207 3.8 mg (Sled) (Treatment A) to M207 3.8 mg (MACAP) (Treatment B) to M207 3.8 mg (MiniMac) (Treatment C), each worn for 30 minutes on the upper arm.
- To compare the PK, safety and tolerability of these 3 formulations of M207 3.8 mg to intranasal zolmitriptan 2.5 mg (Treatment D).

2.2 Endpoints

Safety and Tolerability

- Incidence of adverse events
- Change in physical exam findings from predose to 8 hr postdose
- Changes in vital signs from predose to 10 minutes, 60 minutes, and 2, 4 and 12 hr postdose
- Changes in ECG parameters from predose to 15 minutes and 12 hr postdose
- Scores from the investigator's visual skin assessment for erythema, edema, bruising and bleeding at the patch application sites from predose to 30 minutes, 60 minutes, 8 hr and 24 hr postdose

Pharmacokinetics

- Cmax - maximum observed plasma concentrations
- Tmax - time to maximum concentration
- AUC0-t - the area under the plasma concentration time profile from hour 0 to the last detectable concentration at time t.
- AUC0-30min - the area under the plasma concentration time profile from minute 0 to minute 30.
- AUC0-60min - the area under the plasma concentration time profile from minute 0 to minute 60.
- AUC0-120min - the area under the plasma concentration time profile from minute 0 to minute 120
- Kel - apparent elimination rate constant will be estimated by linear regression of the log-transformed plasma concentrations during the terminal log-linear decline phase.
- t½ - apparent half-life (t½) values will be calculated as 0.693/Kel.
- AUC0-inf - the AUC value extrapolated to infinity will be calculated as the sum of AUC0-t, and the area extrapolated to infinity, calculated by the concentration at time t (Ct) divided by k.
- AUC0-inf(m/p) – metabolite to parent ratio of AUC0-inf
- %Frel - bioavailability relative to each treatment assignment

3. STUDY DESIGN

This is a single-center, open-label, randomized, four-way crossover study. The study population will consist of 24 healthy volunteers (12 women and 12 men) 18 to 50 years of age in general good health. Following review of all Screening procedures, eligible subjects will be enrolled into the dosing phase of the study. The interval between screening and first treatment will be no more than 30 days.

Eligible subjects will be admitted into the clinic on the day before the first dosing. Subjects will be required to stay in the clinic for the entire duration of the study (unless medically necessary to leave the clinic as instructed by the principal investigator and/or for non-medically related reasons considered on a case by case basis).

Subjects will fast for at least 10 hours during the night preceding dosing and until at least 2 hours after dosing. Water is allowed ad libitum, as well as tea and coffee in moderate amounts. The following morning (between 0630 and 0930), subjects will receive that day's scheduled treatment (A, B, C, or D). The treatments are described in Section 5. Hour 0 will be the time of second patch application.

Each subject will receive each of the 4 study treatments once, followed by in-clinic monitoring and extensive blood sample collections for PK analysis. All AEs,

including any skin irritations and sensations as well as concomitant medication usage will be documented.

Depending on the treatment assignment, two M207 patches (Treatments A, B, and C) will be applied to the upper arm by means of a handheld reusable applicator with an application energy of 0.26 Joules. No lotions, ointments, or powders may be applied to the upper arm where M207 will be applied for 12 hours before or after applying M207. Used patches will be removed 30 minutes after application of the second patch. The patches will be collected and frozen in storage until shipped for analysis of remaining drug. For Treatment D (nasal spray), the dose will be administered, after the subject blows his/her nose, to either the right or left nostril with the subject's head tilted slightly backward.

Dosing will occur approximately 48 hours apart from the time of patch application, until completion of dosing in randomized order per the treatment sequence schedule. Treatments sequences ABDC, BCAD, CDBA, and DACB will be used. At the end of each dosing day, the safety data from the subjects will be evaluated. If tolerability is deemed to be acceptable by the Principal Investigator, a decision will be made to proceed to the next dosing day. After completion of the four dosing days (one in each treatment period), subjects will be assessed one final time and dismissed from the study.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Safety Population

The safety population will include all subjects who received any amount of study drug.

Pharmacokinetic Population

The PK population will include all subjects who were dosed and who have an evaluable PK profile.

4.2 Preliminary Analysis of Pharmacokinetic Data

Celerion will perform a preliminary analysis of plasma zolmitriptan and n-desmethyl zolmitriptan PK data. PK parameters will be calculated using quality-controlled plasma zolmitriptan and n-desmethyl zolmitriptan concentration data and actual sampling times.

5. TREATMENT DESCRIPTIONS

The treatments descriptions will be described as:

Treatment	Short Description	Long Description
Treatment A	M207 3.8 mg (Sled)	M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
Treatment B	M207 3.8 mg (MACAP)	M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
Treatment C	M207 3.8 mg (MiniMac)	M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
Treatment D	Zolmitriptan 2.5 mg (Intranasal)	Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D)

6. PHARMACOKINETIC ANALYSIS

6.1 Measurements and Collection Schedule

Blood samples for the determination of plasma zolmitriptan and n-desmethyl zolmitriptan concentrations will be collected predose and 0.0333 (2 minutes), 0.0833 (5 minutes), 0.1667 (10 minutes), 0.25 (15 minutes), 0.3333 (20 minutes), 0.5 (30 minutes), 0.75 (45 minutes), 1, 1.5, 2, 4, 8, 12, and 24 hours postdose.

Following removal of the patches 30 minutes postdose, the subjects' skin will be swabbed and both the patches and skin swabs will be analyzed for residual zolmitriptan.

All plasma concentration data will be included in the calculation of the individual PK parameters, the individual concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times). All deviations and excluded data will be provided and discussed in the CSR.

6.2 Bioanalytical Method

6.2.1 Plasma Zolmitriptan

Plasma concentrations of zolmitriptan will be determined using a high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) method validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Syneos Health. The analytical range (lower limit of quantitation [LLOQ] – upper limit of quantitation [ULOQ]) for zolmitriptan in plasma is expected to be 100 to 20000 pg/mL.

6.2.2 Plasma N-Desmethyl Zolmitriptan

Plasma concentrations of n-desmethyl zolmitriptan will be determined using a HPLC-MS/MS method validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Syneos Health. The analytical range for n-desmethyl zolmitriptan in plasma is expected to be 50 to 10000 pg/mL.

6.2.3 Residual Zolmitriptan in Patches and Skin Swabs

Residual amounts of zolmitriptan in patches and skin swabs will be determined using HPLC-MS/MS methods validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Syneos Health. The analytical range for zolmitriptan in patches and skin swabs is expected to be 7.5 to 1500 µg.

6.3 Investigational Product and PK Analyte Information

6.3.1 Zolmitriptan

Plasma will be analyzed for zolmitriptan concentrations. The analyte can be described with the following structure and molecular weight (MW) of 287.36 g/mol (Figure A). Zolmitriptan will be administered transdermally to subjects in 3.8 mg doses via Zosana M207 (Zolmitriptan Microneedle System) patches (2 patches x 1.9 mg/patch) made from 3 different types of equipment, and intranasally via a commercially available nasal spray (Zomig® Nasal Spray) at a dose of 2.5 mg (0.1 mL spray x 2.5 mg/0.1 mL).

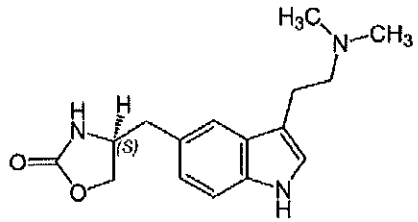


Figure A: Zolmitriptan (MW = 287.36 g/mol)

6.3.2 N-Desmethyl Zolmitriptan

Plasma will be analyzed for n-desmethyl zolmitriptan concentrations. The analyte can be described with the following structure and molecular weight (MW) of 273.34 g/mol (Figure B).

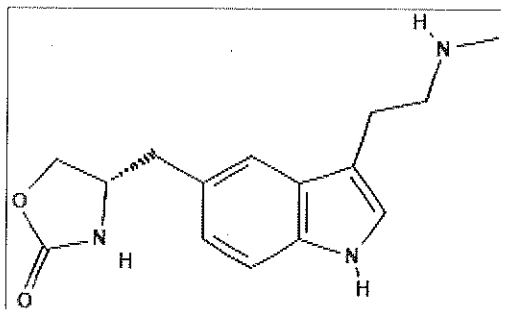


Figure B: N-Desmethyl Zolmitriptan (MW = 273.34 g/mol)

6.4 Pharmacokinetic Concentrations

Plasma concentrations of zolmitriptan and n-desmethyl zolmitriptan as determined at the collection times and per the bioanalytical method described in Section 6.1 and Section 6.2, respectively, will be used for the calculation of the plasma zolmitriptan and n-desmethyl zolmitriptan PK parameters.

6.5 NonCompartmental Pharmacokinetic Analysis and Parameter Calculation

The appropriate noncompartmental PK parameters will be calculated from the plasma zolmitriptan and n-desmethyl zolmitriptan concentration-time data using Phoenix® WinNonlin® Version 7.0 or higher. Actual sample times will be used in the calculations of the PK parameters. The calculation of the actual times will be in respect to the start of patch administration (Treatments A, B, and C) or in respect to the start time of intranasal administration (Treatment D) of zolmitriptan on Day 1. All PK parameters included in the protocol are listed in Table 6.1 below, and are defined as appropriate for study design.

