Title: Specified Drug-Use Survey of Zafatek Tablets “Survey on long-term use in patients with type 2 diabetes mellitus”

NCT Number: NCT03555591

Statistical analysis plan Approve Date: 07-Apr-2022

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

Statistical Analysis Plan

(Final Analysis)

Product:	Zafatek Tablets
Surveillance study title:	Specified Drug-Use Survey “Survey on long-term use in patients with type 2 diabetes mellitus”
Protocol Number:	Trelagliptin-5001
Sponsor:	Takeda Pharmaceutical Company Limited

Takeda Pharmaceutical Company Limited
Director of Biostatistics Dept.

Seal

Month Day Year

First Version: Prepared on April 7, 2022

Table of Contents

1 Definitions of Terms, etc.

1.1 List of Terms and Abbreviations

- This drug: Zafatek Tablets is abbreviated as “this drug.”
- Adverse drug reactions, etc.: An abbreviation for the term “adverse drug reactions or infections.” Adverse drug reactions are adverse events with a causal relationship to this drug other than “Not related.” “Adverse drug reactions or infections” is used in titles of this statistical analysis plan, and “adverse drug reactions, etc.” is used in the text and tables.
- Serious adverse events:
  - Adverse events that are assessed as “serious” by the investigator. Note that events listed in the MedDRA code list (PT code) of the Important Medical Events List will be handled as serious even when the investigator’s assessment is “non-serious.”
- Summary statistics: General term for the number of patients, mean, standard deviation, maximum, minimum, and quartiles
- Patients without collected case report form: Enrolled patients from whom a case report form was not collected
- Patients with collected case report form: Enrolled patients from whom a case report form was collected
- Age: If the date of the start of treatment with this drug is less than the birth date, age will be calculated according to: Year of the start of treatment with this drug – Year of birth – 1. If the date of the start of treatment with this drug is the same as the birth date or over, age will be calculated according to: Year of the start of treatment with this drug – Year of birth. If the day of birth is unknown, it will be taken to be the first day of the month in calculations.
- Duration of type 2 diabetes mellitus (months):
  - Actual number (Units: months) = [Month of the start of initial treatment with this drug] − [Timing of diagnosis of type 2 diabetes mellitus] + 1
    If the month in which type 2 diabetes mellitus was diagnosed is unknown, it will be taken to be January.
- Severity of renal impairment: The severity of renal impairment at patient enrollment or the severity of renal impairment assessed based on the creatinine clearance, whichever is severer.
  - Severity of renal impairment (Creatinine clearance)
    Normal: ≥80.0
    Mild: ≥50.0 and <80.0
    Moderate: ≥30.0 and <50.0

Severe: <30.0

- Creatinine clearance (mL/min): Calculated using the following Cockcroft-Gault formula (each is rounded off to the nearest whole number).
  Male: [(140 – age) × body weight (kg)] ÷ [72 × serum creatinine (mg/dL)]
  Female: 0.85 × [(140 – age) × body weight (kg)] ÷ [72 × serum creatinine (mg/dL)]
  Note that these will be calculated when all values used for calculation have been measured in the same VISIT, and the value calculated from the test date and date of birth will be used for the age. Furthermore, when the serum creatinine value recorded in the enrollment form is used, the value calculated from the initial treatment date and the date of birth will be used for the age.

- Severity of impaired liver function: The severity of impaired liver function at patient enrollment or the severity of impaired liver function assessed based on the total bilirubin, AST, ALT, and symptoms (concurrent diseases), whichever is severer. A patient will be assessed as normal if the severity of impaired liver function at patient enrollment is missing and none of the following criteria apply.

  - Severity of impaired liver function (total bilirubin)
    Mild: ≥1.6 and <3.0
    Moderate: ≥3.0 and <10
    Severe: ≥10

  - Severity of impaired liver function (AST or ALT)
    Mild: ≥50 and <100
    Moderate: ≥100 and <500
    Severe: ≥500

  - Severity of impaired liver function (symptoms [concurrent diseases])

PT term	Severity
Hepatic cirrhosis	Severe
Hepatocellular carcinoma	Severe
Metastases to liver	Severe
Hepatomegaly	Moderate
Hepatic mass	Moderate
Hepatic steatosis	Moderate
Autoimmune hepatitis	Moderate
Nonalcoholic steatohepatitis	Moderate
Nonalcoholic fatty liver disease	Moderate

- Overdoses or excessive intake: An overdose or excessive intake will be taken for a patient responding even in one instance that "The dosing frequency was inadvertently misunderstood as daily, and consequently two or more doses were taken in a week" or "This drug was taken together with another daily medication, and consequently two or more doses were inadvertently taken in a week," as a reason for there being a "Week in which two or more doses were taken" in the "Treatment noncompliance details and reasons," or for a patient responding even in one instance that "A larger dose than prescribed was taken" in the "Treatment noncompliance details."

- HOMA-β: [Fasting insulin level (μU/mL) × 360] ÷ [Fasting blood glucose level (mg/dL) – 63]

1.2 Analysis Populations

A "safety population" and an "efficacy population" have been set as the analysis populations for this surveillance study. The analysis populations are defined as follows.

Safety population

The definition of "safety population" for this Statistical Analysis Plan is "patients who receive at least 1 dose of this drug and for whom safety is evaluable among patients from whom a case report form was collected." A patient for whom any of the following conditions apply will be excluded from the safety population.

- This drug not administered
- Before administration of contract period
- Enrolled on or after Day 15 of prescription for this drug

Efficacy Population

The definition of "efficacy population" for this Statistical Analysis Plan is "patients in the safety population, without any significant protocol violations and for whom efficacy is evaluable." Patients in the safety population, for whom any of the following conditions apply will be excluded from the efficacy population.

