Statistical Analysis Plan

Protocol No.: CP-2018-002

"A randomized open-label four-way crossover study to compare the pharmacokinetics, safety, and tolerability of M207 3.8 mg (administered as two 1.9 mg patches) at two different application locations (upper arm and thigh) for 30 minutes with intranasal zolmitriptan 2.5 mg and 1 hour wear time (upper arm) in healthy volunteers"

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Sponsor

Zosano Pharma Corporation
34790 Ardentech Court,
Fremont, CA 94555,
United States

Prepared by

Cliantha Research Limited
Sigma-1 Corporate
B/H Rajpath Club
Opposite Mann Party Plot
Off. S.G. Highway, Bodakdev
Ahmedabad-380054
Gujarat, India
Tel# +91 -79 – 66135628
Fax# +91 -79 – 66135602

Approval Page

Document Approvals		
Name	**Title/Area of Expertise**	**Signature & Date**
Mr. Brijesh Shukla	Author – Biostatistician	bshukla 05JAN19
Mr. Rakesh Phawde	Reviewer – Lead Biostatistician	RRPhawde 05 JAN 19
Donald Kellerman	Vice President, Clinical Development and Medical Affairs, Zosano Pharma	06 JAN-2019

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
ALT	Alanine aminotransferase
AP	Alkaline phosphatase
AST	Aspartate aminotransferase
AUC	Area under the curve
AUC_{30min}	Area under the curve from minute 0 to minute 30
AUC_{60min}	Area under the curve from minute 0 to minute 60
AUC_{120min}	Area under the curve from minute 0 to minute 120
AUC_t	Area under the curve from 0 hours to the last measureable concentration
AUC_{inf}	Area under the curve extrapolated to infinity
BMI	Body Mass Index
BP	Blood pressure
BSAP	Bone specific alkaline phosphate
C	Celsius
CBC	Complete blood count
C_t	Concentration at time t
CFR	Code of Federal Regulations
CM	Concomitant medication
cm^2	Centimeter squared
C_{max}	Maximum observed plasma concentrations
CPK	Creatinine phosphokinase
CRF	Case report form
dL	Deciliter
ECG	Electrocardiogram
EDTA	Ethylenediaminetetraacetic acid
F	Fahrenheit
GCP	Good Clinical Practice
GGT	gamma glutamyl transpeptidase
H	Hour
HCl	Hydrochloride
HRT	Hormone replacement therapy
ICF	Informed consent form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IM	Intramuscular
IRB	Institutional Review Board
IV	Intravenous
J	Joules

Abbreviation	Definition
k	Apparent elimination rate constant
kg	Kilogram
KIU	Kilo international units
µg	Microgram
L	Liter
LDH	Lactate dehydrogenase
LOCF	Last observation carry forward
µm	Micrometer
mL	Milliliters
mmol	millimole(s)
NSAID	Nonsteroidal anti-inflammatory drug
OCT	Optical Coherence Tomography
PD	Pharmacodynamics
PE	Physical examination
PK	Pharmacokinetics
PPI	Proton pump inhibitors
PRSPB	Bruising
PTH	Parathyroid hormone
SAE	Serious adverse event
SC	Subcutaneous
SD	Standard deviation
$t_{½}$	Apparent half life
TEAE	Treatment-emergent adverse event
TGA	Therapeutic Goods Administration
T_{max}	Time to maximum concentration
ZP	Zosano Pharma
M207	Zosano intracutaneous microneedle system containing zolmitriptan

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1.0 Introduction

This statistical analysis plan (SAP) is intended to give a detailed description of the summaries and the analyses for the study. The analyses outlined in this document are designed in support of clinical protocol CP-2018-002.

- This Statistical Analysis Plan (SAP) should be finalized prior to database lock, final analysis of pharmacokinetics and before the treatment codes are applied to the analysis data.

- The Statistical analysis will be initiated after completion of impact assessment of protocol deviation.

2.0 Study Title

A randomized open-label four-way crossover study to compare the pharmacokinetics, safety, and tolerability of M207 3.8 mg (administered as two 1.9 mg patches) at two different application locations (upper arm and thigh) for 30 minutes with intranasal zolmitriptan 2.5 mg and 1 hour wear time (upper arm) in healthy volunteers

3.0 Study Objectives

1. To compare the pharmacokinetics, safety and tolerability of M207 3.8 mg administered to either the upper arm or thigh, particularly with respect to skin irritation (erythema, edema, bruising, bleeding)

2. To compare the pharmacokinetics, safety and tolerability of M207 3.8 mg worn for either 30 minutes or 1 hour on the upper arm

3. To compare the pharmacokinetics, safety and tolerability of M207 3.8 mg to intranasal zolmitriptan 2.5 mg

4.0 Study Description

4.1 Randomization and Blinding

The 24 subjects are planned to receive each of the four treatments (A, B, C, D) 48 hours apart.

The order of receiving of the investigational products for each subject will be determined according to a randomization schedule which will be appropriate to the study design. Subjects will be randomized to one of the four sequences: either ABCD or BDAC or CADB or DCBA. Equal allocation of the sequence will be ensured.

The randomization schedule will be generated using SAS® statistical software (Version: 9.4; SAS Institute Inc, USA), by a biostatistician of Cliantha Research Limited. The randomization schedule will be maintained under controlled access.

The personnel involved in the dispensing of investigational products will be accountable for ensuring compliance to randomization schedule.

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.

4.2 Pharmacokinetic Variables

Serial blood sampling PK assessments will be performed at 0.00 (pre-dose), 2, 5, 10, 15, 20, 30, 45, 60, 90 min, 2 hr, 4 hr, 8 hr, 12 hr and 24 hr post dose for each treatment period.

Concentrations of zolmitriptan and it's metabolite n-desmethyl zolmitriptan in plasma will be measured for the formulations using a validated assay.

Based on the concentration data below pharmacokinetic parameters will be calculated using Phoenix® WinNonlin® professional software (Version 6.4 or higher).

Pharmacokinetic Parameters: Cmax, Tmax, AUCt, AUCi, AUC(0-30mins), AUC(0-60mins), AUC(0-120mins), Kel, Tmax, tHalf and AUC_%Extrap_obs.

4.3 Safety Assessment

The safety of zolmitriptan 2.5 mg and M207 3.8 mg patch will be assessed on the basis of:

1) Vital signs monitoring
2) Adverse Events (AEs) monitoring
3) Clinical laboratory tests
4) Physical examinations
5) ECG
6) Concomitant medications
7) Investigator visual skin assessment

4.4 Sample Size

No formal sample size calculation was performed. In previous studies of Zosano Pharma transdermal products in healthy volunteers, a sample size of 24 was sufficient to provide directional information on tolerability, as well as adequate information on pharmacokinetics, and comparative pharmacokinetics for various regimens.

4.5 Study Design, Treatment and Plan

This is a single-center, open-label, randomized, four-way crossover study. Each subject will receive each of the four study treatments once, followed by in-clinic monitoring and extensive blood sample collection for pharmacokinetic analysis.

Dosing will occur approximately 48 hours apart, until completion of dosing in randomized order per the treatment sequence tables. Plasma samples from the dosing days will be sent to the analytical laboratory for analysis and tolerability for each of the dose levels will be summarized.

After completion of the four dosing days, subjects will be assessed one final time and dismissed from the study.

Investigational Products:

M207 Intracutaneous Microneedle System

The Zosano M207 Intracutaneous Microneedle System is a novel drug delivery technology which consists of a disposable titanium patch centered on an adhesive backing with microneedles that are dry-coated with the drug product formulation, and a reusable handheld applicator that ensures that the patch is applied with a defined application speed and energy to the site of administration.

M207 systems consist of zolmitriptan coated titanium array with an adhesive backing that is applied using proprietary patch applicators. Descriptions of the 1.9 mg patches used in the study are described below.

Zolmitriptan Nasal Spray

Zolmitriptan nasal spray is a commercially available product (Zomig® Nasal Spray) and will be purchased for use in this study. The dose used in this study will be 2.5 mg/0.1 ml. This dose should be administered to either the right or left nostril with the subject's head tilted slightly backward.

M207 1.9 mg

The M207 1.9 mg consists of a 3 cm^2 titanium array of microprojections that are nominally 340 μm in length coated with 1.9 mg of zolmitripan. The array is applied to the center of a 5 cm^2 tan adhesive patch. The patch is attached to the interior of a white to off-white polycarbonate ring co-molded with a desiccant, packaged in a cup.

Study treatments are:

Treatment A: M207 3.8 mg administered as two 1.9 mg patches, 30 min wear time (upper arm application)

Treatment B: M207 3.8 mg administered as two 1.9 mg patches, 30 min wear time (thigh application)

Treatment C: M207 3.8 mg administered as two 1.9 mg patches, 1 hour wear time (upper arm application)

Treatment D: Intranasal zolmitriptan 2.5mg

4.6 Subject Population

The study population will consist of 24 healthy volunteers (12 women and 12 men) 18 to 50 years of age in general good health.

4.7 Number of Subjects

A sufficient number of subjects will be enrolled to ensure application of 24 healthy subjects.

4.8 Study Duration

Screening is 1 day (up to 30 days prior to dosing); in-clinic duration of study participation for each subject is approximately 2 weeks total (includes 4 treatment periods), and the final end of study visit occurs on one day.

4.9 Withdrawal/Discontinuation Criteria

The Participation in the study is completely voluntary and a subject can choose to withdraw from the study at any time. In addition, a subject can be withdrawn for any of the following reasons: the Principal Investigator decides that continuing the drug may be harmful, a subject is non-compliant with the protocol, a subject has a serious reaction to the treatment, or the study is stopped by the Independent Ethics Committee, US Food and Drug Administration (FDA), or Zosano Pharma.

In order to complete all treatments for each dose, additional subjects may be enrolled to account for subjects who withdraw or are discontinued from the study. If a subject does not complete all planned treatments, the reason and date of withdrawal from the study must be recorded in the CRF. Zosano Pharma should be notified immediately if a subject withdraws prematurely from the study.

5.0 Endpoints

5.1 Safety and Tolerability

- Incidence of adverse events
- Change in physical examination findings from pre-dose to 12 hours post-dose
- Changes in vital signs from pre-dose to 10 min, 60 min, 2 hour, 4 hour, and 12 hour post-dose
- Changes in ECG parameters from pre-dose to 15 min, 60 min, 8 hour, and 12 hour post-dose
- Scores from an investigator visual skin assessment for erythema, edema, bruising and bleeding at the patch application sites from pre-dose to 30 min (for 30 min wear time treatment assignments only), 60 min (for 60 min wear time treatment assignment only), 12 hour and 24 hour post-dose
- Changes in clinical labs from screening to end of study
- Patch adhesion score at time of application at 30 min and 60 min post-dose (for 60 min wear time treatment assignment only)

5.2 Safety Overview

M207 consisting of two patches of 1.9 mg (3.8 mg), 30 minute upper arm application, has been studied in healthy volunteers (in clinic) and subjects with migraine (outpatient). This regimen has been generally well-tolerated, with adverse events observed (dizziness and chest tightness) of those typically reported for triptans. Adverse events reported were almost always within the first few minutes after patch application. It is anticipated that systemic exposure with forearm application will be not significantly different than that seen with upper arm application, based on our experience with glucagon. Also, since Cmax was generally observed, on average, at around 15 minutes, wearing the patches for 1 hours will probably not be associated with higher Cmax levels than 30 minutes and should not result in different tolerability issues.

6.0 Study Populations (Definition of Populations for Analysis)

6.1 Pharmacokinetic Population

PK population is defined as below:

- Concentration data of subjects, who complete at least two periods of the study, will be included in the pharmacokinetic and statistical analysis. Concentration

and pharmacokinetic data of other subjects will be presented in the report if available, but will not be included in the statistical analysis.

- Data from any subject with missing concentration values in any period (like missed blood samples, lost samples, samples unable to be quantitated) may be used for bioavailability evaluation if pharmacokinetic parameters can be reliably estimated using the remaining data points otherwise that specific pharmacokinetic parameter data will be excluded from the bioavailability evaluation.
- If any subject has all BLQ/zero values in any period, then the subject will be excluded from the bioavailability evaluation analysis from that particular period.
- If the pre-dose concentration appears to be >5% of the Cmax in any subject in any period, then the subject will be excluded from the statistical analysis in that period.
- Kel and related elimination phase parameters will not be estimated for cases that do not exhibit a terminal log-linear phase in the concentration versus time profile.

6.2 Safety Population

Safety analysis will be performed on all randomized subjects receiving at least one dose of investigational product. Subjects' safety data will be presented according to the treatment they actually received.

Drop-outs within a 24-hour period are not anticipated; however should they occur prior to 2 hours after patch application then additional eligible subjects may be enrolled.

7.0 Incomplete and Missing Data

No adjustment or imputation will be utilized for missing values or for subjects who withdraw prior to completing the study. In case of missing data for skin assessment, LOCF (last observation carried forward) method will be used.

8.0 Study Subjects and Conduct

Subject accountability will be tabulated for each study treatment and for all subjects combined by summarizing the number of subjects who are randomly assigned to treatment, complete the study, prematurely discontinue, and the reason for discontinuation. A listing will be presented to describe dates of withdrawal and the reason for discontinuation for each discontinued subject. A listing of study treatment administration will be provided.

9.0 Demographic Characteristics

Individual subject demographics will be presented in listings. Demographic characteristics such as age, gender, race, ethnicity, height, weight and body mass index (BMI) will be summarized and tabulated for all randomized subjects. Descriptive statistics will be presented for age, height, weight and BMI. Frequency counts and percentage will be presented for gender, race and ethnicity.

10.0 Prior and Concomitant Medications

Subjects will be asked to refrain from taking either prescription or OTC medications from the time of Screening until the completion of the study, except for those discussed in this section. All concomitant medications taken during the study will be recorded on the concomitant medications case report form (CRF) with indication for use, totally daily dosage, and dates of drug administration.

Subjects must discontinue use of herbal or over-the-counter medications (with the exception of all medications listed below) for 48 hours prior to treatment days and throughout the study.

If the medication end date is known and medication end date is prior to the first dose of study treatment it will be classified under prior medication. If the end date of the medication is unknown, it will be considered as concomitant medication. A subject listing of all prior and concomitant medications and related information (e.g.: dose, unit, frequency etc.) will be presented.

11.0 Pharmacokinetic Analysis

Pk analysis will be performed on the pharmacokinetic population (see section 6.1).

