Statistical Analysis Plan

NCT Number: NCT05107960

Title: Special Drug Use Surveillance; AZILVA Tablets and AZILVA Granules 1% in Pediatric Use

Study Number: TAK-536-4001

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Certain information within this document has been redacted (ie, specific content is masked irreversibly from view) to protect either personally identifiable information or company confidential information.

Note; This document was translated into English as the language on original version was Japanese.

Statistical Analysis Plan

(Final Analysis)

Product Name	: Azilva Tablets, Azilva Granules 1%
Surveillance Title	: <Pediatric Use> Special Drug Use Surveillance
Sponsor	: Takeda Pharmaceutical Company Limited

Head of Biostatistics Office,

Takeda Pharmaceutical Company Limited

Ver. 1: Prepared on October 23, 2024

Table of Contents

1 Definitions of Terms

1.1 List of Terms and Abbreviations

- Azilsartan: Azilsartan is the generic term for Azilva Tablets and Azilva Granules 1%.
- Adverse event: An adverse event occurring after the administration of azilsartan.
- Adverse reactions, etc.: An abbreviation for the term "adverse reactions/infections." Adverse events other than any assessed as "not related" to azilsartan by investigators. In this statistical analysis plan, "adverse reactions/infections" will be used in the titles, and "adverse reactions, etc." will be used in the text and tables.
- Serious adverse event: An adverse event assessed as being "serious" by investigators. Based on the Important Medical Events List, events listed in the MedDRA Code List (PT code) will be handled as serious even if assessed by investigators as "non-serious."
- "Related" to azilsartan: An adverse event with a causal relationship other than "unrelated" to azilsartan.
- "Not related" to azilsartan: An adverse event for which a causal relationship to azilsartan was ruled out.
- Summary statistics: A collective term for sample size, mean, standard deviation, maximum, minimum, and quartile values.
- Patients for whom no CRFs were collected: Enrolled patients for whom no CRFs were collected.
- Patients for whom CRFs were collected: Enrolled patients for whom CRFs were collected.
- Age: Age (at the time azilsartan is prescribed) will be used. If age (at the time azilsartan is prescribed) is missing, age will be derived as follows.

  If the birth month is prior to the month at the start of azilsartan treatment, age will be calculated as the year at the start of azilsartan treatment - birth year - 1. If the birth month is the same as or after the month at the start of azilsartan treatment, age will be calculated as the year at the start of azilsartan treatment - birth year. However, if the birth month is unknown, it will be calculated as January.
- Duration of azilsartan treatment (days): End of azilsartan treatment date - start of azilsartan treatment date + 1

  Wash out periods, if any, will be excluded from the duration of azilsartan treatment (days).

  If the end of azilsartan treatment date is unknown or treatment continues past the end of the observation period, the vital signs/body weight measurement date or the laboratory tests date, whichever is last, will be used as the end of azilsartan treatment date.

- Antihypertensives *Within 3 months prior to start of treatment:

  Antihypertensives taken prior to start of azilsartan treatment (that are used with or without azilsartan). Any antihypertensive meeting any of the following conditions that is reported in the "Concomitant medication (antihypertensive other than azilsartan) treatment status" section of the CRF. The CRF states the following: "Document any antihypertensives other than azilsartan that are used from 3 months before the start of azilsartan treatment up to 12 months after the start of azilsartan treatment or until discontinued. Any antihypertensives that are discontinued within 3 months before the start of azilsartan treatment should also be documented." Therefore, no statistical analysis of the 3-month period prior to azilsartan treatment will be performed in the analysis.

  · Start of treatment date before start of azilsartan treatment date

  · End of treatment date before start of azilsartan treatment date

  · Ongoing since 3 months before the start of azilsartan treatment

- Concomitant medication (antihypertensive other than azilsartan) *After the start of azilsartan treatment:

  Antihypertensives administered during azilsartan treatment period. Any antihypertensive meeting any of the following conditions that is reported in the "Concomitant medication (antihypertensive other than azilsartan) treatment status" section of the CRF.