- Other than a target disease
- Has severe ketosis, diabetic coma or precoma, or type 1 diabetes mellitus
- Has a severe infection, perioperative status, or serious trauma
- Has severe renal impairment or on dialysis due to end-stage renal failure
- Has a history of hypersensitivity to any of the ingredients of this drug

1.3 Number of Digits to Display

- Percentage (%)
  Incidence or occurrence rate of adverse events or adverse drug reactions, etc.:
  Rounded off to two decimal places, and expressed to two decimal places.
  Other than the above:
  Rounded off to one decimal place, and expressed to one decimal place.

- Summary statistics

  Mean, median, and first and third quartiles:

  Raw data will be rounded off from the second decimal place, and expressed to one decimal place.

  Standard deviation:

  Raw data will be rounded off from the third decimal place, and expressed to two decimal places.

  Minimum and maximum:

  Values will be expressed to the same number of digits as that for target data.

1.4 Important Identified Risks, Important Potential Risks, and Important Missing Information

- Important identified risks
  - Hypoglycaemia: An event that includes "hypoglycaemia" in the PT term
- Important potential risks
  - Skin disorder: An event corresponding to the SOC, "Skin and subcutaneous tissue disorders"
  - Pancreatitis acute: An event (preferred term) corresponding to a narrow term of the SMQ, "pancreatitis acute," or an event classified according to a broad term of the SMQ, "pancreatitis acute" and that is associated with a laboratory test value (blood tests and urinalyses)
  - Proarrhythmia with prolonged QT/QTc interval: Torsade de pointes, sudden death, cardiac death, sudden cardiac death, cardiac arrest, cardio-respiratory arrest, ventricular tachycardia, ventricular tachyarrhythmia, ventricular arrhythmia, ventricular fibrillation, cardiac fibrillation, ventricular flutter, altered state of consciousness, syncope, loss of consciousness, seizure, epilepsy, electrocardiogram QT prolonged, long QT syndrome, congenital long QT syndrome, electrocardiogram QT interval abnormal, electrocardiogram repolarisation abnormality, electrocardiogram U wave abnormal (preferred terms)
  - Intestinal obstruction: An event corresponding to a narrow term of the SMQ, "gastrointestinal obstruction"
  - Infection: An event corresponding to the SOC, "Infections and infestations"
  - Malignant tumor: An event corresponding to the SOC, "Neoplasms benign, malignant and unspecified (incl cysts and polyps)"
  - Pemphigoid: Pemphigoid, ocular pemphigoid (preferred term)
- Important missing information

- Safety when administered in patients with renal impairment: Events occurring in patients with concurrent diseases for which the HLGT is “nephropathy” or “renal disorder (other than nephropathy),” the HLT is “renal function test” or “renal therapeutic procedure,” and among these, the PT term is an illness that includes dialysis (but this excludes urinary tract disease and renal calculus).
- Safety when administered in patients with impaired liver function: Events occurring in patients with concurrent diseases corresponding to a broad term of the SMQ, “liver disorder”
- Safety when administered in elderly patients: Events occurring in patients ≥65 years of age
- Effect on cardiovascular risk: Events classified according to a broad term of the SMQ, “myocardial infarction” or a broad term of the SMQ, “central nervous system haemorrhage and cerebrovascular disease”

1.5 Handling of Time Windows

Evaluable data (data that is not missing and deemed usable) and data within the acceptable range will be used for each test, observation, and evaluation variable. If there are multiple evaluable data within the same acceptable range, the value from a test, observation, or evaluation date that is closest to the reference date will be used, and if the difference from that of the reference date is the same or no reference date has been specified, the latter of the values will be used. Furthermore, differences from a reference date will be determined based on the number of days after treatment. Of the laboratory tests, however, only the HbA1c, fasting blood glucose, fasting insulin, HOMA-β, and fasting glucagon levels are specified for the final evaluation.

Vital signs and laboratory tests

Evaluation timepoints	Reference date	Acceptable window
		Number of days after treatment
At the start of treatment with this drug	Number of days after treatment: -1	-30 to 1
1 month after the start of treatment with this drug	Number of days after treatment: 30	2 to 60
3 months after the start of treatment with this drug	Number of days after treatment: 90	61 to 135
6 months after the start of treatment with this drug	Number of days after treatment: 180	136 to 270
12 months after the start of treatment with this drug	Number of days after treatment: 360	271 to 450
18 months after the start of treatment with this drug	Number of days after treatment: 540	451 to 630
24 months after the start of treatment with this drug	Number of days after treatment: 720	631 to 810
30 months after the start of treatment with this drug	Number of days after treatment: 900	811 to 990
36 months after the start of treatment with this drug	Number of days after treatment: 1080	991 to 1170
At the final evaluation	Number of days after treatment: -	2 to 1170

Electrocardiography

Evaluation timepoints	Reference date	Acceptable window
		Number of days after treatment
At the start of treatment with this drug	Number of days after treatment: -1	-30 to 1
1 month after the start of treatment with this drug	Number of days after treatment: 30	2 to 60
3 months after the start of treatment with this drug	Number of days after treatment: 90	61 to 135
6 months after the start of treatment with this drug	Number of days after treatment: 180	136 to 270
12 months after the start of treatment with this drug	Number of days after treatment: 360	271 to 540
24 months after the start of treatment with this drug	Number of days after treatment: 720	541 to 900
36 months after the start of treatment with this drug	Number of days after treatment: 1080	901 to 1170

Waist circumference

Evaluation timepoints	Reference date	Acceptable window
		Number of days after treatment
At the start of treatment with this drug	Number of days after treatment: -1	-30 to 1
6 months after the start of treatment with this drug	Number of days after treatment: 180	2 to 270
12 months after the start of treatment with this drug	Number of days after treatment: 360	271 to 540
24 months after the start of treatment with this drug	Number of days after treatment: 720	541 to 900
36 months after the start of treatment with this drug	Number of days after treatment: 1080	901 to 1170

1.6 Other Handling

- Case report forms with information entered for patient enrollment, Case Report Form 1 (from baseline to 12 months after the start of treatment), and Case Report Form 2 (from 12 months to 36 months after the start of treatment) will be the target of this analysis.
- Time to onset of adverse events (or adverse drug reactions, etc.): [Calculated from the onset date of the adverse event (or adverse drug reaction, etc.)] – [the start date of treatment with this drug] + 1. For adverse events (or adverse drug reactions, etc.) with an unknown day of onset, the first day of the month will be used in the calculation. However, if the month and year of the start of treatment with this drug = the month and year of onset of the adverse event (or adverse drug reaction, etc.), the start day of initial treatment with this drug will be used in the calculation.

