Protocol

A Multicenter, Open-label, Randomized, Comparative Study to Evaluate the Efficacy and Safety of Electric Smart Insulin Pen DIA:CONN P8 in Patients with Type 1, Type 2 or Pancreatogenic Diabetes Mellitus

Under Multiple Dose Insulin Therapy

Protocol Number	P8_S301
Version No.	1.0
Version Date	26 Feb 2024
Investigational Medical Device	DIA:CONN P8
Target Patients	Patients with type 1, type 2 and pancreatogenic diabetes mellitus on multiple daily insulin injections
Sponsor	G2E Co., Ltd.
Coordinating Investigator	Jae Hyeon Kim, MD, PhD, Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center

[Protocol Signature Page]

Title: A Multicenter, Open-label, Randomized, Comparative Study to Evaluate the Efficacy and Safety of Electric Smart Insulin Pen DIA:CONN P8 in Patients with Type 1, Type 2 or Pancreatogenic Diabetes Mellitus Under Multiple Dose Insulin Therapy

Protocol Number:	P8_S301	**Version (Date):**	1.0 (26 Feb 2024)

I have read and reviewed this protocol and understand and agree that it contains all the information necessary for conducting the study. I will make reasonable efforts to ensure the completion of this study within the planned schedule. I will conduct this study in accordance with the Declaration of Helsinki, Good Clinical Practice guidelines for medical devices, and all applicable local regulations.

Principal Investigator

Printed Name _____

Signature _____

Date (DD/MMM/YYYY) _____

Sponsor

Printed Name _____

Signature _____

Date (DD/MMM/YYYY) _____

[Table of Contents]

[Appendix List]

[Protocol Revision History]

Document history including this protocol:

Version	Date	Summary of Changes
1.0	26 Feb 2024	Initial protocol

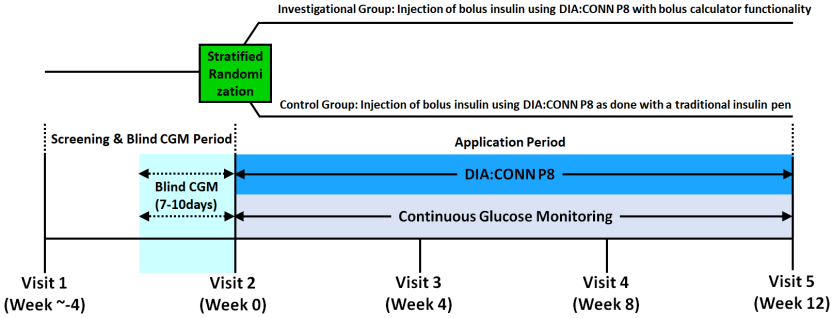
[Protocol Synopsis]

Sponsor	G2E Co., Ltd.
Product Name	DIA:CONN P8
Study Title	A Multicenter, Open-label, Randomized, Comparative Study to Evaluate the Efficacy and Safety of Electric Smart Insulin Pen DIA:CONN P8 in Patients with Type 1, Type 2 or Pancreatogenic Diabetes Mellitus Under Multiple Dose Insulin Therapy
Study Identifier	P8_S301
Coordinating Investigator	Professor Jae Hyeon Kim, Division of Endocrinology and Metabolism, Samsung Medical Center
Study Site and Principal Investigator	Samsung Medical Center and 9 other sites Refer to [Appendix 1] List of the Study Staff and Investigational Medical Device Managers
Study Period	Approximately 18 months from the date of IRB approval at the investigational site
Target Indication	Type 1, type 2, and pancreatogenic diabetes mellitus
Study Objective	To evaluate the efficacy and safety of the electric smart insulin pen DIA:CONN P8 in patients with type 1, type 2, and pancreatogenic diabetes mellitus on multiple daily insulin injections. For this primary purpose, the difference in glycated hemoglobin change between the investigational group and control group will be assessed following a 12-week administration of bolus insulin through multiple daily injections. The investigational group will use DIA:CONN P8 with bolus calculator functionality and the control group will utilize only the insulin injection and tracking functions of the DIA:CONN P8 as done with a traditional insulin pen.
Study Phase and Design	Multicenter, open-label, randomized, controlled study
Number of Subjects	120 (investigational group: 60, control group: 60, accounting for a 10% dropout rate) ※ Rationale for calculation: existing study [Diabetes Care 35(5):984-990, 2012]

Investigational Medical Device (IMD)	Investigational Medical Device: DIA:CONN P8 **[Investigational Group]** Bolus insulin will be injected with an electric smart insulin pen ➢ Insulin will be injected using DIA:CONN P8 with bolus calculator functionality, and subjects will receive education on carbohydrate counting and bolus calculator adjustment **[Control Group]** Bolus insulin will be injected in a manner similar to that of a commercially available traditional insulin pen ➢ Insulin will be injected using only the insulin injection and injection tracking functions of DIA:CONN P8 by manually entering the insulin dose in numbers
Application Method and Duration of IMD	**[Blind CGM Period]** During this period, all subjects will use two DIA:CONN P8 devices, each used for the injection of basal insulin and bolus insulin. Subjects will manually enter and inject the doses, utilizing only the insulin injection and tracking functions as done with a traditional insulin pen. Considering the domestic product approval status, a long-acting insulin which is compatible with DIA:CONN P8 (e.g., Lantus Injection) must be injected for basal insulin. **[Application Period]** All subjects randomized to either the investigational group or control group will use the two DIA:CONN P8 devices provided during the Blind CGM Period continuously until the end of the 12-week Application Period. **1) Investigational group** For the 12-week Application Period of the investigational group, the same method used in the Blind CGM Period will be applied for basal insulin; subjects will manually enter and inject the dose while utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen. For bolus insulin, subjects will enter the carbohydrate count or select a meal in the DIA:CONN P8 smartphone app, which includes bolus calculator functionality, and the app will automatically calculate and set the injection dose using the entered carbohydrate count and other indicators. Subjects will then use DIA:CONN P8 to manually inject the calculated insulin dose. **2) Control group** For the 12-week Application Period of the control group, the same method used in the Blind CGM Period will be applied; subjects will manually enter and inject the basal insulin and bolus insulin doses, utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen.

Inclusion Criteria	1) Aged ≥ 19 years and < 75 years 2) Diagnosed with type 1, type 2, or pancreatogenic diabetes mellitus within one year prior to Screening (i.e., disease duration is at least one year) 3) Continued use of multiple daily insulin injections* for at least 3 months prior to Screening, regardless of whether the subject has used continuous glucose monitoring (CGM). *Defined as, 'dosing of long-acting insulin in combination with ultra-rapid-acting/rapid-acting insulin,' 'dosing of premixed insulin (e.g., insulin aspart/insulin degludec, etc.) in combination with ultra-rapid-acting/rapid-acting insulin,' or 'dosing of premixed insulin at least three times per day'. 4) HbA1c level of ≥ 7.5% and ≤ 12.0% at Screening 5) Capable of injecting basal insulin and bolus insulin using the investigational medical device provided in this study (i.e., DIA:CONN P8) 6) A subject and/or their legally authorized representative who has voluntarily provided written informed consent to participate in this study, including medical care and study use involving CGM and investigational medical device (i.e., DIA:CONN P8)
Exclusion Criteria	1) Administration of medication(s) which may affect glucose metabolism (e.g., corticosteroids, immunosuppressants, etc.) within 3 months prior to Screening (However, subjects on a stable, maintenance dose for at least 6 months prior to Screening are able to participate.) 2) Subjects with clinically significant cardiovascular disease within 6 months prior to Screening 3) Estimated glomerular filtration rate (eGFR) of < 15 mL/min at Screening 4) Unable to engage in education due to severe systemic disorders (e.g., end-stage renal disease requiring dialysis, liver cirrhosis of Child-Pugh Class C or higher, etc.) 5) Subjects with severe diabetic complications (e.g., diabetic foot, diabetic retinopathy, etc.) 6) Pregnant or lactating women 7) Women of childbearing potential who are planning for pregnancy or do not agree to use at least one medically acceptable effective contraceptive method* from Screening until the end of their participation in the study *Medically acceptable contraceptive methods include: intrauterine devices (IUDs), such as a loop or Mirena; the double-barrier method, defined as both male and female partners using contraceptives (i.e., condom/ femidom, diaphragm, or cervical cap); non-oral contraceptives (e.g., injection, vaginal ring, patch, etc.); or total abstinence. Sole use of oral contraceptives or periodic abstinence (e.g., basal body temperature method, fertility awareness method, etc.) is not permitted. However, postmenopausal females (i.e., at least 1 year without menstruation) or females/males who have received sterilization (e.g., vasectomy, tubal ligation, etc.) are not required to agree to the use of contraceptive methods to participate in the study.

	8) Participated in another studies involving an investigational drug or investigational medical device within 3 months prior to Screening 9) Otherwise deemed ineligible by the investigator to participate in this study
Methodology	**[Blind CGM Period]** All subjects who have voluntarily provided informed written consent to participate in this study and are deemed eligible based on the inclusion/exclusion criteria will undergo the blind CGM period of 7 to 10 days before the Baseline Visit (i.e., Randomization). During the Blind CGM Period, all subjects will be provided with a CGM and two DIA:CONN P8 devices for the injection of basal insulin and bolus insulin. Throughout this period, subjects will receive education on the basics of how to use the insulin pen and CGM, then use DIA:CONN P8 to manually enter and inject the basal insulin and bolus insulin doses, utilizing only the insulin injection and tracking functions as done with a traditional insulin pen. Considering the domestic product approval status, a long-acting insulin compatible with DIA:CONN P8 (e.g., Lantus Injection) must be injected for basal insulin. The insulin injection dose and injection time (i.e., time of day) logged in DIA:CONN P8 and the subject's blood glucose data logged in the CGM app will be collected. If a subject's compliance (i.e., rate of CGM use) during their scheduled Blind CGM Period of 7-10 days is below 70%, it will be considered a screen failure, and one re-attempt of the blind CGM period will be allowed. **[Application Period]** Subjects randomized to the investigational group or control group will visit the study site up to five times during the 12-week Application Period, including the Baseline Visit, and will undergo the following process: **1) Investigational group** At Baseline, the investigational group will receive education on carbohydrate counting and bolus calculator adjustment methods, install and receive education on DIA:CONN P8 and the DIA:CONN smartphone app, and install and receive education on CGM and the CGM app. For the 12-week Application Period, the same method used in the Blind CGM Period will be applied for basal insulin; subjects will manually enter and inject the dose while utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen. For bolus insulin, subjects will enter the carbohydrate count or select a meal in the DIA:CONN P8 smartphone app, which includes bolus calculator functionality, and the app will automatically calculate and set the injection dose using the entered carbohydrate count and other indicators. Subjects

	will then use DIA:CONN P8 to manually inject the calculated insulin dose. Data such as the insulin injection dose and injection time (i.e., time of day) will be tracked in the DIA:CONN P8 device and smartphone app. **2) Control group** The control group will receive education on the basics of how to use the insulin pen and CGM and will implement CGM while maintaining their multiple daily insulin injections. For the 12-week Application Period, the same method used in the Blind CGM Period will be applied; subjects will manually enter and inject the basal insulin and bolus insulin doses, utilizing only the insulin injection and injection tracking functions of DIA:CONN P8. Data such as the insulin injection dose and injection time (i.e., time of day) will be recorded on the DIA:CONN P8 device and smartphone app.  **[Study Schematic]**
Endpoints and Assessment Methods	**[Primary Efficacy Endpoint]** Change in HbA1c (%) at Week 12 compared to Baseline **[Secondary Efficacy Endpoints]** 1) Percentage of subjects with HbA1c <7% at Week 12 2) Core CGM endpoints over 12 weeks* • Percentage of Time In Range (TIR) (70-180 mg/dL) • Percentage of Time Below Range (TBR) (<54 mg/dL) • Percentage of TBR (<70 mg/dL) • Percentage of Time Above Range (TAR) (>180 mg/dL) • Percentage of TAR (>250 mg/dL) • Mean glucose, Glucose Management Indicator (GMI) • Coefficient of Variation (CV) (%) *Percentage will be presented for subjects with CGM data ≥70% 3) Core CGM endpoints at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 10 to 12)* • Percentage of TIR (70-180 mg/dL) • Percentage of TBR (<54 mg/dL) • Percentage of TBR (<70 mg/dL) • Percentage of TAR (>180 mg/dL)

	• Percentage of TAR (>250 mg/dL) • Mean glucose, GMI • CV (%) *Percentage will be presented for subjects with CGM data ≥70% 4) Percentage of subjects satisfying both percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) < 1% over 12 weeks 5) Percentage of subjects satisfying both percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) < 1% at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) 6) Percentage of subjects with ≥5% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) 7) Percentage of subjects with ≥10% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) 8) Insulin dose: Type of insulin, total number of daily bolus injections, basal insulin dose, rapid-acting insulin dose for each meal 9) Dosing behavior • Missed dose (no bolus –30 to +60 min) • Late dosing (+15 to +60 min) • Percentage of days with ≥3 daily bolus injections over 12 weeks 10) Number of days in which three bolus calculation modes (i.e., fixed meal mode, estimated meal mode, carbohydrate counting mode) were used from Baseline to Week 12 11) Total individual education hours for the investigational group **[Safety Endpoints]** 1) Adverse events 2) Laboratory tests, vital signs, physical examination
Statistical Analysis Method	**<u>Primary Efficacy Analysis</u>** For the change in HbA1c (%) from Baseline to Week 12, descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) will be presented by group. In order to compare the investigational group and control group, covariance analysis adjusted for Baseline values, CGM use status, and stratification factor (i.e., type of diabetes) will be performed. The results of the covariance analysis will be summarized with the least squares mean (LSM) and standard error (SE) of each group, the LSM difference between groups and its 95% confidence interval, and two-sided *p*-value.

Secondary Efficacy Analysis

1) Percentage of subjects with HbA1c <7% at Week 12

The percentage of subjects with HbA1c <7% at Week 12 and the 95% confidence interval will be presented by group. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use status and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value.

2) Core CGM endpoints over 12 weeks

For the core CGM endpoints over 12 weeks, the percentage of subjects with CGM data ≥70% and descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) for the change from Baseline will be presented by group. In order to compare the investigational group and control group, covariance analysis adjusted for Baseline values, CGM use status, and stratification factor (i.e., type of diabetes) will be performed. The results of the covariance analysis will be summarized with the LSM and SE of each group, the LSM difference between groups and its 95% confidence interval, and two-sided *p*-value.

3) Core CGM endpoints at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12)

For the core CGM endpoints over 12 weeks, the percentage of subjects with CGM data ≥70% and descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) for the change from Baseline will be presented by group. In order to compare the investigational group and control group, covariance analysis adjusted for Baseline values, CGM use status, and stratification factor (i.e., type of diabetes) will be performed. The results of the covariance analysis will be summarized with the LSM and SE of each group, the LSM difference between groups and its 95% confidence interval, and two-sided *p*-value.

4) Percentage of subjects satisfying both percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% over 12 weeks

The percentage of subjects simultaneously satisfying percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% over 12 weeks will be presented along with the 95% confidence interval. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression

	analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value. 5) Percentage of subjects satisfying both percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) The percentage of subjects simultaneously satisfying percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) will be presented along with the 95% confidence interval. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value. 6) Percentage of subjects with ≥5% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) The percentage of subjects with ≥5% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) will be presented along with the 95% confidence interval. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value. 7) Percentage of subjects with ≥10% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) The percentage of subjects with ≥10% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) will be presented along with the 95% confidence interval. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use status and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value.

8) Insulin dose: Type of insulin, total number of daily bolus injections, basal insulin dose, rapid-acting insulin dose for each meal

For the insulin dose, descriptive statistics will be presented for continuous variables. Comparison between the investigational group and control group will be performed using either a two-sample t-test or Wilcoxon rank sum test, depending on whether the normality assumption is satisfied. For categorical data, the frequency and percentage will be presented for each category. Depending on whether more than 20% of cells have an expected frequency of <5, Pearson's chi-square test or Fisher's exact test will be used to compare the investigational group and control group.

9) Dosing behavior
- Missed dose (no bolus –30 to +60 min)
- Late dosing (+15 to +60 min)
- Percentage of days with ≥3 daily bolus injections over 12 weeks

For the endpoints listed above, descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) will be presented. Comparison between the investigational group and control group will be performed using either a two-sample t-test or Wilcoxon rank sum test, depending on whether the normality assumption is satisfied.

10) Number of days in which three bolus calculation modes (i.e., fixed meal mode, meal estimation mode, carbohydrate counting mode) were used from Baseline to Week 12

Descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) will be presented for the number of days each of the three bolus calculation modes were used from Baseline to Week 12 in the investigational group.

11) Total individual education hours for the investigational group

Descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, maximum) will be presented for the total individual hours spent on education (i.e., education on carbohydrate counting and bolus calculator adjustment methods, education on DIA:CONN P8 and the DIA:CONN P8 smartphone app, education on CGM and the CGM app) for the investigational group.

Safety Analysis

1) Adverse events (AEs)

All adverse events collected during the study period will be analyzed. For adverse events, adverse device effects (ADEs), unanticipated adverse device effects (UADEs), and serious adverse events/serious adverse device

	effects (SAEs/SADEs), the number of subjects who experienced the event, incidence rate, 95% confidence interval of the incidence rate, and the number of events will be presented. For comparison of incidence rates between the investigational and control groups, Pearson's chi-square test or Fisher's exact test will be performed depending on whether more than 20% of cells have an expected frequency of less than 5. All adverse events will be coded according to the System Organ Class (SOC) and Preferred Term (PT) of the Medical Dictionary for Regulatory Activities (MedDRA) and will be presented by group. 2) Laboratory tests, vital signs, and physical examination For laboratory tests, vital signs, and physical examination, within-group and between-group comparisons will be conducted. For within-group comparisons: for continuous variables, descriptive statistics will be presented and mean changes from Baseline will be analyzed using a paired t-test or Wilcoxon signed-rank test; For categorical variables, shift tables will be prepared and analyses such as McNemar's test will be performed. For between-group comparisons: for continuous variables, mean changes from Baseline will be analyzed using either a two-sample t-test or Wilcoxon rank-sum test, depending on whether the assumption of normality is met; For categorical variables, Pearson's chi-square test or Fisher's exact test will be performed depending on whether more than 20% of cells have an expected frequency of less than 5.