  · Start of treatment date is on or after start of azilsartan treatment date, or end of treatment date is on or after start of azilsartan treatment date

  · Start of treatment date is prior to start of azilsartan treatment date, and continues past end of observation period

  · Ongoing since 3 months before start of azilsartan treatment, and continues past end of observation period

- Time of onset of adverse event (or adverse reaction, etc.): Calculated as the date of onset of adverse event (or adverse reaction, etc.) - start of azilsartan treatment date + 1.

- Duration of disease:
  Actual number (unit: year) = (year when first azilsartan dose initiated - year when hypertension was diagnosed) + (month when the first azilsartan dose initiated - month when hypertension was diagnosed)/12 (rounded off to first decimal place).
  If the month of diagnosis is unknown, it will be calculated as January of the reported year.
  If the year of diagnosis is unknown, it will be considered to be missing data.

- BMI (kg/m^2): Calculated as body weight (kg)/height $(m)^2$ (rounded off to first decimal place).

- eGFR (mL/min/1.73m^2): Calculated using the following formula for estimating GFR in Japanese children, as reported by the Pediatric Chronic Kidney Disease Task Force. The most recently measured height (Ht (m)) will be used to calculate the serum Cr reference value, based on which the eGFR will be calculated (rounded off to the second decimal place).

  <Pediatric eGFR (mL/min/1.73 m^2)>

  110.2 × serum Cr reference value (mg/dL)/actual serum Cr value (mg/dL) + 2.93

  <Serum Cr reference value (mg/dL)>

  Males: $-1.259\ Ht^5 + 7.815\ Ht^4 - 18.57\ Ht^3 + 21.39\ Ht^2 - 11.71\ Ht + 2.628$

  Females: $-4.536\ Ht^5 + 27.16\ Ht^4 - 63.47\ Ht^3 + 72.43\ Ht^2 - 40.06\ Ht + 8.778$

  Uemura O, et al. Clin Exp Nephrol. 2014

1.2 Analysis Sets

In this surveillance, the "safety analysis set" and the "efficacy analysis set" will be used as the analysis sets. These are defined as follows.

- Safety analysis set

This is defined as "patients for whom the CRF is locked, who receive at least one dose of azilsartan and can be assessed for safety." Patients for whom the CRF is locked will be excluded from the safety analysis set if the following conditions are applicable.

  · No azilsartan treatment
  · Enrolled 15 or more days after date on which azilsartan is first prescribed
  · Adverse event status unknown

- Efficacy analysis set

This is defined as "patients of the safety analysis set who have no major protocol violations and can be assessed for efficacy." Patients of the safety analysis set will be excluded from the efficacy analysis set if the following conditions are applicable.

  · Violation of inclusion criteria
  · Violation of exclusion criteria

1.3 Number of Digits Displayed

- Percentages (%)
  Incidence of adverse events or adverse reactions, etc.:
  Round off the third decimal place and display to the second decimal place.
  All others:
  Round off the second decimal place and display to the first decimal place.

- Summary statistics
  Mean, 1st quartile, median, 3rd quartile:
  Round off the second digit of the source data and display to the first digit of the source data.
  Standard deviation:
  Round off the third digit of the source data and display to the second digit of the source data.
  Minimum, maximum:
  Display the same number of digits as the source data.

- Confidence interval
  Round off the third digit of the source data and display to the second digit of the source data.

1.4 Safety Specification

- Important identified risks
  - Hypotension-related events: Events corresponding to MedDRA PT codes 10005731 (blood pressure ambulatory decreased), 10005737 (blood pressure diastolic decreased), 10066077 (diastolic hypotension), 10053356 (blood pressure orthostatic decreased), 10005734 (blood pressure decreased), 10005758 (blood pressure systolic decreased), 10084013 (post procedural hypotension), 10062300 (procedural hypotension), 10013573 (dizziness), 10013578 (dizziness postural), 10021097 (hypotension), 10031127 (orthostatic hypotension), 10036653 (presyncope), 10042772 (syncope), 10047340 (vertigo), 10047348 (vertigo positional), 10024855 (loss of consciousness), 10012373 (depressed level of consciousness), 10009192 (circulatory collapse), 10040560 (shock), 10040581 (shock symptom), 10083659 (hypotensive crisis).