2 Number of Study Sites, Number of Patients Enrolled, and Patient Composition

2.1 Disposition of patients

Analysis target:	All enrolled patients (Enrolled patients)	
Analysis items:	Enrolled patients	
	Number of surveillance study sites	
	Patients without collected case report form	
	Patients with collected case report form	
	Patients excluded from safety evaluation*	
	Reason for exclusion (duplicate tabulation)	[This drug not administered, Before administration of contract period, Enrolled on or after Day 15 of prescription for this drug]
	Patients included in safety evaluation*	
	Patients excluded from efficacy evaluation*	
	Reason for exclusion (duplicate tabulation)	[Other than target diseases, Has severe ketosis, diabetic coma or precoma, or type 1 diabetes mellitus, Has a severe infection, perioperative status, or serious trauma, Has severe renal impairment or on dialysis due to end-stage renal failure, Has a history of hypersensitivity to any of the ingredients of this drug]
	Patients included in efficacy evaluation*	
	Completion status	[Completed, Discontinued]

Analysis method: The following analyses will be performed on the above analysis items and a patient composition chart will be prepared.

Furthermore, the number of surveillance study sites will also be calculated for the enrolled patients. Note that when the same medical institution has different clinical departments for each surveillance study, it will be counted as one medical institution. For patients excluded from the safety evaluation and patients excluded from the efficacy evaluation, the number of patients for each reason for exclusion will be tabulated and a listing will be prepared.

* “Patients included in safety evaluation” refers to the “safety population,” and “patients excluded from safety evaluation” refers to patients excluded from the “safety population.” Similarly, “patients included in efficacy evaluation” refers to the “efficacy population,” and “patients excluded from efficacy evaluation” refers to patients in the “safety population” who are excluded from the “efficacy population.”

（1） Frequency tabulation

3 Patient Background

3.1 Patient Background

Analysis target:	Safety population	
Analysis items:	Sex	[Male, Female]
	Age (years)	[Min<= - <65, 65<= - <=Max]
		[Min<= - <75, 75<= - <=Max]
	Duration of type 2 diabetes mellitus (years)	[Min<= - <2, 2<= - <5, 5<= - <10, 10<= - <=Max]
	Body weight (kg)	
	BMI (kg/m^2)	[Min<= - <18.5, 18.5<= - <25.0, 25.0<= - <30.0, 30.0<= - <=Max]
	Height (cm)	
	Inpatient/outpatient category	[Outpatient, Inpatient]
	Presence or absence of hypersensitivity diathesis	[No, Yes, Unknown]
	Presence or absence of concurrent diseases	[No, Yes]
	Breakdown of concurrent diseases (duplicate tabulation)	
	Diabetic complication	[Diabetic nephropathy, Diabetic retinopathy, Diabetic neuropathy]
	Lifestyle disease	[Hypertension, Dyslipidaemia, Hyperuricaemia]
	Pancreatic and biliary tract disease	[Pancreatitis, Cholecystolithiasis]
	Liver disease	[Hepatic steatosis, Hepatitis alcoholic, Chronic hepatitis, Hepatic cirrhosis]
	Renal disease	[Nephrotic syndrome, Glomerulonephritis, Chronic renal failure]
	Cardiac and cerebrovascular diseases	[Cardiac failure (NYHA Classes I, II, III, IV), Myocardial infarction, Angina pectoris, Cerebral infarction (including cerebral infarction sequelae)]
	Allergic disease	[Bronchial asthma, Pollinosis, Rhinitis allergic, Dermatitis allergic]
	Malignant tumor	[Gastric cancer, Lung cancer, Colorectal cancer, Pancreatic cancer]
	Presence or absence of medical history	[No, Yes, Unknown]

	Breakdown of medical history (duplicate tabulation)	[Pancreatitis, Cholecystolithiasis]
	History of smoking	[Never smoked, Currently smoking, Smoked in the past but not currently, Unknown]
	History of alcohol consumption	[Yes, No, Unknown]
	Presence or absence of renal impairment	[No, Yes]
	Severity of renal impairment	[Normal, Mild, Moderate, Severe]
	Presence or absence of impaired liver function	[No, Yes]
	Severity of impaired liver function	[Normal, Mild, Moderate, Severe]
	HbA1c (NGSP value)	[<6.0%, 6.0 to <7.0%, 7.0 to <8.0%, ≥8.0%, unknown]
	Fasting blood glucose	
	Fasting glucagon	
	Serum creatinine (mg/dL)	
	Creatinine clearance (mL/min)	

Analysis method: The following analyses of the above analysis variables will be performed. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Frequency tabulation of discrete data and summary statistics of continuous data

4 Treatment Details

4.1 Duration of treatment with this drug and completion status

Analysis target:	Safety population	
Analysis items:	Duration of treatment with this drug	
	Completion status	[Completed, Discontinued]
	Reason for discontinuation of treatment with this drug (duplicate tabulation)	[Because treatment goal was achieved, Due to occurrence of adverse event, Because the patient no longer visits the hospital due to transfer to another hospital, etc., Pregnancy, Due to inadequate response, Other]
Analysis method:	The following analyses of the above analysis variables will be performed. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients. (1) Frequency tabulation of discrete data and summary statistics of continuous data	