[Study Schedule]

Period	Screening & Blind CGM Period[a)]		Application Period			
Visit	Visit 1 Screening		Visit 2 Baseline	Visit 3	Visit 4[b)] (☎)	Visit 5
Timepoint	Week ~–4		Week 0	Week 4	Week 8	Week 12
Visit Window	-		-	±10 days	±10 days	±10 days
Obtain written informed consent	●					
Demographic information[1)]	●					
Basic information on target indication	●					
Prior/concomitant medications	●		●	●	●	●
Medical and surgical history	●					
Body measurements and vital signs[2)]	●		●	●	(●)	●
Physical examination	●		●	●	(●)	●
Laboratory tests[3)]	●		●			●
Pregnancy test[4)]	●					●
Evaluation of inclusion/exclusion criteria	●		●			
Randomization			●			
CGM application	~10 days ◄►		◄►			
DIA:CONN P8 application[5)]	~10 days ◄►		◄►			
Adverse event monitoring			●	●	●	●

a) The Blind CGM Period is to be conducted for 7 to 10 days within the maximum 4 weeks between the Screening Visit and Baseline Visit (i.e., Randomization). If possible, it is recommended to schedule the start of the Blind CGM Period so that the Blind CGM Period (7 to 10 days) ends at the Baseline Visit (e.g., start 10 days prior to the date scheduled for Baseline Visit).

b) Visit 4 may be conducted as an on-site visit or telephone visit. If conducted by telephone, the subject's concomitant medication history, blood glucose measurement results, and occurrence of adverse events should be confirmed via telephone interview and logged in detail in the case report form. For the investigational group, education on carbohydrate counting and bolus calculator adjustment methods will be conducted remotely. Vital signs and physical examination will only be performed during on-site visits and may be omitted for telephone visits.

1) The subject's date of birth (age), gender, and smoking history will be investigated.

2) Body measurements (height, weight, BMI) will be taken only during the Screening Visit (Visit 1). Vital signs (blood pressure, pulse, temperature) will be measured at every visit (however, vital signs will be excluded when Visit 4 is conducted by telephone).

3) Laboratory tests will be performed for the items listed below. At Screening (Visit 1), non-fasting c-peptide, glycated hemoglobin (HbA1c), and creatinine results may be substituted with results from laboratory tests conducted within the past 2 weeks, if available.

Visit 1	Hematology: non-fasting c-peptide, HbA1c, creatinine (eGFR*)

Visit 2, Visit 5	Hematology: CBC, HbA1c, fasting glucose, BUN, total cholesterol, HDL-cholesterol, LDL-cholesterol, TG, AST, ALT, creatinine (eGFR) Urinalysis: routine urine analysis, urine albumin, urine creatinine

*eGFR is calculated using the 2021 CKD-EPI Creatinine formula, and normal status is recorded.

4) For women of childbearing potential, excluding those with confirmed sterilization or menopause, a pregnancy test (i.e., urine hCG pregnancy test) will be performed to confirm pregnancy status. Menopause will be determined based on 12 or more consecutive months of amenorrhea.

5) During the Blind CGM Period, all subjects will use two DIA:CONN P8 devices, each used for the injection of basal insulin and bolus insulin. Subjects will manually enter and inject the doses, utilizing only the insulin injection and tracking functions as done with a traditional insulin pen. Considering the domestic product approval status, a long-acting insulin which is compatible with DIA:CONN P8 (e.g., Lantus Injection) must be injected for basal insulin. If a subject's compliance (i.e., rate of CGM use) during the scheduled Blind CGM Period (7–10 days) is below 70%, it will be considered a screen failure, and one re-attempt of the blind CGM period will be allowed.
All subjects randomized to either the investigational group or control group will use the two DIA:CONN P8 devices provided during the Blind CGM Period continuously until the end of the 12-week Application Period.
For the 12-week Application Period of the investigational group, the same method used in the Blind CGM Period will be applied for basal insulin; subjects will manually enter and inject the dose while utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen. For bolus insulin, subjects will enter the carbohydrate count or select a meal in the DIA:CONN P8 smartphone app, which includes bolus calculator functionality, and the app will automatically calculate and set the injection dose using the entered carbohydrate count and other indicators. Subjects will then use DIA:CONN P8 to manually inject the calculated insulin dose.
For the 12-week Application Period of the control group, the same method used in the Blind CGM Period will be applied; subjects will manually enter and inject the basal insulin and bolus insulin doses, utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen.

[Abbreviations and Terms]

Abbreviation	Full term
ADE	Adverse Device Effect
AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CGM	Continuous Glucose Monitoring
CRF	Case Report Form
CV	Coefficient of Variation
eGFR	estimated Glomerular Filtration Rate
FA set	Full Analysis Set
GMI	Glucose Management Indicator
HDL-cholesterol	High-Density Lipoprotein-cholesterol
IRB	Institutional Review Board
ITT	Intention To Treat
IWRS	Interactive Web Response System
LDL-cholesterol	Low-Density Lipoprotein-cholesterol
LOCF	Last Observation Carried Forward
LSM	Least Squares Mean
MedDRA	Medical Dictionary for Regulatory Activities
PP set	Per-Protocol set
PT	Preferred Term
SE	Standard Error
SIP	Smart Insulin Pen
SOC	System Organ Class
TAR	Time Above Range
TBR	Time Below Range
TG	Triglyceride
TIR	Time In Range

1. Study Title

A Multicenter, Open-label, Randomized, Comparative Study to Evaluate the Efficacy and Safety of Electric Smart Insulin Pen DIA:CONN P8 in Patients with Type 1, Type 2 or Pancreatogenic Diabetes Mellitus Under Multiple Dose Insulin Therapy

2. Name and Location of Study Sites

Samsung Medical Center and 9 other sites

Refer to [Appendix 1] List of the Study Staff and Investigational Medical Device Managers

3. Name and Title of the Principal Investigator, Study Staff, and Co-Investigators

Coordinating Investigator: Professor Jae Hyeon Kim, Division of Endocrinology and Metabolism, Samsung Medical Center

The list of principal investigators, study staff, and co-investigators for each study site will be managed in a separate document: [Appendix 1].

4. Name and Title of Managers Responsible for Managing the Investigational Medical Device

The list of investigational medical device managers for each study site will be managed in a separate document: [Appendix 1].

5. Name and Address of Study Sponsor

Sponsor: G2E Co., Ltd.

Representative: Jeong Chang-Bum

Address: 206, 242 Digital-ro, Guro-gu, Seoul, Tel: +82-2-2621-2297

Contract Research Organization: CMIC Korea Co., Ltd.

Representative: CHAN PEY NI

Address: 10F, Gangnam N Tower, 129 Teheran-ro, Gangnam-gu, Seoul, Tel: +82-2-3708-3600

6. Study Purpose and Background

6.1 Study Purpose

To evaluate the efficacy and safety of the electric smart insulin pen DIA:CONN P8 in patients with type 1, type 2, and pancreatogenic diabetes mellitus on multiple daily injections.

For this primary purpose, the difference in glycated hemoglobin change between the investigational group and control group will be assessed following a 12-week administration of bolus insulin through multiple daily injections. The investigational group will use DIA:CONN P8 with bolus calculator functionality and the control group will utilize only the insulin injection and tracking functions of the DIA:CONN P8 as done with a traditional insulin pen.

6.2 Study Background

Disease Background

Diabetes mellitus refers to a metabolic disorder characterized by elevated blood glucose levels. According to the diagnostic criteria in the clinical guidelines of the Korean Diabetes Association (KDA) and the American Diabetes Association (ADA), diabetes is diagnosed if: 1) HbA1c is 6.5% or higher; 2) fasting plasma glucose (FPG) is 126 mg/dL or higher after at least 8 hours of fasting; 3) a plasma glucose level ≥200 mg/dL at two hours after a 75-g oral glucose tolerance test; or 4) the presence of typical symptoms of diabetes (e.g., polyuria, polydipsia, unexplained weight loss) with a random plasma glucose level ≥200 mg/dL.[1,2]

The International Diabetes Federation's Diabetes Atlas (10th edition, 2021) estimates that globally, there are 537 million people with diabetes, representing approximately 10.5% of the adult population aged 20–79 years. This number is projected to rise to 643 million by 2030, 783 million by 2045, with a prevalence rate of 12.2%.[3] The age-standardized prevalence rate of diabetes was approximately 6.1% in 2021.[4] In Korea, the age- standardized prevalence of diabetes among those aged 19 years and older was approximately 10.3% in 2021, exceeding the global prevalence rate.[5]

According to World Health Organization (WHO) statistics, approximately 41 million people died from non-communicable diseases (NCDs) in 2019 alone, accounting for about 74% of all deaths (57 million).[6] Diabetes is one of the four leading non-communicable causes of death (cardiovascular disease, cancer, chronic respiratory disease, diabetes), resulting in approximately 2 million deaths worldwide in 2019 alone.[6]

Based on numerous studies showing that strict blood glucose control reduces the risk of microvascular complications (e.g., diabetic retinopathy, neuropathy) and macrovascular complications (e.g., myocardial infarction, stroke, etc.) in diabetic patients, the importance of sustained blood glucose control in these patients is well established.[1,7] Domestic clinical guidelines recommend an ideal blood glucose control target of HbA1c below 6.5%, but specify that this should be individualized considering the patient's condition and goal awareness.[1] In contrast, U.S. clinical guidelines recommend a blood glucose control target of HbA1c <7.0% for non-pregnant adults, specifying that the target may be adjusted based on the patient's status (life expectancy, duration of diabetes, etc.).[8]

Insulin Therapy

Insulin therapy is a crucial treatment method for diabetes patients. It is vital for blood glucose management not

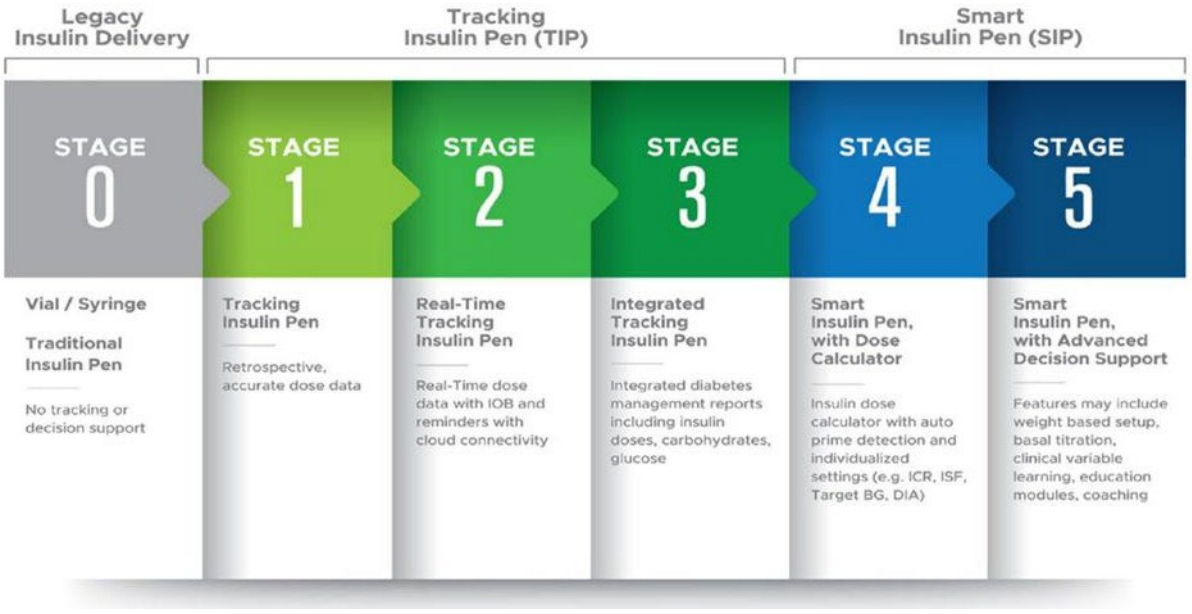
only in type 1 diabetes patients who do not produce insulin, but also in type 2 diabetes patients with increased insulin resistance, and in patients with pancreatogenic diabetes, which is diabetes that develops secondarily due to pancreatectomy. Among insulin delivery methods, the 'pen-type insulin' delivered via an insulin pen is the most common approach. It is convenient, easy to use, and allows for more precise dosing compared to traditional vial or syringe formats.

For most patients with type 1 or type 2 diabetes requiring insulin, multiple daily injections (MDI) are necessary to mimic the body's natural insulin secretion pattern. This multiple daily injection therapy involves administering long-acting insulin or basal insulin to maintain stable insulin levels in the body during normal times, combined with short-acting insulin or rapid-acting insulin administered before meals to manage post-meal blood sugar spikes.

When initiating insulin therapy, factors such as the type of insulin, administration method, timing of administration, single and daily dosage, blood glucose monitoring, and dietary and exercise management must be considered for each individual patient. Based on this, highly individualized insulin treatment should be provided. Among these, the type of insulin, administration method, and dosage regimen (administration timing, dosage) immediately impact the patient's blood glucose levels. Inappropriate administration can lead to hyperglycemia or hypoglycemia, posing a threat to the patient's life, making this an area requiring extreme caution.

Smart Insulin Pen

Conventional insulin pens lack functions to track administration times or doses, or to support decision-making. This means patients must independently determine and administer the injection volume, and administration cannot be observed, leaving them constantly exposed to the aforementioned risks. To address this, as part of digital health management, the tracking insulin pen (TIP) was developed, followed by the smart insulin pen (SIP), which incorporates features like automatic dose calculation.



[Figure1] Smart Insulin Pen Roadmap

The Smart Insulin Pen (SIP) corresponding to stages 4–5 of the SIP roadmap proposed by Kerr and Warshaw provides a solution to most of the challenges we face when using vials, syringes, or traditional insulin pens (e.g., delayed/missed insulin doses, dose and time tracking, insulin dose calculation technology which takes into account carbohydrate counting, etc.). Furthermore, the greatest advantage is that the technology's interface—the device connecting the user (i.e., the patient) to the device—is located on the patient's smartphone.[9,10]
Studies using connected smart insulin pens (SIPs) in real-world settings among type 1 diabetes patients reported improved insulin adherence. This was achieved through reduced bolus dose omissions, improved timing of meals, and increased time in range (TIR).[11] These results suggest that the use of a connected smart insulin pen may lead to improved glycemic control through reduced HbA1c, enhanced TIR, absence of increased hypoglycemia rates, stricter adherence to diabetes treatment guidelines, and reduced diabetes-related complications.[12,13,14]

Background of Study Conduct

The investigational medical device used in this study, DIA:CONN P8, is a reusable smart insulin pen (SIP) linked to a continuous glucose monitor (CGM). It is a Class 4 medical device which was approved in Korea in 2023 and corresponds to Stage 4 in the roadmap shown in [Figure 1]. As a Class 2 medical device serving as a U-healthcare gateway software, it interfaces with the DIA:CONN diabetes management platform to provide real-time updates on the patient's recent blood glucose levels, active insulin status, and other relevant data. It also functions as a bolus calculator to help administer the precise insulin dose needed to manage blood glucose. Additionally, caregivers can monitor the patient's condition in real-time through the DIA:CONN Follower app, while medical staff can use DIA:CONN CareWeb to track insulin dosage, blood glucose trends, patient blood glucose data, and statistical information, enabling comprehensive blood glucose management.
G2E Co., Ltd. is conducting this study to evaluate the efficacy and safety of the smart insulin pen (SIP) DIA:CONN P8 when used in combination with a linked application and a continuous glucose monitor (CGM). This aims to establish clinical evidence enabling diabetes patients receiving insulin therapy in Korea to undergo safer and more efficient insulin treatment without the risk of hypoglycemia. Furthermore, it is anticipated that this will provide an opportunity to potentially change the paradigm of insulin therapy in Korea.

7. Subject Selection Criteria, Exclusion Criteria, Sample Size, and Rationale

7.1 Inclusion Criteria

1) Aged ≥ 19 years and < 75 years
2) Diagnosed with type 1 or type 2, or pancreatogenic diabetes mellitus within one year prior to Screening (i.e., disease duration is at least one year)
3) Continued use of multiple daily insulin injections* for at least 3 months prior to Screening, regardless of whether the subject has used CGM

   *Defined as, 'dosing of long-acting insulin in combination with ultra-rapid-acting/rapid-acting insulin,' 'dosing of premixed insulin (e.g., insulin aspart/insulin degludec, etc.) in combination with ultra-rapid-acting/rapid-acting insulin,' or 'dosing of premixed insulin at least three times per day'.
4) HbA1c level of ≥ 7.5% and ≤ 12.0% at Screening
5) Capable of injecting basal insulin and bolus insulin using the investigational medical device provided in this study (i.e., DIA:CONN P8).
6) A subject and/or their legally authorized representative who has voluntarily provided written informed consent to participate in this study, including medical care and study use involving CGM and investigational medical device (i.e., DIA:CONN P8)

7.2 Exclusion Criteria

1) Administration of medication(s) which may affect glucose metabolism (e.g., corticosteroids, immunosuppressants, etc.) within 3 months prior to Screening (However, subjects on a stable, maintenance dose for at least 6 months prior to Screening are able to participate.)
2) Subjects with clinically significant cardiovascular disease within 6 months prior to Screening
3) eGFR of < 15 mL/min at Screening
4) Unable to engage in education due to severe systemic disorders (e.g., end-stage renal disease requiring dialysis, liver cirrhosis of Child-Pugh Class C or higher, etc.)
5) Subjects with severe diabetic complications (e.g., diabetic foot, diabetic retinopathy, etc.)
6) Pregnant or lactating women
7) Women of childbearing potential who are planning for pregnancy or do not agree to use at least one medically acceptable contraceptive method* from Screening until the end of their participation in the study

   * Medically acceptable contraceptive methods include: intrauterine devices (IUDs), such as a loop or Mirena; the double-barrier method, defined as both male and female partners using contraceptives (i.e., condom/ femidom, diaphragm, or cervical cap); non-oral contraceptives (e.g., injection, vaginal ring, patch, etc.); or total abstinence. Sole use of oral contraceptives or periodic abstinence (e.g., basal body temperature method, fertility awareness method, etc.) is not permitted.