Table 6.1. Noncompartmental Pharmacokinetic Parameters to be Calculated

Parameter	Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
Cmax	Cmax	Maximum observed plasma concentrations	Taken directly from bioanalytical data
Tmax	Tmax	Time to maximum concentration	Taken from clinical database as the difference in the time of administration and the time of the blood draw which is associated with the Cmax.
AUC0-last	AUC0-t	Area under the plasma concentration-time profile from hour 0 to the last detectable concentration at time t	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC0-30min	AUC0-30min	Area under the plasma concentration-time profile from minute 0 to minute 30	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC0-60min	AUC0-60min	Area under the plasma concentration-time profile from minute 0 to minute 60	Calculated using the Linear Trapezoidal with Linear Interpolation Method
AUC0-120min	AUC0-120min	Area under the plasma concentration-time profile from minute 0 to minute 120	Calculated using the Linear Trapezoidal with Linear Interpolation Method
k	Kel	Apparent elimination rate constant	Estimated by linear regression of the log-transformed plasma concentrations during the terminal log-linear decline phase
t1/2	t½	Apparent half-life	Calculated as 0.693/Kel
AUC0-inf	AUC0-inf	Area under the plasma concentration-time curve from minute 0 extrapolated to infinity	Calculated as AUC0-t + (Clast/Kel) where Clast is the last observed/measured concentration
AUC0-inf(m/p)	AUC0-inf(m/p)	Metabolite to parent ratio of the area under the plasma concentration-time curve from minute 0 extrapolated to infinity	Calculated as AUC0-inf of n-desmethyl zolmitriptan x (molecular weight of zolmitriptan/molecular weight of n-desmethyl zolmitriptan)/AUC0-inf of zolmitriptan, where the molecular weights of zolmitriptan and n-desmethyl zolmitriptan are 287.36 g/mol and 273.34 g/mol, respectively.
Frel (zolmitriptan only)	%Frel	Relative bioavailability	Bioavailability relative to each treatment assignment will be calculated as follows: %Frel(A/B) = AUC0-inf(A)/AUC0-inf(B)x100 %Frel(A/C) = AUC0-inf(A)/AUC0-inf(C)x100 %Frel(A/D) = [AUC0-inf(A)/Dose(A)]/[AUC0-inf(D)/Dose(D)]x100 %Frel(B/C) = AUC0-inf(B)/AUC0-inf(C)x100 %Frel(B/D) = [AUC0-inf(B)/Dose(B)]/[AUC0-inf(D)/Dose(D)]x100 %Frel(C/D) = [AUC0-inf(C)/Dose(C)]/[AUC0-inf(D)/Dose(D)]x100

For the calculation of the PK parameters, plasma zolmitriptan and n-desmethyl zolmitriptan concentrations below the limit of quantitation (BLQ) prior to the first quantifiable concentration will be set to 0.00 and plasma concentrations BLQ after the first quantifiable concentration will be treated as missing.

Pharmacokinetic parameters will not be calculated for subjects with less than 3 consecutive postdose time points with quantifiable concentrations. Subjects for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only.

For Treatments A, B, and C, subjects for whom one or both patches detach either partially or completely prior to the completion of the 30 minute wear time may be excluded from any statistics. For Treatment D, subjects who vomit or who experience nasal drip within twice the median Tmax value of 3 hours for the study drug, i.e., within first 6 hours postdose, may be excluded from any statistics.

The Kel will be determined using linear regressions composed of least 3 data points. The Kel will not be assigned if 1) the terminal elimination phase is not apparent, 2) if Tmax is one of the 3 last data points, or 3) if the R^2 value is less than 0.75. In cases where the Kel interval is not assigned, the values of any AUC requiring Kel for extrapolation, t½, AUC0-inf, AUC0-inf(m/p), and %Frel are considered not calculable and will not be reported. Wherever the resulting t½ is more than half as long as the sampling interval, the Kel values and associated parameters (any AUC requiring Kel for extrapolation, t½, AUC0-inf, AUC0-inf(m/p), and %Frel) may not be presented as judged appropriate and in accordance with Celerion SOPs.

The nominal doses of Treatments A, B, and C (3.8 mg), and Treatment D (2.5 mg) will be used in the calculation of the different %Frel parameters.

6.6 Data Summarization and Presentation

For the preliminary PK analysis, all zolmitriptan and n-desmethyl zolmitriptan PK concentrations and/or PK parameter descriptive statistics will be generated using Phoenix® WinNonlin® Version 7.0 or higher. For the final PK analysis, all zolmitriptan and n-desmethyl zolmitriptan PK concentrations and/or PK parameter descriptive statistics will be generated using SAS® Version 9.3 or higher.

The plasma concentrations of zolmitriptan and n-desmethyl zolmitriptan will be listed and summarized by treatment and time point for all subjects in the PK Population. Plasma concentrations of zolmitriptan and n-desmethyl zolmitriptan will be presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including sample size (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, and maximum will be calculated for all nominal concentration time points Excluded subjects will be included in the concentration listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ

values will be presented as "BLQ" in the concentration listings and footnoted accordingly.

The residual amounts of zolmitriptan in each patch and on the skin surface beneath each patch will be listed and the residual amounts of zolmitriptan in both patches combined and on the skin surfaces under both patches combined will be summarized by treatment for all subjects in the PK Population. Residual amounts of zolmitriptan that are BLQ will be set to 0.00. Residual amounts of zolmitriptan in patches and skin swabs will be presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including sample size (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, and maximum will be calculated for residual amounts of zolmitriptan in both patches combined and on the skin surfaces under both patches combined. Excluded subjects will be included in the listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as "BLQ" in the listings and footnoted accordingly.

Mean and individual plasma concentration-time profiles will be presented on linear and semi-log scales. Linear mean plots will be presented with and without SD.

Plasma zolmitriptan and n-desmethyl zolmitriptan PK parameters will be listed and summarized by treatment for all subjects in the PK Population. Pharmacokinetic parameters will be reported to 3 significant figures for individual parameters, with the exception of Tmax, which will be presented with 2 decimal places. Summary statistics (n, Mean, SD, CV%, SEM, minimum, median, maximum, geometric mean (Geom Mean), and geometric CV% (Geom CV%)) will be calculated for plasma zolmitriptan and n-desmethyl zolmitriptan PK parameters. Excluded subjects will be listed in the PK parameter tables, but will be excluded from the summary statistics and noted as such in the tables.

The level of precision for each concentration and PK parameter statistic will be presented as follows: minimum/maximum in same precision as in bioanalytical data and/or parameter output, mean/median/geometric mean in one more level of precision than minimum/maximum, SD/SEM in one more level of precision than mean/median/geometric mean, n will be presented as an integer, and CV%/geometric CV% will be presented to the nearest tenth.

6.7 Statistical Analysis of PK Parameters

No inferential statistics will be performed on the PK data from this study.

7. SAFETY

All case report form (CRF) data will be listed by subject and chronologically by assessment time points. This will include rechecks, unscheduled assessments, and early termination.

Applicable continuous variables will be summarized using n, arithmetic mean, SD, minimum, median, and maximum.

The level of precision will be presented as follows: minimum/maximum in the same precision as in the database, mean/median in one more precision level than minimum/maximum, SD in one more precision level than mean/median, and n will be presented as an integer.

Where individual data points are missing because of dropouts or other reasons, the data will be summarized based on reduced denominators.

No inferential statistics will be performed for safety assessments.

7.1 Subject Disposition

Subjects will be summarized by number of subjects enrolled (randomized), completed, and discontinued the study with discontinuation reasons by randomized treatment sequence and overall. The number of subjects in the safety population will also be summarized. The individual subject's dosing status will also be provided along with their completion status and date of study completion.

7.2 Demographics

Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index [BMI]) by randomized treatment sequence and overall. Weight, height and BMI will be summarized at screening. Age will be derived from date of birth to date of informed consent. Frequency counts will be provided for categorical variables (race, ethnicity, and sex) for each randomized treatment sequence and overall.

7.3 Adverse Events

All adverse events (AEs) occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 20.1.

Each AE will be graded on a 3-point severity scale (mild, moderate, severe). Similarly, the causal relationship of the study drug to the AE will be described using a 3-point relationship scale (probably related, possibly related, not related). All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, treatment, severity, relationship to study medication, and action; however, only treatment-emergent AEs (TEAEs) will be summarized.

A TEAE is defined as an AE that is starting or worsening at the time of or after study drug administration. Each TEAE will be attributed to a treatment based on the onset date and time of the AE. An AE that occurs during the washout period between drugs will be considered treatment-emergent to the last drug administered prior to onset of the AE.

If the onset time of an AE is missing and the onset date is the same as the treatment dosing date, then the AE will be considered treatment emergent in the current treatment. If onset time of an AE is missing and the onset date does not fall on a dosing date, then the AE will be considered treatment emergent for the last treatment administered. If the onset date of an AE is missing, then the AE will be considered treatment emergent and attributed to each treatment on the study, unless the onset date is known to have occurred within or between specific treatment periods or otherwise specified.

TEAEs will be tabulated by System Organ Class (SOC) and Preferred Term. Summary tables will include number of subjects reporting the AE and as percent of number of subjects dosed by treatment. The number of AEs will be tabulated in a similar manner. Tables which tabulate the number of TEAEs by severity and relationship to study drug will also be included.

Serious adverse events (SAEs), if present, will also be listed. Applicable narratives will be included in the CSR.

7.4 Clinical Laboratory Tests

Standard clinical laboratory tests (chemistry, hematology, urinalysis, and serum pregnancy for all women) will be performed at Screening and End of Study (EOS, Day 3 of Period 4) or upon early termination. A serum pregnancy test will also be completed for all women on Day -1 of Period 1. Urine drug screen and alcohol testing will be performed at Screening and on Day -1 of Period 1. Screening serological tests for HIV, Hepatitis B and Hepatitis C will be performed. All clinical laboratory test results will be presented in by-subject data listings.

Out-of-normal range flags will be recorded as follows: high (H) and low (L) for numerical results and did-not-match (*) for categorical results. If a value fails the reference range, it will automatically be compared to a computer clinically significant (CS) range. If the value falls within the computer CS range, it will be noted as "N" for not clinically significant. If the value fails (i.e., fall outside of the CS range) the computer CS range, it will be flagged with a "Y" which prompts the PI to determine how the out-of-range value should be followed using 4 Investigator flags: "N", not clinically significant, "R", requesting a recheck, "^", checking at the next scheduled visit, or "Y", clinically significant. To distinguish the PI flag from the computer CS range flags, the PI flags of "N" and "Y" will be presented as "-" and "+", respectively, in the data listing. Additionally, the PI will provide a 4th flag when the

3rd flag indicates "R" or "^". This 4th flag is intended to capture final CS (+)/NCS (-) when the 3rd flag does not document significance.

Out-of-range serum chemistry, hematology and urinalysis values and corresponding recheck results will be listed. Results that are indicated as CS by the PI (in either PI flag) will be listed in a table.