2 Number of Surveillance Site, Number of Enrolled Patients, and Patient Disposition

2.1 Disposition of Cases

Analysis population:	All enrolled patients (enrolled patients)	
Analytical parameters:	Enrolled patients	
	Surveillance sites	
	Patients for whom no CRFs were collected	
	Patients for whom CRFs were collected	
	Patients excluded from safety analysis*	
	Reason for exclusion (counted more than once)	[No azilsartan treatment; enrolled 15 or more days after date on which azilsartan is first prescribed; adverse event status unknown]
	Safety analysis set	
	Patients excluded from efficacy analysis*	
	Reason for exclusion (counted more than once)	[Inclusion criteria violation [discovered after the fact], Exclusion criteria violation [discovered after the fact]]
	Efficacy Analysis Set	

Analysis methods: The following analyses will be performed for the above analytical parameters, and a patient disposition chart will be prepared.

The number of surveillance sites will also be shown for enrolled patients. The same site having different clinical departments in the surveillance will be counted as one site.

If there are no reasons for excluding any patients, 0 subjects will be displayed.

Listings will be prepared in which the number of patients excluded from the safety and efficacy analyses will be tabulated by each reason for exclusion.

*"Patients excluded from safety analysis" refers to patients for whom CRFs are collected who are excluded from the "safety analysis set." Similarly, "patients excluded from efficacy analysis" refers to patients in the “safety analysis set” who are excluded from the “efficacy analysis set.”

(1) Frequency tabulations

3 Patient Characteristics

3.1 Patient Characteristics

Analysis population:	Safety analysis set	
Analytical parameters:	Sex	[Male, female]
	Age (years)	[6, 7, 8, 9, 10, 11, 12, 13, 14, 15]
	Body weight (kg)	[Min <= - <20.0, 20.0 <= - <30.0, 30.0 <= - <40.0, 40.0 <= - <50.0, 50.0 <= - <60.0, 60.0 <= - <70.0, 70.0 <= - <80.0, 80.0 <= - <= Max]
	BMI (kg/m^2)	[Min <= - <15.0, 15.0 <= - <18.0, 18.0 <= - <21.0, 21.0 <= - <24.0, 24.0 <= - <27.0, 27.0 <= - <= Max]
	Inpatient/outpatient status (at baseline)	[Outpatient, inpatient]
	Comorbidities	[No, yes]
	Medical history	[No, yes, unknown]
	Predisposition to hypersensitivity	[No, yes, unknown]
	eGFR (mL/min/1.73m^2)	[Min <= - <30, 30 <= - <45, 45 <= - <60, 60 <= - <90, 90 <= - <= Max]
	Systolic blood pressure (mmHg)	
	Diastolic blood pressure (mmHg)	
	Pulse rate (bpm)	
	Disease duration (years)	[Min <= - <1, 1 <=- <2, 2 <= - <3, 3 <= - <4, 4 <= - <= Max]
	Antihypertensive treatment *Within 3 months prior to start of treatment	[No, yes]
Analysis methods:	Frequency tabulations of discrete data will be prepared and summary statistics of categorical data will be calculated for the above analytical parameters.	

4 Comorbidities

4.1 List of Comorbidities

Analysis population:	Safety analysis set
Analytical parameters:	Case number
	Disease name
Analysis methods:	Listings of the above analytical parameters will be prepared.

