NCT02873221

Study ID: UBR-MD-04

Title: A Multicenter, Randomized, Open-Label Extension Study to Evaluate the Long-Term Safety and Tolerability of Oral Ubrogepant in the Acute Treatment of Migraine With or Without Aura

Statistical Analysis Plan Amd 2 Date: 04-Sept-2018

1. Title Page

STATISTICAL ANALYSIS PLAN

A MULTICENTER, RANDOMIZED, OPEN-LABEL EXTENSION STUDY TO EVALUATE THE LONG-TERM SAFETY AND TOLERABILITY OF ORAL UBROGEPANT IN THE ACUTE TREATMENT OF MIGRAINE WITH OR WITHOUT AURA

Amendment 2: 2018-09-04

Protocol Number:	UBR-MD-04 Amendment 2
Development Phase:	3
Product Name:	Ubrogepant
Study Statistician:	[redacted].
Sponsor:	Allergan Pharmaceuticals 2525 Dupont Drive Irvine, California USA 92612 +1-714-246-4500 +1-800-347-4500

2. Table of Contents

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Table 3-1 Abbreviations and Definitions of Terms

Abbreviation/Term	Definition
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	body mass index
C-SSRS	Columbia–Suicide Severity Rating Scale
CFB	change from baseline
CHD	coronary heart disease
CSR	clinical study report
CV	cardiovascular
eCRF	electronic case report form
ECG	electrocardiogram, electrocardiographic
FDS	Functional Disability Scale
HEOR	Health Economics and Outcomes Research
INR	international normalized ratio
IWRS	interactive web response system
kg	kilogram(s)
LOCF	last observation carried forward
m	meter(s)
MedDRA	Medication Dictionary for Regulatory Activities
mg	milligrams
mITT	modified intent-to-treat
MQoLQ	migraine quality of life questionnaire
PCS	potentially clinically significant
PF	pain free
PK	pharmacokinetic
PR	pain relief
PT	preferred term
QTc	QT interval corrected for heart rate
QTcB	QT interval corrected for heart rate using the Bazett formula ($QTcB = QT/(RR)^{1/2}$)
QTcF	QT interval corrected for heart rate using the Fridericia formula ($QTcF = QT/(RR)^{1/3}$)
SAE	serious adverse event
SAP	statistical analysis plan
SAS	Statistical Analysis Software
SD	standard deviation
SE	standard error

Abbreviation/Term	Definition
SI	Le Système International d'Unités (International System of Units)
SOC	system organ class
SPF	sustained pain freedom
TBL	total bilirubin
TEAE	treatment-emergent adverse event
ULN	upper limit of normal
US	United States of America
WHO	World Health Organization

4. Introduction

This statistical analysis plan (SAP) details comprehensive, technical specifications of the statistical analyses of the efficacy and safety data outlined and/or specified in the protocol amendment #***2*** dated 06 Dec 2017 of Study UBR-MD-04. Specifications of tables, figures, and data listings are contained in a separate document. The SAP for health economics and outcomes research (HEOR) data will be prepared separately.

This document is organized into 3 main sections:

1. Study overview
2. Statistical Methodology and Study Endpoints
3. Data Handling and Analysis Conventions

4.1 Study Design Summary

Structure: Multicenter, randomized, open-label, 52-week extension study; randomization to the ubrogepant arms (50 and 100 mg) will be blinded.

Duration: 52 weeks

Study Treatment Groups: usual care, ubrogepant 50 mg, or ubrogepant 100 mg

Controls: Not applicable

Dosage/Dose Regimen: Patients randomized to either of the ubrogepant arms will treat up to 8 migraine attacks (of any pain severity) every 4 weeks at home for a total 1 year. Patients have the option to take a second dose of ubrogepant if the patient has either a nonresponding migraine or a migraine recurrence. The second dose of ubrogepant will be identical to the first dose.

Patients randomized to the usual-care arm will be instructed to treat their migraine with medications that they routinely use to relieve a migraine attack.

Randomization/ [redacted] Patients will be randomized (1:1:1) to 1 of the following 3 treatment groups: usual care, ubrogepant 50 mg, or ubrogepant 100 mg. The study is open-label; however, randomization to the ubrogepant arms (50 and 100 mg) will be blinded.

[redacted]

Number of Participants: Approximately 1200 patients will be randomized (400 patients per arm) from approximately 200 centers in the United States.

4.2 Study Objectives and Endpoints

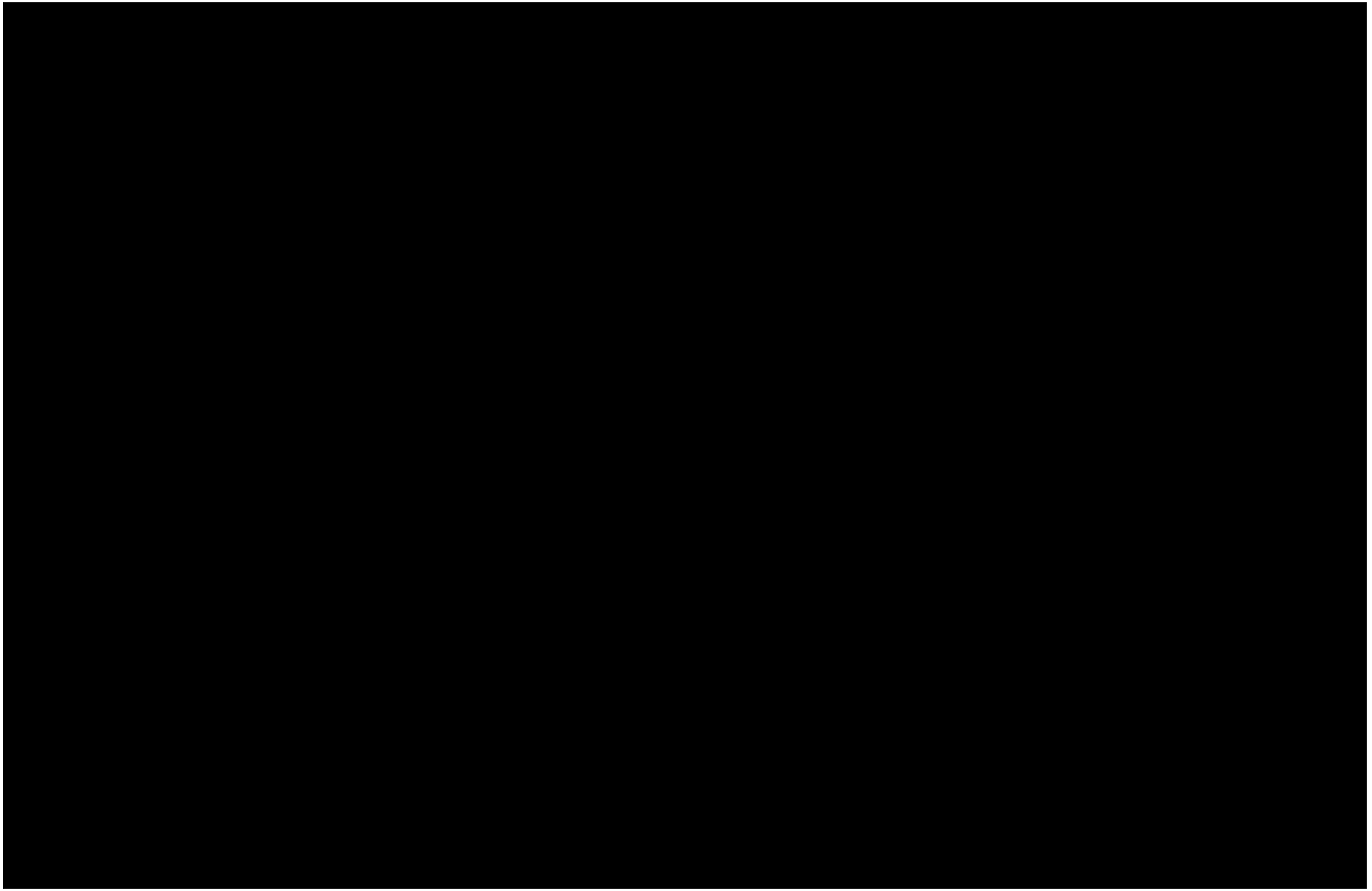
Each study objective is presented with corresponding endpoint(s) below:

Table 4-1 Study Objectives and Corresponding Endpoints

Objectives	Endpoints
Primary • [PO1] To evaluate the safety and tolerability of intermittent treatment with ubrogepant for the acute treatment of migraine over 1 year	[redacted]

Objectives	Endpoints
	 **Safety Assessments** • Adverse events (AE), clinical laboratory values, vital signs, electrocardiogram (ECG), physical examinations, and the Columbia–Suicide Severity Rating Scale (C-SSRS)

4.3 Schedule of Activities



5. Statistical Methodology and Study Endpoints

5.1 Statistical Methods Planned in the Protocol and Determination of Sample Size

This statistical analysis plan (SAP) will be approved prior to database lock. The SAP expands the statistical section of the protocol and contains a detailed description of methods to analyze data collected in the study. The text portion of the SAP will be included in the clinical study report (CSR) report as Appendix 16.1.9.

5.1.1 Statistical and Analytical Plans

Statistical analyses will be conducted using [redacted].

5.1.1.1 Common Conventions

5.1.1.1.1 Analysis Populations

The analysis populations will consist of participants as defined below:

Table 5-1 Analysis Populations

Population	Definition	Study Treatment
Screened	All screened participants who signed informed consent	—
Intent-to-Treat (ITT)	All randomized participants.	Randomized assignment
Modified Intent-to-Treat (mITT)	All randomized patients who received at least 1 dose of IP (ubrogepant) and had at least 1 posttreatment efficacy assessment in this study. The mITT population is only defined for the ubrogepant arms, as no posttreatment efficacy measurements will be collected from patients in the usual-care arm.	Randomized assignment
Safety	The Safety population is defined separately below for the ubrogepant arms and the usual-care arm. Ubrogepant arms: All randomized patients who received ≥ 1 dose of treatment. Usual care arm: All randomized patients in the usual-care arm. The purpose of the usual care arm is to contextualize any safety findings that may occur in the ubrogepant treated patients over the course of 12 months. As such, data from all patients randomized to the usual care arm, regardless of whether the patient used medication to treat migraine, will be included in the safety analyses.	Actual received

5.1.1.1.2 Study Treatments

The following treatment groups are defined for this study:

- Usual Care
- Ubrogepant 50 mg
- Ubrogepant 100 mg

5.1.1.1.3 Statistical Methodology

The methodologies defined below apply as specified to individual endpoints defined in this SAP. All statistical tests will be 2-sided hypothesis tests performed at the 5% level of significance for main effects. All confidence intervals will be 2-sided 95% confidence intervals, unless stated otherwise.

Table 5-2 Statistical Methodology

Methodology		Description
M1	Categorical counts	• Number of participants in individual categories o Participants with ≥ 1 qualifying event counted once per individual category

M2	Categorical descriptives	• Number and percentage of participants in individual categories
		  o Participants with ≥ 1 qualifying event counted once per individual category
		• N1 if proportion denominator ≠ number of participants in the population (standard percentage denominator)
		  o N1 = participants with non-missing baseline value

M3	PCS descriptives	• Number and percentage of participants meeting potentially clinically significant (PCS) criteria
		  o Participants with ≥ 1 qualifying event counted once per PCS category
		• Percentage denominator = number of participants with all non-missing non-PCS baseline and >=1 non-missing postbaseline assessment
		  o Unevaluable assessments considered missing

M4	Shift analysis	• Number and percentage of participants in individual baseline and postbaseline categories • Percentage denominator = number of participants in individual baseline categories • N1 = participants with non-missing values at both baseline and the specified postbaseline analysis visit
M5	Continuous descriptives	• N1, mean, standard deviation (SD), median, minimum, maximum • N1 = participants with non-missing value
M6	CFB descriptives	• Continuous descriptives for baseline, postbaseline, and change from baseline (CFB) values • N1 = participants with non-missing values at both baseline and the specified postbaseline analysis visit

M7	Responder	• Categorical descriptives using proportions for responders and nonresponders
		  o Nonresponders include:
		  ▪ Participants who do not meet responder criteria
		• N1 = all participants unless otherwise specified

M8	Logistic regression model	• Measures the relationship between the binomial dependent variable (number of events among number of treated attacks) and independent variables:
		  o fixed effect terms:
		  ▪ treatment (ubrogepant 50 mg, ubrogepant 100 mg)
		  ▪ time
		  ▪ treatment-by-time interaction
		  o Random effect term:
		  ▪ patient

Methodology	Description
	• Odds ratio for comparing the percentage of treated attacks with PF at 2 hours for a given 3-month interval with that for the first 3-month interval and its 95% confidence interval will be derived from the mixed logistic regression model for each of the 2 ubrogepant treatment groups. ○ Calculate two-sided p-values

CFB = change from baseline.
Raw and derived data listings will be provided, and will be fully defined in the table, figure, and data listing specification document.

5.1.1.1.4 Missing Data

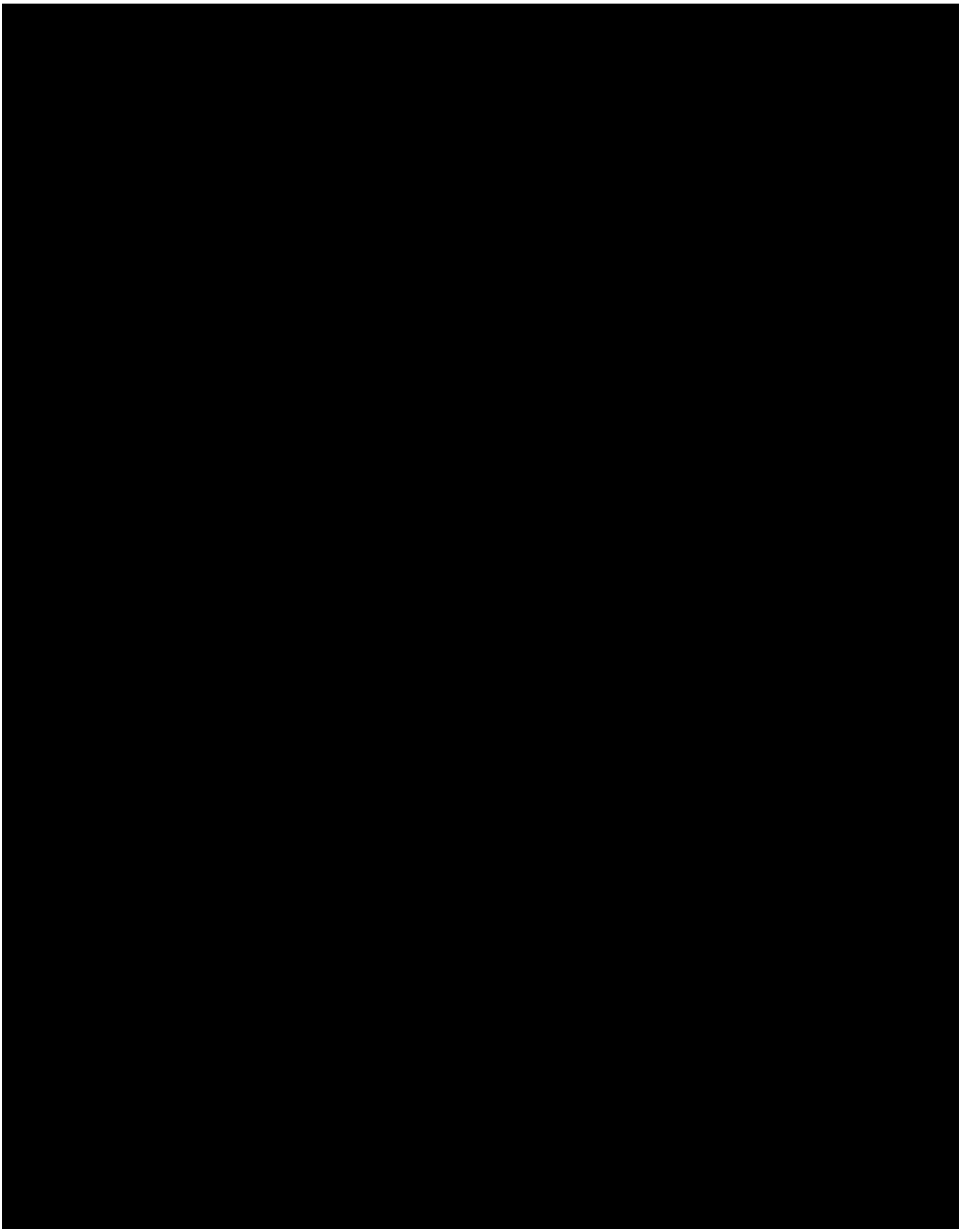
General missing data handling conventions are specified for methodologies in Section 5.1.1.1.3 and summarized as follows:

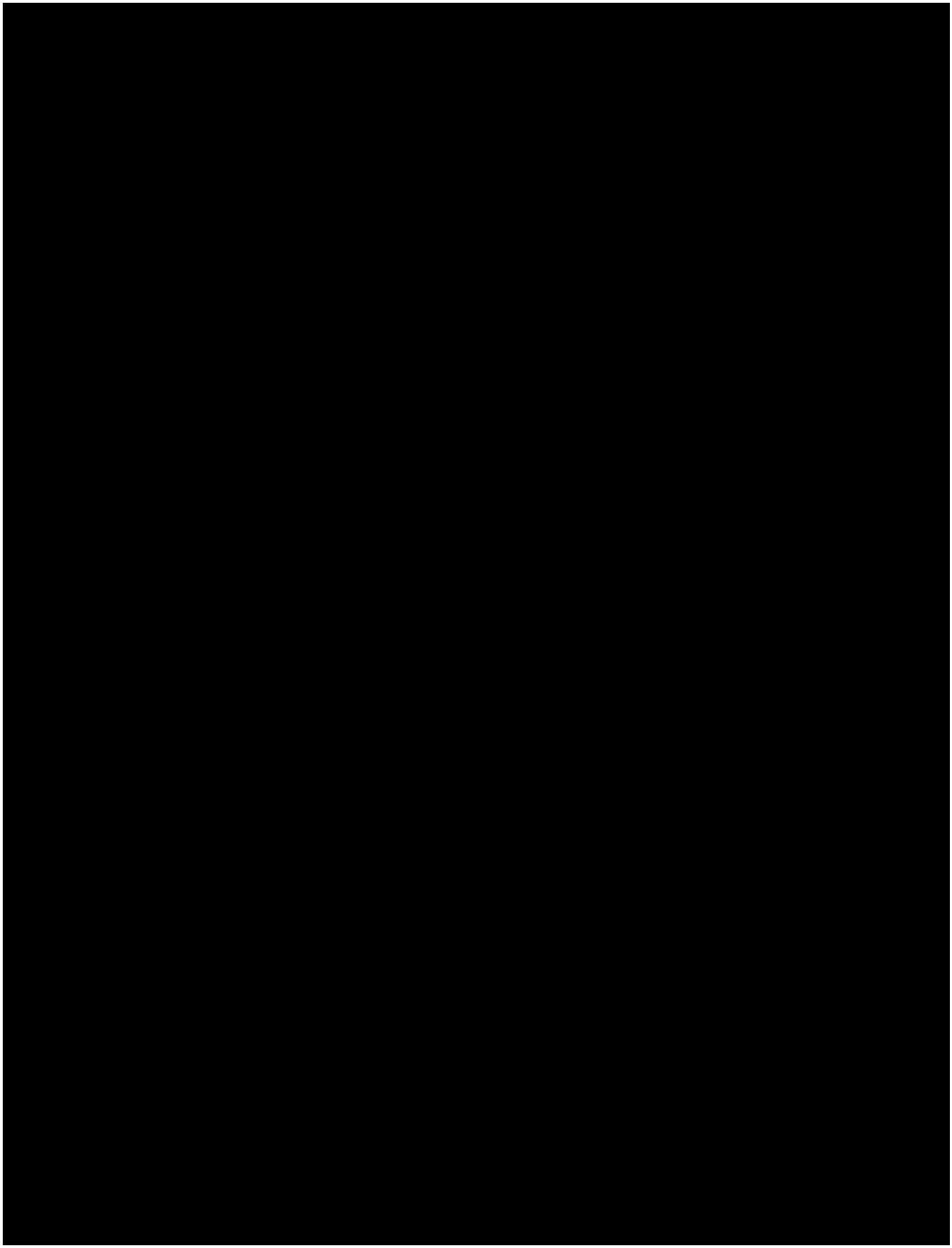
Table 5-3 Missing Data Handling by Endpoint Type

Parameter type	Timing	Missing Data Handling
Responder	Treatment Period	• If missing headache severity, migraine-associated symptoms, use Observed Cases (OC)

A conservative approach will used to resolve the incompatibility between the answers to the headache recurrence questions at the 24- and 48-hour time points for each treated attack by setting the answer to the recurrence question at the 48-hour time point the same as the answer to the recurrence question at the 24-hour time point, when the 24-hour time point recurrence question indicates headache recurrence between 2 and 24 hours but the 48-hour time point recurrence question indicates either no or a less severe headache recurrence between 2 and 48 hours for the same treated attack.

[redacted]





[redacted]

5.1.1.2 Demographics

5.1.1.2.1 Analysis Populations

The distribution of participants within the analysis populations will be summarized as follows:

Table 5-4 Analysis Population Summaries

Population	Description	Timing	Methodology
Screened Population	Distribution overall and within sites in total Distribution by lead-in study treatment and within extension study in total	—	Categorical counts
ITT, mITT, and Safety populations	Distribution overall and within sites in total and by treatment group Distribution by lead-in study treatment and by extension study treatment	—	Categorical counts

5.1.1.2.2 Participant Disposition

Participant disposition encompasses the distribution of participants who enter, complete, and discontinue each specified analysis period, along with eCRF-reported discontinuation reasons from each respective analysis period. Participant disposition will also be presented for the relevant subgroups including sex, age group, race, CV risk category, and renal function class. The subgroups are defined in the lead-in studies. Participant disposition will be summarized as follows:

Table 5-5 Participant Disposition Summaries

Parameter	Description	Timing	Methodology
Screening disposition[1]	Distribution in the Screened Population in total	Screening Period	Categorical descriptives
Treatment disposition[1]	Distribution in the Safety Population and ITT Population in total and by treatment group for all participants and by subgroups: • by sex, • by age group (<40 years vs ≥40 years) • by age subgroup (<65 years vs ≥65 years) • by race (white vs non-white) • by cardiovascular risk category (high risk, moderate risk, and low risk) • by renal function class (normal,	Treatment Period	Categorical descriptives

Parameter	Description	Timing	Methodology
	mild renal impairment, moderate renal impairment)		
4 Week Safety Follow-up disposition[1]	Distribution in the Safety Population and ITT Population in total and by treatment group for all participants and by subgroups: • by sex, • by age group (<40 years vs ≥40 years) • by age subgroup (<65 years vs ≥65 years) • by race (white vs non-white) • by cardiovascular risk category (high risk, moderate risk, and low risk) • by renal function class (normal, mild renal impairment, moderate renal impairment)	Post-treatment Period	Categorical descriptives

[1] Participant disposition will be listed and participants who prematurely discontinued will be listed.

CV risk subgroup will be derived as a categorical variable with three categories based on NCEP ATP III: Category 1 (High Risk): > 20% 10-year CV risk, Category 2 (Moderate Risk): 10 - 20% 10-year CV risk, and Category 3 (Low Risk): <10% 10-year CV risk.

Renal function class will be derived as a categorical variable based on baseline eGFR as shown in Table 5-6. Since only a few participants are classified into the categories of severe renal impairment or ESRD, renal function class for subgroup analyses will focus on the following categories: Normal, Mild renal impairment, Moderate renal impairment. A listing of all AEs for participants with severe renal impairment or ESRD will be provided including treatment group, participant ID, study center, and baseline eGFR.

Table 5-6 Classification of Renal Function Based on Estimated GFR (eGFR)

Stage	Renal Function Class	eGFR[a] (mL/min/1.73m^2)
1	Normal	≥ 90
2	Mild renal impairment	60-89
3	Moderate renal impairment	30-59
4	Severe renal impairment	15-29
5	End Stage Renal Disease (ESRD)	<15 not on dialysis

[a] eGFR: estimate of GFR based on a Modification of Diet in Renal Disease (MDRD) equation.

5.1.1.2.3 Protocol Deviations

Protocol deviations will be defined in Protocol Deviation Requirement Specification, including importance classification. Protocol deviations will be summarized as follows:

Table 5-7 Protocol Deviation Summary

Parameter	Description	Timing	Methodology
Major protocol deviations[1]	Distribution in the ITT Population in total and by treatment group	—	Categorical descriptives

[1] Protocol deviations will be listed.

5.1.1.2.4 Demographics

Demographics will be summarized in total and by treatment group for the ITT, Safety, and mITT populations, as follows:

Table 5-8 Demographic Summaries

Parameter	Description	Timing	Methodology
Age[1]	Age (years) relative to informed consent date	Informed consent in the lead-in study	Continuous descriptives
Age group	Age group 1: • <20 • 20 to 29 • 30 to 39 • 40 to 49 • 50 to 59 • 60 to 69 • ≥ 70 Age group 2: • <40 • ≥40 Age group 3: • <65 • ≥65	Informed consent in the lead-in study	Categorical descriptives

Sex, race, and ethnicity[1]	• eCRF categories
	• Race group
	  ○ White
	  ○ Non-white
		Screening Period in the lead-in study	Categorical descriptives

[1] Participant demographics will be listed.

5.1.1.2.5 Baseline Characteristics

Baseline characteristics will be summarized in total and by treatment group for the ITT, Safety, and mITT populations as follows:

Table 5-9 Baseline Characteristics Summaries

Parameter	Description	Timing	Methodology
Baseline characteristics[1]	• Height (m) • Weight (kg) • Body mass index (BMI) ○ Weight (kg) / height (m)^2	Latest assessment in Screening Period in the lead-in study	Continuous descriptives
Cardiovascular risk[2]	Cardiovascular risk factor subgroup • low risk • moderate risk • high risk	Randomization date in the lead-in study	Categorical descriptives

Parameter	Description	Timing	Methodology
Renal function class[2]	Renal function class subgroup • Normal • Mild renal impairment • Moderate renal impairment	Randomization date in the lead-in study	Categorical descriptives
Randomization strata[3]	Previous response to triptans • Triptan Responder • Triptan Insufficient Responder • Triptan Naïve Triptan Insufficient Responder will be further classified into subcategories • Insufficient Efficacy • Insufficient Tolerability • Contraindications/Warnings or Precautions Current use of prophylactic concomitant medication for migraine (Yes, No)	Randomization date in the lead-in study	Categorical descriptives

[1] Participant baseline characteristics will be listed.
[2] Summary for Safety population only.
[3] Participant randomization scheme and codes will be listed.

5.1.1.2.6 Medical History

Medical history, encompassing abnormalities and surgeries reported as occurring before the Screening Visit in the lead-in study, will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 20.1 or newer. Unique participants who report medical history events will be summarized by MedDRA system organ class (SOC) and preferred term (PT) in total and by treatment group for the Safety Population as follows:

Table 5-10 Medical History Summary

Parameter	Description	Timing	Methodology
Medical history[1]	Abnormalities and surgeries occurring before the Screening Visit by treatment group	Screening Period in the lead-in study	Categorical descriptives

SOCs will be sorted alphabetically; PTs will be sorted in descending frequency in the highest dose group.
[1] Participant medical history will be listed.

5.1.1.2.7 Migraine History

Migraine history (based on the lead-in study), including diagnosis, duration of disorder, previous use of prophylaxis treatment, average frequency of moderate to severe migraines per month in past 3 months, and acute treatments will be reported in total and by treatment group for the Safety Population as follows:

Table 5-11 Migraine History Summary

Parameter	Description	Timing	Methodology
Migraine Diagnosis[1]	• With Aura • Without Aura • Both	Screening Period in the lead-in study	Categorical descriptives
Previous Prophylaxis Migraine Treatment[1]	Yes or No	Screening Period in the lead-in study	Categorical descriptives
Acute Migraine Treatment[1]	Categorize as Yes or No, and subcategorize the Yes by:	Screening Period in the lead-in	Categorical descriptives

Parameter	Description	Timing	Methodology
	• Triptan • Ergot or Ergot Combinations • NSAID • Opiate or Opiate Combination • Antiemetic Agent • Barbiturates • Other	study	
Migraine Disorder Duration[1]	In the Table summarize in Years, in the Listing show original data in Years and Months	Screening Period in the lead-in study	Continuous descriptives
Average Frequency of Moderate to Severe Migraines per Month in Last 3 Months	N/A	Screening Period in the lead-in study	Continuous descriptives

[1] Participant migraine history will be listed.

5.1.1.2.8 Prior and Concomitant Medications

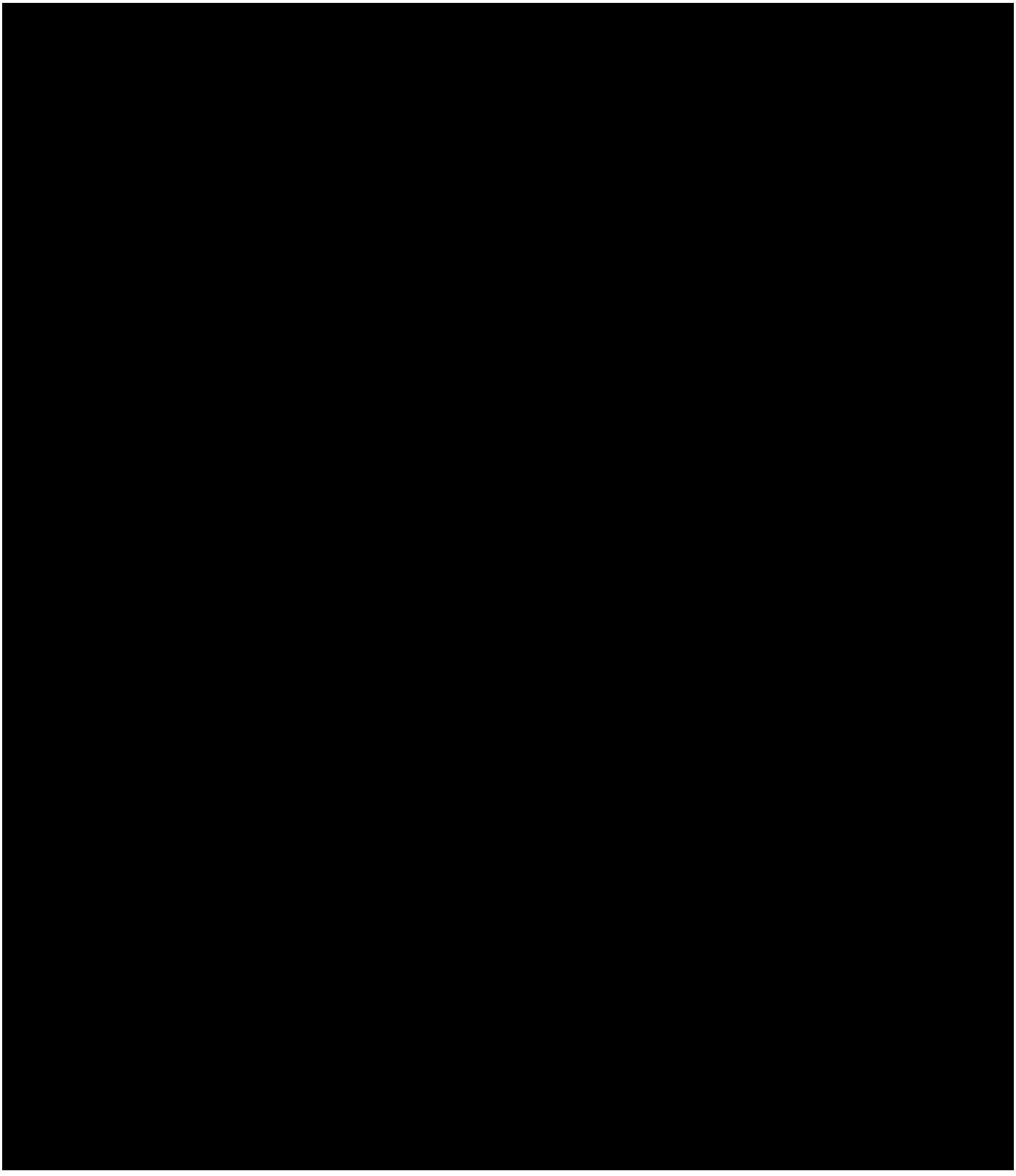
Medications will be coded using the World Health Organization (WHO) Drug Dictionary, version March 2016 or newer. Unique participants who reported medications will be summarized by Anatomical Therapeutic Chemical (ATC) 4 class and PT in total and by treatment group for the Safety Population as follows:

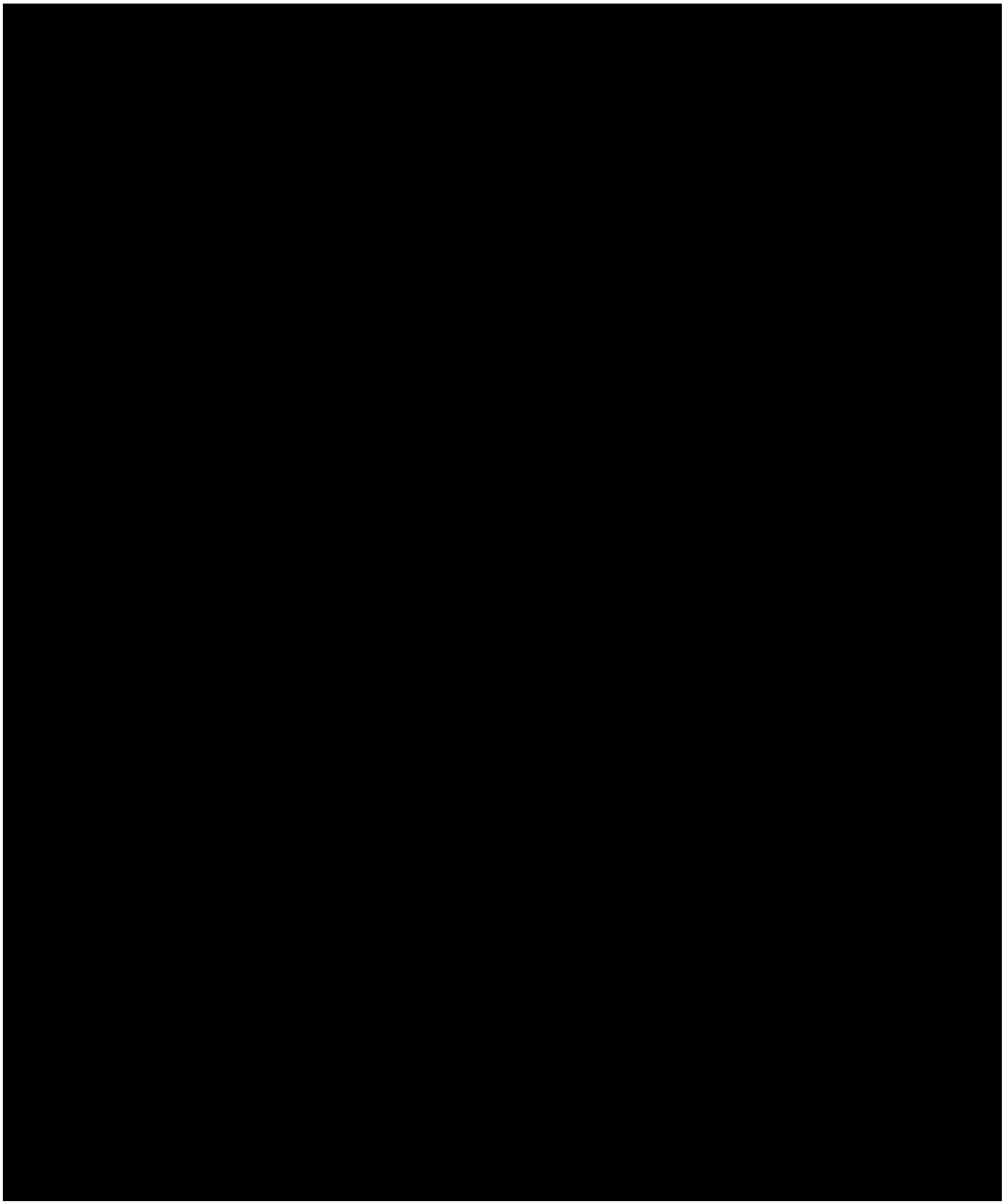
Table 5-12 Medication Summaries

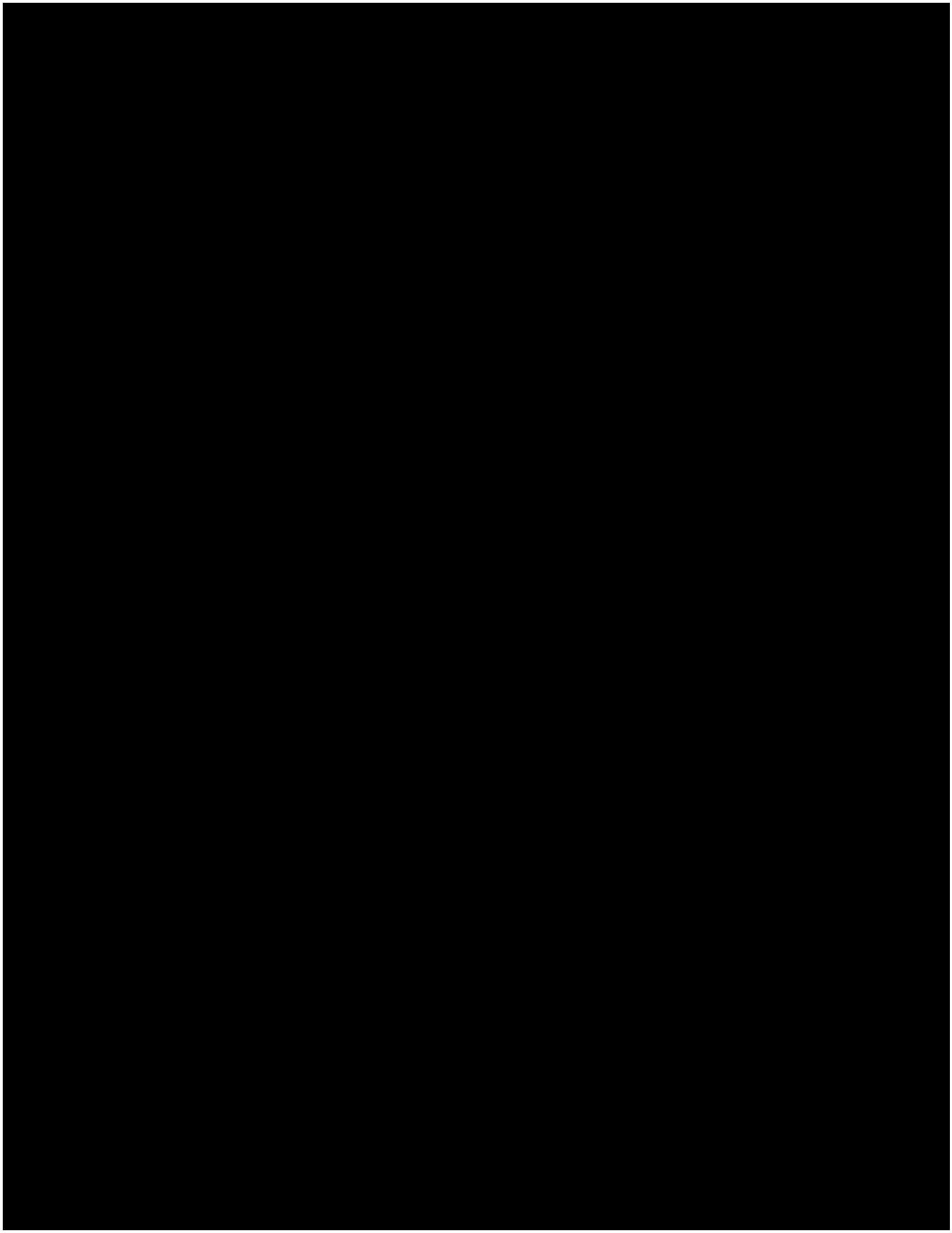
Parameter	Description	Timing	Methodology
Prior medications[1]	Medications taken ≥ 1 time before the study treatment start date of the lead-in study, regardless of medication end date	Screening Period in the lead-in study	Categorical descriptives
Concomitant medications[1]	Medications taken ≥ 1 time on or after the randomization date, regardless of medication start date	Treatment Period	Categorical descriptives

ATC4 classes will be sorted alphabetically; PTs will be sorted in descending frequency in the highest dose group.
[1] Participant prior and concomitant medication will be listed.

[redacted]







[redacted]

[redacted]

[redacted]

5.1.1.4 Safety Analyses

Safety analyses will be based on the Safety Population.

Baseline assessments for applicable safety endpoints are defined as follows:

Table 5-16 Safety Endpoint Baseline Definitions

Parameter	Description	Timing
• Clinical laboratory evaluations • Vital signs • Electrocardiograms (ECGs)	eCRF- or (standardized) vendor-provided assessments	Latest non-missing assessment before the first dose of treatment in the lead-in study

5.1.1.4.1 Study Treatment Exposure and Compliance

Study treatment exposure will be listed for the Safety Population.

The listing of treatment exposure will indicate whether the participant took the optional second dose in addition to the first dose for each attack.

For safety analyses only, the number of treated migraine attacks will be determined based on the date and time (if available from eDiary) doses were taken. Starting with the first dose taken by each participant, doses will be sorted based on the date and time (if available from eDiary) each dose was taken. Subsequent doses that are separated by at least 2 calendar days or 48 hours will be considered the initial treatment for a separate and distinct migraine attack. Doses taken within the 2-calendar day/48-hour window of the initial dose will be considered as additional doses treating the same attack. As such, the treatment label (initial dose or optional second dose) will be ignored. The extent of exposure to study treatment will be summarized as follows:

Table 5-17 Treatment Exposure Summaries

Parameter	Description	Timing	Methodology
Number of participants with study participation by 3-month interval	For all participants: • total number (%) of participants who completed 3 months • total number (%) of participants who completed 6 months • total number (%) of participants who completed 9 months • total number (%) of participants who completed 12 months Subgroup analyses: • by Sex • by Age Group: <40 vs ≥40 • by Age Group: <65 vs ≥65 • by Race White vs All other races • by CV risk category • by renal function class	Treatment period	Categorical descriptives
Number of participants with study participation by 3-month interval among those who treated at least 2 migraine attacks per month on average during the completed interval	• total number (%) of participants who completed 3 months • total number (%) of participants who completed 6 months • total number (%) of participants who completed 9 months • total number (%) of participants who completed 12 months	Treatment period	Categorical descriptives
Number of migraine attacks treated over the entire duration of the study[1]	• total number of migraine attacks treated with only one dose • total number of migraine attacks treated with two or more doses • total number of doses taken	Treatment period	Continuous descriptives
Number of attacks treated with study treatment per month[1]	• >= 8 • >= 6 and < 8 • >= 4 and < 6 • >= 2 and < 4 • < 2	Treatment period	Categorical descriptives
Average number of attacks treated with study treatment per month[1]	For all participants: • >= 8 • >= 6 and < 8 • >= 4 and < 6 • >= 2 and < 4 • < 2 Subgroup analyses: • by Sex • by Age Group: <40 vs ≥40 • by Age Group: <65 vs ≥65 • by Race White vs All other races • by CV risk category • by renal function class	Treatment period	Categorical descriptives
Maximum number of attacks treated with study treatment per	• >= 8 • >= 6 and < 8 • >= 4 and < 6	Treatment period	Categorical descriptives

Parameter	Description	Timing	Methodology
month, defined as maximum of monthly total number attacks treated with study treatment among months 1-12 for each participant[1]	• >= 2 and < 4 • < 2		
Number of months with the number of attacks treated with study treatment in each category[1]	For each category: • >= 8 • >= 6 and < 8 • >= 4 and < 6 • >= 2 and < 4 • < 2	Treatment period	Categorical descriptives
Average number of study treatment taken per month[1]	• >= 16 • >= 14 and < 16 • >= 12 and < 14 • >= 10 and < 12 • >= 8 and < 10 • >= 6 and < 8 • >= 4 and < 6 • >= 2 and < 4 • < 2	Treatment period	Categorical descriptives

Analysis visits defined in Section 6.2.2.
[1] Participants in the ubrogepant treatment arms only. No imputation for the last incomplete month.

Treatment compliance for this study will be summarized as follows:

Table 5-18 Treatment Compliance Summaries

Parameter	Description	Timing	Methodology
Overdosing[1]	Participants who took more than 2 doses within 48 hours or 2 calendar days (if time information is not available)		Listing

[1] Participants in the ubrogepant treatment arms only.

5.1.1.4.2 Adverse Events

The following adverse event (AE) terms are defined:

Table 5-19 AE Terms

Term	Description
Treatment-emergent	An event that initially occurs or increases in intensity on or after the initial dose of treatment of the lead-in study. An event that occurs after Visit 16 for participants with Visit 16, or more than 30 days after the last visit or last treatment, whichever is later, for participants without Visit 16 will not be considered as treatment-emergent.

Term	Description
On-therapy	An event where: • Treatment start date of the lead-in study ≤ event start date ≤ Visit 16 for participants with Visit 16, or within 30 days after the last visit or last treatment, whichever is later, for participants without Visit 16

AEs, encompassing abnormalities and surgeries reported as occurring after the Screening Visit, will be coded using MedDRA version 20.1 or newer. Unique participants reporting AEs in the following AE categories will be summarized by treatment group for the Safety Population as follows:

Table 5-20 AE Summaries

Parameter	Description	Timing	Methodology
Overall summary	Overall summary only for the following categories: • Treatment-emergent AEs (TEAEs) • Treatment-related TEAEs • On-therapy serious adverse events (SAEs) • Deaths • AEs leading to discontinuation Subgroup analyses by Cardiovascular Risk Category and by renal function class	From randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16	Categorical descriptives
TEAEs	Summary by • SOC and PT for all participants and by subgroup analyses: o by Sex o by Age Group <40 vs ≥40 o by Age Group <65 vs ≥65 o by Race White vs All other races o by cardiovascular risk category o by renal function class • SOC and PT for concomitant medication classes used by at least 10% of participants in at least one treatment group • SOC, PT, and AE onset time intervals o <3 months o ≥3 and <6 months o ≥6 and <9 months o ≥9 and <12 months o ≥12 months • SOC, PT, and average number of migraine attacks treated with study treatment per month o ≥2 o ≥4 o ≥6	From randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16	Categorical descriptives

Parameter	Description	Timing	Methodology
	○ ≥8 • SOC, PT, and severity • SOC, PT, and causal relationship to the study treatment • Type (Mild, Moderate, Severe, related, not related) • SOC and PT for TEAEs occurring in ≥ 2% of participants in any ubrogepant treated dose group (and greater than placebo)		
Common TEAEs	Summary by PT • Includes TEAEs occurring in ≥ 2% of participants in any treatment group	From randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16	Categorical descriptives
On-therapy SAEs[1]	Overall summary and by PT	From randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16	Categorical descriptives
On-therapy fatal SAEs	Participants who report On-therapy fatal SAEs will have their fatal SAEs and all AEs listed	From randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16	Categorical descriptives
AEs leading to discontinuation[2]	Overall summary and by PT	From randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16[2]	Categorical descriptives
TEAEs of specific interest[3]	Overall summary and by PT for the following type of TEAEs: • Hepatic Injury TEAEs • Cardiac Arrhythmias TEAEs • Central Nervous System Vascular Disorders TEAEs • Embolic and Thrombotic Events TEAEs • Hypertension TEAEs • Ischaemic Heart Disease TEAEs • Suicide/self-injury TEAEs • Triptan-associated TEAEs • Abuse-related TEAEs	From randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16	Categorical descriptives

SOCs will be sorted alphabetically; PTs will be sorted in descending frequency in the highest dose group.
If more than 1 AE is coded to the same participant, the participant will be counted only once for that preferred term using the greatest severity

Parameter	Description	Timing	Methodology

If more than 1 AE is coded to the same participant, the participant will be counted only once for that preferred term using the strictest causal relationship to treatment for the summarization by causal relationship
[1] Participants who report ≥ 1 SAE will have their SAE listed.
[2] If the discontinued date is from randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16, then AEs leading to discontinuation will be summarized and listed
[3] Participants who reported ≥ 1 AEs in the corresponding category will have these AEs listed.