   However, postmenopausal females (i.e., at least 1 year without menstruation) or females/males who have received sterilization (e.g., vasectomy, tubal ligation, etc.) are not required to agree to the use of contraceptive methods to participate in the study.
8) Participated in another study involving an investigational drug or investigational medical device within 3 months prior to Screening
9) Otherwise deemed ineligible by the investigator to participate in this study

7.3 Number of Subjects

120 subjects in total

	Investigational group	Control group	Total number of subjects
Number of subjects	53	53	106
Number of subjects considering a 10% dropout rate	60	60	120

8. Study Period

Approximately 18 months from the date of Institutional Review Board (IRB) approval at the study site

- Subject recruitment period: Approximately 6 months
- Participation period for each subject: Approximately 5 months (Screening and Blind CGM Period: 4 weeks; Application Period: 12 weeks; Safety Follow-up: 4 weeks; Total: 20 weeks)
- Post-study data management, statistical analysis, and clinical study report preparation: Approximately 6 months

However, the planned study period may be extended or shortened depending on subject enrollment rate, changes in post-study procedures, etc.

9. Methodology

9.1 Study Design

This study is designed as a 12-week, multicenter, open-label, randomized, comparative study.

[Blind CGM Period]

All subjects who have voluntarily provided written informed consent to participate in this study and are deemed eligible based on the inclusion/exclusion criteria will undergo the Blind CGM Period for 7 to 10 days prior to the Baseline Visit (i.e., Randomization). During the Blind CGM Period, all subjects will be provided with a continuous glucose monitor (CGM) and two DIA:CONN P8 devices, each used for basal insulin and bolus insulin injection. During this period, subjects will receive education on the basic instructions of using the insulin pen and CGM, then use DIA:CONN P8 to manually enter and inject the basal insulin and bolus insulin doses, utilizing only the insulin injection and tracking functions as done with a traditional insulin pen. Considering the domestic product approval status, a long-acting insulin which is compatible with DIA:CONN P8 (e.g., Lantus Injection) must be injected for basal insulin.

The insulin injection dose and administration time (time of day) recorded on the DIA:CONN P8 and smartphone app, as well as the subject's blood glucose information recorded on the CGM app, will be collected. If a subject's compliance (i.e., rate of CGM use) during the scheduled Blind CGM Period (7–10 days) is below 70%, it will be considered a screen failure, and one re-attempt of the blind CGM period will be allowed.

[Application Period]

Subjects randomized to the investigational group or control group will visit the study site up to five times during the 12-week Application Period, including the Baseline Visit, and will undergo the following process:

1) Investigational group

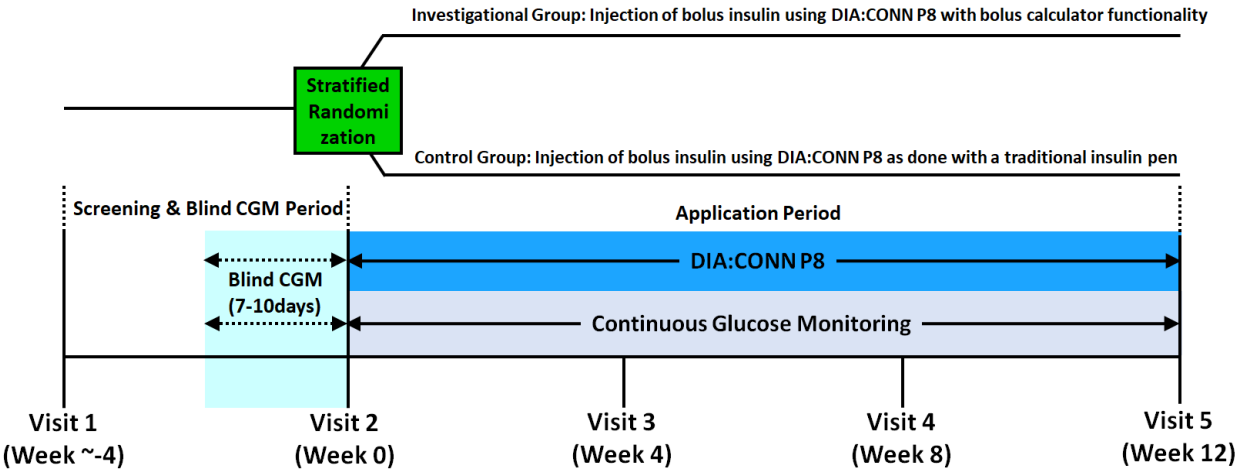
At Baseline, the investigational group will receive education on carbohydrate counting and bolus calculator adjustment methods, install and receive education on DIA:CONN P8 and the DIA:CONN smartphone app, and install and receive education on CGM and the CGM app. For the 12-week Application Period, the same method used in the Blind CGM Period will be applied for basal insulin; subjects will manually enter and inject the dose while utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen. For bolus insulin, subjects will enter the carbohydrate count or select a meal in the DIA:CONN P8 smartphone app, which includes bolus calculator functionality, and the app will automatically calculate and set the injection dose using the entered carbohydrate count and other indicators. Subjects will then use DIA:CONN P8 to manually inject the calculated insulin dose. Data such as the insulin injection dose and injection time (i.e., time of day) will be tracked in the DIA:CONN P8 device and smartphone app.

2) Control group

The control group will receive education on the basics of how to use the insulin pen and CGM and will implement CGM while maintaining their multiple daily insulin injections. For the 12-week Application Period, the same method used in the Blind CGM Period will be applied; subjects will manually enter and inject the basal insulin

and bolus insulin doses, utilizing only the insulin injection and injection tracking functions of DIA:CONN P8. Data such as the insulin injection dose and injection time (i.e., time of day) will be tracked in the DIA:CONN P8 device and smartphone app.

Efficacy and safety will be assessed at Week 4 (Visit 3), Week 8 (Visit 4), and Week 12 (Visit 5) following baseline application of the investigational medical device.



[Study Schematic]

9.2 Randomization

The randomization table will be generated prior to the start of the study by an independent statistician who is not directly involved in this study. Randomization numbers will be generated using SAS® (Version 9.4 or higher, SAS Institute, Cary, NC, USA), applying a stratified block randomization method. This ensures subjects to be centrally assigned to either the investigational group or control group in a 1:1 ratio based on diabetes type (i.e., type 1, type 2).
Central randomization will be performed using an interactive web response system (IWRS). Investigators will assign screening numbers to subjects in the order the subjects provide their written informed consent, and finally assign randomization numbers to subjects meeting the inclusion/exclusion criteria in the order of their enrollment.

9.3 Blinding

This study is conducted as a multicenter, open-label, randomized, comparative study; therefore, blinding for subjects and investigators are not required.

9.4 Concomitant Medications

9.4.1 Permitted Concomitant Medications

The following medications are permitted during the study period.

- Medications that subjects were taken prior to participation in this study and that are deemed unlikely to affect the interpretation of the study results may be permitted at the investigator's discretion.
- Medications used intermittently for the treatment of other diseases or adverse events should be administered concomitantly after consultation with the investigator.

When administering any concomitant medication, information on the medication should be logged in the medical record and details in the subject's Case Report Form (CRF).

9.4.2. Prohibited Concomitant Medications

The following medications should not be used during the study period without the investigator's approval.
However, medications that may affect glucose metabolism and have been taken at the same dose for at least 6 months prior to Screening may be continued during the study period, provided that dose adjustments for these medications are not permitted.

- Drugs which may increase blood glucose: glucocorticoids, corticosteroids, immunosuppressants, oral contraceptives, anticonvulsants, growth hormones, sugar-containing liquid medications, etc.

9.5 Investigational Medical Devices

Product Name	Electric Smart Insulin Pen (*Under domestic law, the product name is designated in Korea as "U-Healthcare External Insulin injection pen".)
Product Approval Number and Class	Approval No. 23-490, Class 4
Model Name	DIA:CONN P8
Model No.	DIA:CONN P8b and 1 other
Manufacturer	G2E Co., Ltd.
Intended Use	**U-Healthcare External Insulin Injection pen**: An external insulin delivery device that automatically injects insulin to control blood glucose levels for remote diabetes management. **Class 2 U-Healthcare Gateway Software**: Software that collects, monitors, analyzes, and retrieves biometric data measured by U- Healthcare medical devices via wired/wireless technology, and encrypts the collected data for transmission to medical institutions for remote medical services.
Storage	1. Storage Environment A. Temperature: -25 ~ 5℃ or 5~35℃ (Maximum relative humidity 90%), or 35~70℃ (50ha Under vapor pressure B. Humidity: 10~90% RH C. Atmospheric Pressure: 700~1060 mbar 2. Operating Environment A. Temperature: 5~40°C B. Humidity: 15~90% RH C. Atmospheric pressure: 700~1060 mbar
Expiration date	Not applicable

9.5.1. Shape, Structure, and Dimensions

1. Principle of Action

This product is a portable external insulin injection pen designed to automatically deliver a set amount of insulin to the patient. It is powered by an internal battery, and it enables the precise injection of insulin from the cartridge into the body via a user-operated control button. In addition, the user application, implemented as a mobile application (DIA:CONN APP) installed on a portable smartphone, can be used in conjunction with the external insulin injection pen via Bluetooth communication. In addition, a user application (DIA:CONN APP)

installed on a portable smartphone can be paired with the external insulin injection pen via Bluetooth communication. The user application transmits insulin delivery settings configured by the user to the paired external insulin injection pen, and insulin injection can be performed after user confirmation. Injection execution is initiated either by pressing the confirmation button directly on the external injection pen or by user authentication through an app-to-pen verification sequence using a one-time secure token key. The user application also allows users to view insulin delivery information, and when connected to an already approved personal continuous glucose monitoring (CGM) system, it enables access to glucose measurement records obtained from the device.

1. Appearance

(1) Exterior Photos

A. Main device

<table>
<tr>
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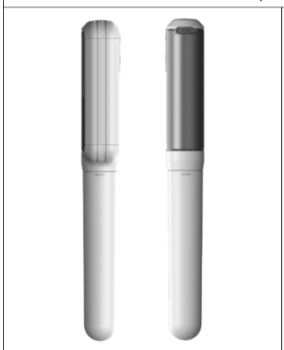
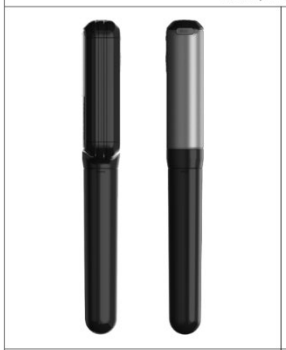
Front, Rear Side

Left, Right


Up, Down
DIA:CONN P8w (White)
</td>
<td>


Front, Rear Side

Left, Right


Up, Down
DIA:CONN P8b (Black)
</td>
</tr>
</table>

B. Components

<table>
<tr>
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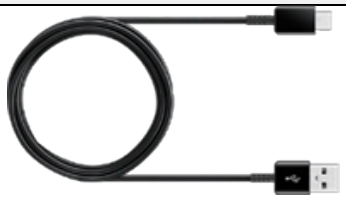

USB Cable
</td>
<td>


Portable Pouch
</td>
</tr>
</table>

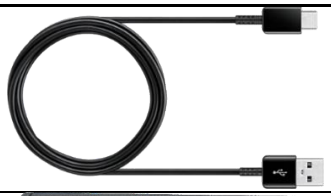
(2) Exterior Structure

A. Main Device

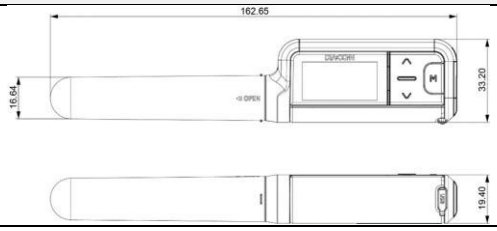
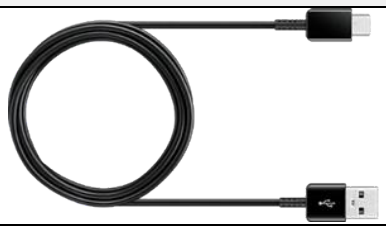
No.	Name	Description
A	Pen Cap	A needle to inject insulin and cartridge protection cover
B	Main device	Main device for insulin injection management
C	Cartridge Holder A	Classification of cartridge holder according to the insulin pharmaceuticals
C1	Cartridge Holder B	Classification of cartridge holder according to the insulin pharmaceuticals
D	Function Buttons	Up/down button: If set up/down menu, quantity is plus (up) or minus (down) M button: Back, Cancel, Magic key (If click 1 sec on main screen, it moves to main) ACT button: Injection, Change of setting, Pushing 5 seconds make the power off or on
E	OLED Screen	The screen for GUI realization shows information
E1	LED Indicator	This is an area to show warning or whether something runs, and the LED below is in red if the warning happens. But whether something runs is connected to changing the screen contents, and LED above blinks in green once.
F	C type USB port	Charging port for device
G	Plunger	When injecting insulin, this is a connected part to give pressure on piston

B. Components

No.	Figure	Name	Description

1		USB Cable	Used to charge or connect with PC(Main: USB-Type C / PC: USB-Type A)
2		Portable Pouch	This is to make main device, cable, insulin cartridge and needle portable.

2. Dimensions

A. Main Device

-Weight: 65 g -Dimensions: 33.2 x 162.65 x 19.4 mm
B. Components- USB Cable

-Weight: 28.6 g -Dimensions: 1 m

9.5.2. Instructions for use

9.5.2.1. DIA:CONN P8

1. Getting Started

A) Charging the Power Supply

The new products come with the battery charged to about 50%. However, because insufficient battery power may hinder insulin delivery, it should be fully charged with the charger before normal use.

B) Alarm

1) Injection blockage warning

If insulin delivery cannot be performed due to an unstable connection between the cartridge and needle or tissue hardening at the injection site, the 'Injection Blockage warning' screen will appear, and the amount of insulin not delivered will be displayed.

When an injection blockage occurs, the device stops the injection and displays a standby screen. After the standby time completes, the "Injection blockage warning" screen appears.

(a) When the injection blockage warning screen appears, remove the inserted needle from the body.

(b) Run the priming procedure(air removal procedure) to check for needle blockages and ensure that the device is capable of delivering insulin. If insulin is not expelled during the procedure, replace the needle and repeat priming process.

(c) Once insulin delivery is possible after air removal procedure, attempt injection at a different injection site. In this case, due to the previous injection blockage, the device will first attempt to deliver the uninjected dose.

2) When an insulin shortage alarm occurs:

This alarm occurs when the programmed injection dose exceeds the remaining insulin in the cartridge in use. The alarm screen displays the amount of insulin that could not be delivered due to insufficient cartridge volume. After replacing the cartridge, the remaining insulin can be delivered through the the “uninjected set screen”

(a) When the insulin shortage alarm occurs, remove the inserted needle from the patient.

(b) Remove the needle and cartridge according to the procedure, and replace with a new cartridge following the cartridge replacement procedure. Cartridge replacement includes the air removal procedure.

(c) After completing the cartridge replacement, administer insulin injection through the the “uninjected set screen”

* The cartridge volume indicated by the device is based on the device’s recognition and may differ slightly from the actual volume in the cartridge.

3) When the battery shortage warning occurs

If the P8's internal battery falls below 9%, insulin delivery functions will be restricted. It is recommended to keep the battery level at 50% or higher during P8 use by charging it regularly.

When a battery shortage warning occurs, dismiss the alarm and charge the device.

Users should prepare a backup battery or charger before going out in case of emergencies.

* If the battery level is below 10%, the DIA:CONN P8 restricts the use of motor-driven functions such as injection, air removal, and cartridge replacement for user safety. Other settings-related functions remain available.

4) No Injection warning during charging

For user safety, the injection function is restricted while the device is charging. All other functions remain fully operational.

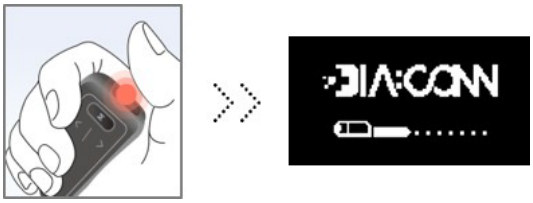
If injection must be performed during charging, check the battery level. If necessary, remove the charging cable and proceed with injection.

C) Initial Setup

When turning on a P8 with a sufficiently charged battery, verify that the power turns on normally. If the battery is not sufficiently charged, use it only when fully charged.

First Use of the Pen The DIA:CONN P8 is provided in a factory reset state. Therefore, the user must complete the initial setup before using the DIA:CONN P8.

1) Powering on the P8



(a) Ensure the battery is fully charged using the charger, then press and hold the ACT button for at least 5 seconds to turn on the pen.

(b) The pen booting screen appears as it powers on.

2) Initial Language Settings

(a) After the booting screen appears, the 'Language Settings' screen will display.

(b) Press the [△] or [▽] button to select your preferred language.

(c) Once the language is selected, press [ACT] to complete the language selection.

* You can change the language later in Settings – Language.

3) Date/Time Settings

(a) After completing the initial language setting, the screen moves to 'Date/Time Setting'. The initial date/time displayed is the manufactured date.

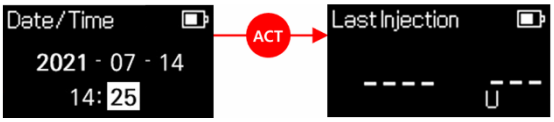
(b) On the settings screen, press the [△] or [▽] button to select the year, then press the [ACT] button to move to the next setting item.

(c) Set the month, day, and hour information using the same method.

* If you need to change a previous setting, press the [M] button to move back to the previous setting item.

(d) Finally, after setting the minute information, press the [ACT] button to complete the date/time setting.

(e) The initial setup is completed, and the device returns to the main screen. Since there is no insulin injection history or cartridge replacement record yet, the related fields show "- - - - ".



***The initial setup is set to enter sleep mode and turn off the screen if the device remains idle for 30 seconds (default setting) or longer. To turn the screen back on, press and hold the [ACT] button.**

D) Cartridge Replacement

1) Prepare the Cartridge

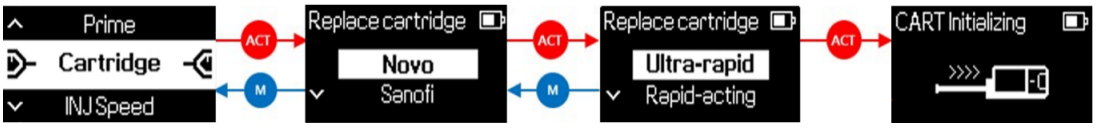
Before replacing the cartridge, remove the pen cap and cartridge holder as shown in the illustration. Prepare the cartridge and the pen needle to be inserted into the P8.