7.5 Vital Signs

Single measurements of body temperature, respiratory rate, blood pressure (systolic and diastolic), and pulse rate will be performed at the following time points:

Table 7.1. Vital Signs Collection Time Points

Vital Sign Measurement	Period	Day	Time Point
Systolic and Diastolic Blood Pressure, Pulse Rate, Respiration Rate, Temperature*	Screen		
	1, 2, 3, 4	-1**	
		1	Predose, 10 min, 60 min, 2 hours, 4 hours, and 12 hours postdose
	4	3	End of Study or Early Termination
* Temperature will only be collected at screening, on Day -1 of Period 1, and End of Study or upon early termination. ** Period 1 only			

All vital signs data will be listed by subject. Descriptive statistics will be reported for vital signs parameters, excluding temperature, by treatment and assessment time point. Change from baseline will be summarized in a similar manner. Baseline will be defined as the result closest and prior to dosing in each period, including unscheduled or recheck results, whichever is later. This will typically be the predose measurement collected on Day 1 prior to dosing. Change from baseline will not be calculated for the End of Study time point. Postdose unscheduled events or rechecks will not be included in summaries. Similarly, early termination results will not be included in summaries.

7.6 Electrocardiogram

Safety 12-Lead ECG parameters (i.e., HR, PR, QRS, QT, and QTcF [QT corrected for heart rate using Fridericia's equation]) will be measured at the following time points:

Table 7.2. Safety 12-lead ECG Collection Time Points

ECG Parameter	Period	Day	Time Point
HR, PR, QRS, QT, QTcF	Screen		
	1, 2, 3, 4	1	Predose, 15 min, and 12 hours postdose

ECG Parameter	Period	Day	Time Point
	4	3	End of Study or Early Termination

All ECG parameters will be listed by subject and time point of collection with QTcF > 450 msec and change from baseline > 30 msec flagged. Descriptive statistics will be reported for ECG parameters by treatment and assessment time point. Change from baseline will be summarized in a similar manner. Baseline will be defined as the result closest and prior to dosing in each treatment period, including unscheduled or recheck results, whichever is later. This will typically be the predose measurement collected on Day 1 prior to dosing. Change from baseline will not be calculated for the End of Study time point. Postdose unscheduled events or rechecks will not be included in summaries. Similarly, early termination results will not be included in summaries.

7.7 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Dictionary Version 01Mar2019-b3 and listed.

7.8 Physical Examination

Physical examinations will be performed at Screening and 8 hours postdose in each period and EOS (Day 3 of Period 4). Abnormal findings will be reported as medical history or adverse events. All abnormal findings will be listed.

7.9 Investigator Visual Skin Assessment

Each M207 patch site (where a patch has been removed) will be observed by the investigator for erythema, edema, bruising, and bleeding assessments at the following time points:

Table 7.3. Investigator Visual Skin Assessment Time Points

Skin Assessment	Period*	Day	Time Point
Erythema, Edema, Bruising, Bleeding	1, 2, 3, 4	1	Predose, 30 min, 60 min, 8 hours, and 24 hours postdose
* The skin assessments will be performed at the specified time points for Treatments A, B, C. The predose assessment will also be performed prior to Treatment D dosing.			

The erythema evaluations will be performed using the following scale:
0 = None
1 = Mild redness
2 = Moderate colored redness

3 = Beet colored redness

The edema evaluations will be performed using the following scale:
0 = None
1 = Slight edema
2 = Moderate edema
3 = Severe edema

Bruising assessments (visual rating) will be performed using the following scale:
0 = None
1 = ≤ 25% application site has bruising spots
2 = ≥ 26 to ≤ 50% application site has bruising spots
3 = > 50% application site has bruising spots

Bleeding will be assessed using the following scale:
0 = None
1 = Pink color on skin
2 = Visible blood drop
3 = Active bleeding

Scales from the investigator skin assessment of the application sites will be listed by subject and summarized. For each treatment period, assessments will be performed for each patch application site, separately. For the purpose of the analysis, the worst scale between the two patches at each treatment will be used in the summary statistics. For each type of assessment, frequency counts and percentages showing the number of subjects obtaining each scale by treatment and time point will be provided. Percentages will be based on the number of non-missing results per treatment and time point. Descriptive statistics will also be provided for each type of assessment scales by treatment and time point. The average scale for each assessment will be plotted against time.

8. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

The analyses described in this SAP are aligned with those analyses described in the protocol.

9. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Conference on Harmonization (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. Note that all summary tables and figures will be generated using SAS® Version 9.3 or higher and/or using Phoenix® WinNonlin® Version 6.3 or higher, as appropriate.

9.1 In-text Summary Tables and Figures

The following is a list of table and figure titles that will be included in the text of the CSR. Tables and figures will be numbered appropriately during compilation of the CSR.

Section 10:

Table 10-1 Subject Disposition Summary

Section 11:

Table 11-1 Demographic Summary

Figure 11-1 Arithmetic Mean (SD) Plasma Zolmitriptan Concentration-Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Predose to 24 Hours Postdose)

Figure 11-2 Arithmetic Mean (SD) Plasma Zolmitriptan Concentration-Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Predose to 2 Hours Postdose)

Table 11-2 Summary of Plasma Zolmitriptan Pharmacokinetics for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers

Table 11-3 Relative Bioavailability Between Each Treatment for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers

Table 11-4 Residual Amounts of Zolmitriptan in M207 Patches and on Skin Swabs for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes in Healthy Volunteers

Figure 11-3 Arithmetic Mean (SD) Plasma N-Desmethyl Zolmitriptan Concentration-Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers

Section 12:

Table 12-1 Treatment-Emergent Adverse Event Frequency by Treatment- Number of Subjects Reporting the Event (% of Subjects Dosed)

Figure 12-1 Mean Investigator Visual Erythema Assessment Scale by Time Profile

Figure 12-2 Mean Investigator Visual Edema Assessment Scale by Time Profile

Figure 12-3 Mean Investigator Visual Bruising Assessment Scale by Time Profile

Figure 12-4 Mean Investigator Visual Bleeding Assessment Scale by Time Profile

9.2 Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the report. Table and figure titles may be renumbered as appropriate during the compilation of the report.

14.1 Demographic Data Summary Tables

Table 14.1.1 Summary of Disposition (All Randomized Subjects)
Table 14.1.2 Subject Dosing Status and Study Disposition (Safety Population)
Table 14.1.3 Demographic Summary (Safety Population)

14.2 Pharmacokinetic Data Summary Tables and Figures

14.2.1 Plasma Zolmitriptan Tables

Table 14.2.1.1 Plasma Zolmitriptan Concentrations (pg/mL) for M207 3.8 mg (Sled) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment A) (Pharmacokinetic Population)
Table 14.2.1.2 Plasma Zolmitriptan Concentrations (pg/mL) for M207 3.8 mg (MACAP) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment B) (Pharmacokinetic Population)
Table 14.2.1.3 Plasma Zolmitriptan Concentrations (pg/mL) for M207 3.8 mg (MiniMac) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment C) (Pharmacokinetic Population)
Table 14.2.1.4 Plasma Zolmitriptan Concentrations (pg/mL) for Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Treatment D) (Pharmacokinetic Population)
Table 14.2.1.5 Plasma Zolmitriptan Pharmacokinetic Parameters for M207 3.8 mg (Sled) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment A) (Pharmacokinetic Population)
Table 14.2.1.6 Plasma Zolmitriptan Pharmacokinetic Parameters for M207 3.8 mg (MACAP) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment B) (Pharmacokinetic Population)

14.2.2 Plasma Zolmitriptan Figures

Figure 14.2.2.1 Arithmetic Mean (SD) Plasma Zolmitriptan Concentration Versus Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Predose to 24 Hours Postdose) (Linear Scale) (Pharmacokinetic Population)

Figure 14.2.2.2 Arithmetic Mean (SD) Plasma Zolmitriptan Concentration Versus Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Predose to 2 Hours Postdose) (Linear Scale) (Pharmacokinetic Population)

Figure 14.2.2.3 Arithmetic Mean Plasma Zolmitriptan Concentration Versus Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Predose to 24 Hours Postdose) (Linear Scale) (Pharmacokinetic Population)

Figure 14.2.2.4 Mean Plasma Zolmitriptan Concentration Versus Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Predose to 2 Hours Postdose) (Linear Scale) (Pharmacokinetic Population)

14.2.3 Plasma N-Desmethyl Zolmitriptan Tables

Table 14.2.3.1 Plasma N-Desmethyl Zolmitriptan Concentrations (pg/mL) for M207 3.8 mg (Sled) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment A) (Pharmacokinetic Population)

Table 14.2.3.2 Plasma N-Desmethyl Zolmitriptan Concentrations (pg/mL) for M207 3.8 mg (MACAP) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment B) (Pharmacokinetic Population)

Table 14.2.3.3 Plasma N-Desmethyl Zolmitriptan Concentrations (pg/mL) for M207 3.8 mg (MiniMac) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment C) (Pharmacokinetic Population)

Table 14.2.3.4 Plasma N-Desmethyl Zolmitriptan Concentrations (pg/mL) for Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Treatment D) (Pharmacokinetic Population)

Table 14.2.3.5 Plasma N-Desmethyl Zolmitriptan Pharmacokinetic Parameters for M207 3.8 mg (Sled) on the Upper Arm for

14.2.4 Plasma N-Desmethyl Zolmitriptan Figures

14.3 Safety Data Summary Tables and Figures

14.3.1 Displays of Adverse Events

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subject Dosed) (Safety Population)

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Drug – Number (%) of Subjects Reporting the Event (Safety Population)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events (Safety Population)

14.3.3 Narratives of Deaths, other Serious and Certain other Significant Adverse Events

14.3.4 Abnormal Laboratory Value Listing (each patient)

Table 14.3.4.1 Out-of-Range Clinical Laboratory Values and Recheck Results (Safety Population)

Table 14.3.4.2 Clinically Significant Values According to PI and Recheck Results (Safety Population)

14.3.5 Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data

14.3.5.1 Vital Sign, Electrocardiogram and Investigator Visual Skin Assessment Tables

Table 14.3.5.1.1 Vital Sign Summary and Change From Baseline (Safety Population)

Table 14.3.5.1.2 12-Lead Electrocardiogram Summary and Change From Baseline (Safety Population)

Table 14.3.5.1.3 Frequency Counts of Investigator Visual Skin Assessment (Safety Population)

Table 14.3.5.1.4 Summary of Investigator Visual Skin Assessment (Safety Population)

14.3.5.2 Investigator Visual Skin Assessment Figures

Figure 14.3.5.2.1 Mean Investigator Visual Erythema Assessment Scale by Time Profile (Safety Population)

Figure 14.3.5.2.2 Mean Investigator Visual Edema Assessment Scale by Time Profile (Safety Population)

Figure 14.3.5.2.3 Mean Investigator Visual Bruising Assessment Scale by Time Profile (Safety Population)

Figure 14.3.5.2.4 Mean Investigator Visual Bleeding Assessment Scale by Time Profile (Safety Population)

9.3 Section 16 Data Listings

Note: Hepatitis and HIV results that are provided by the clinical laboratory will not be presented in subject data listings and will not be included in any database transfer.