5 Treatment

5.1 Azilsartan and Concomitant Medication (Antihypertensives Other Than Azilsartan, and Medication Other Than Antihypertensives) Treatment Status

Analysis population:	Safety analysis set
Analytical parameters:	Case number
	Initial azilsartan dose (mg)
	Change in daily dose
	Mean azilsartan daily dose (mg)
	Duration of azilsartan treatment (days)
	Discontinuation of azilsartan
	Reason for discontinuation of azilsartan
	Concomitant medication (antihypertensive other than azilsartan) treatment *After start of azilsartan treatment
	Breakdown of concomitant medication (antihypertensive other than azilsartan) treatment *After start of azilsartan treatment
	Concomitant medication (other than antihypertensive) treatment
	Breakdown of concomitant medication (other than antihypertensives)
Analysis methods:	Listings of the above analytical parameters will be prepared.

6 Safety Information

If 0 adverse events are reported in the safety analysis set, no tabulations will be prepared for Sections 6.1.2, 6.2, 6.4, 6.5, and 6.6. If 0 patients are excluded from safety analysis, no tabulations will be prepared for Section 6.3. If 1 or more patients are excluded from safety analysis and 0 adverse events are reported, tabulations will be prepared for Section 6.3.1, and no tabulations will be prepared for Section 6.3.2.

6.1 Incidence of Adverse Events and Adverse Reactions/Infections

6.1.1 Incidence of Adverse Events

Analysis population: Safety analysis set

Analytical parameters: Adverse events

Analysis methods: The following analyses will be performed for the above analytical parameter.

(1) Number of patients with adverse events

(2) Number of adverse events

(3) Incidence of adverse events

(4) Type of adverse events

Each analysis will be carried out as follows.

[Number of patients with adverse events]

- The number of patients who experience adverse events.

[Number of adverse events]

- The number of adverse events that occur. If the same adverse event occurs more than once in the same patient, the total number of events will be tabulated.

[Incidence of adverse events]

- This will be calculated as the number of patients with adverse events divided by the number of patients in the safety analysis set multiplied by 100.

[Type of adverse events]

- Adverse events will be coded using the MedDRA/J. These will be broadly classified by SOC, and will be tabulated by PT within those classifications. Those in the SOC of "investigations" will be tabulated by HLGT (sorted in ascending order of HLGT code, but without listing the codes) and tabulated by PT.
- In SOC tabulations, the number of patients with adverse events and the incidence of adverse events will be documented in order of SOC international consensus. If the same SOC occurs more than once in the same patient, the patient will be counted only once for that SOC.

- In PT tabulations, the number of patients with adverse events and the incidence of adverse events will be documented in ascending order of PT code. If the same PT occurs more than once in the same patient, the patient will be counted only once for that PT.

6.1.2 Incidence of Adverse Reactions/Infections

Analysis population: Safety analysis set

Analytical parameters: Adverse reactions, etc.

Analysis methods: The following analyses will be performed for the above analytical parameter.

(1) Number of patients with adverse reactions, etc.

(2) Number of adverse reactions, etc.

(3) Incidence of adverse reactions, etc.

(4) Types of adverse reactions, etc.

Each analysis will be carried out as follows.

[Number of patients with adverse reactions, etc.]

· The number of patients who experience adverse reactions, etc.

[Number of adverse reactions, etc.]

· The number of adverse reactions, etc. that occur. If the same adverse reaction, etc. occurs more than once in the same patient, the total number of events will be tabulated.

[Incidence of adverse reactions, etc.]

· This will be calculated as the number of patients with adverse reaction, etc. divided by the number of patients in the safety analysis set multiplied by 100.

[Types of adverse reactions, etc.]

· Adverse reactions, etc. will be coded using the MedDRA/J. These will be broadly classified by SOC, and will be tabulated by PT within those classifications. Those in the SOC of "investigations" will be tabulated by HLGT (sorted in ascending order of HLGT code, but without listing the codes) and tabulated by PT.

· In SOC tabulations, the number of patients with adverse reactions, etc. and the incidence of adverse reactions, etc. will be documented in order of SOC international consensus. If the same SOC occurs more than once in the same patient, the patient will be counted only once for that SOC.

· In PT tabulations, the number of patients with adverse reactions, etc. and the incidence of adverse reactions, etc. will be documented in ascending order of PT code. If the same PT occurs more than once in the same patient, the patient will be counted only once for that PT.