4.2 Previous Therapeutic Drugs (Antidiabetic Drugs) and Concomitant Drugs (Antidiabetic Drugs)

Analysis target:	Safety population	
Analysis items:	Previous therapeutic drug (antidiabetic drug) treatment status	[No, Yes]
	Breakdown of previous therapeutic drugs (antidiabetic drugs) (duplicate tabulation)	[α-Glucosidase inhibitors, thiazolidinediones, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, antidiabetic combination products] The denominator for percentages will be the number of patients with a previous therapeutic drug (antidiabetic drug) treatment status of "Yes."
	Concomitant drug (antidiabetic) treatment status	[No, Yes]

	Breakdown of concomitant drugs (antidiabetics) (Duplicate tabulation)	[α-Glucosidase inhibitors, thiazolidinediones, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, antidiabetic combination products] The denominator for percentages will be the number of patients with a concomitant drug (antidiabetic drug) treatment status of "Yes."
Analysis method:	The following analyses of the above analysis variables will be performed. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients. (1) Frequency tabulation	

4.3 Concomitant Drugs (Non-Antidiabetic)

Analysis target:	Safety population	
Analysis items:	Concomitant drug (non-antidiabetic) treatment status	[No, Yes]
Analysis method:	The following analyses of the above analysis variables will be performed. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients. (1) Frequency tabulation	

4.4 Treatment Compliance Status With This Drug

Analysis target:	Safety population	
Analysis items:	Treatment Compliance Status With This Drug	[≥90% of the doses were taken once weekly as prescribed. ≥70% of the doses were taken once weekly as prescribed. ≥50% of the doses were taken once weekly as prescribed. <50% of the doses were taken once weekly as prescribed. No dose taken, Unknown treatment compliance status]

Analysis method: This tabulation, in which the incidences at each evaluation timepoint (1 month after the start of treatment with this drug, 3 months after the start of treatment with this drug, 6 months after the start of treatment with this drug, 18 months after the start of treatment with this drug, 24 months after the start of treatment with this drug, 30 months after the start of treatment with this drug, and 36 months after the start of treatment with this drug or at the discontinuation of treatment) will be tabulated, will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

4.5 Overdoses or Excessive Intake

Analysis target: Safety population

Analysis items: Overdoses or Excessive Intake [No, Yes]

Analysis method: The following analyses of the above analysis variables will be performed. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Frequency tabulation

5 Matters Pertaining to Safety

5.1 Occurrence Status of Adverse Events and Adverse Drug Reactions or Infections

5.1.1 Occurrence Status of Adverse Events

Analysis target: Safety population

Analysis items: Adverse events

Analysis method: The following analyses of the above analysis variables will be performed. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrences of adverse events

(2) Number of occurrences of adverse events

(3) Incidence of adverse events

(4) Adverse event type

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrences of adverse events]

- Number of patients with an occurrence of an adverse event.

[Number of occurrences of adverse events]

- Number of adverse events that occurred. Note that the total number of adverse events will be tabulated if there are multiple occurrences of the same adverse event in the same patient.

[Incidence of adverse events]

- The following will be calculated: [Number of patients with occurrence of adverse event] / [Number of patients included in safety evaluation] × 100.

[Adverse event types]

- Adverse events will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the SOC is “Investigations,” they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.
- When recording the number and incidence of patients with adverse events according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC.
- When recording the number and incidence of patients with adverse events according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT.

5.1.2 Occurrence Status of Adverse Drug Reactions or Infections

Analysis target: Safety population

Analysis items: Adverse drug reactions, etc.

Analysis method: The following analyses of the above analysis variables will be performed. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.

(2) Number of occurrences of adverse drug reactions, etc.

(3) Incidence of adverse drug reactions, etc.

(4) Type of adverse drug reactions, etc.

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrence of adverse drug reaction, etc.]

- Number of patients with an occurrence of an adverse drug reaction, etc.

[Number of occurrences of adverse drug reactions, etc.]

- Number of adverse drug reactions, etc., that occurred. Note that the total number of adverse drug reactions, etc., will be tabulated if there are multiple occurrences of the same reaction in the same patient.

[Incidences of adverse drug reactions, etc.]

- The following will be calculated: [Number of patients with occurrence of adverse drug reaction, etc.] / [Number of patients included in safety evaluation] × 100.

[Types of adverse drug reactions, etc.]

- Adverse drug reactions, etc., will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the SOC is “Investigations,” they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.
- When recording the number and incidence of patients with adverse drug reactions, etc., according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC.
- When recording the number and incidence of patients with adverse drug reactions, etc., according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT.

5.2 Occurrence Status of Adverse Events Corresponding to the Safety Specification (Tabulation According to Risk)

Analysis target: Safety population

Analysis items: Adverse events corresponding to important identified risks (hypoglycaemia), corresponding to important potential risks (skin disorder, pancreatitis acute, proarrhythmia with prolonged QT/QTc interval, intestinal obstruction, infection, malignant tumor, and pemphigoid), and corresponding to important missing information (safety when administered in patients with renal impairment, safety when administered in patients with impaired liver function, safety when administered in elderly patients, and effect on cardiovascular risk)

Analysis method: The following analyses of the above analysis variables will be performed. Note that each of these targeted risks will be defined according to the definitions in Section 1.4, Important Identified Risks, Important Potential Risks, and Important Missing Information. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

Number of patients with occurrences of adverse events

(1) Number of occurrences of adverse events

(2) Incidence of adverse events

(3) Adverse event type

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrences of adverse events]

- Number of patients with an occurrence of an adverse event.

[Number of occurrences of adverse events]

- Number of adverse events that occurred. Note that the total number of adverse events will be tabulated if there are multiple occurrences of the same adverse event in the same patient.

[Incidence of adverse events]

- The following will be calculated: [Number of patients with occurrence of adverse event] / [Number of patients included in safety evaluation] × 100.

[Adverse event types]

- Adverse events will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the SOC is “Investigations,” they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.

- When recording the number and incidence of patients with adverse events according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC.
- When recording the number and incidence of patients with adverse events according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT.