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the TFLs for the CSR. The following is a list of appendix numbers and titles that will be included as data listings:

16.1 Study Information

Appendix 16.1.9 Statistical Methods

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

16.2 Subject Data Listings

16.2.1 Subject Discontinuation

Appendix 16.2.1 Subject Discontinuation (All Randomized Subjects)

16.2.2 Protocol Deviations

Appendix 16.2.2 Protocol Deviations

16.2.3 Subjects Excluded from Pharmacokinetic Analysis

Appendix 16.2.3 Subjects Excluded from Pharmacokinetic Analysis

Note: Appendices 16.2.2 and 16.2.3 are generated in MS Word for inclusion in the study report.

16.2.4 Demographic Data

Appendix 16.2.4.1	Demographics (Safety Population)
Appendix 16.2.4.2	Physical Examination Abnormal Findings (Safety Population)
Appendix 16.2.4.3	Medical and Surgical History (Safety Population)
Appendix 16.2.4.4	Substance Use (Safety Population)

16.2.5 Compliance and/or Drug Concentration Data

Appendix 16.2.5.1.1	Inclusion Criteria
Appendix 16.2.5.1.2	Exclusion Criteria
Appendix 16.2.5.2	Subject Eligibility (Safety Population)
Appendix 16.2.5.3	Check-in Responses (Safety Population)
Appendix 16.2.5.4	Test Compound Administration Times (Safety Population)
Appendix 16.2.5.5	Blood Draw Times (Safety Population)
Appendix 16.2.5.6	Meal Times (Safety Population)
Appendix 16.2.5.7	Prior and Concomitant Medications (Safety Population)

16.2.6 Individual Pharmacokinetic Response Data

Appendix 16.2.6.1	Plasma Zolmitriptan Concentration Versus Time Profiles for Subject <X> for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg (Linear Scale)
Appendix 16.2.6.2	Plasma N-Desmethyl Zolmitriptan Concentration Versus Time Profiles for Subject <X> for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg (Linear Scale)
Appendix 16.2.6.3	Residual Amounts of Zolmitriptan in M207 Patches for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg (Safety Population)
Appendix 16.2.6.4	Residual Amounts of Zolmitriptan on Skin Swabs for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg (Safety Population)

16.2.7 Adverse Events Listings

Appendix 16.2.7.1.1	Adverse Events (I of II) (Safety Population)
Appendix 16.2.7.1.2	Adverse Events (II of II) (Safety Population)
Appendix 16.2.7.2	Adverse Event Non-Drug Therapy (Safety Population)

16.2.8 Listings of Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1.1	Clinical Laboratory Report - Serum Chemistry (Safety Population)
Appendix 16.2.8.1.2	Clinical Laboratory Report - Hematology (Safety Population)
Appendix 16.2.8.1.3	Clinical Laboratory Report - Urinalysis (Safety Population)
Appendix 16.2.8.1.4	Clinical Laboratory Report - Urine Drug Screening (Safety Population)
Appendix 16.2.8.1.5	Clinical Laboratory Report - Comments (Safety Population)
Appendix 16.2.8.2	Vital Signs (Safety Population)
Appendix 16.2.8.3	12-Lead Electrocardiogram (Safety Population)
Appendix 16.2.8.4	Investigator Visual Skin Assessments (Safety Population)

10. TABLE AND FIGURE SHELLS

The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables that will be presented and included in the final report. Unless otherwise noted, all in-text tables will be presented in Times New Roman font size 9 and all post-text tables will be presented in Courier New font size 9. These tables will be generated off of the Celerion AdaM Model 2.1 and AdaM Implementation Guide 1.1.

10.1 In-text Summary Tables Shells

In-text Table 10-1 will be in the following format:

Table 10-1 Subject Disposition Summary

	Randomized Treatment Sequence				
Disposition	**ABDC**	**BCAD**	**CDBA**	**DACB**	**Overall**
Enrolled (Randomized)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Safety Population	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Completed Study	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)
Discontinued Early	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)
<Reason1>	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)
<Reason2>	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)

Treatment A: < description>
Treatment B: < description>
Treatment C: < description>
Treatment D: < description>

<AE =Adverse event >

Source: Table 14.1.1
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_disp.sas DDMMMYYYY HH:MM

In-text Table 11-1 will be in the following format:

Table 11-1 Demographic Summary

		Randomized Treatment Sequence				
Trait	**Category/Statistics**	**ABDC**	**BCAD**	**CDBA**	**DACB**	**Overall**
Sex	Male	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Female	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Race	Asian	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	American Indian or Alaska Native	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Black or African American	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Native Hawaiian or Pacific Islander	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	White	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Ethnicity	Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Not Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Age* (yrs)	n	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX

Treatment A: < description>
Treatment B: < description>
Treatment C: < description>
Treatment D: < description>
BMI = Body mass index
*Age is derived from birth date to date of informed consent .

Source: Table 14.1.3
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_dem.sas DDMMMYYYY HH:MM

Programmer Notes: Height (cm), Weight(kg), and BMI (kg/m²) at screening will be also summarized in the table above.

Table 11-2 Summary of Plasma Zolmitriptan Pharmacokinetics for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers

Pharmacokinetic Parameters	M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)	Zolmitriptan 2.5 mg (Intranasal)
AUC0-30min (pg•hr/mL)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
AUC0-60min (pg•hr/mL)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
AUC0-120min (pg•hr/mL)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
AUC0-t (pg•hr/mL)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
AUC0-inf (pg•hr/mL)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Cmax (pg/mL)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Tmax (hr)	XXX.X (XX.X, XX.X) [n=xx]	XXX.X (XX.X, XX.X) [n=xx]	XXX.X (XX.X, XX.X) [n=xx]	XXX.X (XX.X, XX.X) [n=xx]
t½ (hr)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Kel (1/hr)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
Zolmitriptan 2.5 mg (Intranasal): Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D)
AUC and Cmax values are presented as geometric mean and geometric CV%.
Tmax values are presented as median (min, max).
Other parameters are presented as arithmetic mean (± SD).
NA = Not applicable
Source: Tables 14.2.1.5 to 14.2.1.8

Notes for Generating the Actual Table:

Presentation of Data:

- n will be presented as an integer (with no decimal). If n is the same for all parameters within a given treatment for all 4 treatments, the n will be presented in the treatment header only.
- Summary statistics will be presented with same precision as defined in post-text shells

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell: Two additional treatment columns were added.

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

Table 11-3 Relative Bioavailability Between Each Treatment for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers

Pharmacokinetic Parameters	Geom Mean (Geom CV%)
%Frel(A/B) (%)	XXX.X (XX.X) [n=xx]
%Frel(A/C) (%)	XXX.X (XX.X) [n=xx]
%Frel(A/D) (%)	XXX.X (XX.X) [n=xx]
%Frel(B/C) (%)	XXX.X (XX.X) [n=xx]
%Frel(B/D) (%)	XXX.X (XX.X) [n=xx]
%Frel(C/D) (%)	XXX.X (XX.X) [n=xx]
M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A) M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B) M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C) Zolmitriptan 2.5 mg (Intranasal): Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D) Source: Table 14.2.1.13	

Notes for Generating the Actual Table:

Presentation of Data:

- n will be presented as an integer (with no decimal). If n is the same for all parameters, the n will be presented along with the "Geom Mean (Geom CV%)" header.
- Geom Mean and Geom CV% will be presented with same precision as defined in post-text shells

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell: One column was deleted.

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

Table 11-4 Residual Amounts of Zolmitriptan in M207 Patches and on Skin Swabs for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes in Healthy Volunteers

PharmacokineticParameters	M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)
Residual Amount in Both Patches Combined (mg)	XX.X (XX.X) [n=xx]	XX.X (XX.X) [n=xx]	XX.X (XX.X) [n=xx]
Residual Amount on Both Skin Surfaces Combined (mg)	XX.X (XX.X) [n=xx]	XX.X (XX.X) [n=xx]	XX.X (XX.X) [n=xx]
Actual Dose Administered (mg)	XX.X (XX.X) [n=xx]	XX.X (XX.X) [n=xx]	XX.X (XX.X) [n=xx]

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
Actual Dose Administered = Nominal Dose – Residual Amount in Both Patches Combined – Residual Amount on Both Skin Surfaces Combined
Source: Tables 14.2.1.14 to 14.2.1.16

Notes for Generating the Actual Table:

Presentation of Data:

- n will be presented as an integer (with no decimal). If n is the same for all parameters within a given treatment for all 3 treatments, the n will be presented in the treatment header only.
- Summary statistics will be presented with same precision as defined in post-text shells

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell: One additional treatment column was added.