2) Navigate to the Menu

(a) Press and hold the [M] button for about 1 second on the main screen to enter the menu screen.

(b) Press the [△] and [▽] buttons to move to the 'Cartridge' menu, then press the [ACT] button.

3) Cartridge and Insulin type Settings



(a) On the settings screen, press the [△] or [▽] button to select the 'Cartridge Manufacturer' information, then press the [ACT] button to proceed to the next screen.

* **Select from Novo, Sanofi, Lilly, Berlin, or DIA:CONN.**

(b) On the next settings screen, press the [△] or [▽] button to select the 'Insulin Type' information, then press the [ACT] button.

* **Select form Ultra-Rapid, Rapid, Long, Intermediated Acting or Mixed.**

(c) Once the cartridge settings are complete, the plunger will move to its initial state.

4) Inserting the Cartridge

(a) Once the plunger is reset and the screen flashes "Please insert a new cartridge" (for up to 5 minutes), insert the new insulin cartridge prepared earlier into the cartridge holder.

* **Two types of cartridge holders are provided, and the appropriate holder type must be used for each cartridge.**

(b) Then, attach the holder with the cartridge inserted to the P8 device.

2. Basic Operation Guide

A) Basic Button Operation

△ Up button

- Navigates up the menu list
- Increases the numerical value
- Moves up through the settings menu

∇ Down button

- Navigates down the menu list
- Decreases numerical value
- Moves down through the setting menu

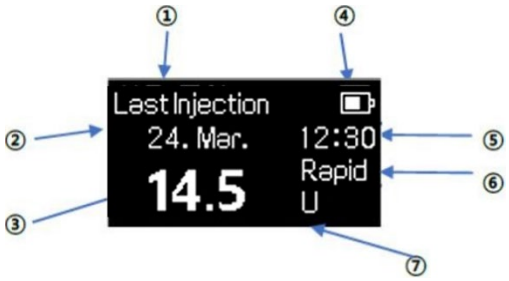
ACT button

- Turns on the pen (Press for 5 seconds)
- Turns on the display (Press once)
- Starts injection
- Goes to next screen or save settings

M button

- Moves to menu list screen (press for 1 second)
- Returns to the previous screen
- Moves to previous item in the settings

B) Main Screen



① **Recent Injection Amount**

② **Current Date**

③ **Remaining Injection Volume**

④ **Remaining battery icon**

⑤ **Current Time**

⑥ **Insulin Type**

⑦ **Insulin injection unit**

3. Menu description

A) Injection insulin

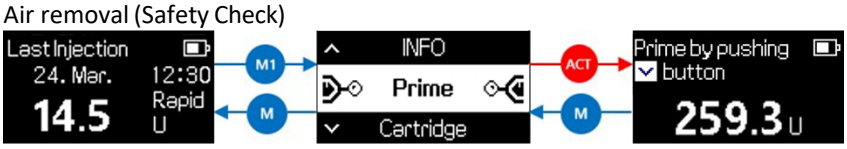
1) Attaching the Needle

(a) Before attaching the needle, wash your hands thoroughly and clean the insulin injection port with an antiseptic swab.

(b) Remove the protective paper cover from the top of the new needle. To attach the needle, rotate it firmly onto the rubber part at the end of the cartridge.

(c) Remove both the outer protective cap and the inner needle cap from the new pen needle. Keep the outer cap for use when removing the needle after injection.

2) Air removal (Safety Check)



(a) Press and hold the [M] button for 1 second on the main screen to enter the menu screen.

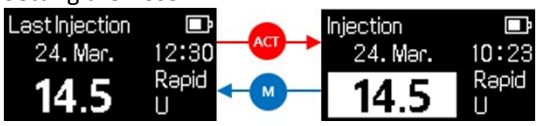
(b) Select the "Prime" menu and press the [ACT] button to move to the prime screen.

(c) When the "Prime" screen appears, hold the P8 with the attached needle facing upward. Tap the cartridge holder with your finger or similar object to move any air bubbles in the cartridge to the top as much as possible.

(d) Once you are ready to prime, press the [▽] button once to start the priming process. Continue priming until several drops of insulin come out continuously.

(e) After confirming that insulin is coming out, press the [M] button to stop priming, then press the [ACT] button to return to the main screen.

3) Setting the Dose



(a) On the main screen, press the [ACT] button to move to the “injection procedures” screen.

(b) On the “injection procedures” screen, The dose is preset to the most recent injection amount. If you wish to adjust the dose, press the [△] or [▽] button to set the desired amount. Pressing the button briefly changes the dose in 0.1 U increments, while pressing and holding changes it in 1 U increments. (*The dose can be set from a minimum of 0.5 U to a maximum of 60 U.)

4) Injecting

(a) Once settings are complete, place the P8 on a flat surface and disinfect the injection site with an antiseptic swab.

(b) Pinch the skin so that it forms a thickness of about 5 cm, then insert the needle quickly and firmly into the skin at a 45-90° angle in one motion.

(c) After inserting the needle, press and release the [ACT] button once to start the injection. If you need to stop the injection during delivery, follow the procedure described in "Stopping an Injection".

(d) Once the injection begins, the injection amount number on the P8 "Injection procedures screen" will decrease. When injection is complete, the screen will changes to "Waiting!".

(e) When the waiting time reaches 0 seconds, the P8 emits a short beep once. This indicates that injection is complete; and you may remove the needle from the skin at this time.

*** If blood appears at the injection site, apply gentle pressure for a few minutes until the bleeding stops.**

B) Air Removal

1) When the "Attach new needle!" screen appears, attach the prepared pen needle to the P8. After the needle is securely attached, press the [ACT] button to move to the "Prime" screen.
2) When the "Prime" screen appears, hold the P8 with the attached needle facing upward. Tap the cartridge holder with your finger or similar object to move any air bubbles in the cartridge to the top as much as possible.
3) Once you are ready to prime, press the [▽] button once to start the priming process. Continue priming until several drops of insulin come out continuously.
4) After confirming that insulin is coming out, press the [M] button to stop priming, then press the [ACT] button to complete the cartridge replacement process.

C) Cartridge Replacement

1) After the cartridge is attached, press the [ACT] button. The screen will change to " Cartridge Connecting," and the plunger will begin to move to final connection.
2) When the plunger reaches the cartridge and the maximum cartridge capacity is detected, the plunger movement will stop, and the screen will switch to "Attach new needle!" screen.

D) Injection Speed Setting

DIA:CONN P8 provides a function allowing the user to adjust the insulin injection rate. For injection rates are available: 0.2 U/sec, 0.5 U/sec, 1.0 U/sec, and 2.0 U/sec. To set the speed, follow these steps.

1) Press and hold the [M] button for 1 second on the main screen to move to the menu screen.
2) On the menu screen, select the "Injection Speed" menu and press [ACT].
3) When the injection speed setting screen appears, navigate to the desired option using the [△] or [▽] buttons, then press [ACT] to complete the injection speed setting.

E) Settings

1) Volume

(a) Go to Main Screen >> Menu List >> Settings >> Voice set menu.
(b) Use the [△] or [▽] buttons to select the desired volume level, then press the [ACT] button to save the setting. If you press [M] during setting process, you will return to the previous screen and the changes will not be saved.
*However, even if the volume is adjusted through the volume settings, the volume of warning alarms will sound at the designated default level.

2) Date/Time

(a) Go to Main Screen >> Menu List >> Settings >> Date/Time set menu.

(b) From the initially selected 'Year' item, use the [△] or [▽] button to change to the desired year, then press the [ACT] button to move to the next item.
(c) Set the remaining 'Month', 'Day', and 'Hour' items in the same manner.
*To modify the previous item, press the [M] button.
(d) Finally, set the 'Minute' item and press the [ACT] button to save the date/time and return to the main screen.

3) Language

(a) Go to Main Screen >> Menu List >> Settings >> Language Set menu.
(b) Select your desired language from the list ('Korean', 'English', 'German') and press the [ACT] button to save the setting information.
(c) Once applied, all screens will change to the selected language.

4) Screen time

The 'Screen Time' refers to the duration the screen remains on after the device has completed its operation. Device enters sleep mode immediately after the screen turns off. Follow these steps to configure the setting.

(a) Go to Main Screen >> Menu List >> Settings >> Screen Time Set menu.
(b) Use the [△] or [▽] buttons to select the desired screen light duration.
* The screen light duration can be set from 10 seconds to 60 seconds, adjustable in 10-second increments
(c) Press the [ACT] button to save the setting.

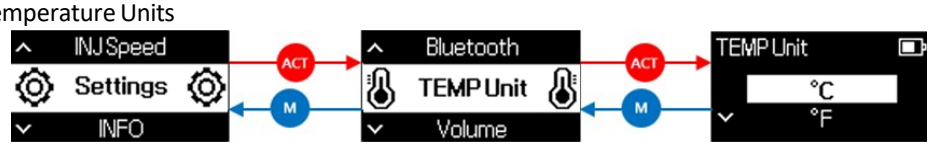
5) Bluetooth

DIA:CONN P8 is equipped with Bluetooth Smart, allowing data to be transmitted to an app installed on a smart device. For data transfer to occur, Bluetooth on the P8 pen must be activated and connected to the dedicated app. To activate Bluetooth on the P8 pen, follow the steps below:

(a) Go to Main Screen >> Menu List >> Settings >> Bluetooth Set menu.
(b) Use the [△] or [▽] button to select one of "On (Always)", "On (When in Use)", or "Off", then press the button to confirm your select. The Bluetooth connection status based on the setting is as follows

- **On (Always)** : Bluetooth connection possible in all situations (except Deep Sleep mode)
- **On (When in Use)** : Bluetooth connection is possible only when the screen is on
- **Off** : Bluetooth connection is not possible

6) Temperature Units



(a) Go to Main Screen >> Menu List >> Settings >> Temperature Unit Set screen.
(b) Press the [△] or [▽] button to select the desired unit from 'C (Celsius)' or 'F (Fahrenheit)', then press the [ACT] button to save the setting.

F) Information

1) Go to Main Screen >> Menu List >> Information menu, and then press the [ACT] button.
2) On the Information screen, you can check the current P8 device software version and the device's unique identification number (serial number).

9.5.2.2. DIA:CONN P8 Smartphone App

A. Caution

Even if you have used the DIA:CONN app before, you must read this manual before use. Failure to follow the instructions may result in too much or too little insulin being delivered.

B. Instructions for Use

This is a home pen injector for single-patient use by patients with diabetes or patients aged 7 years and older to self-administer the desired dose of insulin under the supervision of an adult caregiver. The pen injector is compatible with Lilly Humalog® U-100 3.0 mL cartridges, Novo Nordisk Novolog® U-100 3.0 mL cartridges, Novo Nordisk Fiasp® U-100 3.0 mL cartridges, and disposable detachable and fixed pen needles (not included). The pen injector allows for the injection of the desired dose in increments of 0.1 units, ranging from 0.5 to 60 units.

For insulin dosing based on carbohydrate intake, the healthcare professional must provide patient- specific target blood glucose, insulin-to-carbohydrate ratio, and insulin sensitivity parameters to be programmed into the software prior to use.
For insulin dosing based on fixed/estimated meal sizes, the healthcare professional must provide patient-specific fixed/estimated meal sizes to be programmed into the software prior to use.

For detailed instructions on using the DIA:CONN smartphone app, refer to [Appendix 4] DIA:CONN P8 and DIA:CONN Smartphone App Usage Guidelines.

9.5.3. Packaging and Labeling of Medical Devices for the Study

The sponsor supplies investigational medical devices to the medical device manager at the study site. Labeling of the medical device for the study should comply with Article 43, Paragraph 2 of the Enforcement Rules of the Medical Device Act and should be entered as follows.

The marking "For the Study Use"
Product name and model
Lot number and date of manufacture, or expiration date
Storage conditions
Name of manufacturer or importer
The statement "Not for use for purposes other than Studies"

9.5.4. Use and Management of Investigational Medical Devices

Medical devices for studies must be managed by a person designated by the head of the respective study institution. These devices must be handled and stored according to the instructions provided in the labeling and must bear the statement “For the study use only.” The investigational medical device manager is responsible for tasks such as receipt, inventory control, subject-specific assignment, and return of the investigational medical devices, and must maintain all related records.

1) The principal investigator and the medical device manager (hereinafter referred to as “the manager”) share responsibility for the management of investigational medical devices at the study site.
2) The manager must perform tasks including receipt, inventory management, subject-specific use, and return of investigational medical devices, maintain records of these activities, and periodically report relevant information to the principal investigator.
3) Records maintained pursuant to item 2) must include, for each subject: the period of investigational medical device use, lot or serial number, expiration or validity date, medical device identification code, and subject identification code.
4) The manager must maintain medical records verifying that the investigational medical device was used for each subject according to the instructions described in the study protocol and must confirm that the inventory of investigational medical devices matches the usage records.
5) Investigational medical devices must be stored according to the conditions specified by the sponsor and in compliance with applicable laws and regulations.
6) The principal investigator must confirm that investigational medical devices are used and managed in accordance with the study protocol.
7) The principal investigator, study staff, or the manager must explain the correct method of use of the investigational medical device to each subject and verify that subjects follow these instructions appropriately.
8) The sponsor must determine whether to retrieve and dispose of unused or returned investigational medical devices in cases of study suspension or termination, or when the principal investigator fails to conduct the study according to the protocol. In such cases, the manager must return unused investigational medical devices to the sponsor after consultation with the principal investigator and retain the return receipt.

10. Observation Variables and Methods

10.1. Assessment Variables at each Visits

10.1.1. Visit 1 (Screening, Week ~–4)

Subjects who agree to participate in this study must voluntarily provide their written consent on the informed consent form, either by themselves or through an authorized representative, prior to undergoing any procedures related to the study.

(1) Obtain written informed consent.
(2) Investigate the subject's demographic information, baseline information on the target disease, prior/concurrent medications, medical history, and surgical history.
(3) Measure body measurements (height, weight, BMI) and vital signs (blood pressure, pulse, temperature).
(4) Conduct physical examination.
(5) Perform laboratory tests.
(However, non-fasting c-peptide, glycated hemoglobin (HbA1c), and creatinine results may be substituted with results from laboratory tests conducted within the past 2 weeks, if available.)
(6) For women of childbearing potential only, a pregnancy test is performed.
(7) Evaluate eligibility/exclusion criteria.
(8) A continuous glucose monitor (CGM) will be provided along with two DIA:CONN P8 devices for the injection of basal insulin and bolus insulin. The CGM for blind monitoring will be applied at the study site, and the two provided DIA:CONN P8 devices must be used until the end of the study.
   - All subjects will perform blind CGM period using only the insulin injection and tracking functions of the DIA:CONN P8 for 7 to 10 days prior to the Baseline Visit (i.e., Randomization). During the Blind CGM Period, subjects will receive education on the basics of how to use the insulin pen and CGM, attach the provided CGM, and use the DIA:CONN P8 like a traditional insulin pen—manually entering and injecting basal insulin and bolus insulin doses by utilizing only the insulin injection and tracking functions.
   - However, participants unable to undergo the Blind CGM Period at the day of Screening will schedule a separate visit within the Screening Period for CGM attachment and DIA:CONN P8 issuance.

10.1.2. Visit 2 (Baseline, Week 0)

The Baseline Visit will occur after the blind CGM period. During this visit, the subject's final eligibility to participate in the study will be determined, and the investigational medical device will be applied according to the randomization results.

(1) Confirm changes in the administration status of prior/concomitant medication compared to the previous visit.
(2) Measure vital signs (blood pressure, pulse, body temperature).
(3) Conduct physical examination.
(4) Perform laboratory tests.
(5) Assess blind CGM compliance. If a subject’s compliance (i.e., rate of CGM use) during their scheduled Blind CGM Period of 7-10 days is below 70%, it will be considered a screen failure, and one re-attempt of the blind CGM period will be allowed.
(6) Based on all test and evaluation results to date, including the Screening Visit, a final assessment is made to determine if subjects meet the inclusion/exclusion criteria.

(7) Randomize and provide a randomization number.

(8) Verify the subject's blood glucose information from the previous visit and ensure continuous CGM attachment.

(9) Apply the investigational medical device.

- The investigational group will receive education on carbohydrate counting and bolus calculator adjustment methods, install and receive education on DIA:CONN P8 and the DIA:CONN smartphone app, and install and receive education on CGM and the CGM app. Individual education time should be confirmed. For the 12-week Application Period, the same method used in the Blind CGM Period will be applied for basal insulin; subjects will manually enter and inject the dose while utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen. For bolus insulin, subjects will use the bolus calculator functionality of the DIA:CONN P8 to inject insulin.
- The control group will receive education on the basics of how to use the insulin pen and CGM. For the 12-week Application Period, the same method used in the Blind CGM Period will be applied; subjects will manually enter and inject the basal insulin and bolus insulin doses, utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen.

(10) Investigate the occurrence and details of any adverse events since the last visit.

10.1.3. Visit 3 (4-week Efficacy Assessment, Week 4±10 days)

This visit (Visit 3) is for evaluating the efficacy and safety of the investigational medical device at the 4-week mark following its application.

(1) Confirm whether there have been any changes in concomitant medication administration compared to the previous visit.

(2) Measure vital signs (blood pressure, pulse, body temperature).

(3) Conduct physical examination.

(4) Review the subject's blood glucose information from the previous visit and ensure continuous CGM attachment.

(5) Apply the investigational medical device.

The investigational group will receive education on carbohydrate counting and bolus calculator adjustments required for using the DIA:CONN P8, and individual education hours will be confirmed. The control group will receive education on the basics of how to use the insulin pen and CGM.

(6) Investigate whether any adverse events occurred since the last visit and their details.

10.1.4. Visit 4 (Week 8±10 days)

This visit (i.e., Visit 4) may be conducted as an on-site visit or telephone visit.

If conducted by telephone, the subject's concomitant medication history, blood glucose measurement results, and occurrence of any adverse events are confirmed via telephone interview and logged in detail in the CRF. For the investigational group, education on carbohydrate counting and bolus calculator adjustment methods will be conducted remotely.