5.1.1.4.3 Clinical Laboratory Assessments

Clinical laboratory assessments will be summarized by treatment group for the Safety Population as follows:

Table 5-21 Clinical Laboratory Summaries

Endpoint	Description	Timing	Methodology
Number and percentage of participants with Potentially Clinically Significant (PCS) values[1]	Summary by laboratory category, parameter, and PCS criteria • Parameters and PCS criteria specified in Section 6.3.5.1 • N1 (percentage denominator) = Participants with non-missing non-PCS baseline and >=1 postbaseline parameter assessment	Randomization to End of Study[3]	PCS descriptives
Descriptives[2]	Summary by laboratory category and parameter in SI units and in conventional units and analysis visit • Parameters specified in Section 6.3.5.3	Randomization to End of Study[3]	CFB descriptives
Shift from baseline	Summary by laboratory parameter and category • Low, normal, and high categories provided by central laboratory • Parameters specified in Section 6.3.5.3	End of Study[3]	Shift analysis
Liver function findings[4]	Summary of number and percentage by hepatic laboratory parameter and PCS categories. Definition of PCS categories see Table 6-10 in Section 6.3.4.2.	Randomization to End of Study[3]	Categorical descriptives
Adjudication results of ALT or AST elevations[5]	Summary of relationship of ALT or AST elevation to study medication for participants with adjudicated case (i.e., ALT ≥ 3xULN and/or AST ≥ 3xULN) by the following categories: • Probable • Possible • Unlikely • Insufficient data Summary will be provided for the incidence by number of participants and by number of events	Randomization date to End of Study[3]	Categorical descriptives

ALT = aspartate aminotransferase; AST = aspartate aminotransferase; TBL = total bilirubin; ALP = alkaline phosphatase; INR = international normalized ratio; ULN = upper limit of normal.
[1] Participants who report ≥ 1 postbaseline PCS value will have their laboratory visits with PCS values and all AEs listed.
[2] Clinical laboratory results and comments will be listed.
[3] Analysis visits defined in Section 6.2.2.

Endpoint	Description	Timing	Methodology

[4] Details of all participants with any liver function laboratory findings will be listed. For participants who met ALT ≥ 3xULN or AST ≥ 3xULN, their ALT, AST, TBL, ALP, and INR assessments, and all AEs will be listed for all study visits. In addition, if available, their abnormal liver biochemistries risk factors, liver disease signs and symptoms, liver diagnostic tests, specialist consultation, liver lab tests, and drug screen will also be listed.
[5] Participants with at least one adjudicated case (i.e. ALT ≥ 3xULN or AST ≥ 3xULN) will be listed with their ALT and AST assessments, adjudication dates, adjudication results and confounding factors for all study visits.

Evaluation of drug-induced serious hepatoxicity (eDISH) plot (scatter plot of maximum total bilirubin vs. maximum ALT) will be generated. The ALT, AST, total bilirubin, and ALP values over time will be overlaid on the same plot along with indicators for dosing times for each participant with ALT or AST elevation (≥ 3 × ULN).

5.1.1.4.3.1 Potential Hy's Law

Potential Hy's Law criteria will be summarized by treatment group for the Safety Population as follows:

Table 5-22 Potential Hy's Law Summaries

Endpoint	Description	Timing	Methodology
Potential Hy's Law within 24-hour window	Number and percentage of participants with postbaseline assessment of the following laboratory parameters based on blood draws collected within a 24-hour period: • ALT or AST ≥ 3 × ULN • TBL ≥ 2 × ULN • ALP < 2 × ULN	Randomization to End of Study[1]	Categorical descriptives
Potential Hy's Law without window (e-DISH)	Number and percentage of participants with postbaseline assessment of the following laboratory parameters at any time: • Maximum ALT or AST ≥ 3 × ULN • Maximum TBL ≥ 2 × ULN	Randomization to End of Study[1]	Categorical descriptives

e-DISH = evaluation of drug-induced serious hepatotoxicity.
ALT = alanine aminotransferase; AST = aspartate aminotransferase; TBL = total bilirubin.
ALP = alkaline phosphatase; ULN = upper limit of normal.
[1] Analysis visits defined in Section 6.2.2.

Participants who meet the Potential Hy's Law criteria will have their ALT, AST, TBL, and ALP assessment listed for all study visits.

5.1.1.4.4 Vital Signs

Vital signs will be summarized by treatment group for the Safety Population as follows:

Table 5-23 Vital Signs Summaries

Endpoint	Description	Timing	Methodology
PCS values[1]	Summary of number and percentage of participants by parameter and PCS criteria • Parameters and PCS criteria specified in Section 6.3.6.1	Randomization to End of Study[1]	PCS descriptives
Descriptives[3]	Summary by parameter and analysis visit • Parameters specified in Section 6.3.6.2	Randomization to End of Study[2]	CFB descriptives
Measures	Summary of number number and percentage of	Randomization to	Summary

Endpoint	Description	Timing	Methodology
meeting criteria[4]	participants with post-treatment vital sign measurement meeting any of following criteria will by treatment group: • Systolic Blood Pressure: < 90 mmHg, > 140 mmHg, > 160 mmHg • Diastolic Blood Pressure: < 50 mmHg, > 90 mmHg, > 100 mmHg • Pulse Rate: < 60 bpm, > 100 bpm • Temperature: > 38.0 °C, < 36.0 °C • Respiratory rate: < 12 breaths/min, > 20 breaths/min	End of Study[2]	

[1] Participants who report ≥ 1 postbaseline PCS value will have their vital sign visits with PCS values and all AEs listed.
[2] Analysis visits defined in Section 6.2.2.
[3] Participant vital signs will be listed.
[4] A listing of AEs for participants with postbaseline values meeting the criteria will be also provided.

5.1.1.4.5 Electrocardiograms

Electrocardiograms (ECGs) will be summarized by treatment group for the Safety Population as follows:

Table 5-24 ECG Summaries

Endpoint	Description	Timing	Methodology
PCS values[1]	Summary of number and percentage of participants by parameter and PCS criteria • Parameters and PCS criteria specified in Section 6.3.7.2 • N1 (percentage denominator) = Participants with non-missing non-PCS baseline and >=1 postbaseline parameter assessment	Randomization to End of Study[2]	PCS descriptives
Descriptives	Summary by parameter and analysis visit • Parameters specified in Section 6.3.7.3	Randomization to End of Study[2]	CFB descriptives
Shift from baseline	Summary by parameter and category • Normal; abnormal, not clinically significant; abnormal, clinically significant provided by investigator • Parameters specified in Section 6.3.7.3	End of Study[2]	Shift analysis
Clinically significant ECG abnormalities	A listing showing ECG parameters for participants with postbaseline clinically significant ECG abnormalities according to the investigator's overall interpretation	Randomization to End of Study[2]	Listing
Descriptives of measures meeting criteria	Summary of number and percentage of participants with post-treatment QTcF >450 ms, >480 ms, and >500 ms will be tabulated by treatment group	Randomization to End of Study[2]	Descriptives

[1] Participants who report ≥ 1 postbaseline PCS value will have their ECG visits with PCS values and all AEs listed.
[2] Analysis visits defined in Section 6.2.2.

5.1.1.4.6 Cardiovascular Risk

Patients will be categorized into 1 of 3 coronary heart disease (CHD) risk subgroups (low, moderate, or high risk) based on NCEP ATP III guideline. Subgroup analyses of TEAEs by cardiovascular (CV) risk category will be provided for the Safety Population.

Table 5-25 Cardiovascular Risk Summaries

Endpoint	Description	Timing	Methodology
TEAEs	• Subgroup analyses by CV risk category for overall summary and by SOC and PT	From randomization date to Visit 16 for participants with Visit 16, or within 30 days after last visit or last treatment, whichever is later, for participants without Visit 16	Categorical descriptives

5.1.1.4.7 Suicidality Analyses

Suicidality will be summarized by treatment group for the Safety Population as follows:

Table 5-26 Suicidality Summaries

Endpoint	Description	Timing	Methodology
C-SSRS[1]	Summary by number and percentage of participants with suicidal ideation and suicidal behavior for each study phase listed in the timing column	Lifetime History, 6 months prior to Screening in the lead-in study, Treatment phase, Safety Follow-up phase	Categorical descriptives

[1] Participants with all values, including participant number, treatment group, visit number, intensity of suicidal ideation, suicidal behavior type, and lethality of suicidal behavior will be listed.

5.1.1.5 Subgroup Analyses

Subgroups analyses will be done for disposition (Table 5-6), treatment exposure (Table 5-16), and TEAEs (Table 5-19) for sex, age group (<40 vs ≥40, and <65 vs ≥65), race (White vs. all other races), cardiovascular risk category, and renal function class.

5.1.1.6 Interim Analyses

The interim analysis will occur when at least 300 ubrogepant participants (with a minimum of 2 migraines treated with ubrogepant per month, on average) have been enrolled in the study for 6 months, and 200 ubrogepant participants (with a minimum of 2 migraines treated with ubrogepant per month, on average) have been enrolled in the study for 1 year.

The treatment assignments will be unblinded to the Allergan staff for the interim analyses. The interim analyses will include all analyses specified in this SAP except for efficacy analyses.

[redacted]

5.2 Changes in the Conduct of the Study or Planned Analyses

Prior to database lock, there were no changes in study conduct or planned analyses from what was described in the protocol and detailed in the SAP.

5.2.1 Changes in the Conduct of the Study

Not applicable.

5.2.2 Changes to Analyses Prior to Database Lock

During study UBR-MD-04, it was reported that Participant [redacted] attempted to conceal her pregnancy [redacted]. Therefore, the participant will be excluded from the mITT and safety populations, but will remain in the ITT population. This change is made after interim lock and prior to the final database lock.

6. Data Handling and Analysis Conventions

6.1 Study Treatment Conventions

6.1.1 Analysis Days

Treatment day is defined as follows:

Table 6-1 Analysis Day Definitions

Term	Description

Treatment Day	Relative to randomization date
	If analysis date ≥ randomization date:
	• Day = analysis date – randomization date + 1
	  o Day 1 = randomization date
	If analysis date < randomization date:
	• Day = analysis date – randomization date
	  o Day -1 = day before randomization date
	  o There is no Day 0

6.1.2 Missing/Incomplete Treatment End Date

If the investigator is unable to provide the treatment end date, treatment end date will be imputed to the last available dosing record date.

6.2 Analysis Visit Windows

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted] e	[redacted]

[1]X is 1, 2, 3, ...

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

6.2.2 Safety

The safety analysis visit windows for 3-month time interval are defined as follows:

Table 6-4 Safety Analysis Visit Definitions for 3-Month Time Interval

Analysis Phase	Analysis Visit (Derived)	Window
Treatment	Completed 3 months	Treatment Day >= 90
	Completed 6 months	Treatment Day >= 180
	Completed 9 months	Treatment Day >= 270
	Completed 12 months	Completing treatment period per disposition CRF, or discontinued after day 360

Table 6-5 Safety Analysis Visit Definitions for 1-Month Time Interval

Analysis Phase	Analysis Visit (Derived)	Window
Treatment	Months 1	Treatment Day [1, 30]
	Months 2	Treatment Day [31, 60]
	Months 3	Treatment Day [61, 90]
	Months 4	Treatment Day [91, 120]
	Months 5	Treatment Day [121, 150]
	Months 6	Treatment Day [151, 180]
	Months 7	Treatment Day [181, 210]
	Months 8	Treatment Day [211, 240]
	Months 9	Treatment Day [241, 270]
	Months 10	Treatment Day [271, 300]
	Months 11	Treatment Day [301, 330]
	Months 12	Treatment Day [331, end of treatment period]

The analysis visit windows for safety endpoints are defined as follows:

Table 6-6 Safety Analysis Visit Definitions

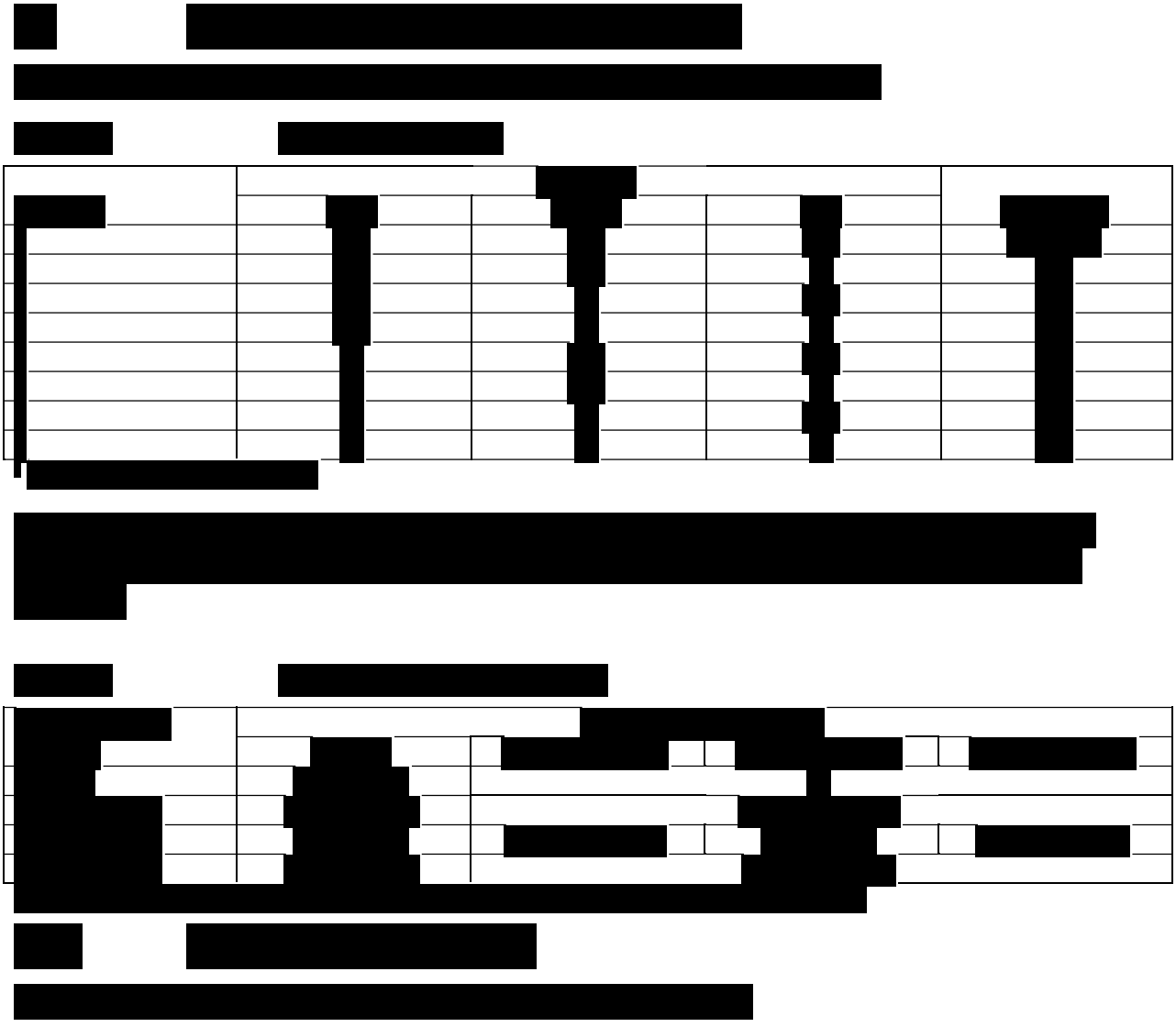
Analysis Phase	Analysis Visit (Derived)	Scheduled Study Visit (eCRF)	Window
Pretreatment	Baseline	Baseline from Lead-in Study	Treatment Day ≤ 1
	Week 4	(Visit 3) Week 4	Treatment Day [2, 42]
	Week 8	(Visit 4) Week 8	Treatment Day [43, 70]
	Week 12	(Visit 5) Week 12	Treatment Day [71, 98]
	Week 16	(Visit 6) Week 16	Treatment Day [99, 126]
	Week 20	(Visit 7) Week 20	Treatment Day [127, 154]
	Week 24	(Visit 8) Week 24	Treatment Day [155, 182]
	Week 28	(Visit 9) Week 28	Treatment Day [183, 210]
	Week 32	(Visit 10) Week 32	Treatment Day [211, 238]
	Week 36	(Visit 11) Week 36	Treatment Day [239, 266]
	Week 40	(Visit 12) Week 40	Treatment Day [267, 294]
	Week 44	(Visit 13) Week 44	Treatment Day [295, 322]
	Week 48	(Visit 14) Week 48	Treatment Day [323, 350]
	Week 52	(Visit 15) Week 52/Early Termination	Treatment Day [351, end of treatment period]

Analysis Phase	Analysis Visit (Derived)	Scheduled Study Visit (eCRF)	Window
	Safety Follow-up	(Visit 16) 4 Week Safety Follow-up	Treatment Day [end of treatment period+1, the last study visit]
	End of study	Final or termination visit	Latest non-missing assessment after randomization date

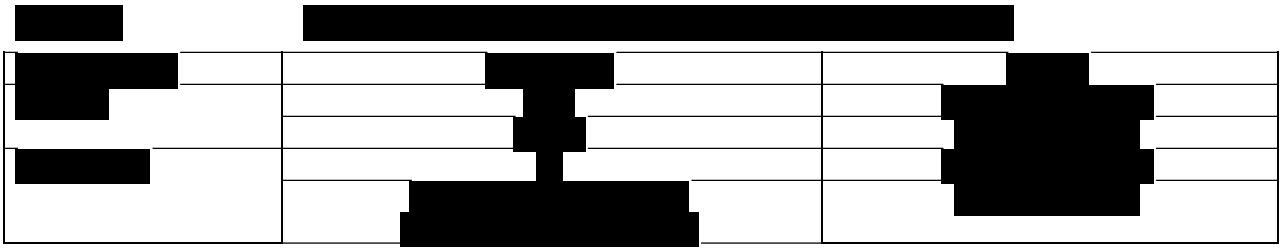
Safety follow-up visit will be presented in analysis tables for clinical laboratory values and vital signs.
End of Study is defined as the last available assessment during treatment and/or safety follow-up period. End of Study results will be presented in analysis tables for safety parameters, including but not limited to electrocardiograms, clinical laboratory values, and vital signs.

The following general conventions for repeated or unscheduled assessments will apply unless otherwise specified:

- The latest non-missing assessment within any analysis window will be flagged as the analysis value for any summaries by analysis visit
- All postbaseline assessments will be considered for PCS categorization
- All assessments will be included in respective listings



[redacted]



6.3.4.2 AE Group of Interest

The preferred terms included in each category are based on standardized MedDRA queries (SMQs) or are custom created where no SMQ exists or is inadequate (as shown in Table 6-10).

Table 6-10 Construction Methods for AE Categories of Clinical Interest

Method	Category
Narrow SMQs	***Cardiac arrhythmias*** • Arrhythmia related investigations, signs and symptoms • Cardiac arrhythmia terms (incl bradyarrhythmias and tachyarrhythmias) ***Central nervous system vascular disorders*** • Central nervous system haemorrhages and cerebrovascular conditions • Central nervous system vascular disorders, not specified as haemorrhagic or ischaemic ***Embolic and thrombotic events*** • Embolic and thrombotic events, arterial • Embolic and thrombotic events, venous • Embolic and thrombotic events, vessel type unspecified and mixed arterial and venous ***Hypertension*** ***Ischaemic heart disease*** • Myocardial infarction • Other ischaemic heart disease ***Suicide/self-injury***
Custom created	***Hepatic injury*** • Hepatic disorders (broad SMQ) • Liver transplant (preferred term) ***Abuse-related*** ***Triptan-associated***

Method	Category

Note: the categories of clinical interest are listed in bolded italics fonts and constructed from Standard MedDRA Query Version 20.1.

The preferred term for the custom-created abuse-related category and triptan-associated category are provided in Table 6-11. The lists of preferred terms for AE categories of clinical interest created using SMQs are provided in Appendix I.

Table 6-11 Preferred Terms for Abuse-Related Category and Triptan-Associated Category

Category	Preferred Terms
Triptan Associated	chest pain; chest discomfort; throat tightness; asthenia; paraesthesia; dysaesthesia; hyperaesthesia
Abuse Related	Affective disorder; Aggression; Confusional state; Disorientation; Dizziness; Drug tolerance; Drug withdrawal syndrome; Euphoric mood; Feeling abnormal; Feeling drunk; Feeling of relaxation; Hallucination; Inappropriate affect; Mood altered; Psychotic disorder; Somnolence; Substance abuse; Substance dependence; Substance use; Substance-induced mood disorder; Substance-induced psychotic disorder; Thinking abnormal

6.3.5 Clinical Laboratory Assessments

6.3.5.1 Potentially Clinically Significant Criteria

Laboratory assessments values meeting *any* of the following PCS low or PCS high criteria will be categorized as PCS:

Table 6-12 Clinical Laboratory PCS Criteria

Laboratory Group	Parameter	SI Unit	PCS Low Limit	PCS High Limit
Hematology	Basophils, absolute cell count	10^9/L	—	> 2.0 × ULN
	Eosinophils absolute cell count	10^9/L	—	> 2 × ULN
	Hematocrit	Ratio	< 0.9 × LLN	> 1.1 × ULN
	Hemoglobin	g/L	< 0.9 × LLN	> 1.1 × ULN
	Lymphocytes absolute cell count	10^9/L	< 0.7 × LLN	> 1.3 × ULN
	Monocytes, absolute cell count	10^9/L	< 0.5 × LLN	> 2.0 × ULN
	Neutrophils absolute cell count	10^9/L	< 0.7 × LLN	> 1.3 × ULN
	Platelet count (thrombocytes)	10^9/L	< 0.5 × LLN	> 1.5 × ULN
	Red blood cell count	10^{12}/L	< 0.9 × LLN	> 1.1 × ULN
	White blood cell count	10^9/L	< 0.9 × LLN	> 1.5 × ULN
Chemistry	Alanine aminotransferase	U/L	—	> 3 × ULN
	Albumin	g/L	< 0.8 × LLN	> 1.2 × ULN

Laboratory Group	Parameter	SI Unit	PCS Low Limit	PCS High Limit
	Alkaline phosphatase	U/L	—	> 3 × ULN
	Aspartate aminotransferase	U/L	—	> 3 × ULN
	Bicarbonate	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Bilirubin, total	µmol/L	—	> 1.5 × ULN
	Blood urea nitrogen	mmol/L	—	> 1.5 × ULN
	Calcium	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Chloride	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Cholesterol, total	mmol/L	—	> 1.6 × ULN
	Creatinine	µmol/L	—	> 1.5 × ULN
	Creatine kinase	U/L	—	> 2.0 × ULN
	Glucose, nonfasting	mmol/L	< 0.8 × LLN	> 2 × ULN
	Lactate dehydrogenase (LDH)	U/L	—	> 3.0 × ULN
	Phosphorus	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Potassium	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Protein, total	g/L	< 0.9 × LLN	> 1.1 × ULN
	Sodium	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Triglycerides	mmol/L	—	> 2.0 × ULN
	Uric acid (urate)	µmol/L	—	> 1.2 × ULN
Urinalysis	Glucose	mmol/L	—	Positive
	pH	pH	< 0.9 × LLN	> 1.1 × ULN
	Protein	g/L	—	Positive
	Specific gravity	—	—	> 1.1 × ULN

LLN = lower limit of normal (value provided by the laboratory); PCS = potentially clinically significant; SI = *Le Système International d'Unités* (International System of Units); ULN = upper limit of normal (value provided by the laboratory).

6.3.5.2 Hepatic Laboratory Abnormalities

The selected event is of clinical interest: Elevated ALT or AST lab value that is ≥ 3 times the ULN. The following laboratory parameters will be summarized:

Table 6-13 Criteria for Hepatic Laboratory Abnormalities

Laboratory Parameter	Categories
ALT	>= 1 × ULN
	>= 1.5 × ULN
	>= 2 × ULN
	>= 3 × ULN
	>= 5 × ULN
	>= 10 × ULN
	>= 20 × ULN
AST	>= 1 × ULN
	>= 1.5 × ULN
	>= 2 × ULN
	>= 3 × ULN
	>= 5 × ULN
	>= 10 × ULN
	>= 20 × ULN
ALT or AST	>= 1 × ULN
	>= 1.5 × ULN
	>= 2 × ULN
	>= 3 × ULN
	>= 5 × ULN
	>= 10 × ULN
	>= 20 × ULN
Bilirubin Total	>= 1 × ULN
	>= 1.5 × ULN
	>= 2 × ULN
	>= 3 × ULN
	>= 5 × ULN
	>= 10 × ULN
	>= 20 × ULN
Alkaline Phosphatase	>= 1 × ULN
	>= 1.5 × ULN
	>= 2 × ULN
	>= 3 × ULN
	>= 5 × ULN

Laboratory Parameter	Categories
	>= 10 × ULN
	>= 20 × ULN
Concurrent Elevations[1]	ALT or AST >= 3 × ULN **AND** Bilirubin Total ≥ 1.5 × ULN
	ALT or AST >= 3 × ULN **AND** Bilirubin Total ≥ 2 × ULN
Potential Hy's Law[1]	ALT or AST ≥ 3 × ULN **AND** Bilirubin Total ≥ 2 × ULN AND ALP < 2 × ULN

LLN = lower limit of normal (value provided by the laboratory); PCS = potentially clinically significant; SI = Le Système International d'Unités (International System of Units); ULN = upper limit of normal (value provided by the laboratory).

[1] Elevations are from the same day

6.3.5.3 Continuous Descriptives and Shift Table Parameters

The following laboratory parameters will be summarized:

Table 6-14 Clinical Descriptive and Shift Table Parameters

Category	Parameters
Chemistry	Sodium, potassium, chloride, bicarbonate, glucose, blood urea nitrogen, creatinine, total bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, creatine kinase, total protein, albumin, calcium, phosphorus, uric acid, total cholesterol, high density lipoprotein, low density lipoprotein, total triglycerides
Hematology	Hemoglobin; hematocrit; red blood cell count; red blood cell indices (mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration); white blood cell count, including differential (neutrophils, lymphocytes, monocytes, eosinophils, and basophils); platelet count
Urinalysis	Specific gravity, pH

6.3.5.4 Character Values

Character values (eg, < 5, negative) will be reviewed prior to database lock and converted to numeric for analysis as appropriate. These conversions will be documented in the ADaM specifications.

6.3.6 Vital Signs

6.3.6.1 Potentially Clinically Significant Criteria

Vital sign values meeting *both* the actual value and change from baseline PCS criteria will be categorized as PCS:

Table 6-15 Vital Sign PCS Criteria

Vital Sign	Flag	Criterion Value	Change From Baseline or Predose
Systolic blood pressure, mm Hg	High	≥ 180	Increase of ≥ 20
	Low	≤ 90	Decrease of ≥ 20
Diastolic blood pressure, mm Hg	High	≥ 105	Increase of ≥ 15

	Low	≤ 50	Decrease of ≥ 15
Pulse rate, bpm	High	≥ 120	Increase of ≥ 15
	Low	≤ 50	Decrease of ≥ 15
Weight, kg	High	—	Increase of ≥ 7%
	Low	—	Decrease of ≥ 7%
Orthostatic SBP change, mm Hg	Low	≤ -20	
Orthostatic DBP change, mm Hg	Low	≤ -15	
Orthostatic Pulse rate change, bpm	High	≥ 25	

SBP = Systolic blood pressure, DBP = Diastolic blood pressure, bpm = beats per minute.

6.3.6.2 Continuous Descriptives and Shift Table Parameters

The following vital sign parameters will be summarized:

Table 6-16 Vital Sign Descriptive and Shift Table Parameters

Parameters		
SBP	Respiratory rate	Weight
DBP	Temperature	BMI
Pulse rate	Orthostatic SBP changes[1]	Orthostatic DBP change[1]
Orthostatic Pulse rate change[1]		

SBP = Systolic blood pressure. DBP = Diastolic blood pressure. BMI=Body Mass Index.
[1]Orthostatic pulse rate change equals standing pulse rate minus sitting pulse rate; orthostatic systolic blood pressure change equals standing systolic blood pressure minus sitting systolic blood pressure; and orthostatic diastolic blood pressure change equals standing diastolic blood pressure minus sitting diastolic blood pressure

6.3.7 Electrocardiograms

6.3.7.1 QTc Derivation

QTc Bazett (QTcB) and QTc Fridericia (QTcF) are derived as follows:

Table 6-17 QTc Derivation

Parameter	Derivation if RR available	Derivation if RR unavailable
QTcB	$\frac{QT}{\text{square root of RR}}$	$\frac{QT}{\text{square root of (60/HR)}}$
QTcF	$\frac{QT}{\text{cubic root of RR}}$	$\frac{QT}{\text{cubic root of (60/HR)}}$

QTcB = QTc Bazett; QTcF = QTcF Fridericia.

6.3.7.2 Potentially Clinically Significant Criteria

ECG values meeting *either* the actual value or change from baseline PCS high criteria will be categorized as PCS:

Table 6-18 ECG PCS Criteria

Parameter	Unit	Criterion Value	Change from Baseline or Predose
QRS duration	msec	≥ 150	—
PR interval	msec	≥ 250	—
QTc (QTcB or QTcF) interval	msec	> 500	Increase of > 60

PCS = potentially clinically significant; QTc = corrected QT interval
QTcB = QTc Bazett; QTcF = QTcF Fridericia.

6.3.7.3 Continuous Descriptives and Shift Table Parameters

The following ECG parameters will be summarized:

Table 6-19 ECG Descriptive and Shift Table Parameters

Parameters		
Heart rate	QRS interval	QT interval
	PR interval	QTcB
	RR interval	QTcF

QTcB = QTc Bazett; QTcF = QTcF Fridericia.

6.4 Imputed Value Listing Conventions

In general, listings will present the actual partial or missing values rather than the imputed values that may be used in endpoint derivation. In instances where imputed values will be presented, imputed values will be flagged. Actual rules will be fully defined in the table, figure, and data listing specification document.

7. Amendment(s)

In Section 5.1.1.4.2, removed triptan-associated and abuse-related AE from Table 5-19, for Table 5-20, triptan-associated and abuse-related TEAE were under TEAE of special interest.

In Table 5-20 (Section 5.1.1.4.2), removed Triptan-associated TEAE from the overall summary row.

In Table 6-4 (Section 6.2.2), updated definition of completing 12 months.

Added details of AE group of special interest (Section 6.3.4.2).

Added Appendix I: Preferred Terms for AE Categories of Clinical Interest Created by SMQs (Section 8.1).

[redacted]

In Section 5.1.1.4.2 added additional analyses of TEAE reported in ≥ 2% of participants in any ubrogepant treated dose group (and greater than placebo) sorted by SOC and then by Preferred Term.

In Section 5.1.1.4.4 added additional analyses of vital signs for measures meeting criteria.

In Section 5.1.1.4.5 added additional analyses of ECG for measures meeting criteria.

[redacted]

In Section 6.4.4, imputation method is changed, missing AE will not be imputed. Updated the imputation of medication end date in case imputed end date is prior to start date, the end date will be imputed the same as the start date.

8. Appendices

8.1 Appendix I: Preferred Terms for AE Categories of Clinical Interest Created by SMQs.

Table 8-1 **List of Preferred Terms for AE Categories of Clinical Interest Created by Narrow SMQs.**

Category	Subcategory	SMQ Type	Preferred Term
Central nervous system vascular disorders (SMQ)	Central nervous system haemorrhages and cerebrovascular conditions (SMQ)	Narrow	Balint's syndrome
		Narrow	Basilar artery aneurysm
		Narrow	Carotid artery aneurysm
		Narrow	Carotid artery dissection
		Narrow	Cerebral endovascular aneurysm repair
		Narrow	Cerebral reperfusion injury
		Narrow	Cerebral ventricular rupture
		Narrow	Cerebrovascular accident prophylaxis
		Narrow	Charcot-Bouchard microaneurysms
		Narrow	Congenital hemiparesis
		Narrow	CSF bilirubin positive
		Narrow	Delayed ischaemic neurological deficit
		Narrow	Hemianaesthesia
		Narrow	Hemiasomatognosia
		Narrow	Hemiparaesthesia
		Narrow	Hemiparesis
		Narrow	Hemiplegia
		Narrow	Intra-cerebral aneurysm operation
		Narrow	Intracranial aneurysm

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Post stroke depression
		Narrow	Posthaemorrhagic hydrocephalus
		Narrow	Vein of Galen aneurysmal malformation
		Narrow	Vertebral artery aneurysm
		Narrow	Vertebral artery dissection
		Narrow	Basal ganglia haematoma
		Narrow	Basal ganglia haemorrhage
		Narrow	Basal ganglia stroke
		Narrow	Basilar artery perforation
		Narrow	Brain stem haematoma
		Narrow	Brain stem haemorrhage
		Narrow	Brain stem microhaemorrhage
		Narrow	Brain stem stroke
		Narrow	Carotid aneurysm rupture
		Narrow	Carotid artery perforation
		Narrow	Central nervous system haemorrhage
		Narrow	Cerebellar haematoma
		Narrow	Cerebellar haemorrhage
		Narrow	Cerebellar microhaemorrhage
		Narrow	Cerebellar stroke
		Narrow	Cerebral aneurysm perforation
		Narrow	Cerebral aneurysm ruptured syphilitic
		Narrow	Cerebral arteriovenous malformation haemorrhagic
		Narrow	Cerebral artery perforation
		Narrow	Cerebral haematoma

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Cerebral haemorrhage
		Narrow	Cerebral haemorrhage foetal
		Narrow	Cerebral haemorrhage neonatal
		Narrow	Cerebral microhaemorrhage
		Narrow	Cerebrovascular accident
		Narrow	Cerebrovascular disorder
		Narrow	Epidural haemorrhage
		Narrow	Extra-axial haemorrhage
		Narrow	Extradural haematoma
		Narrow	Haemorrhage intracranial
		Narrow	Haemorrhagic cerebral infarction
		Narrow	Haemorrhagic stroke
		Narrow	Haemorrhagic transformation stroke
		Narrow	Intracerebral haematoma evacuation
		Narrow	Intracranial haematoma
		Narrow	Intracranial tumour haemorrhage
		Narrow	Intraventricular haemorrhage
		Narrow	Intraventricular haemorrhage neonatal
		Narrow	Meningorrhagia
		Narrow	Perinatal stroke
		Narrow	Periventricular haemorrhage neonatal
		Narrow	Pituitary haemorrhage
		Narrow	Putamen haemorrhage
		Narrow	Ruptured cerebral aneurysm
		Narrow	Spinal cord haematoma
		Narrow	Spinal cord haemorrhage

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Spinal epidural haematoma
		Narrow	Spinal epidural haemorrhage
		Narrow	Spinal subarachnoid haemorrhage
		Narrow	Spinal subdural haematoma
		Narrow	Spinal subdural haemorrhage
		Narrow	Stroke in evolution
		Narrow	Subarachnoid haematoma
		Narrow	Subarachnoid haemorrhage
		Narrow	Subarachnoid haemorrhage neonatal
		Narrow	Subdural haematoma
		Narrow	Subdural haematoma evacuation
		Narrow	Subdural haemorrhage
		Narrow	Subdural haemorrhage neonatal
		Narrow	Thalamus haemorrhage
		Narrow	Vertebral artery perforation
		Narrow	Amaurosis fugax
		Narrow	Basal ganglia infarction
		Narrow	Basal ganglia stroke
		Narrow	Basilar artery occlusion
		Narrow	Basilar artery stenosis
		Narrow	Basilar artery thrombosis
		Narrow	Brachiocephalic arteriosclerosis
		Narrow	Brachiocephalic artery occlusion
		Narrow	Brachiocephalic artery stenosis
		Narrow	Brain hypoxia
		Narrow	Brain stem embolism

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Brain stem infarction
		Narrow	Brain stem ischaemia
		Narrow	Brain stem stroke
		Narrow	Brain stem thrombosis
		Narrow	Capsular warning syndrome
		Narrow	Carotid angioplasty
		Narrow	Carotid arterial embolus
		Narrow	Carotid arteriosclerosis
		Narrow	Carotid artery bypass
		Narrow	Carotid artery calcification
		Narrow	Carotid artery disease
		Narrow	Carotid artery insufficiency
		Narrow	Carotid artery occlusion
		Narrow	Carotid artery restenosis
		Narrow	Carotid artery stenosis
		Narrow	Carotid artery stent insertion
		Narrow	Carotid artery stent removal
		Narrow	Carotid artery thrombosis
		Narrow	Carotid endarterectomy
		Narrow	Carotid revascularisation
		Narrow	Cerebellar artery occlusion
		Narrow	Cerebellar artery thrombosis
		Narrow	Cerebellar embolism
		Narrow	Cerebellar infarction
		Narrow	Cerebellar ischaemia
		Narrow	Cerebellar stroke

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Cerebral arteriosclerosis
		Narrow	Cerebral artery embolism
		Narrow	Cerebral artery occlusion
		Narrow	Cerebral artery restenosis
		Narrow	Cerebral artery stenosis
		Narrow	Cerebral artery thrombosis
		Narrow	Cerebral gas embolism
		Narrow	Cerebral infarction
		Narrow	Cerebral infarction foetal
		Narrow	Cerebral ischaemia
		Narrow	Cerebral microembolism
		Narrow	Cerebral revascularisation
		Narrow	Cerebral septic infarct
		Narrow	Cerebral small vessel ischaemic disease
		Narrow	Cerebral thrombosis
		Narrow	Cerebral vascular occlusion
		Narrow	Cerebral vasoconstriction
		Narrow	Cerebral venous thrombosis
		Narrow	Cerebrovascular accident
		Narrow	Cerebrovascular disorder
		Narrow	Cerebrovascular insufficiency
		Narrow	Cerebrovascular stenosis
		Narrow	Delayed ischaemic neurological deficit
		Narrow	Embolic cerebral infarction
		Narrow	Embolic stroke
		Narrow	Hypoxic-ischaemic encephalopathy

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Inner ear infarction
		Narrow	Ischaemic cerebral infarction
		Narrow	Ischaemic stroke
		Narrow	Lacunar infarction
		Narrow	Lacunar stroke
		Narrow	Lateral medullary syndrome
		Narrow	Migrainous infarction
		Narrow	Millard-Gubler syndrome
		Narrow	Moyamoya disease
		Narrow	Perinatal stroke
		Narrow	Post cardiac arrest syndrome
		Narrow	Post procedural stroke
		Narrow	Precerebral arteriosclerosis
		Narrow	Precerebral artery occlusion
		Narrow	Reversible cerebral vasoconstriction syndrome
		Narrow	Reversible ischaemic neurological deficit
		Narrow	Spinal artery embolism
		Narrow	Spinal artery thrombosis
		Narrow	Stroke in evolution
		Narrow	Subclavian steal syndrome
		Narrow	Thalamic infarction
		Narrow	Thrombotic cerebral infarction
		Narrow	Thrombotic stroke
		Narrow	Transient ischaemic attack
		Narrow	Vascular encephalopathy

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Vascular stent occlusion
		Narrow	Vascular stent restenosis
		Narrow	Vascular stent stenosis
		Narrow	Vertebral artery occlusion
		Narrow	Vertebral artery stenosis
		Narrow	Vertebral artery thrombosis
		Narrow	Vertebrobasilar insufficiency
	Central nervous system vascular disorders, not specified as haemorrhagic or ischaemic (SMQ)	Narrow	Cerebral arteritis
		Narrow	Cerebral capillary telangiectasia
		Narrow	Cerebral circulatory failure
		Narrow	Cerebral congestion
		Narrow	Cerebral hypoperfusion
		Narrow	Dural arteriovenous fistula
		Narrow	Intracranial venous sinus thrombosis
		Narrow	Superior sagittal sinus thrombosis
		Narrow	Transverse sinus thrombosis
		Narrow	Vasculitis cerebral
Suicide/self-injury (SMQ)		Narrow	Assisted suicide
		Narrow	Columbia suicide severity rating scale abnormal
		Narrow	Completed suicide
		Narrow	Depression suicidal
		Narrow	Intentional overdose
		Narrow	Intentional self-injury

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Poisoning deliberate
		Narrow	Self-injurious ideation
		Narrow	Suicidal behaviour
		Narrow	Suicidal ideation
		Narrow	Suicide attempt
		Narrow	Suicide threat
Cardiac arrhythmias (SMQ)	Arrhythmia related investigations, signs and symptoms (SMQ)	Narrow	Chronotropic incompetence
		Narrow	Electrocardiogram repolarisation abnormality
		Narrow	Electrocardiogram RR interval prolonged
		Narrow	Electrocardiogram U wave inversion
		Narrow	Electrocardiogram U wave present
		Narrow	Electrocardiogram U-wave abnormality
		Narrow	Sudden cardiac death
	Cardiac arrhythmia terms (incl bradyarrhythmias and tachyarrhythmias) (SMQ)	Narrow	Bradyarrhythmia
		Narrow	Ventricular asystole
		Narrow	Accessory cardiac pathway
		Narrow	Adams-Stokes syndrome
		Narrow	Agonal rhythm
		Narrow	Atrial conduction time prolongation
		Narrow	Atrioventricular block
		Narrow	Atrioventricular block complete
		Narrow	Atrioventricular block first degree

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Atrioventricular block second degree
		Narrow	Atrioventricular conduction time shortened
		Narrow	Atrioventricular dissociation
		Narrow	Bifascicular block
		Narrow	Brugada syndrome
		Narrow	Bundle branch block
		Narrow	Bundle branch block bilateral
		Narrow	Bundle branch block left
		Narrow	Bundle branch block right
		Narrow	Conduction disorder
		Narrow	Defect conduction intraventricular
		Narrow	Electrocardiogram delta waves abnormal
		Narrow	Electrocardiogram PQ interval prolonged
		Narrow	Electrocardiogram PQ interval shortened
		Narrow	Electrocardiogram PR prolongation
		Narrow	Electrocardiogram PR shortened
		Narrow	Electrocardiogram QRS complex prolonged
		Narrow	Electrocardiogram QT prolonged
		Narrow	Electrocardiogram repolarisation abnormality
		Narrow	Lenegre's disease
		Narrow	Long QT syndrome
		Narrow	Paroxysmal atrioventricular block
		Narrow	Sinoatrial block

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Trifascicular block
		Narrow	Ventricular dyssynchrony
		Narrow	Wolff-Parkinson-White syndrome
		Narrow	Nodal arrhythmia
		Narrow	Nodal rhythm
		Narrow	Sinus arrest
		Narrow	Sinus arrhythmia
		Narrow	Sinus bradycardia
		Narrow	Sinus node dysfunction
		Narrow	Wandering pacemaker
		Narrow	Arrhythmia
		Narrow	Heart alternation
		Narrow	Heart rate irregular
		Narrow	Pacemaker generated arrhythmia
		Narrow	Pacemaker syndrome
		Narrow	Paroxysmal arrhythmia
		Narrow	Pulseless electrical activity
		Narrow	Reperfusion arrhythmia
		Narrow	Withdrawal arrhythmia
		Narrow	Arrhythmia supraventricular
		Narrow	Atrial fibrillation
		Narrow	Atrial flutter
		Narrow	Atrial parasystole
		Narrow	Atrial tachycardia
		Narrow	Junctional ectopic tachycardia
		Narrow	Sinus tachycardia

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Supraventricular extrasystoles
		Narrow	Supraventricular tachyarrhythmia
		Narrow	Supraventricular tachycardia
		Narrow	Anomalous atrioventricular excitation
		Narrow	Cardiac fibrillation
		Narrow	Cardiac flutter
		Narrow	Extrasystoles
		Narrow	Tachyarrhythmia
		Narrow	Accelerated idioventricular rhythm
		Narrow	Cardiac fibrillation
		Narrow	Parasystole
		Narrow	Rhythm idioventricular
		Narrow	Torsade de pointes
		Narrow	Ventricular arrhythmia
		Narrow	Ventricular extrasystoles
		Narrow	Ventricular fibrillation
		Narrow	Ventricular flutter
		Narrow	Ventricular parasystole
		Narrow	Ventricular pre-excitation
		Narrow	Ventricular tachyarrhythmia
		Narrow	Ventricular tachycardia
Embolic and thrombotic events (SMQ)	Embolic and thrombotic events, arterial (SMQ)	Narrow	Acute aortic syndrome
		Narrow	Acute myocardial infarction
		Narrow	Amaurosis
		Narrow	Amaurosis fugax

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Angioplasty
		Narrow	Aortic bypass
		Narrow	Aortic embolus
		Narrow	Aortic surgery
		Narrow	Aortic thrombosis
		Narrow	Aortogram abnormal
		Narrow	Arterectomy
		Narrow	Arterectomy with graft replacement
		Narrow	Arterial bypass occlusion
		Narrow	Arterial bypass operation
		Narrow	Arterial bypass thrombosis
		Narrow	Arterial graft
		Narrow	Arterial occlusive disease
		Narrow	Arterial stent insertion
		Narrow	Arterial therapeutic procedure
		Narrow	Arterial thrombosis
		Narrow	Arteriogram abnormal
		Narrow	Arteriogram carotid abnormal
		Narrow	Arteriotomy
		Narrow	Atherectomy
		Narrow	Atherosclerotic plaque rupture
		Narrow	Atrial appendage closure
		Narrow	Basal ganglia infarction
		Narrow	Basilar artery occlusion
		Narrow	Basilar artery thrombosis
		Narrow	Blindness transient

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Brachiocephalic artery occlusion
		Narrow	Capsular warning syndrome
		Narrow	Carotid angioplasty
		Narrow	Carotid arterial embolus
		Narrow	Carotid artery bypass
		Narrow	Carotid artery occlusion
		Narrow	Carotid artery stent insertion
		Narrow	Carotid artery thrombosis
		Narrow	Carotid endarterectomy
		Narrow	Cerebellar artery occlusion
		Narrow	Cerebellar artery thrombosis
		Narrow	Cerebral artery embolism
		Narrow	Cerebral artery occlusion
		Narrow	Cerebral artery thrombosis
		Narrow	Cerebral hypoperfusion
		Narrow	Cerebrovascular insufficiency
		Narrow	Cerebrovascular stenosis
		Narrow	Coeliac artery occlusion
		Narrow	Coronary angioplasty
		Narrow	Coronary arterial stent insertion
		Narrow	Coronary artery bypass
		Narrow	Coronary artery embolism
		Narrow	Coronary artery occlusion
		Narrow	Coronary artery reocclusion
		Narrow	Coronary artery surgery
		Narrow	Coronary artery thrombosis

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Coronary endarterectomy
		Narrow	Coronary revascularisation
		Narrow	Coronary vascular graft occlusion
		Narrow	Embolia cutis medicamentosa
		Narrow	Embolism arterial
		Narrow	Endarterectomy
		Narrow	Femoral artery embolism
		Narrow	Hepatic artery embolism
		Narrow	Hepatic artery occlusion
		Narrow	Hepatic artery thrombosis
		Narrow	Hypothenar hammer syndrome
		Narrow	Iliac artery embolism
		Narrow	Iliac artery occlusion
		Narrow	Intra-aortic balloon placement
		Narrow	Intraoperative cerebral artery occlusion
		Narrow	Ischaemic cerebral infarction
		Narrow	Ischaemic stroke
		Narrow	Lacunar infarction
		Narrow	Leriche syndrome
		Narrow	Mesenteric arterial occlusion
		Narrow	Mesenteric arteriosclerosis
		Narrow	Mesenteric artery embolism
		Narrow	Mesenteric artery stenosis
		Narrow	Mesenteric artery stent insertion
		Narrow	Mesenteric artery thrombosis
		Narrow	Myocardial infarction

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Myocardial necrosis
		Narrow	Papillary muscle infarction
		Narrow	Penile artery occlusion
		Narrow	Percutaneous coronary intervention
		Narrow	Peripheral arterial occlusive disease
		Narrow	Peripheral arterial reocclusion
		Narrow	Peripheral artery angioplasty
		Narrow	Peripheral artery bypass
		Narrow	Peripheral artery occlusion
		Narrow	Peripheral artery stent insertion
		Narrow	Peripheral artery thrombosis
		Narrow	Peripheral embolism
		Narrow	Peripheral endarterectomy
		Narrow	Popliteal artery entrapment syndrome
		Narrow	Post procedural myocardial infarction
		Narrow	Postinfarction angina
		Narrow	Precerebral artery occlusion
		Narrow	Precerebral artery thrombosis
		Narrow	Profundaplasty
		Narrow	Pulmonary artery occlusion
		Narrow	Pulmonary artery therapeutic procedure
		Narrow	Pulmonary artery thrombosis
		Narrow	Pulmonary endarterectomy
		Narrow	Pulmonary tumour thrombotic microangiopathy
		Narrow	Renal artery angioplasty

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Renal artery occlusion
		Narrow	Renal artery thrombosis
		Narrow	Renal embolism
		Narrow	Retinal artery embolism
		Narrow	Retinal artery occlusion
		Narrow	Retinal artery thrombosis
		Narrow	Silent myocardial infarction
		Narrow	Spinal artery embolism
		Narrow	Spinal artery thrombosis
		Narrow	Splenic artery thrombosis
		Narrow	Splenic embolism
		Narrow	Stress cardiomyopathy
		Narrow	Subclavian artery embolism
		Narrow	Subclavian artery occlusion
		Narrow	Subclavian artery thrombosis
		Narrow	Superior mesenteric artery syndrome
		Narrow	Thromboembolectomy
		Narrow	Thrombotic microangiopathy
		Narrow	Thrombotic thrombocytopenic purpura
		Narrow	Transient ischaemic attack
		Narrow	Truncus coeliacus thrombosis
		Narrow	Vascular pseudoaneurysm thrombosis
		Narrow	Vertebral artery occlusion
		Narrow	Vertebral artery thrombosis
		Narrow	Visual acuity reduced transiently
	Embolic and thrombotic	Narrow	Axillary vein thrombosis

Category	Subcategory	SMQ Type	Preferred Term
	events, venous (SMQ)		
		Narrow	Brachiocephalic vein occlusion
		Narrow	Brachiocephalic vein thrombosis
		Narrow	Budd-Chiari syndrome
		Narrow	Catheterisation venous
		Narrow	Cavernous sinus thrombosis
		Narrow	Central venous catheterisation
		Narrow	Cerebral venous thrombosis
		Narrow	Compression garment application
		Narrow	Deep vein thrombosis
		Narrow	Deep vein thrombosis postoperative
		Narrow	Embolism venous
		Narrow	Hepatic vein embolism
		Narrow	Hepatic vein occlusion
		Narrow	Hepatic vein thrombosis
		Narrow	Homans' sign positive
		Narrow	Iliac vein occlusion
		Narrow	Inferior vena cava syndrome
		Narrow	Inferior vena caval occlusion
		Narrow	Intracranial venous sinus thrombosis
		Narrow	Jugular vein occlusion
		Narrow	Jugular vein thrombosis
		Narrow	Mahler sign
		Narrow	May-Thurner syndrome
		Narrow	Mesenteric vein thrombosis
		Narrow	Mesenteric venous occlusion

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Obstetrical pulmonary embolism
		Narrow	Obstructive shock
		Narrow	Ophthalmic vein thrombosis
		Narrow	Ovarian vein thrombosis
		Narrow	Paget-Schroetter syndrome
		Narrow	Pelvic venous thrombosis
		Narrow	Penile vein thrombosis
		Narrow	Phlebectomy
		Narrow	Portal vein cavernous transformation
		Narrow	Portal vein occlusion
		Narrow	Portal vein thrombosis
		Narrow	Portosplenomesenteric venous thrombosis
		Narrow	Post procedural pulmonary embolism
		Narrow	Post thrombotic syndrome
		Narrow	Postoperative thrombosis
		Narrow	Postpartum venous thrombosis
		Narrow	Pulmonary embolism
		Narrow	Pulmonary infarction
		Narrow	Pulmonary microemboli
		Narrow	Pulmonary thrombosis
		Narrow	Pulmonary vein occlusion
		Narrow	Pulmonary veno-occlusive disease
		Narrow	Pulmonary venous thrombosis
		Narrow	Renal vein embolism
		Narrow	Renal vein occlusion

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Renal vein thrombosis
		Narrow	Retinal vein occlusion
		Narrow	Retinal vein thrombosis
		Narrow	SI QIII TIII pattern
		Narrow	Splenic vein occlusion
		Narrow	Splenic vein thrombosis
		Narrow	Subclavian vein occlusion
		Narrow	Subclavian vein thrombosis
		Narrow	Superior sagittal sinus thrombosis
		Narrow	Superior vena cava occlusion
		Narrow	Superior vena cava syndrome
		Narrow	Thrombophlebitis
		Narrow	Thrombophlebitis migrans
		Narrow	Thrombophlebitis neonatal
		Narrow	Thrombophlebitis superficial
		Narrow	Thrombosed varicose vein
		Narrow	Thrombosis corpora cavernosa
		Narrow	Transverse sinus thrombosis
		Narrow	Vena cava embolism
		Narrow	Vena cava filter insertion
		Narrow	Vena cava filter removal
		Narrow	Vena cava thrombosis
		Narrow	Venogram abnormal
		Narrow	Venoocclusive disease
		Narrow	Venoocclusive liver disease
		Narrow	Venous angioplasty

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Venous occlusion
		Narrow	Venous operation
		Narrow	Venous recanalisation
		Narrow	Venous repair
		Narrow	Venous stent insertion
		Narrow	Venous thrombosis
		Narrow	Venous thrombosis in pregnancy
		Narrow	Venous thrombosis limb
		Narrow	Venous thrombosis neonatal
		Narrow	Visceral venous thrombosis
	Embolic and thrombotic events, vessel type unspecified and mixed arterial and venous (SMQ)	Narrow	Administration site thrombosis
		Narrow	Adrenal thrombosis
		Narrow	Angiogram abnormal
		Narrow	Angiogram cerebral abnormal
		Narrow	Angiogram peripheral abnormal
		Narrow	Application site thrombosis
		Narrow	Arteriovenous fistula occlusion
		Narrow	Arteriovenous fistula thrombosis
		Narrow	Arteriovenous graft thrombosis
		Narrow	Artificial blood vessel occlusion
		Narrow	Atrial thrombosis
		Narrow	Basal ganglia stroke
		Narrow	Bone infarction
		Narrow	Brain stem embolism

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Brain stem infarction
		Narrow	Brain stem stroke
		Narrow	Brain stem thrombosis
		Narrow	Cardiac ventricular thrombosis
		Narrow	Catheter site thrombosis
		Narrow	Cerebellar embolism
		Narrow	Cerebellar infarction
		Narrow	Cerebral congestion
		Narrow	Cerebral infarction
		Narrow	Cerebral infarction foetal
		Narrow	Cerebral ischaemia
		Narrow	Cerebral microembolism
		Narrow	Cerebral septic infarct
		Narrow	Cerebral thrombosis
		Narrow	Cerebral vascular occlusion
		Narrow	Cerebrospinal thrombotic tamponade
		Narrow	Cerebrovascular accident
		Narrow	Cerebrovascular accident prophylaxis
		Narrow	Cerebrovascular disorder
		Narrow	Cerebrovascular operation
		Narrow	Choroidal infarction
		Narrow	Collateral circulation
		Narrow	Coronary bypass thrombosis
		Narrow	Device embolisation
		Narrow	Device occlusion
		Narrow	Device related thrombosis

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Diplegia
		Narrow	Directional Doppler flow tests abnormal
		Narrow	Disseminated intravascular coagulation
		Narrow	Disseminated intravascular coagulation in newborn
		Narrow	Embolic cerebral infarction
		Narrow	Embolic pneumonia
		Narrow	Embolic stroke
		Narrow	Embolism
		Narrow	Foetal cerebrovascular disorder
		Narrow	Graft thrombosis
		Narrow	Haemorrhagic adrenal infarction
		Narrow	Haemorrhagic cerebral infarction
		Narrow	Haemorrhagic infarction
		Narrow	Haemorrhagic stroke
		Narrow	Haemorrhagic transformation stroke
		Narrow	Haemorrhoids thrombosed
		Narrow	Hemiparesis
		Narrow	Hemiplegia
		Narrow	Heparin-induced thrombocytopenia
		Narrow	Hepatic infarction
		Narrow	Hepatic vascular thrombosis
		Narrow	Implant site thrombosis
		Narrow	Incision site vessel occlusion
		Narrow	Infarction
		Narrow	Infusion site thrombosis

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Injection site thrombosis
		Narrow	Inner ear infarction
		Narrow	Instillation site thrombosis
		Narrow	Intestinal infarction
		Narrow	Intracardiac mass
		Narrow	Intracardiac thrombus
		Narrow	Medical device site thrombosis
		Narrow	Mesenteric vascular insufficiency
		Narrow	Mesenteric vascular occlusion
		Narrow	Microembolism
		Narrow	Monoparesis
		Narrow	Monoplegia
		Narrow	Optic nerve infarction
		Narrow	Pancreatic infarction
		Narrow	Paradoxical embolism
		Narrow	Paraneoplastic thrombosis
		Narrow	Paraparesis
		Narrow	Paraplegia
		Narrow	Paresis
		Narrow	Peripheral revascularisation
		Narrow	Pituitary infarction
		Narrow	Placental infarction
		Narrow	Pneumatic compression therapy
		Narrow	Portal shunt procedure
		Narrow	Post procedural stroke
		Narrow	Postpartum thrombosis

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Prosthetic vessel implantation
		Narrow	Quadriparesis
		Narrow	Quadriplegia
		Narrow	Renal infarct
		Narrow	Renal vascular thrombosis
		Narrow	Retinal infarction
		Narrow	Retinal vascular thrombosis
		Narrow	Shunt occlusion
		Narrow	Shunt thrombosis
		Narrow	Spinal cord infarction
		Narrow	Splenic infarction
		Narrow	Splenic thrombosis
		Narrow	Stoma site thrombosis
		Narrow	Stroke in evolution
		Narrow	Surgical vascular shunt
		Narrow	Testicular infarction
		Narrow	Thalamic infarction
		Narrow	Thrombectomy
		Narrow	Thromboangiitis obliterans
		Narrow	Thrombolysis
		Narrow	Thrombosis
		Narrow	Thrombosis in device
		Narrow	Thrombosis mesenteric vessel
		Narrow	Thrombosis prophylaxis
		Narrow	Thrombotic cerebral infarction
		Narrow	Thrombotic stroke

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Thyroid infarction
		Narrow	Tumour embolism
		Narrow	Tumour thrombosis
		Narrow	Ultrasonic angiogram abnormal
		Narrow	Ultrasound Doppler abnormal
		Narrow	Umbilical cord occlusion
		Narrow	Umbilical cord thrombosis
		Narrow	Vaccination site thrombosis
		Narrow	Vascular access site thrombosis
		Narrow	Vascular graft
		Narrow	Vascular graft occlusion
		Narrow	Vascular graft thrombosis
		Narrow	Vascular operation
		Narrow	Vascular stent insertion
		Narrow	Vascular stent occlusion
		Narrow	Vascular stent thrombosis
		Narrow	Vasodilation procedure
		Narrow	Vessel puncture site occlusion
		Narrow	Vessel puncture site thrombosis
		Narrow	Visual midline shift syndrome
Hypertension (SMQ)		Narrow	Accelerated hypertension
		Narrow	Blood pressure ambulatory increased
		Narrow	Blood pressure diastolic increased
		Narrow	Blood pressure inadequately controlled
		Narrow	Blood pressure increased
		Narrow	Blood pressure management

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Blood pressure orthostatic increased
		Narrow	Blood pressure systolic increased
		Narrow	Diastolic hypertension
		Narrow	Eclampsia
		Narrow	Endocrine hypertension
		Narrow	Essential hypertension
		Narrow	Gestational hypertension
		Narrow	HELLP syndrome
		Narrow	Hyperaldosteronism
		Narrow	Hypertension
		Narrow	Hypertension neonatal
		Narrow	Hypertensive angiopathy
		Narrow	Hypertensive cardiomegaly
		Narrow	Hypertensive cardiomyopathy
		Narrow	Hypertensive cerebrovascular disease
		Narrow	Hypertensive crisis
		Narrow	Hypertensive emergency
		Narrow	Hypertensive encephalopathy
		Narrow	Hypertensive end-organ damage
		Narrow	Hypertensive heart disease
		Narrow	Hypertensive nephropathy
		Narrow	Labile hypertension
		Narrow	Malignant hypertension
		Narrow	Malignant hypertensive heart disease
		Narrow	Malignant renal hypertension
		Narrow	Maternal hypertension affecting foetus

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Mean arterial pressure increased
		Narrow	Metabolic syndrome
		Narrow	Neurogenic hypertension
		Narrow	Orthostatic hypertension
		Narrow	Page kidney
		Narrow	Pre-eclampsia
		Narrow	Prehypertension
		Narrow	Procedural hypertension
		Narrow	Renal hypertension
		Narrow	Renal sympathetic nerve ablation
		Narrow	Renovascular hypertension
		Narrow	Retinopathy hypertensive
		Narrow	Secondary aldosteronism
		Narrow	Secondary hypertension
		Narrow	Supine hypertension
		Narrow	Systolic hypertension
		Narrow	Withdrawal hypertension
Ischaemic heart disease (SMQ)	Myocardial infarction (SMQ)	Narrow	Acute coronary syndrome
		Narrow	Acute myocardial infarction
		Narrow	Angina unstable
		Narrow	Blood creatine phosphokinase MB abnormal
		Narrow	Blood creatine phosphokinase MB increased
		Narrow	Coronary artery embolism
		Narrow	Coronary artery occlusion

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Coronary artery reocclusion
		Narrow	Coronary artery thrombosis
		Narrow	Coronary bypass thrombosis
		Narrow	Coronary vascular graft occlusion
		Narrow	Kounis syndrome
		Narrow	Myocardial infarction
		Narrow	Myocardial necrosis
		Narrow	Myocardial reperfusion injury
		Narrow	Myocardial stunning
		Narrow	Papillary muscle infarction
		Narrow	Periprocedural myocardial infarction
		Narrow	Post procedural myocardial infarction
		Narrow	Postinfarction angina
		Narrow	Silent myocardial infarction
		Narrow	Troponin I increased
		Narrow	Troponin increased
		Narrow	Troponin T increased
	Other ischaemic heart disease (SMQ)	Narrow	Angina pectoris
		Narrow	Angina unstable
		Narrow	Anginal equivalent
		Narrow	Arteriosclerosis coronary artery
		Narrow	Arteriospasm coronary
		Narrow	Coronary angioplasty
		Narrow	Coronary arterial stent insertion
		Narrow	Coronary artery bypass
		Narrow	Coronary artery compression

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Coronary artery disease
		Narrow	Coronary artery dissection
		Narrow	Coronary artery insufficiency
		Narrow	Coronary artery restenosis
		Narrow	Coronary artery stenosis
		Narrow	Coronary artery surgery
		Narrow	Coronary brachytherapy
		Narrow	Coronary bypass stenosis
		Narrow	Coronary endarterectomy
		Narrow	Coronary no-reflow phenomenon
		Narrow	Coronary ostial stenosis
		Narrow	Coronary revascularisation
		Narrow	Coronary vascular graft stenosis
		Narrow	Dissecting coronary artery aneurysm
		Narrow	ECG signs of myocardial ischaemia
		Narrow	External counterpulsation
		Narrow	Haemorrhage coronary artery
		Narrow	Ischaemic cardiomyopathy
		Narrow	Ischaemic mitral regurgitation
		Narrow	Microvascular coronary artery disease
		Narrow	Myocardial hypoxia
		Narrow	Myocardial ischaemia
		Narrow	Percutaneous coronary intervention
		Narrow	Prinzmetal angina
		Narrow	Stress cardiomyopathy
		Narrow	Subclavian coronary steal syndrome

Category	Subcategory	SMQ Type	Preferred Term
		Narrow	Subendocardial ischaemia

Table 8-2 List of Preferred Terms for Hepatic Disorder Broad SMQ

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
Congenital, familial, neonatal and genetic disorders of the liver (SMQ)	Narrow	Accessory liver lobe
	Narrow	Alagille syndrome
	Narrow	Cerebrohepatorenal syndrome
	Narrow	Congenital absence of bile ducts
	Narrow	Congenital cystic disease of liver
	Narrow	Congenital hepatic fibrosis
	Narrow	Congenital hepatobiliary anomaly
	Narrow	Congenital hepatomegaly
	Narrow	Cystic fibrosis hepatic disease
	Narrow	Dilatation intrahepatic duct congenital
	Narrow	Glycogen storage disease type I
	Narrow	Glycogen storage disease type III
	Narrow	Glycogen storage disease type IV
	Narrow	Glycogen storage disease type VI
	Narrow	Hepatic hamartoma
	Narrow	Hepatitis neonatal
	Narrow	Hepatocellular damage neonatal
	Narrow	Hepato-lenticular degeneration
	Narrow	Hepatosplenomegaly neonatal
	Narrow	Hereditary haemochromatosis
	Narrow	Neonatal cholestasis

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Neonatal hepatomegaly
	Narrow	Polycystic liver disease
	Narrow	Porphyria acute
	Narrow	Portal venous system anomaly
	Narrow	Progressive familial intrahepatic cholestasis
	Broad	Hyperbilirubinaemia neonatal
	Broad	Jaundice neonatal
	Broad	Kernicterus
	Broad	Porphyria non-acute
Drug related hepatic disorders - comprehensive search (SMQ)	Narrow	Bilirubin excretion disorder
	Narrow	Cholaemia
	Narrow	Cholestasis
	Narrow	Cholestatic liver injury
	Narrow	Cholestatic pruritus
	Narrow	Drug-induced liver injury
	Narrow	Hepatitis cholestatic
	Narrow	Hyperbilirubinaemia
	Narrow	Icterus index increased
	Narrow	Jaundice
	Narrow	Jaundice cholestatic
	Narrow	Jaundice hepatocellular
	Narrow	Mixed liver injury
	Narrow	Ocular icterus