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

In-text Table 12-1 will be in the following format:

Table 12-1 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed)

	Treatment				
Adverse Event*	**M207 3.8 mg (Sled)**	**M207 3.8 mg (MACAP)**	**M207 3.8 mg (MiniMac)**	**Zolmitriptan 2.5 mg (Intranasal)**	**Overall**
Number of Subjects Dosed	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Number of Subjects With TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
System Organ Class 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
System Organ Class 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

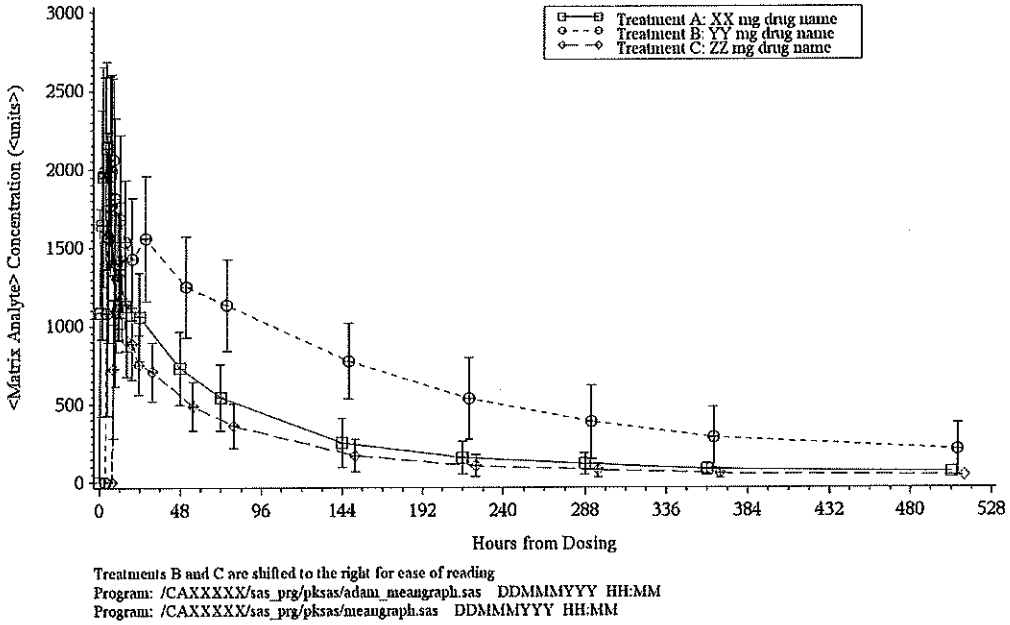
M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
Zolmitriptan 2.5 mg (Intranasal): Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D)
*Adverse events are coded using MedDRA® Version 20.1.
If a subject has 2 or more clinical adverse events, the subject is counted only once within a category. The same subject may appear in different categories.
TEAEs = Treatment-emergent adverse events

Source: Table 14.3.1.1
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_ae.sas DDMMMYYYY HH:MM

10.2 Figures Shells

Figures 11-1 to 11-3, 14.2.2.1, 14.2.2.2, and 14.2.4.1 will be in the following format:

Figure 11-1 Arithmetic Mean (SD) Plasma Zolmitriptan Concentration-Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Predose to 24 Hours Postdose)



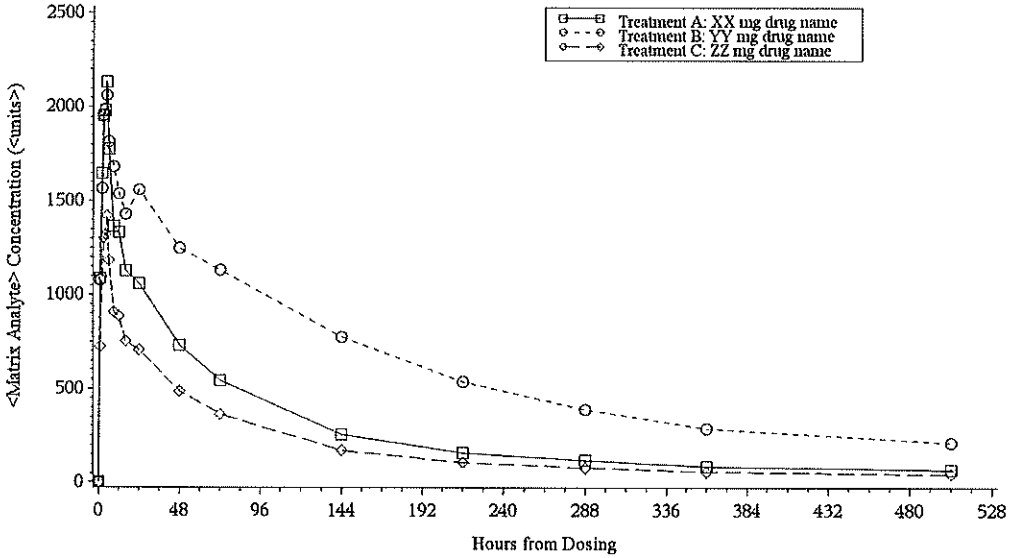
Notes:

- Titles of Figures 14.2.2.1, 14.2.2.2, and 14.2.4.1 will include: "(Pharmacokinetic Population)".
- Legend will include: "M207 3.8 mg (Sled)", "M207 3.8 mg (MACAP)", "M207 3.8 mg (MiniMac)", and "Zolmitriptan 2.5 mg (Intranasal)".
- Y-axis labels will be:
  - Figures 11-1, 11-2, 14.2.2.1, and 14.2.2.2: "Plasma Zolmitriptan Concentration (pg/mL)".
  - Figures 11-3 and 14.2.4.1: "Plasma N-Desmethyl Zolmitriptan Concentration (pg/mL)".
- Plots for Treatments B, C, and D will be shifted to the right for ease of reading and the following footer will be added: "Plots for Treatments B, C, and D are shifted to the right for ease of reading."

Figures 14.2.2.3, 14.2.2.4, and 14.2.4.2 will be in the following format:

Figure 14.2.2.3

Arithmetic Mean Plasma Zolmitriptan Concentration Versus Time Profiles for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Predose to 24 Hours Postdose) (Linear Scale)
(Pharmacokinetic Population)



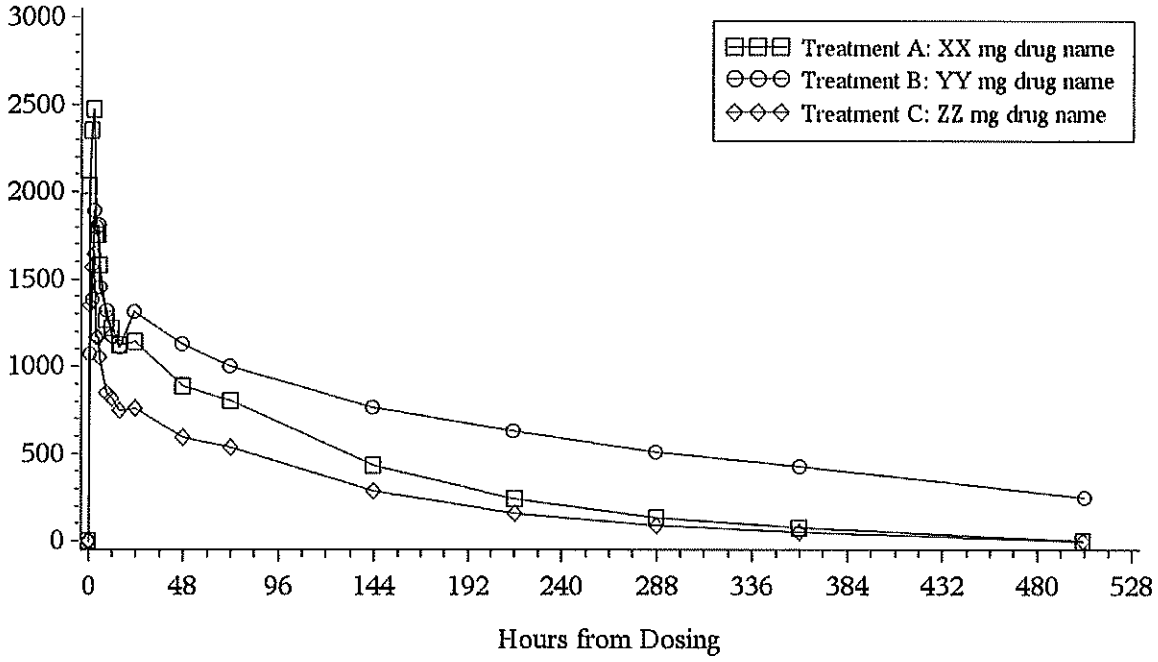
Notes:

- Legend will include: "M207 3.8 mg (Sled)", "M207 3.8 mg (MACAP)", "M207 3.8 mg (MiniMac)", and "Zolmitriptan 2.5 mg (Intranasal)".
- Y-axis labels will be:
  - Figures 14.2.2.3 and 14.2.2.4: "Plasma Zolmitriptan Concentration (pg/mL)".
  - Figure 14.2.4.2: "Plasma N-Desmethyl Zolmitriptan Concentration (pg/mL)".

Figures 12-1 to 12-4 and 14.3.5.2.1 to 14.3.5.2.4 will be in the following format:

Figure 14.3.5.2.1

Mean Investigator Visual Erythema Assessment Scale by Time Profile (Safety Population)



Notes for Generating the Actual Individual Figure:

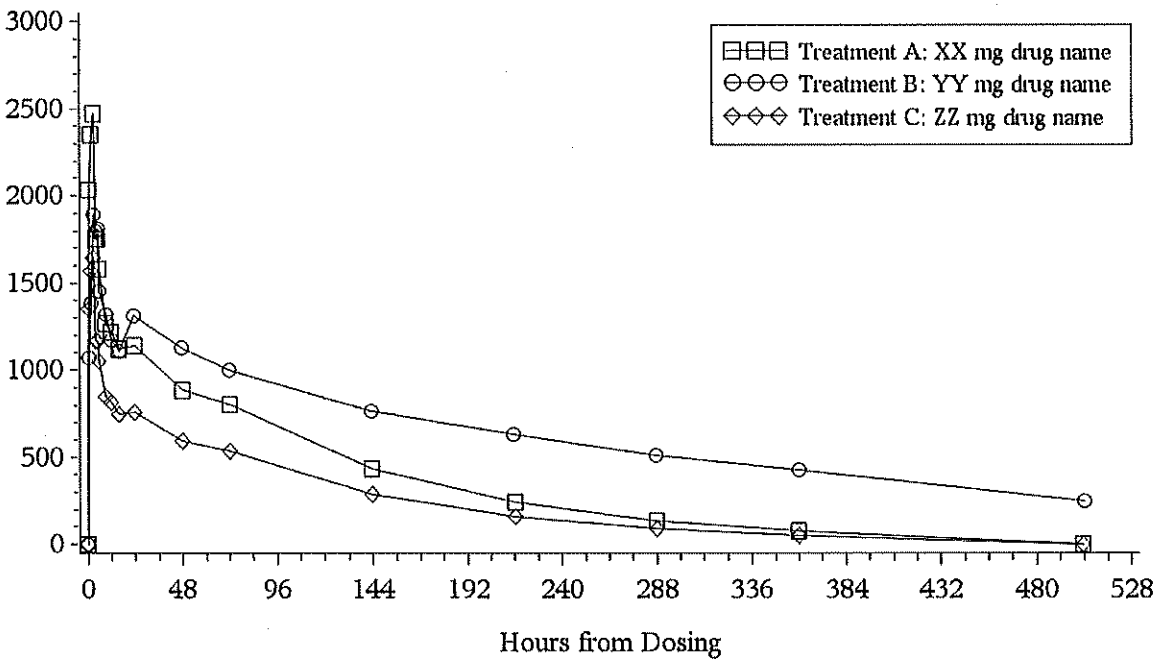
- Legend will include: "M207 3.8 mg (Sled)", "M207 3.8 mg (MACAP)", and "M207 3.8 mg (MiniMac)".
- Y-axis label will be:
  - Figure 12-1 and 14.3.5.2.1: "Investigator Visual Erythema Assessment Scale".
  - Figure 12-2 and 14.3.5.2.2: "Investigator Visual Edema Assessment Scale".
  - Figure 12-3 and 14.3.5.2.3: "Investigator Visual Bruising Assessment Scale".
  - Figure 12-4 and 14.3.5.2.4: "Investigator Visual Bleeding Assessment Scale".

Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_indgraph.sas DDMMMYYYY HH:MM

Appendices 16.2.6.1 and 16.2.6.2 will be in the following format:

Appendix 16.2.6.1

Plasma Zolmitriptan Concentration Versus Time Profiles for Subject <X> for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg (Linear Scale)



Notes for Generating the Actual Individual Figure:

- Legend will include: "M207 3.8 mg (Sled)", "M207 3.8 mg (MACAP)", "M207 3.8 mg (MiniMac)", and "Zolmitriptan 2.5 mg (Intranasal)".
- Y-axis label will be:
  - Appendix 16.2.6.1: "Plasma Zolmitriptan Concentration (pg/mL)".
  - Appendix 16.2.6.2: "Plasma N-Desmethyl Zolmitriptan Concentration (pg/mL)".

Program: /CAXXXXX/sas_prg/pksas/indgraph-all.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_indgraph.sas DDMMMYYYY HH:MM

10.3 Section 14 Summary Tables Shells

Table 14.1.1 will be in the following format:

Part 1 of X

Table 14.1.1 Summary of Disposition (All Randomized Subjects)

	Randomized Treatment Sequence				
Category	ABDC	BCAD	CDBA	DACB	Overall
Enrolled (Randomized)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Safety Population	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Completed Study	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Discontinued Early	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
<Reason1>	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
<Reason2>	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
<AE = Adverse event>

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.1.2 will be in the following format:

Table 14.1.2 Subject Dosing Status and Study Disposition (Safety Population)

Subject Number	Treatment Sequence	Dosed				Study Completion Status	Date
		A	B	C	D		
X	XXXX	Yes	Yes	Yes	Yes	Completed Study	DDMMYYYY
X	XXXX	Yes	Yes	No	Yes	Terminated Study Prematurely	DDMMYYYY
X	XXXX	Yes	Yes	Yes	Yes	Completed Study	DDMMYYYY
X	XXXX	Yes	Yes	Yes	Yes	Completed Study	DDMMYYYY
X	XXXX	Yes	Yes	Yes	Yes	Completed Study	DDMMYYYY
X	XXXX	Yes	Yes	Yes	Yes	Completed Study	DDMMYYYY
		XX	XX	XX	XX		

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.1.3 will be in the following format:

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Table 14.1.3 Demographic Summary (Safety Population)

Trait		Randomized Treatment Sequence ABDC	BCAD	CDBA	DACB	Overall
Sex	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Race	American Indian or Alaska Native	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Asian	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Black or African American	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Native Hawaiian or Pacific Islander	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	White	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Ethnicity	Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Not Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Age* (yr)	n	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
* Age is derived from birth date to date of informed consent.
BMI = Body mass index

Programmer Note: Height (cm), Weight(kg), and BMI (kg/m²) at screening will be also summarized in the table above.
Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.2.1.1 to 14.2.1.4 and 14.2.3.1 to 14.2.3.4 will be in the following format:

Table 14.2.1.1. Plasma Zolmitriptan Concentrations (<units>) for M207 3.8 mg (Sled) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment A) (Pharmacokinetic Population)

Subject Number	Treatment Sequence	Study Period	Sample Times (hr)								
			Predose	XX	XX	XX	XX	XX	XX	XX	XX
X	XXXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	XXXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	XXXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
n			XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%			.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum			XX	XX	XX	XX	XX	XX	XX	XX	XX
Median			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Maximum			XX	XX	XX	XX	XX	XX	XX	XX	XX

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as <0> before the first quantifiable concentration and as missing elsewhere.
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:
Concentrations will be presented to same precision as in bio data.
Summary statistics presentation with respect to the precision of the bio data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal
Programmer Note:
PK Time points are: Predose and 0.0333, 0.0833, 0.1667, 0.25, 0.3333, 0.5, 0.75, 1, 1.5, 2, 4, 8, 12, and 24 hours postdose.
Program: /CAXXXXX/sas_prg/pksas/pk-conc-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/pk-conc-tables-sig.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_conc.sas DDMMMYYYY HH:MM

Tables 14.2.1.5 to 14.2.1.8 and 14.2.3.5 to 14.2.3.8 will be in the following format:

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Table 14.2.1.5. Plasma Zolmitriptan Pharmacokinetic Parameters for M207 3.8 mg (Sled) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment A) (Pharmacokinetic Population)

			Parameters					
Subject Number	Treatment Sequence	Study Period	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
X	XXXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXXX	X	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
n			XX	XX	XX	XX	XX	XX
Mean			XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
SD			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum			XX.X	X.XX	XXX	XXX	XX.X	X.XXX
Median			XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Maximum			XXX	X.XX	XXX	XXX	XX.X	X.XXX
Geom Mean			XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Geom CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- PK Parameters will be presented in the following order and with following units: AUC0-30min (pg•hr/mL), AUC0-60min (pg•hr/mL), AUC0-120min (pg•hr/mL), AUC0-t (pg•hr/mL), AUC0-inf (pg•hr/mL), Cmax (pg/mL), Tmax (hr), $t_{½}$ (hr), and Kel (1/hr).

- For Tables 14.2.3.5 to 14.2.3.8, AUC0-inf(m/p) will be presented after AUC0-inf.
- n will be presented as an integer (with no decimal);
- AUCs, Cmax, and Kel will be presented with, at maximum, the precision of the bio data, and, at minimum, 3 significant figures (to be determined by the PKist once bio data are received).
- Tmax and t1/2 will be presented with 2 decimals. Summary statistics for time-based parameters will be presented as: Mean, Median, and Geom Mean +1; SD +2, Min and Max +0.
- Summary statistics for exposure parameters will be presented as: Mean, Median, and Geom Mean +1; SD and SEM +2, Min and Max +0; CV% and Geom CV% to 1 decimal place.

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_pkparam.sas DDMMMYYYY HH:MM

Tables 14.2.1.9 to 14.2.1.12 and 14.2.3.9 to 14.2.3.12 will be in the following format:

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Table 14.2.1.9. Intervals (Hours) Used for Determination of Plasma Zolmitriptan Kel Values for M207 3.8 mg (Sled) on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment A) (Pharmacokinetic Population)

Subject Number	Treatment	Interval	R^2	n
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X

M207 3.8 mg (Sled) = M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
R^2 = Coefficient of determination
n = Number of points used in Kel calculation
. = Kel value not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Interval start and stop times will be presented to 1 decimal or 3 sig figures min;
- R^2 will be presented to 3 decimals;
- n will be presented as an integer (with no decimal).

Program: /CAXXXXX/sas_prg/pksas/kel-tables-parallel.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_kel.sas DDMMMYYYY HH:MM

Table 14.2.1.13. Relative Bioavailability Between Each Treatment for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes and Intranasal Zolmitriptan 2.5 mg in Healthy Volunteers (Pharmacokinetic Population)

	Parameters					
Subject Number	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
n	XX	XX	XX	XX	XX	XX
Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
Median	XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Maximum	XXX	X.XX	XXX	XXX	XX.X	X.XXX
Geom Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Geom CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
Zolmitriptan 2.5 mg (Intranasal): Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D)
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- PK Parameters will be presented in the following order and with following units: %Frel(A/B) (%), %Frel(A/C) (%), and %Frel(A/D) (%), %Frel(B/C) (%), and %Frel(B/D) (%), and %Frel(C/D) (%).
- n will be presented as an integer (with no decimal);
- Parameters will be presented to 1 decimal place.
- Summary statistics for exposure parameters will be presented as: Mean, Median, and Geom Mean +1; SD and SEM +2, Min and Max +0; CV% and Geom CV% to 1 decimal place.

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_pkparam.sas DDMMMYYYY HH:MM

Tables 14.2.1.14 to 14.2.1.16 will be in the following format:

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Table 14.2.1.14. Residual Amounts of Zolmitriptan in M207 Patches and on Skin Swabs for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes in Healthy Volunteers (Treatment A) (Safety Population)

Subject Number	Treatment Sequence	Study Period	Residual Amount in Patches (mg)	Residual Amount on Skin Swabs (mg)	Actual Dose Administered (mg)
X	XXXX	X	XX	XX	XX
X	XXXX	X	XX	XX	XX
X	XXXX	X	XX	XX	XX
n			XX	XX	XX
Mean			XX.X	XX.X	XX.X
SD			XX.XX	XX.XX	XX.XX
CV%			XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX
Minimum			XX	XX	XX
Median			XX.X	XX.X	XX.X
Maximum			XX	XX	XX

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
Residual Amount in patches = Residual amount in both patches combined
Residual Amount on skin swabs = Residual amount on both skin surfaces combined
Actual Dose Administered = Nominal Dose - Residual Amount in Patches - Residual Amount on Skin Swabs
For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as <0>.
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:
Residual amounts will be presented to same precision as in bio data.
Summary statistics presentation with respect to the precision of the bio data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_pkparam.sas DDMMMYYYY HH:MM

Table 14.3.1.1 will be in the following format:

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Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)

	Treatment				
Adverse Event*	M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)	Zolmitriptan 2.5 mg (Intranasal)	Overall
Number of Subjects Dosed	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)
Number of Subjects With TEAEs	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XXX%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
Zolmitriptan 2.5 mg (Intranasal): Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D)
* Adverse events are coded using MedDRA Version 20.1.
If a subject has 2 or more clinical adverse events, the subject is counted only once within a category. The same subject may appear in different categories.
TEAEs = Treatment-emergent adverse events

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.1.2 will be in the following format:

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Adverse Events (% of Total Adverse Events) (Safety Population)