5.3 Occurrence Status of Adverse Drug Reactions or Infections Corresponding to the Safety Specification (Tabulation According to Risk)

Analysis target: Safety population

Analysis items: Adverse drug reactions, etc., corresponding to important identified risks (hypoglycaemia), corresponding to important potential risks (skin disorder, pancreatitis acute, proarrhythmia with prolonged QT/QTc interval, intestinal obstruction, infection, malignant tumor, and pemphigoid), and corresponding to important missing information (safety when administered in patients with renal impairment, safety when administered in patients with impaired liver function, safety when administered in elderly patients, and effect on cardiovascular risk)

Analysis method: The following analyses of the above analysis variables will be performed. Note that each of these targeted risks will be defined according to the definitions in Section 1.4, Important Identified Risks, Important Potential Risks, and Important Missing Information. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.
(2) Number of occurrences of adverse drug reactions, etc.
(3) Incidence of adverse drug reactions, etc.
(4) Type of adverse drug reactions, etc.

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrence of adverse drug reaction, etc.]

- Number of patients with an occurrence of an adverse drug reaction, etc.

[Number of occurrences of adverse drug reactions, etc.]

- Number of adverse drug reactions, etc., that occurred. Note that the total number of adverse drug reactions, etc., will be tabulated if there are multiple occurrences of the same reaction in the same patient.

[Incidences of adverse drug reactions, etc.]

- The following will be calculated: [Number of patients with occurrence of adverse drug reaction, etc.] / [Number of patients included in safety evaluation] × 100.

[Types of adverse drug reactions, etc.]

- Adverse drug reactions, etc., will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the SOC is “Investigations,” they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.

- When recording the number and incidence of patients with adverse drug reactions, etc., according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC.
- When recording the number and incidence of patients with adverse drug reactions, etc., according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT.

5.4 Occurrence Status of Adverse Drug Reactions or Infections Corresponding to the Safety Specification by Serious or Non-Serious (Tabulation According to Risk)

Analysis target: Safety population

Analysis items: Adverse drug reactions, etc., corresponding to important identified risks (hypoglycaemia), corresponding to important potential risks (skin disorder, pancreatitis acute, proarrhythmia with prolonged QT/QTc interval, intestinal obstruction, infection, malignant tumor, and pemphigoid), and corresponding to important missing information (safety when administered in patients with renal impairment, safety when administered in patients with impaired liver function, safety when administered in elderly patients, and effect on cardiovascular risk)

Stratification items: Seriousness [Serious, Non-serious]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items by each risk. Note that each of these targeted risks will be defined according to the definitions in Section 1.4, Important Identified Risks, Important Potential Risks, and Important Missing Information. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

[Types of adverse drug reactions, etc.]

- Adverse drug reactions, etc., will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the SOC is "Investigations," they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.
- When recording the number and incidence of patients with adverse drug reactions, etc., according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC. However, any difference in seriousness will be counted as 1 patient each for serious and non-serious.
- When recording the number and incidence of patients with adverse drug reactions, etc., according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT. However, any difference in seriousness will be counted as 1 patient each for serious and non-serious.

5.5 Occurrence Status of Adverse Events and Adverse Drug Reactions or Infections in Patients Excluded From Safety Evaluation

5.5.1 Occurrence Status of Adverse Events

Analysis target: Patients excluded from safety evaluation

Analysis items: Adverse events

Analysis method: The following analyses of the above analysis variables will be performed.

(1) Number of patients with occurrences of adverse events

(2) Number of occurrences of adverse events

(3) Incidence of adverse events

(4) Adverse event type

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrences of adverse events]

- Number of patients with an occurrence of an adverse event.

[Number of occurrences of adverse events]

- Number of adverse events that occurred. Note that the total number of adverse events will be tabulated if there are multiple occurrences of the same adverse event in the same patient.

[Incidence of adverse events]

- The following will be calculated: [Number of patients with occurrence of adverse event] / [Number of patients included in safety evaluation] × 100.

[Adverse event types]

- Adverse events will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the SOC is “Investigations,” they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.
- When recording the number and incidence of patients with adverse events according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC.
- When recording the number and incidence of patients with adverse events according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT.

5.5.2 Occurrence Status of Adverse Drug Reactions or Infections

Analysis target: Patients excluded from safety evaluation

Analysis items: Adverse drug reactions, etc.

Analysis method: The following analyses of the above analysis variables will be performed.

(1) Number of patients with occurrence of adverse drug reaction, etc.

(2) Number of occurrences of adverse drug reactions, etc.

(3) Incidence of adverse drug reactions, etc.

(4) Type of adverse drug reactions, etc.

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrence of adverse drug reaction, etc.]

- Number of patients with an occurrence of an adverse drug reaction, etc.

[Number of occurrences of adverse drug reactions, etc.]

- Number of adverse drug reactions, etc., that occurred. Note that the total number of adverse drug reactions, etc., will be tabulated if there are multiple occurrences of the same reaction in the same patient.

[Incidences of adverse drug reactions, etc.]

- The following will be calculated: [Number of patients with occurrence of adverse drug reaction, etc.] / [Number of patients included in safety evaluation] × 100.

[Types of adverse drug reactions, etc.]

- Adverse drug reactions, etc., will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the SOC is "Investigations," they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.
  - When recording the number and incidence of patients with adverse drug reactions, etc., according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC.
- When recording the number and incidence of patients with adverse drug reactions, etc., according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT.

5.6 Occurrence Status of Adverse Events and Adverse Drug Reactions or Infections by Seriousness, Time to Onset, and Outcome

5.6.1 Occurrence Status of Adverse Events by Seriousness, Time to Onset, and Outcome

Analysis target:	Safety population	
Analysis items:	Adverse events	
Stratification items:	Seriousness	[Serious, Non-serious]
	Time to onset	[1–14 days, 15–28 days, 29–84 days, 85–168 days, 169–336 days, 337–504 days, 505–672 days, 673–840 days, 841–1008 days, ≥1009 days]
	Outcome	[Recovered/resolved, Recovering/resolving, Not recovered/resolved, Recovered/resolved with sequelae, Death (due to this event), Unknown]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrences of adverse events
(2) Number of occurrences of adverse events
(3) Incidence of adverse events
(4) Adverse event type

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrences of adverse events]

- Number of patients with an occurrence of an adverse event.

[Number of occurrences of adverse events]

- Number of adverse events that occurred. Note that the total number of adverse events will be tabulated if there are multiple occurrences of the same adverse event in the same patient.

[Incidence of adverse events]

- The following will be calculated: [Number of patients with occurrence of adverse event] / [Number of patients included in safety evaluation] × 100.

[Adverse event types]

- Adverse events will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the

SOC is “Investigations,” they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.

- When recording the number and incidence of patients with adverse events according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC. However, for the same SOC, a single SOC will be selected according to the order of priority at the end.
- When recording the number and incidence of patients with adverse events according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT. However, for the same PT, a single PT will be selected according to the following order of priority.
  Seriousness: Serious → non-serious
  Time to onset: The event that occurred the earliest after administration of this drug
  Outcome: Death (due to this event) → recovered/resolved with sequelae → not recovered/resolved → recovering/resolving → recovered/resolved → unknown

5.6.2 Occurrence Status of Adverse Drug Reactions or Infections by Seriousness, Time to Onset, and Outcome

Analysis target:	Safety population	
Analysis items:	Adverse drug reactions, etc.	
Stratification items:	Seriousness	[Serious, Non-serious]
	Time to onset	[1–14 days, 15–28 days, 29–84 days, 85–168 days, 169–336 days, 337–504 days, 505–672 days, 673–840 days, 841–1008 days, ≥1009 days]
	Outcome	[Recovered/resolved, Recovering/resolving, Not recovered/resolved, Recovered/resolved with sequelae, Death (due to this event), Unknown]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all

patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.
(2) Number of occurrences of adverse drug reactions, etc.
(3) Incidence of adverse drug reactions, etc.
(4) Type of adverse drug reactions, etc.

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrence of adverse drug reaction, etc.]

- Number of patients with an occurrence of an adverse drug reaction, etc.

[Number of occurrences of adverse drug reactions, etc.]

- Number of adverse drug reactions, etc., that occurred. Note that the total number of adverse drug reactions, etc., will be tabulated if there are multiple occurrences of the same reaction in the same patient.

[Incidences of adverse drug reactions, etc.]

- The following will be calculated: [Number of patients with occurrence of adverse drug reaction, etc.] / [Number of patients included in safety evaluation] × 100.

[Types of adverse drug reactions, etc.]

- Adverse drug reactions, etc., will be coded using MedDRA/J. They will be tabulated by broadly classifying according to SOC and then by PT. Note that when the SOC is “Investigations,” they will be tabulated by summarizing according to HLGT (listed in ascending order of HLGT code, but not output) and then by PT.
- When recording the number and incidence of patients with adverse drug reactions, etc., according to SOC, the internationally agreed order of SOCs will be used. Note that multiple occurrences of the same SOC in the same patient will be counted as 1 patient for that SOC. However, for the same SOC, a single SOC will be selected according to the order of priority at the end.
- When recording the number and incidence of patients with adverse drug reactions, etc., according to PT, it will be in ascending order of PT code. Note that multiple occurrences of the same PT in the same patient will be counted as 1 patient for that PT. However, for the same PT, a single PT will be selected according to the following order of priority.

  Seriousness: Serious → non-serious

  Time to onset: The event that occurred the earliest after administration of this drug

Outcome: Death (due to this event) → recovered/resolved with sequelae → not recovered/resolved → recovering/resolving → recovered/resolved → unknown

5.7 Adverse Drug Reaction and Infection Occurrence Status by Patient Background and Treatment Factors

5.7.1 Occurrence Status of Adverse Drug Reactions or Infections by Patient Background Factor and Treatment Factor

Analysis target:	Safety population	
Analysis items:	Adverse drug reactions, etc.	
Stratification items:	Sex	[Male, Female]
	Age (years)	[Min<= - <65, 65<= - <=Max] [Min<= - <75, 75<= - <=Max]
	Duration of type 2 diabetes mellitus (years)	[Min<= - <2, 2<= - <5, 5<= - <10, 10<= - <=Max]
	BMI (kg/m^2)	[Min<= - <18.5, 18.5<= - <25.0, 25.0<= - <30.0, 30.0<= - <=Max]
	Waist circumference (cm)	Male:[Min<= - <85, 85<= - <=Max] Female:[Min<= - <90, 90<= - <=Max]
	Presence or absence of renal impairment	[No, Yes]
	Severity of renal impairment	[Normal, Mild, Moderate, Severe]
	Presence or absence of impaired liver function	[No, Yes]
	Severity of impaired liver function	[Normal, Mild, Moderate, Severe]
	Concomitant antidiabetic drug treatment status	[No, Yes]
	Concomitant antidiabetic drug type (Duplicate tabulation)	[α-Glucosidase inhibitors, Thiazolidinediones, Sulfonylureas, Biguanides, Rapid-acting insulin secretagogues, Insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, Antidiabetic combination products]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.

(2) Incidence of adverse drug reactions, etc.

The calculation method when performing each of the analyses will be as follows.

[Number of patients with occurrence of adverse drug reaction, etc.]

- Number of patients with an occurrence of an adverse drug reaction, etc.

[Incidences of adverse drug reactions, etc.]

- The following will be calculated: [Number of patients with occurrence of adverse drug reaction, etc.] / [Number of patients included in safety evaluation] × 100.

5.7.2 Occurrence Status of Adverse Drug Reactions or Infections by Sex

Analysis target: Safety population

Analysis items: Adverse drug reactions, etc.

Stratification items: Sex [Male, Female]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.
(2) Number of occurrences of adverse drug reactions, etc.
(3) Incidence of adverse drug reactions, etc.
(4) Type of adverse drug reactions, etc.

The tabulation method for each analysis item is the same as that described in Section 5.1.2.

5.7.3 Occurrence Status of Adverse Drug Reactions or Infections by Age Group

Analysis target: Safety population

Analysis items: Adverse drug reactions, etc.

Stratification items: Age (years) [Min<= - <65, 65<= - <=Max]
[Min<= - <75, 75<= - <=Max]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all patients overall, patients with renal impairment, and patients with impaired liver function.

(1) Number of patients with occurrence of adverse drug reaction, etc.
(2) Number of occurrences of adverse drug reactions, etc.
(3) Incidence of adverse drug reactions, etc.
(4) Type of adverse drug reactions, etc.

The tabulation method for each analysis item is the same as that described in Section 5.1.2.

5.7.4 Occurrence Status of Adverse Drug Reactions or Infections by Presence or Absence of Renal Impairment and by Severity of Renal Impairment

Analysis target: Safety population

Analysis items: Adverse drug reactions, etc.

Stratification items:	Presence or absence of renal impairment	[No, Yes]
	Severity of renal impairment	[Normal, Mild, Moderate, Severe]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all patients overall, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.
(2) Number of occurrences of adverse drug reactions, etc.
(3) Incidence of adverse drug reactions, etc.
(4) Type of adverse drug reactions, etc.

The tabulation method for each analysis item is the same as that described in Section 5.1.2.

5.7.5 Occurrence Status of Adverse Drug Reactions or Infections by Presence or Absence of Impaired Liver Function and by Severity of Impaired Liver Function

Analysis target:	Safety population	
Analysis items:	Adverse drug reactions, etc.	
Stratification items:	Presence or absence of impaired liver function	[No, Yes]
	Severity of impaired liver function	[Normal, Mild, Moderate, Severe]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all patients overall, patients with renal impairment, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.
(2) Number of occurrences of adverse drug reactions, etc.
(3) Incidence of adverse drug reactions, etc.
(4) Type of adverse drug reactions, etc.

The tabulation method for each analysis item is the same as that described in Section 5.1.2.

5.7.6 Occurrence Status of Adverse Drug Reactions or Infections by Concomitant Antidiabetic Drug Treatment Status

Analysis target:	Safety population	
Analysis items:	Adverse drug reactions, etc.	
Stratification items:	By Concomitant Antidiabetic Drug Treatment Status	[No, Yes]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.
(2) Number of occurrences of adverse drug reactions, etc.
(3) Incidence of adverse drug reactions, etc.
(4) Type of adverse drug reactions, etc.

The tabulation method for each analysis item is the same as that described in Section 5.1.2.

5.7.7 Occurrence Status of Adverse Drug Reactions or Infections by Concomitant Antidiabetic Drug Type

Analysis target: Safety population

Analysis items: Adverse drug reactions, etc.

Stratification items: Concomitant antidiabetic drug type [α-Glucosidase inhibitors, thiazolidinediones, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, antidiabetic combination products]

Analysis method: For the above analysis items, the following analyses will be performed for each stratum of the stratification items. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

(1) Number of patients with occurrence of adverse drug reaction, etc.
(2) Number of occurrences of adverse drug reactions, etc.
(3) Incidence of adverse drug reactions, etc.
(4) Type of adverse drug reactions, etc.

The tabulation method for each analysis item is the same as that described in Section 5.1.2.

5.8 Time Courses of Test and Measurement Data

5.8.1 Vital Signs and Waist Circumference

Analysis target: Safety population

Analysis items: Systolic blood pressure, diastolic blood pressure, body weight, waist circumference

Analysis method: For each of the above analysis items, summary statistics of test values will be calculated for the safety population at each evaluation timepoint (at the start of treatment with this drug, 1 month after the start of treatment with this drug, 3 months after the start of treatment with this drug, 6 months after the start of treatment with this drug, 12 months after the start of treatment with this drug, 18 months after the start of treatment with this drug, 24 months after the start of treatment with this drug, 30 months after the start of treatment with this drug, and 36 months after the start of treatment with this drug). Summary statistics will be calculated for the change in each analysis item ([test value at each time point after the start of treatment with this drug] − [the test value at the start of treatment with this drug]). Waist circumferences will be analyzed according to sex. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

5.8.2 Laboratory tests

Analysis target: Safety population

Analysis items: Fasting triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, serum creatinine, BUN, albumin urine (albumin urine/creatinine ratio), AST, ALT, gamma-GTP, ALP, total bilirubin, amylase, and lipase

Analysis method: For each of the above analysis items, summary statistics of test values will be calculated for the safety population at each evaluation timepoint (at the start of treatment with this drug, 1 month after the start of treatment with this drug, 3 months after the start of treatment with this drug, 6 months after the start of treatment with this drug, 12 months after the start of treatment with this drug, 18 months after the start of treatment with this drug, 24 months after the start of treatment with this drug, 30 months after the start of treatment with this drug, and 36 months after the start of treatment with this drug). Summary statistics will be calculated for the change in each analysis item ([test value at each time point after the start of treatment with this drug] − [the test value at the start of treatment with this drug]). This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.

5.8.3 Electrocardiography

Analysis target:	Safety population	
Analysis items:	Electrocardiography	[Clinically significant problem has not occurred, Clinically significant problem has occurred]
Analysis method:	For each of the above analysis items, a frequency tabulation of assessment results will be performed for the safety population at each evaluation timepoint (at the start of treatment with this drug, 1 month after the start of treatment with this drug, 3 months after the start of treatment with this drug, 6 months after the start of treatment with this drug, 12 months after the start of treatment with this drug, 24 months after the start of treatment with this drug, and 36 months after the start of treatment with this drug). This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.	

6 Tabulations and Analyses Related to Efficacy

6.1 Time Courses of HbA1c, Fasting Blood Glucose, Fasting Insulin, HOMA-β, and Fasting Glucagon

Analysis target: Efficacy Population

Analysis items: HbA1c, fasting blood glucose, fasting insulin, HOMA-β, fasting glucagon

Analysis method: For each of the above analysis items, summary statistics of test values will be calculated for the efficacy population at each evaluation timepoint (at the start of treatment with this drug, 1 month after the start of treatment with this drug, 3 months after the start of treatment with this drug, 6 months after the start of treatment with this drug, 12 months after the start of treatment with this drug, 18 months after the start of treatment with this drug, 24 months after the start of treatment with this drug, 30 months after the start of treatment with this drug, 36 months after the start of treatment with this drug, and at the final evaluation). Summary statistics will be calculated for the change in each analysis item ([test value at each time point after the start of treatment with this drug] − [the test value at the start of treatment with this drug]). A bar graph of the changes at each evaluation timepoint will also be created for the HbA1c level. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients on HbA1c only.

6.2 Glycemic control target achievement rate

Analysis target: Efficacy Population

Analysis items: Glycemic control target achievement rate

[<6.0%, 6.0 to <7.0%, 7.0 to <8.0%, and ≥8.0%]
[<8.0%, ≥8.0%]
[<7.0%, ≥7.0%]
[<6.0%, ≥6.0%]

Analysis method: A frequency tabulation of glycemic control target achievement rates will be performed for the efficacy population at each evaluation timepoint (at the start of this treatment with this drug, 1 month after the start of this treatment with this drug, 3 months after the start of this treatment with this drug, 6 months after the start of this treatment with this drug, 12 months after the start of this treatment with this drug, 18 months after the start of this treatment with this drug, 24 months after the start of this treatment with this drug, 30 months after the start of this treatment with this drug, 36 months after the start of this treatment with this drug, and at the final evaluation). Bar graphs will also be created (only for the following categories: <6.0%, 6.0 to <7.0%, 7.0 to <8.0%, and ≥8.0%).

6.3 Changes in HbA1c level by patient background factor and treatment factor

Analysis target:	Efficacy Population	
Analysis items:	Change in HbA1c	
Stratification items:	Sex	[Male, Female]
	Age (years)	[Min<= - <65, 65<= - <=Max] [Min<= - <75, 75<= - <=Max]
	Duration of type 2 diabetes mellitus (years)	[Min<= - <2, 2<= - <5, 5<= - <10, 10<= - <=Max]
	BMI (kg/m^2)	[Min<= - <18.5, 18.5<= - <25.0, 25.0<= - <30.0, 30.0<= - <=Max]
	Waist circumference (cm)	Male:[Min<= - <85, 85<= - <=Max] Female:[Min<= - <90, 90<= - <=Max]
	Presence or absence of renal impairment	[No, Yes]
	Severity of renal impairment	[Normal, Mild, Moderate, Severe]
	Presence or absence of impaired liver function	[No, Yes]
	Severity of impaired liver function	[Normal, Mild, Moderate, Severe]
	Baseline HbA1c (%)	[<6.0%, 6.0 to <7.0%, 7.0 to <8.0%, ≥8.0%, unknown]
	Baseline dose of this drug	[100 mg, 50 mg, other]
	Concomitant antidiabetic drug treatment status	[No, Yes]
	Concomitant antidiabetic drug type	[α-Glucosidase inhibitors, Thiazolidinediones, Sulfonylureas, Biguanides, Rapid-acting insulin secretagogues, Insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, Antidiabetic combination products]
Analysis method:	Summary statistics will be calculated for the change in HbA1c level at the final evaluation for each category of the stratification items with the target population being the efficacy population. This tabulation will be performed for all patients overall, patients with renal impairment, patients with impaired liver function, and elderly patients.	

7 Occurrence Status of Adverse Drug Reactions or Infections in Supplementary Pharmacovigilance Plan

7.1 Occurrence Status of Adverse Drug Reactions or Infections in Supplementary Pharmacovigilance Plan (Appended Form 12)

Analysis target: Safety population

Analysis items: Important identified risks

Hypoglycaemia

Important potential risks

Skin disorder

Pancreatitis acute

Proarrhythmia with prolonged QT/QTc interval

Intestinal obstruction

Infection

Malignant tumor

Pemphigoid

Important missing information

Safety when administered in patients with renal impairment

Safety when administered in patients with impaired liver function

Safety when administered in elderly patients

Effect on cardiovascular risk

Stratification items: Seriousness [Serious, Non-serious]

Analysis method: Analyses of the above analysis items will be performed for each stratum of the stratification items according to Notices 1 to 4 of Appended Form 12 of PSEHB/PED Re-Examination Notification No. 0325-10, dated March 25, 2020.

(1) Number of patients with occurrences of important identified risks and the incidence

(2) Number of patients with occurrences of important potential risks and the incidence

(3) Number of patients with occurrences of important missing information and the incidence

Note that the definitions of risks and order of description of risks will be based on Section 1.4, Important Identified Risks, Important Potential Risks, and Important Missing Information.

8 Summary of Patients in Postmarketing Surveillance, etc.

8.1 Summary of Patients in Postmarketing Surveillance, etc. (Attachment Form 16)

Analysis target: Patients with collected case report form

Analysis items:
- Patient No.
- Site name
- Sex
- Date of birth
- Reason for use (Disease code, Disease name)
- Concurrent diseases (Disease code, Disease name)
- Route of administration
- Maximum dose
- Mean dose
- Units
- Duration of use
- Concomitant drugs (Drug code, Drug name)
- Degree of effectiveness
- Adverse drug reactions (Disease code, Disease name, Outcome)
- Case Report Form No.
- Dropout
- Reason for dropout
- Overdoses or Excessive Intake

Analysis method: A listing of the above analysis items will be prepared in accordance with the procedural guidelines for preparing reexamination data entry files specified in the PSEHB/PED Re-Examination Notification No. 1119-3, dated November 19, 2020. An overdose or excessive intake will be indicated by a "Y" for an applicable patient.

Version History (Version Control)

Version	Date	Prepared or changed by	Comments
First version	2022.4.7	PPD	Preparation of first version