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Parenteral nutrition associated liver disease
	Broad	Deficiency of bile secretion
	Broad	Yellow skin
	Narrow	Acute hepatic failure
	Narrow	Acute on chronic liver failure
	Narrow	Acute yellow liver atrophy
	Narrow	Ascites
	Narrow	Asterixis
	Narrow	Bacterascites
	Narrow	Biliary cirrhosis
	Narrow	Biliary cirrhosis primary
	Narrow	Biliary fibrosis
	Narrow	Cholestatic liver injury
	Narrow	Chronic hepatic failure
	Narrow	Coma hepatic
	Narrow	Cryptogenic cirrhosis
	Narrow	Diabetic hepatopathy
	Narrow	Drug-induced liver injury
	Narrow	Duodenal varices
	Narrow	Gallbladder varices
	Narrow	Gastric variceal injection
	Narrow	Gastric variceal ligation
	Narrow	Gastric varices

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Gastric varices haemorrhage
	Narrow	Hepatectomy
	Narrow	Hepatic atrophy
	Narrow	Hepatic calcification
	Narrow	Hepatic cirrhosis
	Narrow	Hepatic encephalopathy
	Narrow	Hepatic encephalopathy prophylaxis
	Narrow	Hepatic failure
	Narrow	Hepatic fibrosis
	Narrow	Hepatic hydrothorax
	Narrow	Hepatic infiltration eosinophilic
	Narrow	Hepatic lesion
	Narrow	Hepatic necrosis
	Narrow	Hepatic steato-fibrosis
	Narrow	Hepatic steatosis
	Narrow	Hepatitis fulminant
	Narrow	Hepatobiliary disease
	Narrow	Hepatocellular foamy cell syndrome
	Narrow	Hepatocellular injury
	Narrow	Hepatopulmonary syndrome
	Narrow	Hepatorenal failure
	Narrow	Hepatorenal syndrome
	Narrow	Hepatotoxicity

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Intestinal varices
	Narrow	Intestinal varices haemorrhage
	Narrow	Liver and small intestine transplant
	Narrow	Liver dialysis
	Narrow	Liver disorder
	Narrow	Liver injury
	Narrow	Liver operation
	Narrow	Liver transplant
	Narrow	Lupoid hepatic cirrhosis
	Narrow	Minimal hepatic encephalopathy
	Narrow	Mixed liver injury
	Narrow	Nodular regenerative hyperplasia
	Narrow	Non-alcoholic fatty liver
	Narrow	Non-alcoholic steatohepatitis
	Narrow	Non-cirrhotic portal hypertension
	Narrow	Oedema due to hepatic disease
	Narrow	Oesophageal varices haemorrhage
	Narrow	Peripancreatic varices
	Narrow	Portal fibrosis
	Narrow	Portal hypertension
	Narrow	Portal hypertensive colopathy
	Narrow	Portal hypertensive enteropathy
	Narrow	Portal hypertensive gastropathy

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Portal vein cavernous transformation
	Narrow	Portal vein dilatation
	Narrow	Portopulmonary hypertension
	Narrow	Renal and liver transplant
	Narrow	Retrograde portal vein flow
	Narrow	Reye's syndrome
	Narrow	Reynold's syndrome
	Narrow	Splenic varices
	Narrow	Splenic varices haemorrhage
	Narrow	Steatohepatitis
	Narrow	Subacute hepatic failure
	Narrow	Varices oesophageal
	Narrow	Varicose veins of abdominal wall
	Narrow	White nipple sign
	Broad	Anorectal varices
	Broad	Anorectal varices haemorrhage
	Broad	Intrahepatic portal hepatic venous fistula
	Broad	Peritoneovenous shunt
	Broad	Portal shunt
	Broad	Portal shunt procedure
	Broad	Small-for-size liver syndrome
	Broad	Spider naevus
	Broad	Splenorenal shunt

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Broad	Splenorenal shunt procedure
	Broad	Spontaneous intrahepatic portosystemic venous shunt
	Broad	Stomal varices
	Narrow	Acute graft versus host disease in liver
	Narrow	Allergic hepatitis
	Narrow	Autoimmune hepatitis
	Narrow	Chronic graft versus host disease in liver
	Narrow	Chronic hepatitis
	Narrow	Graft versus host disease in liver
	Narrow	Hepatitis
	Narrow	Hepatitis acute
	Narrow	Hepatitis cholestatic
	Narrow	Hepatitis chronic active
	Narrow	Hepatitis chronic persistent
	Narrow	Hepatitis fulminant
	Narrow	Hepatitis toxic
	Narrow	Ischaemic hepatitis
	Narrow	Lupus hepatitis
	Narrow	Non-alcoholic steatohepatitis
	Narrow	Radiation hepatitis
	Narrow	Steatohepatitis
	Broad	Granulomatous liver disease
	Broad	Liver sarcoidosis

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Broad	Portal tract inflammation
	Narrow	Benign hepatic neoplasm
	Narrow	Benign hepatobiliary neoplasm
	Narrow	Focal nodular hyperplasia
	Narrow	Haemangioma of liver
	Narrow	Haemorrhagic hepatic cyst
	Narrow	Hepatic adenoma
	Narrow	Hepatic cyst
	Narrow	Hepatic cyst ruptured
	Narrow	Hepatic haemangioma rupture
	Narrow	Hepatic hamartoma
	Narrow	Hepatobiliary cyst
	Narrow	Cholangiosarcoma
	Narrow	Hepatic angiosarcoma
	Narrow	Hepatic cancer
	Narrow	Hepatic cancer metastatic
	Narrow	Hepatic cancer recurrent
	Narrow	Hepatic cancer stage I
	Narrow	Hepatic cancer stage II
	Narrow	Hepatic cancer stage III
	Narrow	Hepatic cancer stage IV
	Narrow	Hepatobiliary cancer
	Narrow	Hepatobiliary cancer in situ

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Hepatoblastoma
	Narrow	Hepatoblastoma recurrent
	Narrow	Hepatocellular carcinoma
	Narrow	Liver carcinoma ruptured
	Narrow	Mixed hepatocellular cholangiocarcinoma
	Broad	Liver ablation
	Narrow	Hepatic neoplasm
	Narrow	Hepatobiliary neoplasm
	Narrow	Alanine aminotransferase abnormal
	Narrow	Alanine aminotransferase increased
	Narrow	Ammonia abnormal
	Narrow	Ammonia increased
	Narrow	Ascites
	Narrow	Aspartate aminotransferase abnormal
	Narrow	Aspartate aminotransferase increased
	Narrow	Bacterascites
	Narrow	Bile output abnormal
	Narrow	Bile output decreased
	Narrow	Biliary ascites
	Narrow	Bilirubin conjugated abnormal
	Narrow	Bilirubin conjugated increased
	Narrow	Bilirubin urine present
	Narrow	Biopsy liver abnormal

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Blood bilirubin abnormal
	Narrow	Blood bilirubin increased
	Narrow	Blood bilirubin unconjugated increased
	Narrow	Bromosulphthalein test abnormal
	Narrow	Child-Pugh-Turcotte score abnormal
	Narrow	Child-Pugh-Turcotte score increased
	Narrow	Computerised tomogram liver
	Narrow	Computerised tomogram liver abnormal
	Narrow	Foetor hepaticus
	Narrow	Galactose elimination capacity test abnormal
	Narrow	Galactose elimination capacity test decreased
	Narrow	Gamma-glutamyltransferase abnormal
	Narrow	Gamma-glutamyltransferase increased
	Narrow	Guanase increased
	Narrow	Hepaplastin abnormal
	Narrow	Hepaplastin decreased
	Narrow	Hepatic artery flow decreased
	Narrow	Hepatic congestion
	Narrow	Hepatic enzyme abnormal
	Narrow	Hepatic enzyme decreased
	Narrow	Hepatic enzyme increased
	Narrow	Hepatic function abnormal
	Narrow	Hepatic hydrothorax

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Hepatic hypertrophy
	Narrow	Hepatic mass
	Narrow	Hepatic pain
	Narrow	Hepatic sequestration
	Narrow	Hepatic vascular resistance increased
	Narrow	Hepatobiliary scan abnormal
	Narrow	Hepatomegaly
	Narrow	Hepatosplenomegaly
	Narrow	Hyperammonaemia
	Narrow	Hyperbilirubinaemia
	Narrow	Hypercholia
	Narrow	Hypertransaminasaemia
	Narrow	Kayser-Fleischer ring
	Narrow	Liver function test abnormal
	Narrow	Liver function test decreased
	Narrow	Liver function test increased
	Narrow	Liver induration
	Narrow	Liver palpable
	Narrow	Liver scan abnormal
	Narrow	Liver tenderness
	Narrow	Mitochondrial aspartate aminotransferase increased
	Narrow	Molar ratio of total branched-chain amino acid to tyrosine
	Narrow	Nuclear magnetic resonance imaging liver abnormal

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Oedema due to hepatic disease
	Narrow	Perihepatic discomfort
	Narrow	Retrograde portal vein flow
	Narrow	Total bile acids increased
	Narrow	Transaminases abnormal
	Narrow	Transaminases increased
	Narrow	Ultrasound liver abnormal
	Narrow	Urine bilirubin increased
	Narrow	White nipple sign
	Narrow	X-ray hepatobiliary abnormal
	Broad	5'nucleotidase increased
	Broad	Blood alkaline phosphatase abnormal
	Broad	Blood alkaline phosphatase increased
	Broad	Blood cholinesterase abnormal
	Broad	Blood cholinesterase decreased
	Broad	Deficiency of bile secretion
	Broad	Glutamate dehydrogenase increased
	Broad	Haemorrhagic ascites
	Broad	Hepatic fibrosis marker abnormal
	Broad	Hepatic fibrosis marker increased
	Broad	Hepatic lymphocytic infiltration
	Broad	Hypoalbuminaemia
	Broad	Leucine aminopeptidase increased

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Broad	Liver iron concentration abnormal
	Broad	Liver iron concentration increased
	Broad	Model for end stage liver disease score abnormal
	Broad	Model for end stage liver disease score increased
	Broad	Periportal oedema
	Broad	Peritoneal fluid protein abnormal
	Broad	Peritoneal fluid protein decreased
	Broad	Peritoneal fluid protein increased
	Broad	Pneumobilia
	Broad	Portal vein flow decreased
	Broad	Portal vein pressure increased
	Broad	Retinol binding protein decreased
	Broad	Urobilinogen urine decreased
	Broad	Urobilinogen urine increased
	Narrow	Acquired antithrombin III deficiency
	Narrow	Acquired protein S deficiency
	Narrow	Anti factor X activity abnormal
	Narrow	Anti factor X activity decreased
	Narrow	Anti factor X activity increased
	Narrow	Antithrombin III decreased
	Narrow	Blood fibrinogen abnormal
	Narrow	Blood fibrinogen decreased
	Narrow	Blood thrombin abnormal

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Blood thrombin decreased
	Narrow	Blood thromboplastin abnormal
	Narrow	Blood thromboplastin decreased
	Narrow	Coagulation factor decreased
	Narrow	Coagulation factor IX level abnormal
	Narrow	Coagulation factor IX level decreased
	Narrow	Coagulation factor V level abnormal
	Narrow	Coagulation factor V level decreased
	Narrow	Coagulation factor VII level abnormal
	Narrow	Coagulation factor VII level decreased
	Narrow	Coagulation factor X level abnormal
	Narrow	Coagulation factor X level decreased
	Narrow	Hyperfibrinolysis
	Narrow	Hypocoagulable state
	Narrow	Hypofibrinogenaemia
	Narrow	Hypoprothrombinaemia
	Narrow	Hypothrombinaemia
	Narrow	Hypothromboplastinaemia
	Narrow	International normalised ratio abnormal
	Narrow	International normalised ratio increased
	Narrow	Protein C decreased
	Narrow	Protein S abnormal
	Narrow	Protein S decreased

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Prothrombin level abnormal
	Narrow	Prothrombin level decreased
	Narrow	Prothrombin time abnormal
	Narrow	Prothrombin time prolonged
	Narrow	Prothrombin time ratio abnormal
	Narrow	Prothrombin time ratio increased
	Narrow	Thrombin time abnormal
	Narrow	Thrombin time prolonged
Hepatic disorders specifically reported as alcohol-related (SMQ)	Narrow	Alcoholic liver disease
	Narrow	Cirrhosis alcoholic
	Narrow	Fatty liver alcoholic
	Narrow	Hepatic steato-fibrosis
	Narrow	Hepatitis alcoholic
	Narrow	Zieve syndrome
Liver infections (SMQ)	Narrow	Acute hepatitis B
	Narrow	Acute hepatitis C
	Narrow	Adenoviral hepatitis
	Narrow	Asymptomatic viral hepatitis
	Narrow	Chronic hepatitis B
	Narrow	Chronic hepatitis C
	Narrow	Congenital hepatitis B infection
	Narrow	Cytomegalovirus hepatitis

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	HBV-DNA polymerase increased
	Narrow	Hepatic amoebiasis
	Narrow	Hepatic candidiasis
	Narrow	Hepatic cyst infection
	Narrow	Hepatic echinococciasis
	Narrow	Hepatic gas gangrene
	Narrow	Hepatic infection
	Narrow	Hepatic infection bacterial
	Narrow	Hepatic infection fungal
	Narrow	Hepatic infection helminthic
	Narrow	Hepatitis A
	Narrow	Hepatitis A antibody abnormal
	Narrow	Hepatitis A antibody positive
	Narrow	Hepatitis A antigen positive
	Narrow	Hepatitis A virus test positive
	Narrow	Hepatitis B
	Narrow	Hepatitis B antibody abnormal
	Narrow	Hepatitis B antibody positive
	Narrow	Hepatitis B core antibody positive
	Narrow	Hepatitis B core antigen positive
	Narrow	Hepatitis B DNA assay positive
	Narrow	Hepatitis B DNA increased
	Narrow	Hepatitis B e antibody positive

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Hepatitis B e antigen positive
	Narrow	Hepatitis B reactivation
	Narrow	Hepatitis B surface antibody positive
	Narrow	Hepatitis B surface antigen positive
	Narrow	Hepatitis B virus test positive
	Narrow	Hepatitis C
	Narrow	Hepatitis C antibody positive
	Narrow	Hepatitis C core antibody positive
	Narrow	Hepatitis C RNA increased
	Narrow	Hepatitis C RNA positive
	Narrow	Hepatitis C virus test positive
	Narrow	Hepatitis D
	Narrow	Hepatitis D antibody positive
	Narrow	Hepatitis D antigen positive
	Narrow	Hepatitis D RNA positive
	Narrow	Hepatitis D virus test positive
	Narrow	Hepatitis E
	Narrow	Hepatitis E antibody abnormal
	Narrow	Hepatitis E antibody positive
	Narrow	Hepatitis E antigen positive
	Narrow	Hepatitis E virus test positive
	Narrow	Hepatitis F
	Narrow	Hepatitis G

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
	Narrow	Hepatitis H
	Narrow	Hepatitis infectious mononucleosis
	Narrow	Hepatitis mumps
	Narrow	Hepatitis non-A non-B
	Narrow	Hepatitis non-A non-B non-C
	Narrow	Hepatitis post transfusion
	Narrow	Hepatitis syphilitic
	Narrow	Hepatitis toxoplasmal
	Narrow	Hepatitis viral
	Narrow	Hepatitis viral test positive
	Narrow	Hepatobiliary infection
	Narrow	Hepatosplenic abscess
	Narrow	Hepatosplenic candidiasis
	Narrow	Herpes simplex hepatitis
	Narrow	Liver abscess
	Narrow	Perinatal HBV infection
	Narrow	Schistosomiasis liver
	Narrow	Sustained viral response
	Narrow	Viral hepatitis carrier
	Narrow	Withdrawal hepatitis
	Broad	Gianotti-Crosti syndrome
	Broad	Portal pyaemia
	Broad	Weil's disease

SMQs under Hepatic disorders (SMQ)	SMQ Type	Preferred Term
Pregnancy-related hepatic disorders (SMQ)	Narrow	Acute fatty liver of pregnancy
	Narrow	Cholestasis of pregnancy