	Treatment				
Adverse Event*	M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)	Zolmitriptan 2.5 mg (Intranasal)	Overall
Number of TEAEs	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
Zolmitriptan 2.5 mg (Intranasal): Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D)
* Adverse events are coded using MedDRA Version 20.1.
TEAEs = Treatment-emergent adverse events

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.1.3 will be in the following format:

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Study Drug – Number (%) of Subjects Reporting the Event (Safety Population)

Adverse Event*	Treatment	Number of Subjects With TEAEs	Severity Grade			Relationship to Study Drug		
			Mild	Moderate	Severe	Probably Related	Possibly Related	Not Related
Abdominal pain	A	X	X	X	X	X	X	X
Constipation	B	X	X	X	X	X	X	X
Dry throat	B	X	X	X	X	X	X	X
Dysmenorrhoea	C	X	X	X	X	X	X	X
Dyspepsia	D	X	X	X	X	X	X	X
Headache	C	X	X	X	X	X	X	X
	D	X	X	X	X	X	X	X
Myalgia	A	X	X	X	X	X	X	X
Nasal congestion	B	X	X	X	X	X	X	X
Skin laceration	C	X	X	X	X	X	X	X
Treatment A		X	X	X	X	X	X	X
Treatment B		X	X	X	X	X	X	X
Treatment C		X	X	X	X	X	X	X
Treatment D		X	X	X	X	X	X	X
Overall		X	X	X	X	X	X	X

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
* Adverse events are coded using MedDRA Version 20.1.
TEAEs = Treatment-emergent adverse events
When a subject experienced the same AE at more than one level of severity during a treatment period, the AE with the maximum severity was counted. When a subject experienced the same AE at more than one level of drug relationship during a treatment period, the most related AE was counted.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.2.1 will be in the following format:

Table 14.3.2.1 Serious Adverse Events (Safety Population)

Programmer Note: Will match 16.2.7 or contain the following statement: "There were no serious adverse events recorded during the study."

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.4.1 Out-of-Range Clinical Laboratory Values and Recheck Results (Safety Population)

Subject Number	Age#/ Sex	Study Period	Day	Hour	Date	Time	Department	Test	Result		Reference Range	Unit
X	XX/X	X	X	XXX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX		X - X	mg/dL
			X	XXX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HYR+	X - X	mg/dL
			X	XXX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HY+	X - X	mg/dL
			X	XXX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HN	X - X	mg/dL

# Age is derived from birth date to date of informed consent. F = Female, M = Male
H = Above reference range, L = Below reference range
Computer: N = Not clinically significant, Y = Clinically significant
PI Interpretation: - = Not clinically significant, R = Recheck requested, ^ = Will be retested later, + = Clinically significant

Programmer Notes: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early termination records chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for. Add fourth flag in the cases that ^ or R are used for the PI flag. This flag will be found in the ClinQuick Extraction.

Program: /CAXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.4.2 Clinically Significant Values According to PI and Recheck Results (Safety Population)

Subject Number	Age#/ Sex	Study Period	Day	Date	Time	Department	Test	Result		Reference Range	Unit
X	XX/X	X	X	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX		X - X	mg/dL
			X	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HYR+	X - X	mg/dL
			X	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HY+	X - X	mg/dL
			X	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HN	X - X	mg/dL

# Age is derived from birth date to date of informed consent. F = Female, M = Male
H = Above reference range
Computer: Y = Clinically significant
PI Interpretation: R = Recheck requested, + = Clinically significant

Programmer Note: All time points for a subject/test with at least one value deemed as CS by the PI will be presented in this table. If there were no CS values as deemed by PI (i.e., no "CS" or "Clinically Significant" in the PI flag [3rd or 4th field] in the laboratory dataset), then this table will contain only the statement: "There were no laboratory values deemed clinically significant by the PI in the study."

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.5.1.1 will be in the following format:

Table 14.3.5.1.1 Vital Sign Summary and Change From Baseline (Safety Population)

Vital Sign (unit)	Time Point	Statistic	Overall	Treatment				Change From Baseline*			
				M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)	Zolmitriptan 2.5 mg (Intranasal)	M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)	Zolmitriptan 2.5 mg (Intranasal)
Testname (unit)	Screening	n	X								
		Mean	X.X								
		SD	X.XX								
		Minimum	XX								
		Median	X.X								
		Maximum	XX								
	Day -1	n	X								
		Mean	X.X								
		SD	X.X								
		Minimum	X.XX								
		Median	XX								
		Maximum	X.X								
	Day 1, Predose	n		X	X	X	X				
		Mean		X.X	X.X	X.X	X.X				
		SD		X.XX	X.XX	X.XX	X.XX				
		Minimum		XX	XX	XX	XX				
		Median		X.X	X.X	X.X	X.X				
		Maximum		XX	XX	XX	XX				
	Day 1, 10 Min	n		X	X	X	X	X	X	X	X
		Mean		X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD		X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum		XX	XX	XX	XX	XX	XX	XX	XX
		Median		X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum		XX	XX	XX	XX	XX	XX	XX	XX

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
Zolmitriptan 2.5 mg (Intranasal): Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D)
*Baseline is the last non-missing assessment prior to dosing in each period (Day 1 Predose).
Supine and sitting measurement were pooled in the summaries.

Programmer Notes: Similar for all time points and vital signs. Change from baseline will not be calculated for the End of Study (Day 3 of Period 4) time point. The End of Study time point will be summarized in the Overall column.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.5.1.2 will be in the following format:

Table 14.3.5.1.2 12-Lead Electrocardiogram Summary and Change From Baseline(Safety Population)

Parameter (unit)	Time Point	Statistic	Overall	Treatment				Change From Baseline*			
				M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)	Zolmitrip-tan 2.5 mg (Intranasal)	M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)	Zolmitrip-tan 2.5 mg (Intranasal)
Parameter (unit)	Screening	n	X								
		Mean	X.X								
		SD	X.XX								
		Minimum	XX								
		Median	X.X								
		Maximum	XX								
	Day 1, Predose	n		X	X	X	X				
		Mean		X.X	X.X	X.X	X.X				
		SD		X.XX	X.XX	X.XX	X.XX				
		Minimum		XX	XX	XX	XX				
		Median		X.X	X.X	X.X	X.X				
		Maximum		XX	XX	XX	XX				
	Day 1, 15 Min	n		X	X	X	X	X	X	X	X
		Mean		X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD		X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum		XX	XX	XX	XX	XX	XX	XX	XX
		Median		X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum		XX	XX	XX	XX	XX	XX	XX	XX

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)

Zolmitriptan 2.5 mg (Intranasal): Zolmitriptan 2.5 mg administered intranasally as a single 2.5 mg/0.1 mL spray (Treatment D)
*Baseline is the last non-missing assessment prior to dosing in each period (Day 1 Predose).

Programmer Notes: Similar for all time points and ECG parameters. Change from baseline will not be calculated for the End of Study (Day 3 of Period 4) time point. The End of Study time point will be summarized in the Overall column.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.5.1.3 will be in the following format:

Table 14.3.5.1.3 Summary of Investigator Visual Skin Assessment (Safety Population)

Skin Assessment	Treatment	Time Point	N	Skin Assessment Scales*			
				0	1	2	3
Erythema	X	Day 1, Predose	X	X (XX.X%)	X (XX.X%)	X (X.XX%)	X (XX.X%)
		Day 1, 30 Min	X	X (XX.X%)	X (XX.X%)	X (X.XX%)	X (XX.X%)
		Day 1, 60 Min	X	X (XX.X%)	X (XX.X%)	X (X.XX%)	X (XX.X%)
		Day 1, 8 Hours	X	X (XX.X%)	X (XX.X%)	X (X.XX%)	X (XX.X%)
		Day 2, 24 Hours	X	X (XX.X%)	X (XX.X%)	X (X.XX%)	X (XX.X%)

<Similar for all skin assessments, treatments and time points>

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
N = Number of non-missing observations. Percentages are based on the number of non-missing observations.
At each treatment and time point, the worst assessment scale between the two dosing patches application sites was used in the summaries.
* Scale descriptions:
Erythema: 0 = None; 1 = Mild redness; 2 = Moderate colored redness; 3 = Beet colored redness
Edema: 0 = None; 1 = Slight edema; 2 = Moderate edema; 3 = Severe edema
Bruising (visual rating): 0 = None; 1 = ≤ 25% application site has bruising spots; 2 = ≥ 26 to ≤ 50% application site has bruising spots; 3 = > 50% application site has bruising spots
Bleeding: 0 = None; 1 = Pink color on skin; 2 = Visible blood drop; 3 = Active bleeding

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.5.1.4 will be in the following format:

Table 14.3.5.1.4 Summary of Investigator Visual Skin Assessment(Safety Population)

Skin Assessment	Time Point	Statistic	Treatment		
			M207 3.8 mg (Sled)	M207 3.8 mg (MACAP)	M207 3.8 mg (MiniMac)
Erythema	Day 1, Predose	n	X	X	X
		Mean	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
	Day 1, 30 Min	n	X	X	X
		Mean	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX

<Similar for all skin assessments and time points>

M207 3.8 mg (Sled): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "Sled" coater and packaged in foil pouches (Treatment A)
M207 3.8 mg (MACAP): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MACAP" coater and packaged in foil cups (Treatment B)
M207 3.8 mg (MiniMac): M207 3.8 mg administered as two 1.9 mg patches 30 min wear time (upper arm application) - made on a "MiniMac" coater and packaged in foil cups (Treatment C)
At each treatment and time point, the worst assessment scale between the two dosing patches application sites was used in the summaries.
* Scale descriptions:
Erythema: 0 = None; 1 = Mild redness; 2 = Moderate colored redness; 3 = Beet colored redness
Edema: 0 = None; 1 = Slight edema; 2 = Moderate edema; 3 = Severe edema
Bruising (visual rating): 0 = None; 1 = ≤ 25% application site has bruising spots; 2 = ≥ 26 to ≤ 50% application site has bruising spots; 3 = > 50% application site has bruising spots
Bleeding: 0 = None; 1 = Pink color on skin; 2 = Visible blood drop; 3 = Active bleeding
Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

11. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final report. These listings will be generated off of the Celerion SDTM Tabulation Model 1.4 mapped in accordance with SDTM Implementation Guide 3.2. All listings will be presented in Courier New font size 9.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Laboratory Group	Test Name	Sex	Age Category	Reference Range	Units
Serum Chemistry	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units
Hematology	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units
	Test Name	XXXXXX	XX	XX - XX	units

<similar for remaining Laboratory Groups and Test Names>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.1.1 Subject Discontinuation (All Randomized Subjects)

Subject Number	Safety Population	Randomized Treatment Sequence	Actual Treatment Sequence	Date of Completion or Discontinuation	Completed Study?	Primary Discontinuation Reason	Specify
X	Yes	XXX	XXX	DDMMMYYYY	YES		
X	Yes	XXX	XXX	DDMMMYYYY	YES		
X	Yes	XXX	XXX	DDMMMYYYY	NO	Adverse Event	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.1 Demographics (Safety Population)

Subject Number	Date Of Birth	Age* (yrs)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m²)	Informed Consent Date
X	DDMMMYYYY	XX	Male	< >	Not Hispanic or Latino	XXX	XX.X	XX.XX	DDMMMYYYY
X	<similar to above>								

* Age is derived from birth date to informed consent.