Vital signs and physical examination will only be performed during on-site visits and may be omitted for telephone visits.

(1) Verify any changes in concomitant medication administration compared to the previous visit.

(2) Measure vital signs (blood pressure, pulse, temperature) **only during on-site visits**.

(3) Conduct physical examination **only during on-site visits**.

(4) Review the subject's blood glucose information since the last visit and ensure CGM is continuously applied.

(5) Apply the study medical device.

For on-site visits, the investigational group will receive education on carbohydrate counting and bolus calculator adjustments required for using the DIA:CONN P8, and individual education hours will be confirmed. The control group will receive education on the basics of how to use the insulin pen and CGM.

For telephone visits, education for both the investigational group and control group will be conducted remotely.

(6) Investigate whether any adverse events have occurred since the last visit and their details.

10.1.5. Visit 5 (12-week Efficacy Assessment and Study Completion Visit, Week 12±10 days)

This visit is for evaluating the efficacy and safety of the investigational medical device at Week 12 and is the final visit.

(1) Confirm any changes in concomitant medication administration compared to the previous visit.

(2) Measure vital signs (blood pressure, pulse, body temperature).

(3) Conduct physical examination.

(4) Perform laboratory tests.

(5) For women of childbearing potential only, a pregnancy test is performed.

(6) Review the subject's blood glucose information from the previous visit.

(7) Retrieve the investigational medical device and CGM.

(8) Investigate whether any adverse events have occurred since the last visit and their details.

10.1.6. Unscheduled Visits

Unscheduled visits may occur at any time upon the subject's (or their representative's) request or when deemed necessary by the investigator.
To this end, the investigator should inform the subject of this possibility during their regular visits to the study site and ensure the subject can contact the investigator immediately if an adverse event occurs. The visit schedule should not be altered due to an unscheduled visit. During an unscheduled visit, examinations and tests may be conducted at the investigator's discretion.

10.1.7. Safety Follow-up Visit

If there are adverse events that have not been resolved by Visit 5 (i.e., the final visit), a safety follow-up visit may be conducted up to 4 weeks after the last application of the investigational medical device.

The investigator should follow up on the adverse event until it recovers to the state or baseline prior to the application of the investigational medical device, or until it can be determined that the adverse event has normalized. During adverse event follow-up, the investigator or a person delegated by the investigator should collect relevant information, such as whether the adverse event has been resolved and the date of resolution, through telephone calls (telephone follow-up) with the subject or by visiting the subject's institution.

10.2. Assessment Method

10.2.1. Obtaining Written Informed Consent

The investigator will explain the study in detail to the subject, answer any questions the subject may have, and ask to participate in the study. If the subject agrees to participate, written informed consent will be obtained from the subject (or their representative). A screening number is assigned in the order the written informed consent is received.

10.2.2. Demographic Information

The subject's date of birth (age), gender, and smoking history are investigated.

10.2.3. Basic Information on Target Indication

Investigate the date of diagnosis (duration of disease), symptoms related to the target disease, medical history, and treatment history (type of insulin, insulin dosage, frequency of administration, use of CGM).

10.2.4. Prior/Concomitant Medications

For prior medications, investigate the medication history and current status (product name, purpose of administration, dosage, duration of administration, etc.) of diabetes medications administered within 3 months prior to Visit 1 (screening), including insulin injection dosage, frequency, and oral diabetes medications. However, for medications that may affect glucose metabolism, information on medications administered within 6 months prior to Screening is collected.

Concomitant medications: Starting from Visit 2 (Baseline) after application of the investigational medical device, the subject's concomitant medication administration status should be assessed at each visit. When concomitant medications are administered (including therapeutic drugs for other diseases or adverse events), detailed information about those medications (product name, purpose of administration, dosage, duration of administration, etc.) should be logged on the CRF.

10.2.5. Medical and Surgical History

Medical and surgical history should be thoroughly investigated and logged through interviews and review of past medical records. Medical and surgical history within the 6 months prior to Visit 1 (Screening) should be collected. However, history of diabetic complications and malignant tumors should be collected regardless of the time period.

10.2.6. Body Measurements and Vital Signs

At Visit 1 (Screening), log the subject's body measurements: height, weight, and BMI.

Vital signs (blood pressure, pulse rate, body temperature) are measured at each visit (except during the Visit 4 telephone visit). Measurements are taken prior to any scheduled tests, according to the study schedule, after the subject has rested for 5 minutes in a seated position.

10.2.7. Physical Examination

A physical examination is conducted at each visit (excluding the telephone visit for Visit 4) using inspection, palpation, percussion, and auscultation to assess health status and identify any abnormalities. The physical examination includes assessment of appearance, skin, head/neck, chest/lungs, heart, abdomen, urinary/genital system, extremities, musculoskeletal system, nervous system, and lymph nodes.

10.2.8. Laboratory Tests

Laboratory tests should be performed for the items listed below. At Screening (Visit 1), non-fasting c-peptide, glycated hemoglobin (HbA1c), and creatinine results may be substituted with results from laboratory tests conducted within the past 2 weeks, if available.

Visit 1	Hematology: non-fasting c-peptide, HbA1c, creatinine (eGFR*)
Visit 2, Visit 5	Hematology: CBC, HbA1c, fasting glucose, BUN, total cholesterol, HDL- cholesterol, LDL-cholesterol, TG, AST, ALT, creatinine (eGFR) Urinalysis: routine urine analysis, urine albumin, urine creatinine

*eGFR is calculated using the 2021 CKD-EPI Creatinine formula, and normal status is recorded.

10.2.9. Pregnancy test

For women of childbearing, excluding those with confirmed sterilization or menopause, a pregnancy test (urine hCG pregnancy test) is performed to confirm pregnancy status. Menopause is determined based on the absence of menstruation for 12 months or more.

10.2.10. Continuous Glucose Monitoring (CGM)

All subjects will measure continuous glucose levels using CGM (Dexcom G7, Dexcom Inc.) from the Blind CGM Period until Visit 5 (end-of-study visit).

The glucose information collected and calculated by CGM is as follows.

- Predicted Glycated Hemoglobin (HbA1c) (%): A predicted HbA1c value used solely for subject monitoring purposes.
- Percentage of TIR (70-180 mg/dL)
- Percentage of TBR (<54 mg/dL)
- Percentage of TBR (<70 mg/dL)
- Percentage of TAR (>180 mg/dL)
- Percentage of TAR (>250 mg/dL)
- Mean glucose, Glucose Management Indicator (GMI)
- Coefficient of Variation (CV) (%)

10.2.11. DIA:CONN P8 Application

[Blind CGM Period]

During this period, all subjects will use two DIA:CONN P8 devices, each used for the injection of basal insulin and bolus insulin. Subjects will manually enter and inject the doses, utilizing only the insulin injection and tracking

functions as done with a traditional insulin pen. Considering the domestic product approval status, a long-acting insulin compatible with DIA:CONN P8 (e.g., Lantus Injection) must be injected for basal insulin.

[Application Period]

All subjects randomized to either the investigational group or control group will continuously use the two DIA:CONN P8 devices provided during the Blind CGM Period throughout this 12-week Application Period.

1) Investigational group

For the 12-week Application Period of the investigational group, the same method used in the Blind CGM Period will be applied for basal insulin; subjects will manually enter and inject the dose while utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen. For bolus insulin, subjects will enter the carbohydrate count or select a meal in the DIA:CONN P8 smartphone app, which includes bolus calculator functionality, and the app will automatically calculate and set the injection dose using the entered carbohydrate count and other indicators. Subjects will then use DIA:CONN P8 to manually inject the calculated insulin dose.

2) Control group

For the 12-week Application Period of the control group, the same method used in the Blind CGM Period will be applied; subjects will manually enter and inject the basal insulin and bolus insulin doses, utilizing only the insulin injection and injection tracking functions of DIA:CONN P8 as done with a traditional insulin pen.

The subject's daily continuous glucose information, carbohydrates, boluses, and other real-time data are displayed on DIA:CONN CareWeb, identical to the [Today] screen of the DIA:CONN P8 app, enabling remote monitoring. The subject's glucose information can be shared with the investigator via DIA:CONN CareWeb, allowing the investigator to monitor the subject's glucose trends through the web portal.

Information collected by the DIA:CONN P8 includes the following.

- Insulin injection information: Injection time, insulin type, insulin dose

10.2.12. Adverse Event Monitoring

Adverse events are collected for all events which occur after obtaining written informed consent. They are confirmed at each visit, starting from the Blind CGM Period using the investigational medical device through Visit 5 (i.e., the final visit). Investigators must instruct subjects to report adverse events immediately upon occurrence. Additionally, investigators must confirm the occurrence of adverse events through medical examinations, including interviews and medical history reviews, during regular visits throughout the study period.

10.3. Endpoints

10.3.1. Primary Efficacy Endpoint

Change in HbA1c (%) at Week 12 compared to baseline

10.3.2. Secondary Efficacy Endpoints

1) Percentage of subjects with HbA1c <7% at Week 12
2) Core CGM endpoints over 12 weeks*
   - Percentage of TIR (70-180 mg/dL)
   - Percentage of TBR (<54 mg/dL)
   - Percentage of TBR (<70 mg/dL)
   - Percentage of TAR (>180 mg/dL)
   - Percentage of TAR (>250 mg/dL)
   - Mean glucose, Glucose Management Indicator (GMI)
   - Coefficient of Variation (CV) (%)

*Percentage will be presented for subjects with CGM data ≥70%

3) Core CGM endpoints at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, 6-8 weeks, Week 8 to 10, Week 10 to 12)*
   - Percentage of TIR (70-180 mg/dL)
   - Percentage of TBR (<54 mg/dL)
   - Percentage of TBR (<70 mg/dL)
   - Percentage of TAR (>180 mg/dL)
   - Percentage of TAR (>250 mg/dL)
   - Mean glucose, GMI
   - CV (%)

*Percentage will be presented for subjects with CGM data ≥70%

4) Percentage of subjects satisfying both percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% over 12 weeks
5) Percentage of subjects satisfying both percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12)
6) Percentage of subjects with ≥5% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12)
7) Percentage of subjects with ≥10% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12)
8) Insulin dose: Type of insulin, total number of daily bolus injections, basal insulin dose, rapid-acting insulin dose for each meal
9) Dosing behavior
   - Missed dose (no bolus –30 to +60 min)

- Late dosing (+15 to +60 min)
- Percentage of days with ≥3 daily bolus injections over 12 weeks

10) Number of days on which three bolus calculation modes (i.e., fixed meal mode, meal estimation mode, carbohydrate counting mode) were used from Baseline to Week 12
11) Total individual education hours for the investigational group

10.3.3. Safety Endpoints

1) Adverse events
2) Laboratory tests, vital signs, physical examination

11. Predicted Adverse Effects and Precautions for Use

11.1. Predicted Adverse Effects

If the information set on the DIA:CONN P8 insulin pen differs from the cartridge type, it may lead to hypoglycemia or hyperglycemia depending on the situation. Additionally, inadvertent button presses may result in unintended dose recording or changes to treatment settings, and such changes could lead to hypoglycemic or hyperglycemic events that may potentially cause serious injury or death. Other commonly reported side effects associated with insulin injections include the following.[15,16,17]

1) Hypoglycemia: Hypoglycemia can occur if insulin is injected in excess of the required amount, used irregularly, or administered while skipping meals or eating insufficiently.
2) Lipodystrophy: Repeated injections in the same area without rotating injection sites can cause fat cells to accumulate in the subcutaneous tissue, forming lumps. If lipodystrophy occurs, avoid injecting in the affected area until the abnormal tissue returns to normal.
3) Bleeding and Bruising: Puncturing a small blood vessel during insulin injection can cause bleeding and bruising. If bleeding occurs, apply firm pressure until it stops.
4) Pain: Pain during insulin injections may occur depending on insulin temperature or alcohol use. To reduce pain, use insulin stored at room temperature. If alcohol is used, ensure the area is completely dry before injection. For high doses of 50 units or more, it is recommended to administer the dose in two separate injections.

Hypoglycemia is defined as a blood glucose level of 3.9 mmol/L (70 mg/dL) or lower and/or requiring intervention. If the subject experiences any of the following major symptoms of hypoglycemia, they should consume orange juice or a beverage/food containing sugar, contact the tester, and visit the testing facility or receive accurate testing/telephone consultation via phone. Additional measures should be taken as necessary.

- Mild: Trembling, cold sweats, rapid heartbeat, dizziness, hunger, blurred vision, anxiety, etc.
- Severe: Confusion, fatigue, yawning, lack of coordination, headache, double vision, aggressive behavior, etc.

11.2. Precautions for Use

1. U-Healthcare External Insulin Infusion System (DIA:CONN P8b, DIA:CONN P8w)

1) Recommendations for Modifications
   (1) This product must not be modified, repaired, or altered without the manufacturer's approval.
   (2) Repair and after-sales (A/S) services for the DIA:CONN P8 may only be performed at A/S centers designated by the manufacturer's headquarters.
   (3) A/S certification facilities must be approved by the manufacturer's headquarters, and at least one A/S specialist who has completed the manufacturer's A/S training program for a designated period (three months or longer) must be present.
   (4) If any modification is made to this product, appropriate inspections must be performed to ensure its continued safe and reliable use.

2) General Precautions
   (1) For safe use of this product, be sure to read this user manual carefully before use and use it according to the user manual. In addition, please familiarize yourself with the basic injection method before real use.

(2) This product is a home medical device manufactured for use in a home environment.

(3) This product is a medical device that must be used under the guidance and prescription of a physician. Any changes to the insulin injection volume must be made according to the physician's instructions.

(4) This product cannot be maintained or operated while in use by the user.

(5) If you are blind or have any problems with sight, do not use this product without the assistance of caregiver.

(6) All users under the age of 14 should be always monitored by parents or medical professionals when injecting insulin.

(7) Please do not share this pen with other people to prevent infection.

(8) Individuals with hypersensitivity to insulin should not use this product.

(9) If the blood glucose is abnormal during use, please contact your healthcare professional.

(10) Individuals without diabetes should not use this product.

(11) The pen and needle must be kept out of sight and out of reach of others, especially children.

(12) Caution is advised as the charging cable may pose a strangulation hazard.

(13) This equipment is suitable for use in residential environments, where CISPR 11 Class B requirements are generally applied. When used in industrial or hospital environments (CISPR 11 Class A), this equipment may not provide adequate protection against radio frequency communication services.

(14) Using accessories and cables other than those specified or provided by the manufacturer of this device may increase electromagnetic emissions or reduce the electromagnetic immunity of this device, causing it to malfunction.

(15) Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should not be used within 30 cm (12 inches) of any part of the device, including cables specified by the manufacturer. Failure to comply may degrade the performance of this device.

3) Precautions for Insulin Injection

(1) This product is designed on the premise of using a single agent of insulin. Therefore, do not randomly mix two or more types of insulin or mix two or more cartridges.

(2) Do not use non-sterile or damaged pen needles. Medical experts strongly recommend not reusing pen needles. It minimizes the risk of infection and clogged pen needles if you use a new needle for each injection. Follow the pen needle instructions and safety guidelines of the manufacturer.

(3) You will need to change the injection site every time you inject. Always follow the instructions given after consulting with your healthcare professional regarding the injection site.

(4) Do not reattach the used needle to the pen after injection. Always remove and dispose of used needles safely after use. Always follow general safety precautions for the removal and disposal of the needle to minimize the unintentional risk of needle penetration and contamination. Otherwise, it may lead to incorrect insulin delivery, leakage of insulin, or unintended needle injury.

(5) Pen needles must never be reused. Reusing needles may cause infection and may result in needle blockage, which can interfere with insulin delivery.

(6) Perform priming before each insulin injection to ensure that the pen is functioning properly. If insulin is not expelled during priming and an injection is attempted, insulin may not be delivered and hyperglycemia may occur.

4) Precautions for Cartridge Replacement

(1) Only one type of insulin cartridge (Basal/ Bolus) can be used with one product. Do not mix different insulin cartridges (Basal/Bolus) in one product.

(2) Proceed with the replacement after accurately checking the cartridge manufacturer and insulin type to be used before replacing the insulin cartridge. If it does not match the pen's setting information, it will not be able to recognize the exact amount of insulin remaining in the cartridge, and the unit amount displayed may differ from the actual amount remaining. This can result in the infusion of an incorrect dose and a hypoglycemic or hyperglycemic state depending on the situation.

(3) Always remove the pen needle first before replacing the cartridge.

(4) During cartridge replacement, do not remove the cartridge holder before the plunger has completely returned to its initial (rewound) position.

(5) Before replacing the insulin cartridge, check the packaging and ensure that the cartridge is not damaged. If the cartridge is damaged, insulin may leak during use or the cartridge may break.

Selecting the correct cartridge manufacturer	When replacing the cartridge, select the correct manufacturer. Supported manufacturers: Novo Nordisk, Sanofi, Lilly, Berlin-Chemie, DIA:CONN (G2E)
Selecting the correct insulin type	When replacing the cartridge, the correct insulin type must be selected. Supported insulin types: Ultra-short-acting, short-acting, long-acting, intermediate-acting, premixed

(6) Verify the manufacturer and insulin type of the cartridge to be replaced before proceeding with replacement.

* If the manufacturer differs, differences in the inner diameter of the cartridge may cause variations in insulin delivery.

* If the insulin type differs, the bolus calculator may recommend an incorrect dose.

(7) Follow the instructions in the user manual when inserting or replacing a cartridge. Always prepare a new cartridge.

(8) Check the insulin cartridge for any damage before replacement.

(9) Dispose of used cartridges in accordance with the disposal procedures of each manufacturer.

(10) When a cartridge is attached to the pen, store the pen at room temperature. Refer to the manufacturer’s information and manual provided with the cartridge for storage methods, shelf life, and usage duration.

(11) When replacing the insulin cartridge, ensure that the cartridge information set on the pen matches the actual manufacturer and insulin type of the cartridge. If the information set on the pen differs from the cartridge type, hypoglycemia or hyperglycemia may occur.

5) Handling and Storage Precautions

(1) Try to always check whether the battery is totally charged. Always make sure the battery is fully charged. Please bring an extra auxiliary battery if needed.

(2) Do not remove the USB cover forcibly. Moisture and dirt can easily penetrate into the product. Always remove the pen needle before replacing the cartridge.

(3) Do not intentionally throw the pen as the impact may damage the pen. Check whether the inserted cartridge is damaged before using it, if an impact occurs during use.

(4) Do not use this product adjacent to or stacked with other devices. It may not work properly. If such use is necessary, you must ensure that this device and other devices are operating normally.

(5) This product alone has no waterproof and protection function against penetration. Exposure to water or moisture can damage and prevent the pen from functioning properly. Put it in the exclusive bag provided when storing the product after use.

(6) Do not modify or disassemble the product. If any part of the product is broken or seems damaged, do not use the product and contact your local supplier or healthcare professional.

(7) Do not expose the product to heat or direct sunlight.

(8) Do not expose the product to flammable materials or its mixtures.

(9) Do not expose the product to electromagnetic waves and/or certain frequencies (CT, MRI, X-rays, etc.). Exposure to electromagnetic waves may damage the pen

(10) Please do not use any liquid or chemical materials (Grease, Lubricant) when cleaning up the product. It may cause deformation or failure of the product

(11) The manufacturer shall not be liable for any problems, damages or malfunctions caused by force majeure or other events beyond its control

(12) Do not expose the DIA:CONN P8 to direct sunlight or dust.

(13) Please do not use liquids, immerse the product in liquid, or use chemical agents when cleaning the device. Improper cleaning may damage the product. If necessary, gently wipe the DIA:CONN P8 device, the cartridge holder, and the pen cap with a dry or slightly damp cloth.

(14) Always remove the needle after each use. Do not store the pen with the needle attached, and do not store it in a refrigerator.

(15) Avoid dropping the pen or hitting it against hard surfaces. If the pen has been dropped or if malfunction is suspected, perform priming prior to insulin injection to confirm proper operation.

6) Precautions for attaching the pen needle and performing the air removal procedure

(1) Compressing the cartridge may cause insulin to leak when attaching the needle.

7) Precautions during air removal

(1) If a blockage occurs during insulin delivery or priming, a warning message may be displayed, and an alarm may sound.

(2) Before setting the injection dose, remove air from the cartridge. Priming is performed to ensure that the attached pen needle is usable and that insulin can be properly delivered. In addition, if air bubbles remain in the cartridge, accurate insulin dosing cannot be achieved.

8) Post-injection handling precautions

(1) Always discard the needle after each injection. This reduces the risk of contamination, infection, insulin leakage, needle blockage, and inaccurate dose delivery. If the needle becomes blocked, insulin may not be delivered at all.

(2) Never re-cap the inner needle cap. Doing so may result in accidental needlestick injury.

2. Class 2 U-Healthcare Gateway Software (DIA:CONN APP for Android / DIA:CONN APP for iOS)

1) Precautions for Using the DIA:CONN Application

(1) Even if you have previously used the DIA:CONN app, you must read this manual before use. Failure to follow the instructions may result in delivering too much or too little insulin.

(2) Do not use the app if any component of the smart device or the DIA:CONN pen appears broken or damaged.

(3) Always carry a spare insulin delivery device in case the DIA:CONN pen is lost or damaged.

2) Contraindications

(1) The DIA:CONN platform is not intended for individuals who are unable or unwilling to:

- perform blood glucose (BG) testing as recommended by their healthcare provider
- maintain sufficient diabetes self-management skills
- visit their healthcare provider on a regular basis

(2) User interaction, compatible devices, and proper device pairing and configuration are required.

(3) Users must log out when the application is not in use.

(4) Users should regularly update the password associated with the account linked to this application.

(5) Users should not install applications of unknown origin on the smart device used with this application, and any previously installed suspicious applications must be deleted.

(6) When updates recommended by the manufacturer are available, users must update to the latest version promptly.

(7) The application should only be used on a trusted network.

(8) If possible, users should install and use reliable security software.

(9) Law restricts the sale of the DIA:CONN system to physicians or by their order.

(10) Important Pediatric User Information

- The following recommendations are intended to help pediatric patients and caregivers manage the DIA:CONN platform safely. Caregivers must consult with the patient's healthcare provider to determine whether therapy with the DIA:CONN platform is appropriate for the child.
- Children should not chew or swallow the pen cap, cartridge components, or other small parts. Small parts pose a choking hazard, and ingestion may cause internal injury or infection.
- For patients who are unable to manage their condition independently, the smart device must always be used under the supervision of a caregiver.
- Careless button presses may lead to unintended dose logging or changes to therapy settings. Such changes may result in hypoglycemic or hyperglycemic events that could potentially cause serious injury or death.

3) Precautions for Supported Devices

(1) This product must be used only with supported mobile devices.

(2) Periodically verify that the app is compatible with the smart device and operating system version. System messages including instructions or warnings may appear. Internet access is required to confirm compatibility (ensure Wi-Fi or cellular data is enabled).

(3) The P8 pen must first be paired with the smart device and the DIA:CONN app. This enables wireless transmission of P8 pen information to the smart device.

(4) The Bluetooth® function of the P8 transmits information to the smart device. To prevent another person's dose data from being transmitted to the smart device, ensure that no one else uses the P8 to administer insulin. The P8 is intended for single-patient use only.

(5) The smart device must have sufficient memory/storage capacity. Without adequate storage, the DIA:CONN app may not install or may be unable to record dose data. Users may need to delete files or applications from the smart device.

4) Precautions for Use

(1) To safely use the dose calculator, it is essential that therapy settings are correct. Always proceed only after consulting with your healthcare provider.

(2) The time settings of the insulin pen and cartridge replacement must be performed accurately.

(3) If the time settings or cartridge replacement of the insulin pen are not performed correctly, use of the DIA:CONN app may not be optimal.

(4) To use the DIA:CONN P8 (DIA:CONN P8) pen properly and safely with the DIA:CONN platform, the smart device must be configured correctly. The device's internal settings take precedence over the DIA:CONN app settings. If the device settings are incorrect, the DIA:CONN app may not function properly.

(5) To prevent unauthorized access to data and settings, the security features of the smart device should be enabled. For safety and security, virus/malware protection software should be used on the smart device.

(6) To receive alarms or alerts, the following must be ensured:

① Verify that notifications are enabled in the settings menu.

② Ensure the application is not closed on the smartphone.

③ Ensure Bluetooth on the smart device is turned on.

④ Verify that the "Do Not Disturb" feature is disabled on the smart device.

⑤ After restarting the smart device, confirm that the application has been launched.

⑥ Set the device volume to an audible level.

⑦ Do not force close the application; ensure it continues running in the background when possible.

⑧ The vibration alerts and notifications of the DIA:CONN app are not different from those of other vibration-enabled apps on the smart device.

(7) Medical device apps, such as the DIA:CONN app, do not have special priority over the smart device's native functions. It is not possible to determine whether a vibration originates from the DIA:CONN app or another app. The only way to confirm the source of a notification is to view the device screen.

(8) Frequently check that the date and time on the device are accurate. When traveling to a different time zone, verify the device's date and time. Enable "Set Automatically" and allow the smart device to manage date and time. For instructions on setting the device's date and time, refer to the device user manual.

(9) When using blood glucose data provided by an external connected device, always verify before injection that the blood glucose measured by the external device matches the blood glucose received by the DIA:CONN app. If there is a discrepancy, blood glucose management may differ from the predicted values.

3. Dexcom G7

1) Warning

(1) No MRI/CT/diathermy — MR unsafe: Do not wear any Dexcom G7 CGM System component during magnetic resonance imaging (MRI) or high-frequency electrical heat (diathermy) treatment. However, it's safe to have a CT scan if you keep the sensor out of the scanned area and cover the sensor with a lead apron during the scan. The Dexcom G7 CGM System hasn't been tested in those situations when used during an MRI scan, diathermy, or in the scanned area of a CT scan. The magnetic fields and heat could damage components of the Dexcom G7 CGM System, which may cause inaccurate sensor readings or prevent alerts. Without sensor readings or alerts, you might miss a severe low/high glucose event.

(2) Read the product instructions before you use your Dexcom G7 CGM System.

(3) Do not ignore low/high symptoms: Use your BG (Blood Glucose) meter to make treatment decisions when your sensor readings do not match your low/high symptoms. If needed, seek immediate medical attention.

(4) No number or no arrow, no CGM treatment decision: Use your BG (Blood Glucose) meter to make treatment decisions when your Dexcom G7 CGM System doesn't show both a number and trend arrow as well as during the 30-minute sensor warmup period.

(5) Do not use if you are on dialysis or critically ill: The Dexcom G7 CGM System performance hasn't been evaluated in these populations and sensor readings may be inaccurate.

(6) Sensor wire breaks off: Do not ignore broken or detached sensor wires. If this happens, please contact technical support at dexcom.com, or your local Dexcom distributor If a sensor wire breaks off or detaches under your skin and you can't see it, do not try to remove it. Contact your healthcare provider if you have symptoms of infection or inflammation — redness, swelling, or pain — at the insertion site.

(7) Where to insert – Arm, abdomen, or buttocks: Users may place the sensor on the abdomen or the back of the upper arm. However, Children from 2 to 6 years old can also choose their upper buttock. Additionally, pregnant women aged 18 years and older should attach only to the back of the upper arm. Other sites have no been validated or approved. Talk to your healthcare provider about the optimal attachment site.

(8) Where to store: You can store your sensors at room temperature or in your refrigerator, between 2~30°C, but not in the freezer.

(9) Inspect: Do not use any damaged or cracked Dexcom G7 CGM System component because it may not work correctly and could cause injuries from electrical shocks

(10) Use as directed: The Dexcom G7 CGM System is small and may pose a choking hazard if swallowed.

(11) Check settings: Make sure your smart device volume is turned up, not muted, and the speaker works. When you have headphones connected, alerts will only sound through the headphones, not on your smart device speaker. Your glucose alerts sound and display information by default even when your volume is low.

(12) Quiet Mode (Vibrate): When this setting is enabled all your Dexcom G7 CGM System Alerts will vibrate. Your Urgent Low Glucose and Technical Alerts will still escalate to sound if not acknowledged.

(13) Quiet Mode (Silence All): When this setting is enabled, all your Dexcom G7 CGM System Alerts will be silent. You won't receive sound or vibration for any alerts. You will still receive visual alerts on your display device. (Exceptions: The alert for the app stopping will still sound.) Check your display device frequently to avoid missing a low/high glucose event.

(14) Bluetooth® wireless technology: Make sure your Bluetooth is on. If not, you won't get readings or alerts.

(15) Use your Dexcom G7 CGM System to make treatment decisions: Do not use Followers' information for treatment decisions, like treating for a low or dosing for a high. Follow your Dexcom G7 CGM System instructions to make treatment decisions.

(16) Follow healthcare provider advice: Share is not intended to replace self-monitoring practices as advised by your healthcare provider.

2) Precautions for Use

(1) Secure internet: Only use a cellular internet connection, a trusted Wi-Fi network (like your home or office), or use a secure internet connection such as a VPN service when using your Dexcom G7 CGM System. Do not use unsecured public Wi-Fi such as guest networks in other's homes, restaurants, schools, libraries, hotels, airports, airplanes, etc. Those could expose your Dexcom G7 CGM System to viruses or hacking.

(2) Check connected devices: When using connected devices such as headphones, Bluetooth speakers, or smartwatches, you may get your alerts on only one, not all. After connecting any devices, make sure that your smart device settings allow you to continue receiving alerts.

(3) Clean and dry skin: If your insertion site and hands aren't clean and dry, you run the risk of infection and the sensor not sticking well. Clean your insertion site with alcohol wipes to prevent infections. Before insertion and during your sensor session, do not apply insect repellent, sunscreen, perfume, or lotion on your insertion site or sensor. This may cause the sensor to not stick well or could damage your Dexcom G7 CGM System.

(4) Hydroxyurea: If you are taking hydroxyurea, your sensor readings will be higher than your actual glucose, which could result in missed hypoglycemia alerts or errors in diabetes management, such as giving yourself a higher dose of insulin due to falsely high sensor glucose values. The level of inaccuracy depends on the amount of hydroxyurea in your body. If you are taking hydroxyurea, you should use your own BG (Blood Glucose) meter.

(5) Be accurate, be quick: If you calibrate your Dexcom G7 CGM System using your BG (Blood Glucose) meter, enter the BG (Blood Glucose) value on your meter within five minutes of measuring your BG (Blood Glucose).

(6) Use fingertips: Use a BG (Blood Glucose) sample from your fingertips when calibrating as blood glucose from other places may be less accurate and not as timely. Calibration is not required but you can do optional BG (Blood Glucose) calibration to align with your meter.

(7) Do not start past the Use By Date: Do not start a sensor past its Use By Date (YYYY-MM-DD) because it may give incorrect results. You can start a new sensor on or before its Use By Date. This gives you full wear.

(8) Check package: Do not use your Dexcom G7 CGM System if the applicator and/or sterile cap has been

damaged or opened, because it might cause an infection. Do not remove cap until ready for insertion.

(9) Where to insert — things to check: The Dexcom G7 CGM System insertion safety guard is enabled until you press the Dexcom G7 CGM System applicator down against your skin. Only do this when ready to insert.
Change your insertion site with each sensor to allow the skin to heal.
Avoid areas:

- With loose skin or without enough fat to avoid muscles and bones
- That get bumped, pushed, or you lie on while sleeping
- Within 8 cm of infusion or injection site
- Near waistband or with irritations, scarring, tattoos, or lots of hair. If needed, trim site with clippers.

(10) Use correct components: Dexcom G7 CGM System components aren't compatible with any previous Dexcom products. Do not mix with different generations.

(11) TSA Security check point: You can wear your G7 sensor when going through walk-through metal detectors and Advanced Imaging Technology (AIT) body scanners. If you do, use your BG (Blood Glucose) meter for treatment decisions until you leave the security area. This is because the Dexcom G7 CGM System hasn't been tested with every x-ray and security scanner and you may not be able to bring a display device.
You can also ask for hand-wanding or full-body pat-down and visual inspection instead of going through any walk through body scanners or putting any part of the Dexcom G7 CGM System in the baggage scanning machine.

(12) Keep your sensor close to display device: Keep your smartphone or receiver within 6 meters of your sensor. Make sure there are no obstacles between your display device and your sensor. Otherwise, they may not be able to communicate.

(13) Get alerts on display device you use: To get your phone app and receiver alerts, set them on the display device you use. Your receiver won't get the alerts you set in your phone app. Likewise, your phone and watch apps won't get the alerts you set on your receiver.

(14) Display device is on: Make sure your display device is turned on or you won't receive sensor readings or alerts.

(15) Test speaker and vibrations: Test your receiver speaker and vibrations regularly. To make sure the speaker and vibrations work, plug in the receiver to charge. The Speaker Test screen appears for a few seconds. Follow the directions on the screen to test the speaker and vibrations. If it doesn't beep and vibrate, contact technical support at dexcom.com or your local Dexcom distributor and use the app or BG (Blood Glucose) meter until the receiver is repaired.

(16) Keep receiver clean and dry: Do not submerge your receiver in water and do not get dirt or water in the USB port. That could damage it.

3) General Precautions

(1) Make sure your smart device settings follow Dexcom's recommended settings. Certain phone settings such as Android's Digital Wellbeing and Apple's Screen Time may prevent notifications if enabled.

(2) Allow Dexcom G7 CGM System app notifications to show on your lock screen. This will ensure you receive Dexcom notifications and allow you to see notifications without unlocking your phone.

(3) Android users must allow Location Permission, Do Not Disturb Access, and Notifications to use the app.

(4) Apple users must allow Location Permission and Critical Alerts to use the phone app.

(5) Battery: Keep the battery charged. For the receiver specifically, you should fully charge the battery if it is to be stored for a period exceeding three months.

(6) Compatibility: Before upgrading your smart device or its operating system, check dexcom.com/compatibility. Automatic updates of the phone or watch app or your device operating

system can change settings or shut down the app.
Always update manually and verify correct device settings afterward.
While connected to the internet, the phone and watch apps check periodically and will display a message if it's not compatible (or no longer compatible) with your phone or your phone's operating system (OS). The message may include a time frame for updates.

(7) Time: Let the date and time on your smart device automatically update when you travel across time zones or switch between standard and daylight saving times. Do not manually change your smart device time because you may not get readings or alerts and it may make the time on the trend screen wrong.
(8) Use electrical equipment as directed.
(9) Use of accessories, cables, adapters, and chargers other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.
(10) Portable radio frequency communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm to any part of the Dexcom G7 CGM System including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.
(11) Use of this equipment adjacent to, or stacked with, other equipment should be avoided because it could result in improper operation.
(12) Not using supplied USB charger and cable may cause the receiver battery to not charge. Do not use if the supplied USB charger or cable is damaged. Store supplied USB charger and cable safely. Misuse of the USB cable can be a strangulation risk.
(13) Do not modify: No modifications to the Dexcom G7 CGM System are allowed.
(14) Read the indications, warnings, precautions, and instructions for your Dexcom G7 Continuous Glucose Monitoring (CGM) System (G7). If you do not, you may have inaccurate sensor readings, missed alerts, and might miss a severe low or high glucose event.
(15) Dexcom does not recommend continuous glucose monitoring for people who can't or won't:
- Use their BG (Blood Glucose) meter to test their blood glucose if their symptoms do not match their sensor readings.
- Keep in touch with their healthcare provider about diabetes management.

(16) Risks and Benefits: The risks and benefits of your Dexcom G7 CGM System are described below. Avoid any risks and enjoy Dexcom G7 CGM System's benefits by following the product instructions.
[1] Risks
- Not getting your alerts
- Using the Dexcom G7 CGM System to make treatment decisions when you shouldn't
- Sensor Insertion Issues
- Adhesive reactions
- Retained sensor wire
- Inaccurate sensor readings

① Missed Alerts

You need to get your alerts to respond to them. To make sure you get important alerts to help you avoid undetected low or high glucose, follow Dexcom's recommended settings, available at dexcom.com/faqs or in the Dexcom G7 CGM System phone app, go to Profile > G7 iPhone Safety and tap Complete guide to Dexcom iPhone Settings or Profile > G7 Android Safety and tap Complete guide to Dexcom Android Settings.

Also, go to the Alerts, Safety Information, and Troubleshooting chapters for helpful information to ensure you get alerts.

② Using the Dexcom G7 CGM System for Treatment Decisions

You can use your Dexcom G7 CGM System for treatment decisions in all but a few situations:

- When you do not have both a number and an arrow
- When how you feel doesn't match your sensor reading

Using your Dexcom G7 CGM System in these situations could result in errors in diabetes management. Go to the Treatment Decisions chapter to find out more. Some users found accuracy between different sensors varied. When you insert each sensor, check if symptoms match your readings and pay attention to its accuracy before deciding to use it for treatment decisions.

For more information on how to make treatment decisions using your Dexcom G7 CGM System, go to the Safety Information, Treatment Decisions, and Alerts chapters.

③ Risk of Interfering Substance

Hydroxyurea is a medication used in the treatment of diseases including cancer and blood disorders; it is known to interfere with sensor readings.

If you are taking hydroxyurea, your sensor readings will be higher than your actual glucose, which could result in missed hypoglycemia alerts or errors in diabetes management, such as giving yourself a higher dose of insulin due to falsely high sensor glucose values. The level of inaccuracy depends on the amount of hydroxyurea in your body. Don't use your Dexcom G7 CGM System for diabetes treatment decisions if you are taking hydroxyurea.

Talk to your physician about alternative glucose monitoring approaches.

With the Dexcom G7 CGM System, you can take a standard or maximum paracetamol/acetaminophen dose of 1 gram (1,000 mg) every 6 hours and still use the sensor readings to make treatment decisions. Taking higher than the maximum dose of paracetamol/acetaminophen (e.g. > 1 gram every 6 hours in adults) may affect the sensor readings and make them look higher than they really are.

④ Sensor Insertion Risks

In rare cases, inserting the sensor can cause infection, bleeding, or pain, and wearing the adhesive patch can irritate your skin. In most patients, the adhesive reactions are mild and resolve within a week. Only a few patients in the Dexcom G7 CGM System studies got slight redness and swelling. Although uncommon, some people get a significant reaction from the sensor adhesive that may take weeks to resolve. No sensor wires detached in studies; however, there is a remote chance a sensor wire could break or detach and remain under your skin. Sterile detached sensor wires usually don't pose a significant medical risk. If a sensor wire breaks off or detaches, remains under your skin, and shows signs of infection or inflammation, contact your healthcare provider and technical support at dexcom.com, or your local Dexcom distributor.

12. Discontinuation or Withdrawal Criteria

12.1. Discontinuation Criteria

If circumstances observed during a study are deemed to make continuing the study unreasonable, the principal investigator must request study discontinuation from the Institutional Review Board (IRB), and the study may be discontinued based on the IRB's decision.
If the sponsor intends to discontinue the study due to safety issues related to the investigational medical device or for other reasons, the sponsor may request discontinuation from the Institutional Review Board (IRB), and the study may be discontinued based on the IRB's decision.

1. Temporary discontinuation for handling an adverse event
2. When the use of the medical device is discontinued to address an adverse event that has occurred
3. Discontinuation due to the occurrence of a serious adverse event/medical device adverse reaction

12.2. Handling of Discontinuation

If a study is discontinued, the principal investigator must compile the CRFs for subjects up to the point of discontinuation, along with the study progress and results, and deliver them to the sponsor. All study-related materials (CRFs, investigational medical devices, investigator's brochure) must be returned to the sponsor.

1. If the principal investigator terminates or discontinues the study early without prior agreement with the sponsor, the principal investigator must immediately notify the sponsor and the Institutional Review Board (IRB) of this fact and submit a detailed written explanation for the early termination or discontinuation.
2. If the sponsor terminates or discontinues a study early, the principal investigator must immediately notify the Institutional Review Board (IRB) of this fact and submit a detailed written explanation for the early termination or discontinuation.
3. If the Institutional Review Board (IRB) terminates or discontinues a study early, the principal investigator must immediately notify the sponsor of this fact and submit a detailed written explanation for the early termination or discontinuation.
4. If the study is terminated early or discontinued in accordance with the provisions of 1 through 3, the principal investigator must immediately inform the subjects of this fact and ensure that appropriate measures and follow-up investigations are conducted.

12.3. Withdrawal Criteria

Subjects who are randomly assigned but unable to participate for any reason throughout the entire duration of this study will be classified as withdrawals. Subjects may discontinue the study at any time upon their own request or may be discontinued at any time at the discretion of the investigator or sponsor for safety, conduct, or administrative reasons.
Subjects may be withdrawn if any of the following conditions apply:

1. The subject or their representative requests withdrawal from study participation
2. If a subject who does not meet the inclusion/exclusion criteria participates in the study
3. When continuous observation is impossible due to the subject's absence
4. If the subject is deemed to require surgery or administration of other medications that may affect safety or efficacy assessment

5. If an adverse event occurs during follow-up that makes continued participation in the study difficult
6. If the subject dies for reasons unrelated to the study
7. Other cases where the investigator determines there is a problem with the subject's participation in the study (e.g., if severe hypoglycemia requiring assistance to recover occurs due to significantly inappropriate device operation, the subject may be withdrawn from the study at the investigator's discretion to switch to conventional insulin pen use).

12.4. Handling of Withdrawal

If a subject withdraws prematurely, the reason for withdrawal and all study-related data up to the point of withdrawal must be logged and retained. If a subject fails to attend a scheduled visit during the study, the subject's well-being must be confirmed, and the reason for the absence must be clearly established.
The investigator should persuade the withdrawn subject to visit the study site as soon as possible after withdrawal is determined to complete the procedures corresponding to Visit 5. If any adverse events that have not been resolved are present at that time, the subject should be followed up until 4 weeks after the last application of the investigational medical device or until resolution, whichever is earlier.

Subjects who have been withdrawn from the study are included in the safety and efficacy analyses unless there is a valid reason or basis for exclusion.
Data obtained through the study must be assigned to analysis groups for efficacy and safety analyses. If missing data occurs, they should be handled according to Section 13.2.2, "Missing Data Handling," of this study protocol.

12.5. Protocol Violation

If it becomes known that a subject violated the protocol during the study, the investigator must promptly notify the sponsor, G2E Co., Ltd., of the violation. The sponsor will determine the seriousness of the case. Furthermore, the sponsor and investigator must jointly decide whether the subject should continue participating in the study. If a subject withdraws from the study due to a protocol violation, the details must be recorded in the CRF. Matters considered serious protocol violations include, but are not limited to, the following:

① Failure to obtain informed consent prior to proceeding with the study procedures
② Violations of inclusion or exclusion criteria that could affect efficacy and safety assessments
③ Administration of contraindicated concomitant medications or implementation of contraindicated therapies during the study period
④ Application of the investigational medical device in a manner inappropriate for evaluating efficacy and safety
⑤ Other violations considered major protocol deviations

Other minor protocol deviations deemed unlikely to affect the interpretation of study results should be accurately documented with the degree of violation or delay and the reason. Through a blind meeting prior to database lock, a comprehensive assessment should be conducted to determine whether they impacted the study, and they should be included in the per-protocol set (PP set) analysis.

12.6. Termination Criteria

The study is considered completed once the subject's Visit 5 procedures are finalized after the initiation of the investigational medical device application.

However, if an adverse event persists at Visit 5, follow-up observation continues until 4 weeks after the last application of the investigational medical device, or until resolution occurs if possible. This involves collecting relevant information—such as whether the adverse event is resolved and the date of resolution—either through a direct visit to the institution or via telephone contact between the investigator or their delegate and the subject. The completion of the final visit for the last enrolled subject is defined as the end of the entire study.

13. Data Analysis and Statistical Considerations

13.1. Analysis Population

13.1.1. Efficacy Analysis Group

This study follows the intention-to-treat (ITT) principle. Efficacy evaluation will be analyzed in two forms: the full analysis set (FA set) and the per-protocol set (PP set). The primary analysis group for efficacy evaluation is the FA set, with analysis of the PP set conducted as a secondary analysis.

FA set

Defined as subjects who received randomization, underwent application of the investigational medical device and blood glucose measurement, and had HbA1c collected at least once.

PP set

Defined as subjects included in the FA set who completed the study without major protocol violations. Exclusion criteria for the PP set are as follows.

1) Withdrawal
2) Violation of inclusion/exclusion criteria
3) Use of prohibited concomitant medications
4) CGM data acquisition rate is below 70%
5) Other major protocol violations

13.1.2. Safety Evaluation Group

Safety evaluation is analyzed as a Safety set.

Safety set

Defined as subjects who applied the investigational medical device and performed at least one blood glucose measurement.

13.2. Statistical Analysis Method

13.2.1. General Principles of Analysis

All statistical analyses were performed using SAS® (version 9.4 or higher, SAS Institute, Cary, NC, USA). Continuous data are presented as the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical data are presented as the frequency and percentage for each category. Normality of continuous data is assessed using the Shapiro-Wilk test. Unless otherwise specified, all tests are two-sided at a 5% significance level.

13.2.2. Missing Data Handling Method

For missing HbA1c values in the FA set during efficacy analysis, the last observation carried forward (LOCF) method is applied to impute missing values. However, missing values are not imputed if HbA1c was not collected

after baseline. For other efficacy and safety analyses, missing values are not imputed; the available data set is used as is for analysis.

13.2.3. Covariate Adjustment

For between-group comparisons of efficacy endpoints, analyses are adjusted for baseline values (for continuous variables), CGM use status, and stratification factor (i.e., type of diabetes).

13.2.4. Interim Analysis

No interim analysis will be conducted prior to the completion of the study.

13.2.5. Multiple Comparisons and Multiplicity

Multiple comparisons and multiplicity are not considered in this study.

13.2.6. Subgroup Analysis

Subgroup analyses will be conducted for the efficacy endpoint (change in HbA1c (%) from baseline at Week 12) and core CGM endpoints, based on bolus calculator mode, age group, diabetes type, and CGM usage status.

13.2.7. Demographic Information and Other Pre-Treatment Characteristics

For demographic information and other pre-treatment characteristics, continuous data will be presented using descriptive statistics (number of observations, mean, standard deviation, median, minimum, and maximum), and categorical data will be presented using frequency and percentage.

13.2.8. Efficacy Analysis

13.2.8.1. Primary Efficacy Analysis

For the change in HbA1c (%) from Baseline to Week 12, descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) will be presented by group. In order to compare the investigational group and control group, covariance analysis adjusted for Baseline values, CGM use status, and stratification factor (i.e., type of diabetes) will be performed. The results of the covariance analysis will be summarized with the LSM and SE of each group, the LSM difference between groups and its 95% confidence interval, and two-sided *p*-value.

13.2.8.2. Secondary Efficacy Analysis

1) Proportion of subjects with HbA1c <7% at Week 12

The percentage of subjects with HbA1c <7% at Week 12 and the 95% confidence interval will be presented by group. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use status and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value.

2) Core CGM endpoints over 12 weeks
   - Percentage of TIR (70-180 mg/dL)
   - Percentage of TBR (<54 mg/dL)
   - Percentage of TBR (<70 mg/dL)
   - Percentage of TAR (>180 mg/dL)
   - Percentage of TAR (>250 mg/dL)
   - Mean glucose, Glucose Management Indicator (GMI)
   - Coefficient of Variation (CV) (%)

For the core CGM endpoints over 12 weeks, the percentage of subjects with CGM data ≥70% and descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) for the change from Baseline will be presented by group. In order to compare the investigational group and control group, covariance analysis adjusted for Baseline values, CGM use status, and stratification factor (i.e., type of diabetes) will be performed. The results of the covariance analysis will be summarized with the LSM and SE of each group, the LSM difference between groups and its 95% confidence interval, and two-sided *p*-value.

3) Core CGM endpoints at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, 6–8 weeks, Week 8 to 10, Week 10 to 12)
   - Percentage of TIR (70-180 mg/dL)
   - Percentage of TBR (<54 mg/dL)
   - Percentage of TBR (<70 mg/dL)
   - Percentage of TAR (>180 mg/dL)
   - Percentage of TAR (>250 mg/dL)
   - Mean glucose, GMI
   - CV (%)

For the core CGM endpoints over 12 weeks, the percentage of subjects with CGM data ≥70% and descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) for the change from Baseline will be presented by group. In order to compare the investigational group and control group, covariance analysis adjusted for Baseline values, CGM use status, and stratification factor (i.e., type of diabetes) will be performed. The results of the covariance analysis will be summarized with the LSM and SE of each group, the LSM difference between groups and its 95% confidence interval, and two-sided *p*-value.

4) Percentage of subjects satisfying both percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% over 12 weeks

The percentage of subjects simultaneously satisfying percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% over 12 weeks will be presented along with the 95% confidence interval. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value.

5) Percentage of subjects satisfying both percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12)

The percentage of subjects simultaneously satisfying percentage of TIR (70-180 mg/dL) >70% and percentage of TBR (<54 mg/dL) <1% at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week

6 to 8, Week 8 to 10, Week 10 to 12) will be presented along with the 95% confidence interval. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value.

6) Percentage of subjects with ≥5% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12)

The percentage of subjects with ≥5% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) will be presented along with the 95% confidence interval. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value.

7) Percentage of subjects with ≥10% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12)

The percentage of subjects with ≥10% increase compared to Baseline in percentage of TIR (70-180 mg/dL) at 2-week intervals starting from Baseline (Week 0 to 2, Week 2 to 4, Week 4 to 6, Week 6 to 8, Week 8 to 10, Week 10 to 12) will be presented along with the 95% confidence interval. In order to compare the investigational group and control group, logistic regression analysis adjusted for CGM use status and stratification factor (i.e., type of diabetes) will be performed. The results of the logistic regression analysis will be summarized with the odds ratio, its 95% confidence interval, and two-sided *p*-value.

8) Insulin dose: Type of insulin, total number of daily bolus injections, basal insulin dose, rapid-acting insulin dose for each meal

For the insulin dose, descriptive statistics will be presented for continuous variables. Comparison between the investigational group and control group will be performed using either a two-sample t-test or Wilcoxon rank sum test, depending on whether the normality assumption is satisfied. For categorical data, the frequency and percentage will be presented for each category. Depending on whether more than 20% of cells have an expected frequency of <5, Pearson's chi-square test or Fisher's exact test will be used to compare the investigational group and control group.

9) Dosing behavior
   - Missed dose (no bolus –30 to +60 min)
   - Late dosing (+15 to +60 min)
   - Percentage of days with ≥3 daily bolus injections over 12 weeks

For the endpoints listed above, descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) will be presented. Comparison between the investigational group and control group will be performed using either a two-sample t-test or Wilcoxon rank sum test, depending on whether the normality assumption is satisfied.

10) Number of days in which three bolus calculation modes (i.e., fixed meal mode, meal estimation mode, carbohydrate counting mode) were used from Baseline to Week 12

Descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, and maximum) will be presented for the number of days each of the three bolus calculation modes were used from Baseline to Week 12 in the investigational group.

11) Total individual education hours for the investigational group

Descriptive statistics (i.e., number of observations, mean, standard deviation, median, minimum, maximum) will be presented for the total individual hours spent on education (i.e., education on carbohydrate counting and bolus calculator adjustment methods, education on DIA:CONN P8 and the DIA:CONN P8 smartphone app, education on CGM and the CGM app) for the investigational group.

13.2.9. Safety Analysis

13.2.9.1. Adverse Events

All AEs collected during the study period will be analyzed. For AEs, ADEs, UADEs, and SAEs/SADEs, the number of subjects who experienced the event, incidence rate, 95% confidence interval of the incidence rate, and the number of events will be presented. For comparison of incidence rates between the investigational and control groups, Pearson's chi-square test or Fisher's exact test will be performed depending on whether more than 20% of cells have an expected frequency of less than 5. All AEs will be coded according to the SOC and PT of MedDRA and will be presented by group.

13.2.9.2. Laboratory tests, vital signs, physical examination

For laboratory tests, vital signs, and physical examination, within-group and between-group comparisons will be conducted. For within-group comparisons: for continuous variables, descriptive statistics will be presented and mean changes from Baseline will be analyzed using a paired t-test or Wilcoxon signed-rank test; for categorical variables, shift tables will be prepared and analyses such as McNemar's test will be performed. **For between-group comparisons: for continuous variables, mean changes from Baseline will be analyzed using either a two-sample t-test or Wilcoxon rank-sum test, depending on whether the assumption of normality is met; for categorical variables, Pearson's chi-square test or Fisher's exact test will be performed depending on whether more than 20% of cells have an expected frequency of less than 5.**

13.2.10. Handling Data from Participants Who Withdrew Early

Data from participants who dropped out prematurely are handled according to the methods for missing data processing described in Section 13.2.2.

13.3. Analysis Timing

No interim analysis will be conducted in this study. The final analysis for preparing the results report will be performed after all subjects have completed their last visit.

13.4. Rationale for Sample Size

The primary objective of this study is to evaluate the efficacy of the DIA:CONN P8 smart insulin pen in reducing HbA1c levels in patients with type 1, type 2, and pancreatogenic diabetes receiving multiple daily insulin injections.

To compare the change in HbA1c from baseline in the investigational group (DIA:CONN P8) versus the control group (using only the insulin delivery and delivery tracking functions of DIA:CONN P8), the following hypothesis and assumptions were established to calculate the number of subjects.

$$H_0 : \mu_T - \mu_C = 0 \quad vs. \quad H_1 : \mu_T - \mu_C \neq 0$$

Where, μ_T : Change in HbA1c from baseline to week 12 in the investigational group

μ_C : Change in HbA1c from baseline to week 12 in the control group The formula for calculating the sample size for the above hypothesis is as follows.

$$n_T = n_C = \frac{2 \cdot (Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2 \cdot \sigma^2}{\mathrm{d}^2}$$

Where, $\mathrm{d} : \mu_T - \mu_C$

σ : Standard deviation of the difference in HbA1c change from baseline between groups

$Z_{1-\alpha/2}$: The normal distribution threshold for Type I error

$Z_{1-\beta}$: The normal distribution threshold for Type II error

To calculate the sample size, we cited the results from Reference [18]. Assuming a difference in change from baseline in HbA1c between the investigational group and control group of -0.6 and a standard deviation of 1.1, with a significance level of 5% (two-sided test) and power of 80%, the minimum sample size per group based on a 1:1 allocation is as follows.

$$n = \frac{2 \cdot (Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2 \cdot \sigma^2}{\mathrm{d}^2}$$

$$= \frac{2 \cdot (1.96 + 0.842)^2 \cdot 1.1^2}{(-0.6)^2}$$

$$\approx 53$$

Therefore, the minimum number of subjects required per group is 53. Considering a 10% dropout rate, 60 subjects per group will be enrolled.

14. Safety Evaluation Criteria, Assessment Methods, and Reporting Methods Including Adverse Events

14.1. Definition of adverse events

14.1.1. Adverse Event

(1) Adverse Event (AE)

Refers to any unintended sign, symptom, or disease occurring in a subject during a study (including abnormal laboratory test results), which does not necessarily have to be causally related to the investigational medical device.

(2) Adverse Device Effect (ADE)

Refers to any harmful and unintended reaction caused by the investigational medical device, where a causal relationship with the investigational medical device cannot be denied.
device cannot be ruled out.

(3) Serious Adverse Event/Adverse Device Effect (Serious AE/ADE)

Refers to an adverse event or adverse device effect caused by a medical device used in a study that meets any of the following criteria:

① Death or a life-threatening event

② Hospitalization is required or hospitalization is prolonged

③ In cases where permanent or significant disability and functional impairment have occurred

④ When the fetus has developed a deformity or abnormality

However, in this study, the following reasons for hospital admission are not considered serious adverse events:

- Hospitalization planned prior to the study
- Hospitalization for health check-ups, cosmetic procedures, or convalescence
- Emergency room visits where the time of arrival does not exceed 24 hours. However, based on the investigator's judgment, an event may be considered a serious adverse event even if it does not exceed 24 hours.

(4) Unexpected Adverse Event/Adverse Device Event (Unexpected AE/ADE)

This refers to cases where the nature or severity of the adverse event or adverse device event differs from what is described in available medical device information, such as the investigator's brochure or the device's supplementary documents.

Even if the situation does not fall under the categories listed above, if a situation arises that is medically considered to have a significant impact on the patient's well-being and health status, the investigator and relevant experts should determine whether it should be regarded as a serious adverse event based on their medical judgment and take appropriate action accordingly.

14.2. Adverse Event Severity Criteria

14.2.1. Severity Evaluation

In accordance with the [Appendix 3] Adverse Event Evaluation Criteria' of the 'Regulations on the Management of Safety Information such as Medical Device Adverse Reactions', the investigator should evaluate the safety test results, including adverse events, for all subjects who received the investigational medical device, based on the following severity criteria.

1) Negligible: No adverse effect on the patient's health status
2) Minor: When a temporary problem unrelated to the patient's underlying condition has occurred or could occur
3) Moderate: A reversible impairment of function (sensory, motor, physiological, or cognitive) unrelated to the underlying disease has occurred or could occur in the patient's health status.
4) Major: Permanent impairment of function (sensory, motor, physiological, intellectual) unrelated to the underlying disease has occurred or may occur
5) Critical: Death or major irreversible impairment of function (sensory, motor, physiological, intellectual) unrelated to the patient's underlying disease or condition has occurred or may occur

14.2.2. Frequency

Based on past adverse event reporting history, domestic and international information collected, and clinical specialist opinions, evaluated according to the following criteria.

1) Very common

This refers to adverse events that occur frequently during the use of the medical device and meet one of the following conditions:

(1) Cases where the same incident has been reported at least once in the past 3 to 6 months
(2) Cases where the same adverse event has not been reported in the past but are judged highly likely to occur within the next 3 to 6 months.

2) Common

This refers to an adverse event commonly occurring during the use of the medical device, meeting one of the following criteria:

(1) Cases where the same incident has been reported at least once within the past 6 months to 1 year
(2) Cases where the same adverse event has not been reported in the past, but it is judged highly likely to occur within the next 6 months to 1 year

3) Uncommon

This refers to an adverse event that occurs occasionally during the use of the medical device and meets one of the following criteria:

(1) Cases where the same incident has been reported at least once within the past 1 to 2 years
(2) Cases where the same adverse event has not been reported in the past but are judged to have a high likelihood of occurring within the next 1 to 2 years

4) Rare

This refers to adverse events that occur rarely during the use of the medical device, meeting one of the following criteria:

(1) Cases where the same incident has been reported at least once within the past 2 to 5 years
(2) Cases where the same adverse event has not been reported in the past but are judged to have a high likelihood of occurring within the next 2 to 5 years

5) Very rare

This refers to cases where the same adverse event has never been reported with the use of the medical device and is judged to have a low likelihood of occurring in the future.

14.2.3. Sensitivity Evaluation

The occurrence of adverse events is evaluated as follows.

1) When an adverse event has been announced by a foreign government or has been identified in another domestic field (e.g., pharmaceuticals, etc.) and is deemed necessary to evaluate in the medical device field
2) When recognized through literature information, academic presentations, post-market surveillance, etc., and deemed necessary for evaluation
3) Cases where the issue has been raised through the media, etc., and there is a possibility that social anxiety may spread due to the acquisition of uncertain information
4) Cases not falling under types 1) to 3) above

14.2.4. Potential Contributing Factor Assessment

Potential factors that could lead to recurrence of the adverse event are evaluated based on the following criteria:

1) Whether there are potential contributing factors that could cause the adverse event to recur, such as issues in use or problems during manufacturing, transportation, or storage
2) Whether corrective actions, such as appropriate training or changes to the manufacturing process are necessary to eliminate the potential contributing factor through additional analysis and evaluation

14.2.5. Assessment of whether the adverse event was foreseeable

Evaluate whether the reported adverse event is already known to the manufacturer or is an adverse event that could occur given the characteristics of the patient and the procedure.

14.2.6. Causality Assessment

Evaluate the cause of the adverse event occurrence based on the following criteria.

1) Medical device issue

When adverse events occur due to device failure, malfunction, or damage despite use in accordance with the manufacturer's intended purpose, method, and precautions.

2) Procedure-Related Issues

When the medical device was used correctly, there were no issues with the patient's condition or underlying disease, but the adverse event occurred due to the practitioner's procedure.

3) Patient-Related Issues

When the medical device was used correctly and the practitioner's procedure was not problematic, but an adverse event occurred due to the patient's condition or underlying disease

4) Unable to evaluate

When the reported adverse event details do not match the actual product, or when multiple factors interacted to cause the event, making the root cause unidentifiable

14.3. Adverse Event Reporting Method

14.3.1. Adverse Event Training

The study principal investigator should educate study staff, clinicians, and others on all adverse events that may occur after using the investigational medical device and instruct them to report all phenomena observed after use.

14.3.2. Adverse Event Reporting

Medical device handlers should report adverse events and other safety information to the Minister of Food and Drug Safety within the timeframe specified below, starting from the date they become aware of such information, in accordance with Article 5 (Reporting of Adverse Events) of the Ministry of Food and Drug Safety Notice 'Regulations on the Management of Safety Information such as Adverse Reactions to Medical Devices'. They should also retain relevant documentation for two years.

1. In cases where adverse events resulting in death or life-threatening conditions occur, reporting must be completed within 7 days. In such cases, detailed information must be additionally reported within 8 days from the initial reporting date.
2. Adverse events causing the side effects specified in the following subparagraphs or where an adverse event has occurred must be reported within 15 days.
   1) When hospitalization or extension of hospitalization is required
   2) Cases causing irreversible or severe disability or functional impairment
   3) Causing congenital malformations or abnormalities
3. Other significant information or other adverse events for which the Minister of Food and Drug Safety has directed reporting must be reported within 30 days.
   1) Adverse events not falling under items 1-2 above (adverse events not covered by Article 51(1) of the Enforcement Rules)
   2) Measures taken based on announcements by foreign governments, etc.

14.3.3. Reporting of Serious Adverse Events

The investigator must report all serious adverse events occurring during the study period to the sponsor within 24 hours (working days) of becoming aware of the event, regardless of its relationship with the investigational medical device, using the designated CRF form (Form No. 1 of the Regulations on the Management of Safety Information such as Adverse Reactions to Medical Devices). If an EDC system failure prevents SAE reporting via the EDC system, report the minimum required SAE information via email or fax to the SAE reporting contact. Once the EDC system is restored, the SAE report must be completed and submitted via the EDC system.
Upon receiving the SAE report, the sponsor should review the information and, if necessary, contact the study coordinator to obtain further details. After reviewing the SAE information, the sponsor should investigate the

causal relationship with the medical device used in the study. The investigator should complete a follow-up report form for serious adverse events, including all new information, and send it to the study sponsor.
The investigator must report serious adverse events according to the reporting deadlines and methods specified in the institution's IRB standard operating procedure (SOP) for the studies.

14.4. Pregnancy

Pregnancy occurring during the study period in female subjects is not considered an adverse event. Similarly, hospitalization for uncomplicated elective abortion (therapeutic abortion is excluded) or for the normal delivery of a healthy newborn is not considered an adverse event.
However, if a female subject becomes pregnant during the study period, she must withdraw from the study. The investigator must complete a pregnancy report form within 24 hours of learning of the pregnancy and report it to the sponsor. Furthermore, if pregnancy is confirmed within 90 days after termination of the study (or discontinuation), the investigator must also complete a pregnancy report form within 24 hours of learning about the pregnancy and report it to the sponsor. Even if a subject discontinues participation or the study ends, the investigator must continue to follow up and report on the progress of the pregnant woman and fetus until delivery.
Serious maternal complications, spontaneous abortion, ectopic pregnancy, stillbirth, neonatal death, congenital anomalies, etc., should be considered serious adverse events. The investigator must report them according to the serious adverse event reporting procedures at 14.3.3.

15. Data Management

15.1. Data Collection/Access

Source documents refer to patient records maintained at the site. Most source documents are hospital or patient charts; in such cases, all information collected and recorded in the patient's CRF must match these charts. This study will collect data using electronic case report forms (eCRFs), and access to and modification of data will be restricted to authorized personnel only.
CGM metrics data and insulin injection data will be collected by downloading the subject's complete data in file format from the DIA:CONN platform.
The investigator must ensure that the sponsor, monitor, auditor, or investigator can directly access relevant materials, including study core documents such as electronic documents.

15.2. Data Protection/Storage

The investigator should store all documents and records related to the conduct of the study in a secure location, maintain security, and retain them for three years from the date of study completion. After the completion of the final report, the investigator should transfer all study documents to the person responsible for storage. If the investigator intends to dispose of or relocate any study records, they must notify the sponsor in advance. However, the sponsor may extend the retention period if deemed necessary. The sponsor must notify the investigator and the head of the study institution in writing regarding the necessity for data retention and the retention period. If the sponsor determines that further retention is no longer necessary, the sponsor must notify the principal investigator and the head of the study institution in writing.

16. Ethical Considerations and Administrative Procedures

16.1. Relevant Laws and Regulations

This study will be conducted in accordance with the Declaration of Helsinki (1964), all international and domestic laws and regulations including the Good Clinical Practice guidelines for medical devices, the approval of the Institutional Review Board (IRB) of the institution to which the principal investigator belongs, and the standard operating procedures (SOPs) of the contract research organization (CRO), CIMIC Korea Co., Ltd.

16.2. Informed Consent Form Template

Written informed consent must be obtained from each subject prior to their participation in the study or before performing any specific non-routine procedure that may pose a risk to the subject. The subject consent form is submitted by the Principal Investigator to the relevant IRB for review and approval before the study commences. Prior to subject recruitment and enrollment, the investigator must explain all aspects of the study, including the effects, adverse events, and safety of the investigational medical device. The investigator must obtain the subject's voluntary written informed consent to participate in the study before initiating the study.
If the subject or their representative is unable to read the consent form, subject brochure, or other documented information, an impartial witness must be present throughout the entire consent process. In such cases, all documented information must be read aloud and explained to the subject or their representative. The subject or representative must then verbally consent to the subject's participation in the study. If possible, they must sign the consent form and write the date by hand. Before the impartial witness also signs the consent form, they must confirm that the documented information was accurately explained to the subject or representative, and that the consent process was conducted according to the free will of the subject or representative.
The original consent form is signed by the patient and the principal investigator (or a person authorized by the principal investigator). The principal investigator or the study coordinator provides the subject with a copy of the signed original consent form. The original consent form is retained by the investigator at the institution. For detailed information regarding subject consent, refer to [Appendix 2] Informed Consent Form.

16.3. Regulations on Compensation for Victims

The principal investigator should compensate the subject in accordance with the subject compensation protocol for any injury caused directly by the investigational medical device, including injuries arising from the correction of adverse events caused by the investigational medical device or injuries occurring during the process of correcting manifested adverse events.

16.4. Standards for Medical Care and Treatment of Subjects After Completion or Withdrawal from the Study

The investigator should ensure that subjects who withdraw from the study can receive alternative treatment. If a subject who has completed the study is deemed to require continued treatment, the investigator should ensure they receive additional treatment. Subjects who experience an adverse event should be followed up until their symptoms improve and abnormal laboratory test values return to within normal limits.
The investigator must report adverse events related to the investigational medical device to the sponsor, G2E Co., Ltd., and provide medical care for the adverse event. The sponsor must ensure the subject receives appropriate medical care either from the investigator, according to the subject's preference, or from another medical institution, in accordance with the principles and compensation standards of the victim compensation

protocol.

16.5. Measures for the Safety Protection of Subjects

The obligations of the study site, the Institutional Review Board (IRB), the investigator, the sponsor, the monitor, and others for protecting the safety of subjects are as follows.

- Study Site

The head of the study institution must ensure the institution has the necessary clinical laboratories, facilities, and specialized personnel for conducting the relevant study. They must also ensure the institution can appropriately conduct the study, including being able to take necessary measures in emergencies.

- Institutional Review Board (IRB)

The IRB must be constituted in accordance with domestic laws/customs, protect the rights, safety, and welfare of subjects, and carefully review the validity of reasons when subjects in vulnerable

situations participate in studies. In performing its duties, the IRB must order the study investigator to take necessary measures, such as suspending part or all of the study, if informed consent is not appropriately obtained, the study is not conducted according to the protocol, or serious adverse events or medical device adverse reactions occur. It must evaluate/approve this study protocol according to the Good Clinical Practice guidelines and regularly assess whether the study is conducted according to the protocol.

- Investigator

The term "investigator" refers to the principal investigator, sub-investigator, and study coordinator. Before enrolling subjects in the study, the investigator must confirm each subject's health status to determine their eligibility for participation. Furthermore, the investigator should be fully knowledgeable about the investigational drug and should make every effort to ensure the safety of the subjects. If medical intervention is required for a subject's concomitant disease that the investigator becomes aware of, the investigator must inform the subject. The investigator must accurately analyze and understand the study protocol and proactively address any issues concerning the subject.

- Sponsor

The sponsor refers to the individual, company, institution, or organization responsible for the planning, management, and financing of a study. The sponsor must ensure that the study subjects, testing methods, and the format and content of case report forms are conducted according to the procedures outlined in the study protocol. The sponsor's inspection plan and procedures should be determined based on the importance of the study, the number of subjects, the type and complexity of the study, the degree of potential risk to subjects, and any previously identified issues in the conduct of the study.

- Monitoring

Monitoring refers to the activity of supervising the progress of a study and reviewing and verifying whether the study is being conducted and documented in accordance with the study protocol, standard operating procedures, Good Clinical Practice guidelines, and relevant regulations. Monitoring of the study will be conducted through regular visits by monitors to the study sites and via telephone, among other methods. During site visits, monitors will review the original subject data, records of investigational medical device management, and data storage (study files) to closely examine the progress of the study and consult with the investigator if issues arise.

- Violation of the Study Protocol

The principal investigator or study director may deviate from or modify the protocol without prior IRB approval to eliminate an immediate risk to a subject. After such an event, the deviation or modification, the reason for it, and any proposed changes to the protocol must be submitted to the IRB for review and approval as soon as possible. If necessary, it must also be submitted to the regulatory authorities.
The principal investigator should report to the IRB any major protocol violations affecting the safety and integrity of the study, as well as any violations deemed significant.

- Confidentiality of Patient Records

All study results and documents should be considered confidential. Investigators, study contractors, and personnel of the sponsor must not disclose study-related information without the sponsor's signed approval. Records that could identify subjects will be kept confidential. All study documents, including CRFs, will record and distinguish subjects using identification codes, not names. Subject identities will remain confidential even when study results are published.

- Publication of Results

The sponsor should prepare a report and inform the investigator of the study results once data from all study sites have been fully analyzed.

All data and results arising from this study are the property of the sponsor, who retains the right to publish the results of this study at any time. The Investigator should not publish, present, or disclose any information related to the results of this study without the Sponsor's prior written informed consent, and should ensure that the Study Coordinator also complies with this requirement. To ensure only accurate and validated data is used, the Investigator must provide all draft manuscripts or presentation materials prepared for publication or presentation to the Sponsor for discussion prior to submission or presentation and should withhold publication until written approval is obtained.

For multi-center studies, the investigator agrees not to publish results from their own institution or any individual institutions before the results from all participating institutions are published. However, this does not apply when the principal investigators of all participating institutions and the sponsor formally consent.

16.6. Quality Control and Reliability Assurance

16.6.1. Monitoring

A monitor designated by the sponsor conducts monitoring of the study through regular site visits and telephone calls. The monitor evaluates the progress of the study and verifies whether the investigator is fulfilling their obligations according to the study protocol and regulations. During site visits, the monitor will verify the storage of original subject records, CRFs, drug management records, and other study-related materials. If any discrepancies or issues are found in the study records, the monitor will discuss them with the investigator.

16.6.2. Audit and Inspection

To ensure the safety of subjects in this study and to obtain accurate, complete, and reliable data, the investigator must retain clinical test results, clinical records, and subjects' medical records as supporting documentation. The principal investigator, study coordinator, and institution participating in this study must permit study-related monitoring, audits, IRB reviews, and regulatory inspections. The investigator must allow direct access to study-related materials upon request by the Ministry of Food and Drug Safety and the IRB.

16.7. Other Matters Necessary for the Safe and Scientifically Sound Conduct of the Study

16.7.1. Supply and Handling of Medical Devices for the Study

The sponsor should not supply medical devices for studies to the manager or others prior to obtaining approval of the study protocol from the Institutional Review Board.
The sponsor should have documented procedures for how the administrator and others handle and store the medical devices for studies. These procedures should include methods for appropriate and safe receipt, handling, storage, and return of unused medical devices for studies.
The sponsor should supply investigational medical devices in a timely manner and maintain records concerning supply to the study site, receipt by the study site, return from the study site, and disposal.
The sponsor should establish and document a system for the return of study medical devices in the event of malfunction or other issues, or upon study termination or expiration of the usage period.

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