6.2 Incidence of Adverse Events and Adverse Reactions/Infections Corresponding to Safety Specification

6.2.1 Incidence of Adverse Events Corresponding to Safety Specification

Analysis population:	Safety analysis set
Analytical parameters:	Adverse events corresponding to the safety specification (important identified risks)
Stratification factors:	Seriousness [Serious, non-serious]
Analysis methods:	Stratified analysis of the above, by stratification factor and by risk, will be performed in the same manner as in Section 6.1.1. If the same SOC/PT occurs more than once in the same patient, the patient will be counted only once for that SOC/PT. However, if the seriousness of the events is different, the events will each be counted as serious or non-serious event, respectively. In addition, the risk will be assessed per the definitions specified in 1.4 Safety Specification.

6.2.2 Incidence of Adverse Reactions/Infections Corresponding to Safety Specification

Analysis population:	Safety analysis set
Analytical parameters:	Adverse reactions, etc. corresponding to the safety specification (important identified risks)
Stratification factors:	Seriousness [Serious, non-serious]
Analysis methods:	Stratified analysis of the above, by stratification factor and by risk, will be performed in the same manner as in Section 6.1.2. If the same SOC/PT occurs more than once in the same patient, the patient will be counted only once for that SOC/PT. However, if the seriousness of the events is different, the events will each be counted as serious or non-serious event, respectively. In addition, the risk will be assessed per the definitions specified in 1.4 Safety Specification.

6.3 Incidence of Adverse Events and Adverse Reactions/Infections in Patients Excluded From Safety Analysis

6.3.1 Incidence of Adverse Events in Patients Excluded From Safety Analysis

Analysis population:	Patients excluded from safety analysis
Analytical parameters:	Adverse events
Analysis methods:	The above will be analyzed in the same manner as in Section 6.1.1.

6.3.2 Incidence of Adverse Reactions/Infections in Patients Excluded from Safety Analysis

Analysis population:	Patients excluded from safety analysis
Analytical parameters:	Adverse reactions, etc.
Analysis methods:	The above will be analyzed in the same manner as in Section 6.1.2.

6.4 Incidence of Adverse Reactions/Infections Leading to Discontinuation of Azilsartan Treatment

6.4.1 Incidence of Adverse Reactions/Infections Leading to Discontinuation of Azilsartan Treatment

Analysis population:	Safety analysis set
Analytical parameters:	Adverse reactions, etc. leading to discontinuation of azilsartan treatment
Analysis methods:	The above will be analyzed in the same manner as in Section 6.1.2.

6.5 Incidence of Adverse Events and Adverse Reactions/Infections by Seriousness, Time of Onset, Outcome, and Causal Relationship to Azilsartan

6.5.1 Incidence of Adverse Events by Seriousness, Time of Onset, Outcome, and Causal Relationship to Azilsartan

Analysis population:	Safety analysis set	
Analytical parameters:	Adverse events	
Stratification factors:	Total	
	Seriousness	[Serious, non-serious]
	Time of onset (day)	[1 <= - <= 14, 15 <= - <= 28, 29 <= - <= 42, 43 <= - <= 56, 57 <= - <= 70, 71 <= - <= 84, 85 <= - <= Max]
		[1 <= - <= 84, 85 <= - <= 168, 169 <= - <= 252, 253 <= - <= 336, 337 <= - <= 420, 421 <= - <= Max]
	Outcome	[Resolved, Resolving, Not resolved, Resolved with sequelae, Death (due to this event), Unknown]
	Causal relationship to azilsartan	[Related, unrelated]
Analysis methods:	Stratified analysis of the above by stratification factor will be performed in the same manner as in Section 6.1.1. If the same SOC/PT occurs more than once in the same patient, the patient will be counted only once for that SOC/PT. However, SOCs that are the same will be handled as one in the following order of priority, and PTs that are the same will be handled as one per the details of one of the stratification factors in the following order of priority. Seriousness: Serious → Non-serious Time of onset 1 (days): 1-14 days → 15-28 days → 29-42 days → 43-56 days → 57-70 days → 71-84 days → ≥ 85 days Time of onset 2 (days): 1-84 days → 85-168 days → 169-252 days → 253-336 days → 337-420 days → ≥ 421 days Outcome: Death (due to this event) → Resolved with sequelae → Not resolved → Resolving → Resolved → Unknown Causal relationship to azilsartan: Related → Not related	

6.5.2 Incidence of Adverse Reactions/Infections by Seriousness, Time of Onset, and Outcome

Analysis population:	Safety analysis set	
Analytical parameters:	Adverse reactions, etc.	
Stratification factors:	Total	
	Seriousness	[Serious, non-serious]
	Time of onset (day)	[1 <= - <= 14, 15 <= - <= 28, 29 <= - <= 42, 43 <= - <= 56, 57 <= - <= 70, 71 <= - <= 84, 85 <= - <= Max]
		[1 <= - <= 84, 85 <= - <= 168, 169 <= - <= 252, 253 <= - <= 336, 337 <= - <= 420, 421 <= - <= Max]
	Outcome	[Resolved, Resolving, Not resolved, Resolved with sequelae, Death (due to this event), Unknown]

Analysis methods: Stratified analysis of the above by stratification factor will be performed in the same manner as in Section 6.1.2. If the same SOC/PT occurs more than once in the same patient, the patient will be counted only once for that SOC/PT. However, SOCs that are the same will be handled as one in the following order of priority, and PTs that are the same will be handled as one per the details of one of the stratification factors in the following order of priority.

Seriousness: Serious → Non-serious

Time of onset 1 (days): 1-14 days → 15-28 days → 29-42 days → 43-56 days → 57-70 days → 71-84 days → ≥ 85 days

Time of onset 2 (days): 1-84 days → 85-168 days → 169-252 days → 253-336 days → 337-420 days → ≥ 421 days

Outcome: Death (due to this event) → Resolved with sequelae → Not resolved → Resolving → Resolved → Unknown

6.6 Incidence of Adverse Reactions/Infections by Patient Characteristics and Treatment Factors

6.6.1 List of Adverse Reactions/Infections by Patient Characteristics and Treatment Factors

Analysis population:	Safety analysis set	
Analytical parameters:	Case number	
	Sex	[Male, female]
	Age (years)	
	Comorbidities	[No, yes]
	Breakdown of comorbidities	
	Initial azilsartan dose (mg)	
	Antihypertensive treatment	
	*Within 3 months prior to start of treatment	[No, yes]
	Date of onset	
	SOC	
	PT	
	Hypotension-related events	[O]
	Seriousness	[Serious, non-serious]
	Outcome	[Resolved, Resolving, Not resolved, Resolved with sequelae, Death (due to this event), Unknown]
	Cause of discontinuation of azilsartan treatment	[Yes, no]
Analysis methods:	Listings of the above analytical parameters will be prepared for patients experiencing adverse reactions, etc.	

7 Efficacy Information

7.1 Changes in Blood Pressure Over Time

Analysis population: Efficacy analysis set

Analytical parameters: Systolic blood pressure (mmHg), diastolic blood pressure (mmHg)

Analysis methods: For each of the above analytical parameters, summary statistics will be calculated for laboratory values at each assessment time point (baseline and after 1 month of azilsartan treatment to after 12 months of azilsartan treatment) as well as changes (laboratory values at each assessment time point after baseline-laboratory values at baseline). Listings will be shown rather than summary statistics when the efficacy analysis set includes 2 or fewer patients. Changes over time in laboratory values will also be plotted individually.

7.2 List of Factors Potentially Affecting Efficacy

Analysis population: Efficacy analysis set

Analytical parameters:

Case number	
Sex	[Male, female]
Age (years)	
Comorbidities	[No, yes]
Breakdown of comorbidities	
Initial azilsartan dose (mg)	
Antihypertensive treatment *Within 3 months prior to start of treatment	[No, yes]
Breakdown of antihypertensive treatment *Within 3 months prior to start of treatment	
Assessment time point	
Systolic blood pressure (mmHg)	
Diastolic blood pressure (mmHg)	

Analysis methods: Listings of the above analytical parameters will be prepared.