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2 Physical Examination Abnormal Findings (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Date	Result	System	Description or Comment
X	Screen				DDMONYYYY	Abnormal	XXXXX	< >
	X	X	X	XXXX	DDMONYYYY	Abnormal	XXXXX	< >
	X	X	X	XXXX	DDMONYYYY	Abnormal	XXXXX	< >

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
HEENT = Head, Eyes, Ears, Nose, Throat

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3 Medical and Surgical History (Safety Population)

Subject Number	Any History?	Study Period	Body System	Category	Date Start	Date End	Ongoing?	Condition or Event
X	XXX	Screen	XXXXXX XXXXX	Medical	DDMMMYYYY		XXXX	XXXXXXX XXXXXX XX
				Surgical	DDMMMYYYY	DDMMMYYYY		
X	XXX	Screen	XXXXXXXX XXXXX	Medical	DDMMMYYYY	DDMMMYYYY		

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.4 Substance Use (Safety Population)

Subject Number	Study Period	Substance	Description of Use	Start Date	End Date
X	Screen	XXXXXXXX XXX	XXXXXXXXXX XXXXXX XXXX	DDMMMYYYY	DDMMMYYYY

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.1 Inclusion Criteria

X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.2 Exclusion Criteria

X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.2 Subject Eligibility (Safety Population)

Subject Number	Study Period	Did subject meet all eligibility criteria?	Specify
X	Screen	YES	
X	Screen	YES	<This column is only presented if data are present.>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3 Check-in Responses (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Date	Time	Check-in Criteria* 1	Check-in Criteria* 2	Specify
X	X	X	-X	XXXXX	DDMMMYYYY	HH:MM	No	NA	Will only be present and populated if
			X	XXXXX	DDMMMYYYY	HH:MM	No	NA	there is a comment present in the study
X	X	X	-X	XXXXX	DDMMMYYYY	HH:MM	No	NA	database.

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
* 1 = Did the Subject report any study restriction violations since the last study visit?; 2 = IF YES TO ANY QUESTION, WAS SUBJECT APPROVED FOR STUDY?
NA = Not applicable

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4 Test Compound Administration Times (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Start Date	Start Time	Compound	Dosage	Laterality	Form	Route	Comments
X	X	X	X	XXXX	DDMMMYYYY	X:XX:XX	XXXXXXXXX	< >	< >	< >	< >	XXXXXXXXXXXXXXXXXX
X	X				DDMMMYYYY	X:XX:XX	XXXXXXXXX	< >	< >	< >	< >	
X	X	X	X	XXXX	DDMMMYYYY	X:XX:XX	XXXXXXXXX	< >	< >	< >	< >	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
NA = Not applicable

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5 Blood Draw Times (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Date	Actual Time	Bioassay	Comments
X	X	X	X	XXXXX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
		<similar for all other time points and subjects>						

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.6 Meal Times (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Event	Actual Date	Start Time	Stop Time	Comments
X	X	X	-X	XXXXX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				XXXXX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
			X	XXXXX	BREAKFAST	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				XXXXX	LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				XXXXX	DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				XXXXX	SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

Subject Number	Any Med?	Treatment	Medication (WHO DD*)	Dosage	Route	Start Date	Start Time	Stop Date	Stop Time	Frequency	Indication	Continuing?	Prior to Study?
1	NO		None										
2	NO		None										
3	YES		CETIRIZINE (CETIRIZINE)	X MG	BY MOUTH	DDMMMYYYY	UNK	DDMMMYYYY	HH:MM	XXXXXXX	XXXXXXX	NO	Yes
		X	PARACETAMOL (PARACETAMOL)	X MG	XXXXXXXXX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXXXXXXX	XXXXXXXX	XX	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
*Concomitant medications are coded with WHO Dictionary Version 01Mar2019-b3.
Med = Medication, UNK = Unknown, WHO DD = World Health Organization Drug Dictionary

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.3 Residual Amounts of Zolmitriptan in M207 Patches for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes in Healthy Volunteers (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Date	Actual Time	Result (µg)
X	X	X	X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.4 Residual Amounts of Zolmitriptan on Skin Swabs for 3 Different Formulations of M207 3.8 mg on the Upper Arm for 30 Minutes in Healthy Volunteers (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Date	Actual Time	Result (µg)
X	X	X	X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX
			X	XXXXX	DDMMMYYYY	HH:MM:SS	XXX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.1.1 Adverse Events (I of II) (Safety Population)

Subject Number	Treatment	TE?	Adverse Event	System Organ Class/ Preferred Term*	Time From Last Dose (DD:HH:MM)	Onset Date	Onset Time	Resolved Date	Resolved Time	Duration (DD:HH:MM)
1			None							
2			None							
3		No	XXXXXXXXXXXX	XXXXXXXXX/ XXXXXXXX	DD:HH:MM	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	DD:HH:MM
			XXXXXXXXXXXXXXXX	XXXXXXX/ XXXXX						
	X	Yes	XXXXXXXXXXXXXXXX	XXXXXXXX/ XXXXXXXXXXX	<similar to above>					

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
* Adverse events are coded using MedDRA Version 20.1.
TE = Treatment-emergent

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.1.2 Adverse Events (II of II) (Safety Population)

Subject Number	Treatment	Adverse Event	Onset Date	Onset Time	Frequency	Severity	Serious	Outcome	Relationship to Study Drug	Action
X		None								
X	X	XXXXXXXXXXXXXXXXX	DDMMMYYYY	XX:XX	Inter.	Mild	NS	Recovered/ Resolved	XXXXXXXX	None

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Serious: NS = Not Serious
Frequency: SE = Single Episode, Inter. = Intermittent, Cont. = Continuous

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.2 Adverse Event Non-Drug Therapy (Safety Population)

Subject Number	Treatment	Adverse Event	Onset		Procedure Given		
			Date	Time	Date	Time	Description
X	X	< >	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	TRENDELENBURG POSITION

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendices 16.2.8.1.1 to 16.2.8.1.4 will be in the following format:

Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Subject Number	Age#/ Sex	Study Period	Day	Date	Time	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)	Parameter6 < Range> (Unit)
X	XX	Screen	.	DDMMMYYYY	HH:MM:SS	XX HN	XX	XX	XX	XX HN	XX
		X	-X	DDMMMYYYY	HH:MM:SS	XX LYR+	XX LN	XX	XX LY-	XX	XX

# Age is derived from birth date to date of informed consent. F = Female, M = Male
H = Above reference range, L = Below reference range
Computer: N = Not clinically significant, Y = Clinically significant
PI Interpretation: - = Not clinically significant, R = Recheck requested, ^ = Will be retested later, + = Clinically significant

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.
Add fourth flag in the cases that ^ or R are used for the PI flag. This flag will be found in the ClinQuick Extraction.

Appendix 16.2.8.1.5 Clinical Laboratory Report - Comments (Safety Population)

Subject Number	Age#/ Sex	Study Period	Day	Date	Department	Test	Result	Unit	Comment
X	X	X	-X	DDMMMYYYY	Other Tests	Fibrinogen	XXX	mg/dL	Not significant in the context of this study.

Age is derived from birth date to date of informed consent. F = Female, M = Male

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.2 Vital Signs (Safety Population)

Subject Number	Study Period	Treatment	Day	Hour	Date	Time	Blood Pressure (mmHg) Test	Systolic/Diastolic	Pulse (bpm)	Respiration (bpm)	Temperature (°C)	Weight (kg)	Comment
X	Screen		.	.	DDMMMYYYY	X:XX:XX	SITX	XXX/ XX	XX	XX	XX	XXX.X	
	X	X	-X	XXX	DDMMMYYYY	X:XX:XX	SITX	XXX/ XX	XX	XX		XXX.X	
		X	X	XXX	DDMMMYYYY	X:XX:XX	SITX	XXX/ XX	XX	XX			

Programmer Note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
For pulse, bpm is beats/minute and for respiration bpm is breaths/minute.
SITX = X-minute sitting, SUPX = X-minute supine, R = Recheck value

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Date	Time	Result	Heart Rate (bpm)	PR (ms)	QRS (ms)	QT (ms)	QTcF* (ms)	Comment
X	Screen		.	.	DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X	XXXXXXXXXXXXX
	X	X	X	XXXX	DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X	XXXXXXXXXXXXXX

Programmer Note: Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
QTcF* = QT corrected for heart rate using Fridericia's correction
= QTc >= 450 ms, @ = QTc change from baseline greater than or equals to 30 ms.

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.4 Investigator Visual Skin Assessments (Safety Population)

Subject Number	Study Period	Treat-ment	Day	Hour	Date	Time	Skin Assessment*				Comments
							Erythema	Edema	Bruising	Bleeding	
X	X	X	X	XXXX	DDMMMYYYY	X:XX	X	X	X	X	
			X	XXXX	DDMMMYYYY	X:XX	X	X	X	X	XXXXXXXXXXXXXX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
* Scale descriptions:
Erythema: 0 = None; 1 = Mild redness; 2 = Moderate colored redness; 3 = Beet colored redness
Edema: 0 = None; 1 = Slight edema; 2 = Moderate edema; 3 = Severe edema
Bruising (visual rating): 0 = None; 1 = ≤ 25% application site has bruising spots; 2 = ≥ 26 to ≤ 50% application site has bruising spots; 3 = > 50% application site has bruising spots
Bleeding: 0 = None; 1 = Pink color on skin; 2 = Visible blood drop; 3 = Active bleeding

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM