Insulin Glargine: A Long-Acting Solution for Type 1 & Type 2 Diabetes Management

Assessing PK, PD, Safety & Tolerability for Improved Glycemic Control

Type of Study

A double-blind, randomized, single-center, two treatment, four period, two sequence, replicate crossover, euglycemic clamp study to demonstrate equivalence in the pharmacokinetic and pharmacodynamic properties of Insulin Glargine 100 U/mL in healthy, adult, human male subjects under fasting condition.

Objective

To demonstrate equivalence in the pharmacokinetic and pharmacodynamic properties of Insulin Glargine 100 U/mL in healthy, adult, human male subjects under fasting condition.

To assess and compare the safety and tolerability of subjects after single-dose administration of both Test and Reference products.

Situational Analysis

An Indian pharmaceutical company was seeking marketing approval for Insulin Glargine 100 U/mL to treat Patients with Type 1 and Type 2 Diabetes.

Molecule Overview

Insulin glargine is a long-acting, recombinant human insulin analog used to lower blood glucose levels. It is indicated for treating diabetes mellitus in adults, adolescents, and children aged 2 years and above.

Insulin glargine regulates glucose metabolism by stimulating peripheral glucose uptake, particularly in skeletal muscle and fat, and inhibiting hepatic glucose production. Additionally, it inhibits lipolysis, reduces proteolysis, and enhances protein synthesis, effectively managing blood glucose levels.

Veeda supported the client in following services for the successful execution of the study

- Study Design & Execution
- Volunteer Recruitment & Retention
- Investigational Product Management (IMP)
- Investigational Product Administration
- Regulatory Applications
- Ethics Committee Submissions
- PK and PD Blood Sample Management
- Case Report Preparation
- Biostatistics & Data Management

Highlights of Results Delivered

48 subjects were enrolled in the study

A total of **12** blood samples for PK measurement were collected in each period

Utilized **192** Clamps

147 Blood Samples for PD Measurement were collected in each period

Study Submitted to **DCGI**

Safety Assessment parameters assessed throughout the study as below

- Subjects were monitored throughout the study to ensure safety and minimize the risk of adverse events (AEs)
- Safety assessments included Medical History, Vital Signs, Clinical Examinations, Clinical Laboratory Tests, Chest X-Ray, and 12-lead ECG
- Pre-dose glucose levels were evaluated for safety before each dosing period
- ECGs were taken approximately 5 hours post-dose and at the time of discharge
- Local tolerability at the injection site was assessed, pre-dose and post-dose
- HbA1c and OGTT tests were conducted before check-in to evaluate diabetic conditions
- Serum electrolytes were checked during screening

Major Study Challenges & Actions

Challenges	Action Plan
Deep-Rooted Technical Complexity: Requires in-depth knowledge of glucose metabolism, insulin response, and intricate understanding of clamping techniques.	**Qualified Personnel:** Highly trained staff having more than 400 Glucose clamp, including investigators, nurses, and project coordinators.
Data Analysis Nuances: Specialized statistical analysis is essential for accurate interpretation of clamp data.	**Statistical Analysis:** Experienced statistical team capable of analyzing GIR data.
Strategic Study Design: Precise alignment of clamp studies with broader drug development goals is critical.	**Study Design Expertise:** Trained investigators who can evaluate the clamp data and Team having experience of Clamp ranging from 8 hrs to 36 hrs.
Volunteer Recruitment and Retention: Identifying and maintaining a reliable pool of volunteers compliant with rigorous study protocols.	**Volunteer Base:** Established database of healthy volunteers accustomed to clamp studies.
Algorithm Precision: Developing and refining algorithms for precise clamp data handling.	**Algorithm Refinement:** Trained investigators capable of analyzing and modifying algorithms.
Medical Contingency Planning: Anticipating & addressing potential medical emergencies during clamp procedures.	**Medical Expertise:** Qualified medical team with ACLS and BLS certification.
Infrastructure Adequacy: Ensuring the availability of a dedicated study unit equipped with advanced technology.	**Study Unit:** Dedicated technicians and 12 Bed phase I units equipped with advanced monitoring and analysis equipment like cardiac safety monitor, YSI Analyzer for glucose analysis.
Cardiac Risk Management: Mitigating the risk of cardiac events through rigorous monitoring and subject selection.	**Cardiac Safety Measures:** Subjects with clinically acceptable 12-lead electrocardiograms (ECGs) were enrolled in the study. An additional ECG recording was conducted 5 hours post-dose.

Conclusion

Within the designated timeline, the study was successfully concluded and submitted to DCGI

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