8 Incidence of Adverse Reactions/Infections in Supplementary Pharmacovigilance Plan

8.1 Incidence of Adverse Reactions/Infections in Supplementary Pharmacovigilance Plan (Attachment Form 12)

Analysis population:	Safety analysis set
Analytical parameters:	Adverse reactions, etc. corresponding to the safety specification (important identified risks)
Stratification factors:	Seriousness [Serious, non-serious]
Analysis methods:	The above analytical parameters will be analyzed, stratified by stratification factor, according to (Notes) 1 through 4 of Attachment Form 12 in PSEHB/PED Reexamination Notification No. 0325-10, dated March 25, 2020. (1) Number of patients and incidence The risk terms that are used and the order in which they are listed will be based on the definitions given in the Important Identified Risks section.

9 Incidence of Adverse Reactions/Infections in Post-Marketing Surveillance

9.1 Incidence of Adverse Reactions/Infections in Post-Marketing Surveillance (Attachment Form 15)

Analysis population: Safety analysis set

Analytical parameters: Adverse reactions, etc.

Analysis methods: The following analyses will be performed for the above analytical parameter.

(1) Status of post-marketing surveillance
   1) Number of patients in safety analysis set
   2) Number of patients with adverse reactions, etc.
   3) Incidence of adverse reactions, etc.

(2) Types of adverse reactions, etc.
   1) Number of patients with adverse reactions, etc. and incidence (by SOC)
   2) Number of patients with adverse reactions, etc. and incidence (by PT)

Each analysis will be carried out as follows.

[Number of patients with adverse reactions, etc.]

· The number of patients who experience adverse reactions, etc.

[Incidence of adverse reactions, etc.]

· This will be calculated as the number of patients with adverse reaction, etc. divided by the number of patients in the safety analysis set multiplied by 100.

[Types of adverse reactions, etc.]

· Adverse reactions, etc. will be coded using the MedDRA/J. These will be broadly classified by SOC, and will be tabulated by PT within those classifications. Those in the SOC of "investigations" will be tabulated by HLGT (sorted in ascending order of HLGT code, but without listing the codes) and tabulated by PT.

· In SOC tabulations, the number of patients with adverse reactions, etc. and the incidence of adverse reactions, etc. will be documented in order of SOC international consensus. If the same SOC occurs more than once in the same patient, the patient will be counted only once for that SOC.

· In PT tabulations, the number of patients with adverse reactions, etc. and the incidence of adverse reactions, etc. will be documented in

ascending order of PT code. If the same PT occurs more than once in the same patient, the patient will be counted only once for that PT.

*"Number of patients in the safety analysis" refers to the "analysis set" in this analysis (see above).

10 Summary of Cases in Post-Marketing Surveillance

10.1 Summary of Cases in Post-Marketing Surveillance (File for Reexamination Data Entries)

Analysis population:	Patients for whom CRFs were collected
Analytical parameters:	Case number
	Name of site
	Sex
	Age
	Reason for use (disease code, disease name)
	Comorbidities (disease code, disease name)
	Route of administration
	Maximum dose
	Mean dose
	Units
	Duration of use (duration of azilsartan treatment)
	Concomitant medications (drug code, drug name)
	Effect size
	Adverse reactions (disease code, disease name, outcome)
	CRF number
	Dropped out
	Reason for dropout
Analysis methods:	Listings of the above analytical parameters will be prepared in accordance with the Guidelines for Preparation of File for Reexamination Data Entries in PSEHB/PED Reexamination Notification No. 1119-3, dated November 19, 2020.

Document History (Version Management)

Version	Date	Created/Modified by	Comments
Ver. 1	2024.10.23	[redacted]	Ver. 1 prepared