All Below Limit of Quantitation (BLQ) concentration values will be set to zero before pharmacokinetic analysis, except in the case where there is a measurable value immediately preceding the BLQ value and a measurable value immediately after the BLQ value. In these instances, the BLQ value will be set to missing.

The actual time of blood collection for all samples collected will be used in the calculation of pharmacokinetic parameters.

Pharmacokinetic parameters: The following pharmacokinetic parameters will be determined from the time and concentration data using a non-compartmental analysis of WinNonlin® professional software (Phoenix® version 6.4 or higher; Pharsight Corporation, USA).

Cmax: Maximum measured plasma concentration over the time span specified.

Tmax: Time of the maximum measured plasma concentration. If the maximum plasma concentration occurs at more than one time point, the first is chosen as Tmax.

AUCt: The area under the plasma concentration versus time curve will be calculated using the linear trapezoidal rule from the zero time point to the last quantifiable concentration.

AUCi: The area under the plasma concentration versus time curve from zero to infinity will be calculated by adding Ct/Kel to AUCt, where Ct is the last quantifiable concentration and Kel is the elimination rate constant.

AUC(0-30mins): The area under the plasma concentration versus time curve will be calculated using the linear trapezoidal rule from the time zero to 30 minutes.

AUC(0-60mins): The area under the plasma concentration versus time curve will be calculated using the linear trapezoidal rule from the time zero to 60 minutes.

AUC(0-120mins): The area under the plasma concentration versus time curve will be calculated using the linear trapezoidal rule from the time zero to 120 minutes.

Kel: The terminal elimination rate constant will be obtained from the slope of the line, fitted by linear least squares regression, through the terminal points of the log (base e) of the concentration versus time plot for these points.

tHalf: The half-life will be calculated by the equation tHalf = 0.693/ Kel

AUC_%Extrap_obs: The residual area in percentage will be determined by the formula, [(AUCi - AUCt)/ AUCi] x 100

Frel – Relative Bioavailability.

Bioavailability relative to other treatment sites of application and wear times will be calculated using the below mentioned formula;

Formula for calculation of Frel;
Frel = 100*(AUC_X*D_Y) / (AUC_Y*D_X); where relative bioavailability measures the bioavailability (estimated as the AUC) of a treatment-X when compared with treatment-Y of the same drug. **D** is the dose administered.

Frel will be calculated for AUCt.

Ratios will be reported for AUC(0-30mins), AUC(0-60mins), AUC(0-120mins), AUCt, AUCi and Cmax.

No value of Kel, AUCi or tHalf will be reported for cases that do not exhibit a terminal log-linear phase in the concentration versus time profile.

- *Descriptive statistics:* Mean, standard deviation, coefficient of variance, Median, Maximum and Minimum for applicable pharmacokinetic parameters will be calculated.

- *Statistical analysis:* Statistical analysis will be performed on pharmacokinetic data of subjects using SAS® statistical software (Version: 9.4 or higher; SAS Institute Inc, USA).
- *Analysis of Variance:* Ln-transformed data of Cmax, AUC(0-30mins), AUC(0-60mins), AUC(0-120mins), AUCt and AUCi will be evaluated statistically using the PROC MIXED procedure from SAS® for difference due to treatment, with period and sequence as a fixed effects and subject within sequence as a random effect.

  All main effects will be tested at 5% level of significance using the Mean Square Error as the error term.
- Two one-sided 90% confidence intervals for the ratio of means between drug formulations will be calculated for Ln-transformed data of Cmax, AUC(0-30mins), AUC(0-60mins), AUC(0-120mins), AUCt and AUCi.

  The data of metabolite n-desmethyl zolmitriptan will be provided as supportive information.

  The comparisons of interest will be treatment A vs. B, A vs. C, A vs. D, B vs. C, B vs. D and C vs. D.

12.0 Assessment Details

Clinical Laboratory Tests

Standard clinical laboratory tests (serum pregnancy for all women, CBC, hematology, and urinalysis) will be performed at Screening and End of Study (or early termination) and urine pregnancy testing for all women at each Admission/baseline visit.

A blood sample at screening will be taken to perform serological tests for HIV, Hepatitis B and Hepatitis C.

Urine drug screen and alcohol (breath) testing will be performed at screening and each Admission/baseline visit. Urine drug screen will test for amphetamine, barbituates, cocaine, cannabinoids, phencyclidine (PCP), opioids, and methamphetamines.

Samples will be analyzed by a local laboratory.

Vital Signs

Vital signs include heart rate, pulse, respiratory rate, as well as systolic and diastolic arterial pressure. Vital signs will be recorded after subjects have been in the seated resting position for 2 minutes. Temperature will be taken at Screening, admission/baseline, and at end of study visit/or early termination only.

Electrocardiograms

A standard 12-lead ECG will be performed by a qualified individual at the site. General morphology and intervals [Heart rate, QRS, PR interval, QRS, QTn, QTcf], of interest will be assessed with each tracing. The principal or sub-investigator must review the tracing and assess it for any clinically significant abnormality.

Investigator Visual Skin Assessments of the Application Sites

Each M207 patch site (where a patch has been removed) will be observed for the following skin assessments pre-dose and immediately after removal of the patches from the subject's skin (and before swabbing) at 30 min (for 30 min wear time treatment groups only), 60 min, 12 hr, 24 hr and at the End of Study/or Early Termination visit.

Erythema

The erythema evaluations will be performed using the following scale:

- 0 = None
- 1 = Mild redness
- 2 = Moderate colored redness
- 3 = Beet colored redness

Edema

The edema evaluations will be performed using the following scale:

- 0 = None
- 1 = Slight edema
- 2 = Moderate edema
- 3 = Severe edema

Bruising

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

Bleeding will be assessed using the following scale:

- 0 = None
- 1 = Pink color on skin
- 2 = Visible blood drop
- 3 = Active bleeding

For example;

Skin assessment score presented in Table-A will be modified as presented in Table-B for statistical analysis using LOCF method.

Table-A

Subject	Skin assessment scoring_Time Points(Hrs)				
	0.0	**30 minutes**	**60 minutes**	**12 hour**	**24 hour**
1	0	0	0	2	2
2	0	2	2	3	Missing
3	0	1	2	2	Missing

Table-B

Subject	Skin assessment scoring_Time Points(Hrs)				
	0.0	**30 minutes**	**60 minutes**	**12 hour**	**24 hour**
1	0	0	0	2	2
2	0	2	2	3	3
3	0	1	2	2	2

Patch Adhesion Assessment

Patch adhesion assessment at the time of application and at 30 min and 60 min post-dose (for 60 min wear time treatment group only) will be checked for the degree of adhesion by investigators should use a 5-point numerical scale in which each score corresponds to a specified range of adhered surface area of each patch, as follows:

0 = ≥ 90% adhered (essentially no lift off the skin)

1 = ≥ 75% to < 90% adhered (some edges only lifting off the skin)

2 = ≥ 50% to < 75% adhered (less than half of the patch lifting off the skin)

3 = > 0% to < 50% adhered (not detached, but more than half of the patch lifting off the skin without falling off)

4 = 0% adhered (patch detached; completely off the skin).

For example;

Adhesion Data:

Actual Adhesion score presented in below Table;

Subject	Adhesion scoring_Time Points(Hrs)		
	0.0	30 minutes	60 minutes
1	0	0	0
2	0	2	2
3	0	1	1

13.0 Subject Disposition

An overall summary of subject's disposition will be presented using a clear accounting of all subjects who entered the study, subjects who completed the study and subjects who do not complete the study, along with the reason of not completing the study. Randomized subjects who do not complete the study due to any reason will be considered as withdrawal.

Subject wise data listings will be sorted by subject number; listing will include subject number, treatment, reason for discontinuation, discontinuation period, date & time.

14.0 Protocol Deviations/Violation

Protocol Deviation is defined as less serious non-compliance which needs adequate documentation and Protocol Violation is defined as serious non-compliance with the protocol resulting in the exclusion of a randomized subject from the study. Listing will be provided for subjects with protocol deviation/violation in the study.

15.0 Handling of data from visit

Tabulation of descriptive statistics will be performed primarily using SAS® (release 9.4 or higher).

16.0 Safety Analyses

Safety analyses will be performed on safety population set (refer section 6.2). All safety data will be listed by subject, treatment group and parameter, separate listings of all abnormal laboratory findings will be provided, and clinically significant abnormalities will be recorded as AEs.

16.1 Adverse Events

Adverse events (AEs) will be mapped to preferred term and body-organ system using MedDRA™. The number and percentage of subjects reporting AEs will be

summarized by AE preferred term and AE body-organ system. Adverse events will be summarized by severity and relationship to study drug also.

In particular, AE summary tables will be presented for the following:

- AE overview
- AE incidence
- AEs by severity
- AEs leading to study drug discontinuation
- AEs by relationship

Each participant will be counted only once within each summation level (SOC; preferred term). If a participant experiences more than one AE within each summation level only, the AE with the strongest relationship or the maximum severity, as appropriate, will be included in the summaries of relationship and severity.

Adverse events will be attributed to the most recent dose taken, i.e., AEs occurring post-dose but prior to the next dose, will be attributed to the most recent dose by using the date and time the AE occurred. Adverse events occurring after the first dose of study drug are considered treatment emergent.

16.1.1 Missing and Partial AE Onset Date/Time

In the event that only a partial end date (month/year) is available, and month/year occurs before that of the first study drug administration date, the adverse event will be considered as non-treatment emergent. However, if the onset date is a partial date (month/year) and month/year occurs on or after that of study drug administration date, the following cases will be considered:

- If month/year of the onset date is greater than the month/year of study drug administration date, the adverse event will be considered treatment-emergent.

- If month/year of the onset date is equal to the month/year of study drug administration date, and the end date is present, the end date will be used to determine if the adverse event is treatment emergent. If the end date is on or after study drug administration date, the adverse event will be considered treatment-emergent; otherwise, if the adverse event stopped before study drug administration date, then it will not be treatment-emergent;

- If month/year of the onset date is equal to the month/year of study drug administration date, and the end date is a partial date, the adverse event will be considered treatment emergent.

- If adverse event onset date is known and time is missing then the time will be considered as post dose.

16.2 Vital Signs

Descriptive summaries of actual values and changes from pre-dose to 10 min, 60 min (1 hr), 120 min, 240 min (4 hr), and 720 minutes (12 hr) post-dose will be calculated for heart rate, systolic blood pressure, and diastolic blood pressure and presented by treatment group.

16.3 ECG

Descriptive summaries of actual values and changes from pre-dose by treatment group will also be provided for the quantitative ECG parameters of rhythm, heart rate, PR interval, QRS interval, QT, QTcF, (Fridericia's) corrections for heart rate.

16.4 Investigator Skin Assessments

Scores of the investigator skin assessments of the application sites at 30 min (30 min wear time assignment only), 60 min (1 hr), 12 hours and 24 hours post-dose will be summarized by treatment group using frequency tables.

16.5 Clinical Laboratory Evaluations

Clinical laboratory values will be displayed in data listings, including a listing of all abnormal results. Clinically significant values will be flagged.

16.6 Physical examination

Results of physical examinations conducted throughout the study will be presented in data listings, including abnormalities.

17.0 Medical history

Medical history data will be presented in listings.

18.0 Patch Adhesion

Adhesion scores will be summarized by time point and treatment group using frequency tables. Mean adhesion scored by time point and treatment group will also be provided. The means of the per treatment group mean adhesion score for the different test products will be compared.

19.0 Residual Drug Analyses

Analyses will be performed to quantify the amount of drug remaining on the M207 patch system and the amount of drug recovered from the skin of the subject following removal of each of the patches. A description of the disposition of the remaining drug will be presented. The results from analysis of residual zolmitriptan on the skin and the residual zolmitriptan on the used patches will provide a basis for the calculation of the total amount of drug delivered from each treatment.

20.0 Extent of Exposure

Extent of exposure summarizes the actual number of treatments received by all dosed subjects, the amount of drug dosed and the total cumulative dose received by each subject over the course of the study.

Mock Tables

For all the summary and analysis tables, reference of listing and generation date & time of table will be provided, and for the listing generation date & time of listing will be provided. All summary and analysis tables will be provided in CSR based on the ICH E3 guideline. Given mock tables can be added or modified based on study requirement.

Summary Table 12.1: Extent of Exposure for all Dosed Subjects

Subject	Treatment Received	Total Number of Doses Taken	Treatment Dose	Total Exposure
Subjects Who Completed the Study				
XX, XX	ABCD	X	XX mg	XX mg
Subjects Who Discontinued Prematurely				
XXXX	ABCD	X	XX mg	XX mg

Treatment A: M207 3.8 mg administered as two 1.9 mg patches, 30 min wear time (upper arm application)

Treatment B: M207 3.8 mg administered as two 1.9 mg patches, 30 min wear time (thigh application)

Treatment C: M207 3.8 mg administered as two 1.9 mg patches, 1 hour wear time (upper arm application)

Treatment D: Intranasal zolmitriptan 2.5mg

Summary Table 14.1.1: Summary of Subject Disposition

	Sequence				Total
	ABCD	BDAC	CADB	DCBA	
Subjects Randomized	XX	XX	XX	XX	XX
Subjects Treated (Safety Population)	XX	XX	XX	XX	XX
Subjects Completed	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Subjects Discontinued	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Adverse Event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Non Compliance	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Physician Decision	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Withdrawal by Subject	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Study Termination	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Other					

Treatment A: M207 3.8 mg administered as two 1.9 mg patches, 30 min wear time (upper arm application)
Treatment B: M207 3.8 mg administered as two 1.9 mg patches, 30 min wear time (thigh application)
Treatment C: M207 3.8 mg administered as two 1.9 mg patches, 1 hour wear time (upper arm application)
Treatment D: Intranasal zolmitriptan 2.5mg

Note: Percentages are calculated using the number of subjects treated as the denominator.
Note: Subject 104 was randomized to sequence CADB but was given sequence ABCD.
Note: Subject XXX dropped out after Period Y due to personal reasons.

Summary Table 14.1.2.1: Summary of Demographics

		Dosed	Completed
Subjects	N	XX	XX
Gender, n (%)	Male	XX (XX.XX%)	XX (XX.XX%)
	Female	XX (XX.XX%)	XX (XX.XX%)
Ethnicity, n (%)	Not Hispanic or Latino	XX (XX.XX%)	XX (XX.XX%)
	Hispanic or Latino	XX (XX.XX%)	XX (XX.XX%)
Race, n (%)	Asian	XX (XX.XX%)	XX (XX.XX%)
	White	XX (XX.XX%)	XX (XX.XX%)
	Black or African American	XX (XX.XX%)	XX (XX.XX%)
	Native Hawaiian or Other Pacific Islander	XX (XX.XX%)	XX (XX.XX%)
	American Indian or Alaska Native	XX (XX.XX%)	XX (XX.XX%)
	Other	XX (XX.XX%)	XX (XX.XX%)
	Multiple	XX (XX.XX%)	XX (XX.XX%)
Age (Years)	Mean (±SD)	XX (±X)	XX (±X)
	Median	XX	XX

		Dosed	Completed
	Min	XX	XX
	Max	XX	XX
BMI (kg/m^2)	Mean (±SD)	XX.X (±X.X)	XX.X (±X.X)
	Median	XX.X	XX.X
	Min	XX.X	XX.X
	Max	XX.X	XX.X
Height (cm)	Mean (±SD)	XX.X (±X.X)	XX.X (±X.X)
	Median	XX.X	XX.X
	Min	XX.X	XX.X
	Max	XX.X	XX.X
Weight (kg)	Mean (±SD)	XX.X (±X.X)	XX.X (±X.X)
	Median	XX.X	XX.X
	Min	XX.X	XX.X
	Max	XX.X	XX.X
Note: - BMI: Body Mass Index, N = Number of subjects in each group, n=number of subjects in each category.			

Summary Table 14.1.2.2. Summary of Mean Demographic Data (± SD)

	All Subjects Dosed (N = XX)			**Subjects Completed (N = XX)**			**Subjects Included in PK Analysis (N = XX)**		
	All (N = XX)	**Males (N = XX)**	**Females (N = XX)**	**All (N = XX)**	**Males (N = XX)**	**Females (N = XX)**	**All (N = XX)**	**Males (N = XX)**	**Females (N = XX)**
Age (years)	XX.X (±XX.XX)			XX.X (±XX.XX)			XX.X (±XX.XX)		
Weight (kg)	XX.X (±XX.XX)			XX.X (±XX.XX)			XX.X (±XX.XX)		
Height (cm)	XX.X (±XX.XX)			XX.X (±XX.XX)			XX.X (±XX.XX)		
BMI (kg/m2)	XX.X (±XX.XX)			XX.X (±XX.XX)			XX.X (±XX.XX)		

Summary Table 14.2.1.1: Descriptive Statistics of Zolmitriptan Pharmacokinetic Parameters

Variable / Parameters	Cmax (Unit)				AUCt (Unit)			
	Treatment (A) - M207 Arm 30 minutes	Treatment (B) - M207 Thigh 30 minutes	Treatment (C) - M207 Arm 60 minutes	Treatment (D) - INT Spray 2.5	Treatment (A) - M207 Arm 30 minutes	Treatment (B) - M207 Thigh 30 minutes	Treatment (C) - M207 Arm 60 minutes	Treatment (D) - INT Spray 2.5
N Mean Std Dev Minimum Median Maximum Coeff of Variation								

Variable / Parameters	Tmax (Unit)				Kel (Unit)			
	Treatment (A) - M207 Arm 30 minutes	Treatment (B) - M207 Thigh 30 minutes	Treatment (C) - M207 Arm 60 minutes	Treatment (D) - INT Spray 2.5	Treatment (A) - M207 Arm 30 minutes	Treatment (B) - M207 Thigh 30 minutes	Treatment (C) - M207 Arm 60 minutes	Treatment (D) - INT Spray 2.5
N Mean Std Dev Minimum Median Maximum Coeff of Variation								

Variable / Parameters	AUC0-0.5 (Unit)				AUC0-1 (Unit)			
	Treatment (A) - M207 Arm 30 minutes	Treatment (B) - M207 Thigh 30 minutes	Treatment (C) - M207 Arm 60 minutes	Treatment (D) - INT Spray 2.5	Treatment (A) - M207 Arm 30 minutes	Treatment (B) - M207 Thigh 30 minutes	Treatment (C) - M207 Arm 60 minutes	Treatment (D) - INT Spray 2.5
N								
Mean								
Std Dev								
Minimum								
Median								
Maximum								
Coeff of Variation								

Variable / Parameters	AUC0-2 (Unit)				AUCi (Unit)			
	Treatment (A) - M207 Arm 30 minutes	Treatment (B) - M207 Thigh 30 minutes	Treatment (C) - M207 Arm 60 minutes	Treatment (D) - INT Spray 2.5	Treatment (A) - M207 Arm 30 minutes	Treatment (B) - M207 Thigh 30 minutes	Treatment (C) - M207 Arm 60 minutes	Treatment (D) - INT Spray 2.5
N								
Mean								
Std Dev								
Minimum								
Median								
Maximum								
Coeff of Variation								

Variable / Parameters	tHalf (Unit)				AUC_Extp_obs (Unit)			
	Treatment (A) - M207 Arm 30 minutes	**Treatment (B) - M207 Thigh 30 minutes**	**Treatment (C) - M207 Arm 60 minutes**	**Treatment (D) - INT Spray 2.5**	**Treatment (A) - M207 Arm 30 minutes**	**Treatment (B) - M207 Thigh 30 minutes**	**Treatment (C) - M207 Arm 60 minutes**	**Treatment (D) - INT Spray 2.5**
N Mean Std Dev Minimum Median Maximum Coeff of Variation								

Summary Table 14.2.1.2: Descriptive statistics of Zolmitriptan concentration (unit) data

	Variable	Time (hrs)														
		0.000	0.033	0.083	0.167	0.250	0.333	0.500	0.750	1.000	1.500	2.000	4.000	8.000	12.000	24.000
Treatment (A) - M207 Arm 30 minutes	N															
	Mean															
	Std Dev															
	Minimum															
	Median															
	Maximum															
	Coeff of Variation															
Treatment (B) - M207 Thigh 30 minutes	N															
	Mean															
	Std Dev															
	Minimum															
	Median															
	Maximum															
	Coeff of Variation															

	Variable	Time (hrs)														
		0.000	0.033	0.083	0.167	0.250	0.333	0.500	0.750	1.000	1.500	2.000	4.000	8.000	12.000	24.000
Treatment (C) - M207 Arm 60 minutes	**N**															
	Mean															
	Std Dev															
	Minimum															
	Median															
	Maximum															
	Coeff of Variation															
Treatment (D) - INT Spray 2.5	**N**															
	Mean															
	Std Dev															
	Minimum															
	Median															
	Maximum															
	Coeff of Variation															

Note: All the above provided concentration descriptive will also be provided for metabolite n-desmethyl zolmitriptan as a supportive information.

Summary Table 14.2.2.1: Summary of Statistical Analysis for M207 patches compared to Intranasal zolmitriptan

PARAMETER	INT Spray 2.5 (D) LEAST SQUARE MEANS Ln DATA	M207 Arm 30 (A) LEAST SQUARE MEANS Ln DATA	M207 Arm 60 (C) LEAST SQUARE MEANS Ln DATA	M207 Thigh 30 (B) LEAST SQUARE MEANS Ln DATA	INT Spray 2.5 (D)GEOMETRIC MEANS	M207 Arm 30 (A)GEOMETRIC MEANS	M207 Thigh 30 (B)GEOMETRIC MEANS	M207 Arm 60 (C) GEOMETRIC MEANS
Cmax								
AUCt								
AUC(0-0.5hr)								
AUC(0-1hr)								
AUC(0-2hr)								
AUCi								

PARAMETER	INTRA-SUBJECT CV (%)	(M207 Arm 30 (A)/ INT Spray 2.5 (D))RATIO	(M207 Thigh 30 (B)/ INT Spray 2.5 (D))RATIO	(M207 Arm 60 (C)/ INT Spray 2.5 (D))RATIO	(M207 Arm 30 (A)/ M207 Thigh 30 (B))RATIO	(M207 Arm 30 (A)/ M207 Arm 60 (C))RATIO	(M207 Thigh 30 (B)/ M207 Arm 60 (C))RATIO
Cmax							
AUCt							
AUC(0-0.5hr)							
AUC(0-1hr)							
AUC(0-2hr)							
AUCi							

PARAMETER	90% CONFIDENCE INTERVAL FOR M207 Arm 30 (A) and INT Spray 2.5 (D)	90% CONFIDENCE INTERVAL FOR M207 Thigh 30 (B) and INT Spray 2.5 (D)	90% CONFIDENCE INTERVAL FOR M207 Arm 60 (C) and INT Spray 2.5 (D)	90% CONFIDENCE INTERVAL FOR M207 Arm 30 (A) and M207 Thigh 30 (B)	90% CONFIDENCE INTERVAL FOR M207 Arm 30 (A) and M207 Arm 60 (C)	90% CONFIDENCE INTERVAL FOR M207 Thigh 30 (B) and M207 Arm 60 (C)	POWER TOST
Cmax							
AUCt							
AUC(0-0.5hr)							
AUC(0-1hr)							
AUC(0-2hr)							
AUCi							

Note: All the above provided summary table of statistical analysis will be provided for metabolite n-desmethyl zolmitriptan as a supportive information.

Summary Table 14.3.1.1: Overview of Adverse Event

	Treatment			
	Treatment (A)	**Treatment (B)**	**Treatment (C)**	**Treatment (D)**
subjects who received study treatment				
subjects who discontinued due to AEs				
subjects with at least one AE				
Total number of AEs				
Total number of SAEs				
Source: Appendix 16.2.1 and 16.2.7				

Summary Table 14.3.1.2: Incidence of AE by SOC and PT by Treatment Group

	Treatment			
System Organ Class / Preferred Term	**Treatment (A) (N= XX) n (%)**	**Treatment (B) (N= XX) n (%)**	**Treatment (C) (N= XX) n (%)**	**Treatment (D) (N= XX) n (%)**
Number of AEs				
Number of subjects with at least one AE				
System Organ Class				
Preferred Term				

Abbreviations: AE=Adverse Event; SOC=System Organ Class; PT=Preferred Term;
N=number of subjects dosed for each treatment; n=number of subjects reporting at least one incidence of the specified AE.
Medical Dictionary used: MedDRA Version XX.X

Summary Table 14.3.1.3: Summary of Treatment Emergent Adverse Events by SOC, PT and Severity

System Organ Class / Preferred Term	**Treatment A** (N=XX) **n (%)**	**Treatment B** (N=XX) **n (%)**	**Treatment C** (N=XX) **n (%)**	**Treatment D** (N=XX) **n (%)**
Number of subjects with at least one AE	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Mild	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Moderate	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Severe	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
System Organ Class 1	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Preferred Term 1	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Mild	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Moderate	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Severe	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
System Organ Class 2	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Preferred Term 2				
----	----	----	----	----

Abbreviations: N=Number of subjects in specified treatment group; n = number of subjects in specified category.
Notes: 2) A subject is counted only once at the highest severity, in the severity sub-categories.
Medical Dictionary used: MedDRA Version XX.X

Summary Table 14.3.1.4: Summary of Treatment Emergent Adverse Events by SOC, PT and Causality

System Organ Class / Preferred Term	**Treatment A** (N=XX) **n (%)**	**Treatment B** (N=XX) **n (%)**	**Treatment C** (N=XX) **n (%)**	**Treatment D** (N=XX) **n (%)**
Number of subjects with at least one AE	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Not Related	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Possibly Related	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Probably Related	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
System Organ Class 1	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Preferred Term 1	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Not Related	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Possibly Related	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Probably Related	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)

Abbreviations: N=Number of subjects in specified treatment group; n = number of subjects in specified category.
Notes: Multiple reports of same TEAE (for Summary Table 9) / SAE (for Summary Table 10) for the same subject were counted once.
Medical Dictionary used: MedDRA Version XX.X

Listing 1: Listing of Adhesion Score for Test Treatment (A) - M207 Arm 30 minutes

Subject	Sequence	Pre-Dose	30 minutes
XXXX			
XXXX			
XXXX			

Listing 2: Listing of Adhesion Score for Test Treatment (B) - M207 Thigh 30 minutes

Subject	Sequence	Pre-Dose	30 minutes
XXXX			
XXXX			
XXXX			

Listing 3: Listing of Adhesion Score for Test Treatment (C) - M207 Arm 60 minutes

Subject No.	Sequence	Pre-Dose	30 minutes	60 minutes	Mean Score
XXXX					
XXXX					
XXXX					

Summary Table 14.3.2: Descriptive Statistics by Treatment for Adhesion

Variable	N	Mean	Std Dev	Minimum	Maximum	Median
Treatment (A) - M207 Arm 30 minutes						
Treatment (B) - M207 Thigh 30 minutes						
Treatment (C) - M207 Arm 60 minutes						

Summary Table 14.3.4: Descriptive Statistics by Treatment for ECG Parameters

Heart Rate							
Variables		**0 minutes**	**15 minutes**	**60 minutes**	**8 hour**	**12 hour**	**48 hour**
Treatment (A) - M207 Arm 30 minutes	**N**						
	Mean						
	Std Dev						
	Minimum						
	Maximum						
	Median						

Note: Same tables needs to be followed for rest of the treatments and variables i.e. PR Interval, QRS Interval, QT Interval and QTcF.

Summary Table 14.3.4.1: Descriptive Statistics by Treatment for Vital Signs

Systolic_blood_pressure								
Variables		**0 minutes**	**10 minutes**	**60 minutes**	**2 hour**	**4 hour**	**12 hour**	**48 hour**
Treatment (A) - M207 Arm 30 minutes	**N**							
	Mean							
	Std Dev							
	Minimum							
	Maximum							
	Median							

Note: Same tables needs to be followed for rest of the treatments and variables i.e. Diastolic_blood_pressure, Heart_Rate, Respiratory_rate and Body Temprature.

Summary Table 14.3.5: Descriptive Statistics by Treatment for Investigator Visual Skin Evaluation

Erythema							
Variables		**Pre-dose**	**30 minutes**	**60 minutes**	**12 hour**	**24 hour**	**48 hour**
Treatment (A) - M207 Arm 30 minutes	**N**						
	Mean						
	Std Dev						
	Minimum						
	Maximum						
	Median						

Note: Same tables needs to be followed for rest of the treatments and variables i.e. Edema, Bruising and Bleeding.

Summary Table 14.3.6: Frequency by Treatment for Investigator Visual Skin Evaluation

Frequency_Erythema							
Variables		**Pre-dose**	**30 minutes**	**60 minutes**	**12 hour**	**24 hour**	**48 hour**
Treatment (A) - M207 Arm 30 minutes	**0**						
	1						
	2						
	3						

Note: Same tables needs to be followed for rest of the treatments and variables i.e. Edema, Bruising and Bleeding.

Summary Table 14.3.7: Descriptive Statistics by Treatment for Adhesion

Variable	N	Mean	Std Dev	Minimum	Maximum	Median
Treatment (A) - M207 Arm 30 minutes						
Treatment (B) - M207 Thigh 30 minutes						
Treatment (C) - M207 Arm 60 minutes						

Listing 14.2.1: Time (unit) and Plasma M207 Concentration (unit) Data of Test Treatment-M207 Arm 30 minutes for Individual Subjects

			Time (hrs)													
			0.000	0.033	0.083	0.167	0.250	0.333	0.500	0.750	1.000	1.500	2.000	4.000	8.000	12.000	24.000
Subject	Sequence	Period	Concentration (unit)														
XXXX																	

Listing 14.2.2: Time (unit) and Plasma M207 Concentration (unit) Data of Test Treatment-M207 Thigh 30 minutes for Individual Subjects

			Time (hrs)													
			0.000	0.033	0.083	0.167	0.250	0.333	0.500	0.750	1.000	1.500	2.000	4.000	8.000	12.000	24.000
Subject	Sequence	Period	Concentration (unit)														
XXXX																	

Listing 14.2.3: Time (unit) and Plasma M207 Concentration (unit) Data of Test Treatment-M207 Arm 60 minutes for Individual Subjects

			Time (hrs)													
			0.000	0.033	0.083	0.167	0.250	0.333	0.500	0.750	1.000	1.500	2.000	4.000	8.000	12.000	24.000
Subject	Sequence	Period	Concentration (unit)														
XXXX																	

Listing 14.2.4: Time (unit) and Plasma M207 Concentration (unit) Data of Test Treatment-INT Spray 2.5 mg for Individual Subjects

			Time (hrs)													
			0.000	0.033	0.083	0.167	0.250	0.333	0.500	0.750	1.000	1.500	2.000	4.000	8.000	12.000	24.000
Subject	Sequence	Period	Concentration (unit)														
XXXX																	

Listing 14.2.5: Pharmacokinetic Parameter and Ratio Values of zolmitriptan for Individual Subjects

Subject	Sequence	Cmax (unit)										AUCt (unit)									
		A	B	C	D	A/B	A/C	A/D	B/C	B/D	C/D	A	B	C	D	A/B	A/C	A/D	B/C	B/D	C/D
XXXX																					

Subject	Sequence	AUC(0-0.5) (unit)										AUC(0-1) (unit)									
		A	B	C	D	A/B	A/C	A/D	B/C	B/D	C/D	A	B	C	D	A/B	A/C	A/D	B/C	B/D	C/D
XXXX																					

Subject	Sequence	AUC(0-2) (unit)										AUCi (unit)									
		A	B	C	D	A/B	A/C	A/D	B/C	B/D	C/D	A	B	C	D	A/B	A/C	A/D	B/C	B/D	C/D
XXXX																					

Listing 14.2.6: Pharmacokinetic Parameter Values of zolmitriptan for Individual Subjects

Subject	Sequence	Tmax (unit)				Kel (unit)				tHalf (unit)			
		A	B	C	D	A	B	C	D	A	B	C	D
XXXX													

Subject	Sequence	REGSTART (unit)				REGEND (unit)				NUMPT				AUC_%Extrap_obs			
		A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
XXXX																	

Note: All the above provided summary table of pharmacokinetics will be same presented for metabolite n-desmethyl zolmitriptan as a supportive information. All treatments lables will be provided in footenote for this table.

Listing 14.2.7: Pharmacokinetic Parameter Frel of zolmitriptan for Individual Subjects

Subject	Sequence	AUCt (unit)			Frel (%)		
		A	B	C	A & B	A & C	B & C
XXXX							

Note: Above mentioned table will be same presented for metabolite n-desmethyl zolmitriptan as a supportive information. All treatments lables will be provided in footenote for this table.

Listing 14.2.8: Amount of Residual Drug on Used Test Treatment-A for Individual Subjects at 30 minutes (Upper Arm Application)

			Time (hrs)	
			0.500	
Subject	Sequence	Period	Amount (unit)	
			Patch-1	Patch-2
XXXX				

Listing 14.2.9: Amount of Residual Drug on Used Test Treatment-B for Individual Subjects at 30 minutes (Thigh Application)

			Time (hrs)	
			0.500	
Subject	Sequence	Period	Amount (unit)	
			Patch-1	Patch-2
XXXX				

Listing 14.2.10: Amount of Residual Drug on Used Test Treatment-C for Individual Subjects at 60 minutes (Upper Arm Application)

			Time (hrs)	
			1.000	
Subject	Sequence	Period	Amount (unit)	
			Patch-1	Patch-2
XXXX				

Listing 14.2.11: Amount of Residual Drug on Skin (3 Swabs) after removing Test Treatment-M207 Arm 30 minutes, Test Treatment-M207 Thigh 30 minutes and Test Treatment-M207 Arm 60 minutes for Individual Subjects

			Treatment-A	Treatment-B	Treatment-C
			Time (hrs)	Time (hrs)	Time (hrs)
			0.500	0.500	1.000
Subject	Sequence	Period	Amount (unit)	Amount (unit)	Amount (unit)
XXXX					

Listing 14.2.12: Listing of Adhesion Score for Test Treatment (A) - M207 Arm 30 minutes

Subject	Sequence	Pre-Dose	30 minutes
XXXX			
XXXX			
XXXX			

Listing 14.2.13: Listing of Adhesion Score for Test Treatment (B) - M207 Thigh 30 minutes

Subject	Sequence	Pre-Dose	30 minutes
XXXX			
XXXX			
XXXX			

Listing 14.2.14: Listing of Adhesion Score for Test Treatment (C) - M207 Arm 60 minutes

Subject No.	Sequence	Pre-Dose	30 minutes	60 minutes	Mean Score
XXXX					
XXXX					
XXXX					

Listing 14.2.15: PK Blood Sampling Time Deviations

Subject	Period	Time Point	Deviation +/- (minutes)	Actual Blood collection time (hr)
XXXX				

Listing 16.1.6: Listing of Subjects Receiving Treatment

Subject	Period	Treatment	Dosing Date (DDMMMYY)	Dosing Start Time (HH:MM)
XXXX				

Listing 16.2.1: Listing of Subject Disposition

Subject	Period	Date of Completion/Discontinuation (DDMMMYYYY)	Status*
XXXX			
*If status is OTHER, specify the reason for non-completion.			

Listing 16.2.2: Protocol Deviations

Period	Subject	Sample Time Point (hours)	#Minutes	Early/Late	Deviation	Impact Assessment
Note: NA: Not Available						

Listing 16.2.2.1: Other Protocol Deviations

Subject	Period	Date of Deviation (DDMMMYYYY)	Deviation
XXXX	1		
	2		
	3		
	4		

Listing 16.2.4: Demographic Data*

Subject	Collection Date (DDMMYYYY)	Age (Years)	Weight (kg)	Height (cm)	BMI (kg/m^2)	Sex	Race	Ethnicity
XXXX								

* Determined at Screening
Note:- BMI: Body Mass Index

Listing 16.2.7: Adverse Events Listings

						ONSET		END							
Subject	**Drug**	**Dosing Time & Date**	**Period**	**Adverse Event**	**Adverse Event (Preferred term)**	**Date (DDMMMYY)**	**Time (HH:MM)**	**Date (DDMMMYY)**	**Time (HH:MM)**	**Severity**	**Serious Y = YES N = NO**	**Relationship to drug**	**Resolution, Other Action Taken**	**Outcome**	**Caused Study Discontinuation Y = YES N = NO**
XXXX															
Medical Dictionary used: MedDRA Version XX.X															

Listing 16.2.7.1: Listing of Prior and Concomitant Medication

Subject	Site	Medication Name Or Therapy	Medication given for	Indication	Dose Per Administration & Unit	Frequency	Route	Start Date (DDMMMYYYY)	End Date (DDMMMYYYY)	P/C
XXXX										

Note: P/C: P=Prior C=Concomitant. Medications that were stopped prior to first dose of study drug are termed as 'Prior'.
WHO DD Version: xxxxxxxx.

Listing 16.2.8: Listing Drug Screen-Alcohol Breath Testing Results at Screening and at Admission/baseline

Subject	Site	Collection Date (DDMMMYYYY)	Collection Time (HHMM)	Visit	Panel Name	Test	Result
XXXX						XXXXXXX	Positive

Listing 16.2.8.1: Listing Abnormal Clinically Significant Lab Results

Subject	Visit	Date	Laboratory Test	Units	Range	Results	Abnormality Flag
XXXX							

Listing 16.2.8.2: Listing of Pregnancy Test Results Performed on Screening and Admission/baseline

Subject	Visit	Pregnancy test performed?	Date of test performed (DDMMMYYYY)	Result
XXXX				

Listing 16.2.8.3: Listing of Patch Retainment and Residual Drug Collection

Subject	Treatment	Patch site	Collection	Collection Date (DDMMMYYYY)	Collection Time (HH:MM)
XXXX					

Listing 16.2.8.4: Listing of Vital Signs Assessments

Subject	Visit	Vital Signs Date (DDMMMYYYY)	Time (HHMM)	Vital Sign (Unit)	Result
XXXX					

Listing 16.2.8.5: Listing of Medical History

Subject	Site	Medical History Category	Medical / Surgical Term	Start Date (DDMMMYYYY)	Stop Date (DDMMMYYYY)	Ongoing
XXXX						

Listing 16.2.8.6: Listing of Physical Examination at Screening and 12 hr

Subject	Site	Visit	Date of Physical Examination (DDMMMYYYY)	Body System	Result	Abnormal Findings	Clinically significant Y = Yes N = No
XXXX							

Listing 16.2.8.7: Listing of Adhesion Assessment at 30 Minute and 60 Minute

Subject	Patch	Adhesion Assessment Time Point	Adhesion Assessment Date (DDMMMYYYY)	Adhesion Assessment Time (HH:MM)	Adhesion Assessment Score	Adhesion Assessment Result
XXXX						

Listing 16.2.8.8: Listing of Investigator Visual Skin Evaluation at Pre-dose, 30 Minute, 60 Minute, 12 hour, 24 hour and EOS/Early Term

Subject	Patch Site	Visual Skin Assessment Time Point	Visual Skin Assessment Date (DDMMMYYYY)	Visual Skin Assessment Time (HH:MM)	Visual Skin Evaluation	Visual Skin Evaluation Score	Visual Skin Evaluation Result
XXXX					Erythema Evaluation		
					Edema Evaluation		
					Bruising Assessment		
					Bleeding Assessment		

Listing 16.2.8.9: Listing of ECG performed on during Screening, Pre-dose, 15 minutes, 60 minutes, 8 hour, 12 hour and End of Study

Subject	Date of ECG performed (DDMMMYYYY)	Time of ECG performed (HH:MM)	ECG Parameters (unit)	Result	Overall Interpretation	If Abnormal, Clinically significant?	If Yes, please specify
XXXX			Heart Rate (beats/min)				
			PR Interval (msec)				
			QRS Interval (msec)				
			QT Interval (msec)				
			QTcF - Fridericia`s Correction Formula (msec)				

Figure 1: Linear Mean Plot of Zolmitriptan Treatments over Time

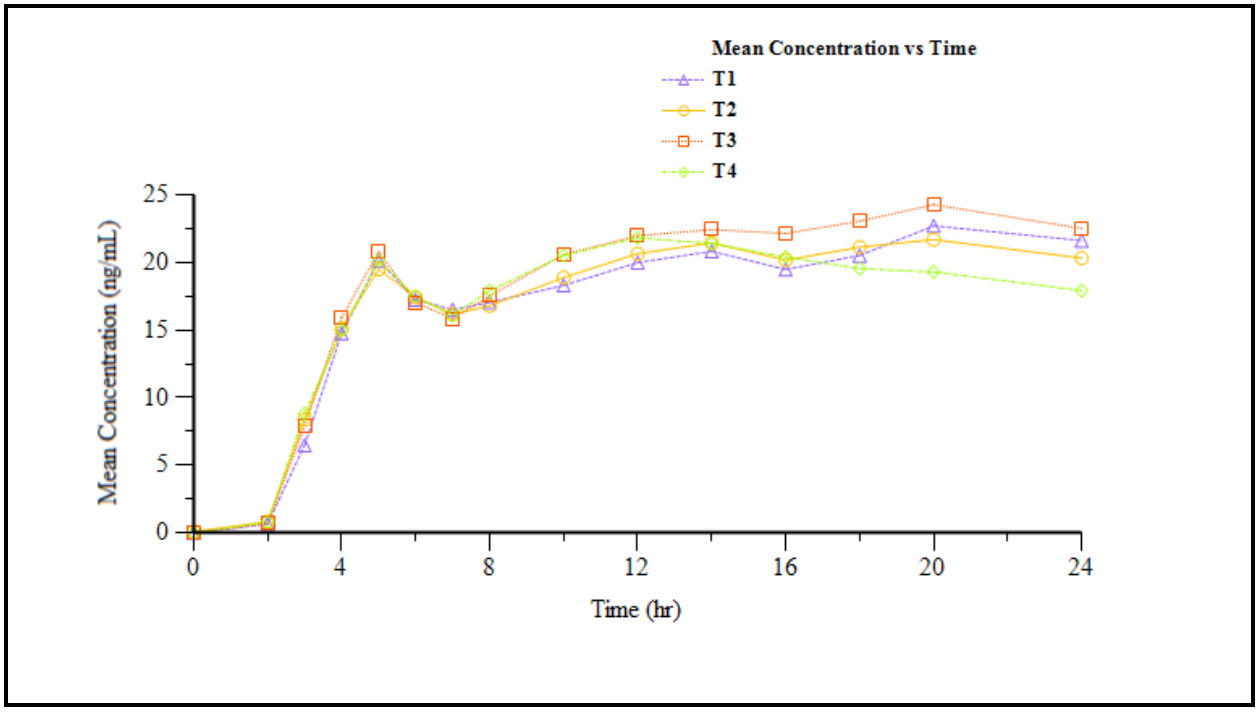

Figure 2: Mean Plot of Zolmitriptan Treatments over First 2 Hours