505(b)(2) Pathway: Bioequivalence and Safety Assessment of Loperamide Hydrochloride ODTs

Evaluating Loperamide Hydrochloride ODTs with Two Reference Formulations

Type of Study

An open-label, balanced, randomized, three-treatment, three-period, three-sequence, single-dose, crossover oral bioequivalence study. It compares Loperamide Hydrochloride Orally Disintegrating Tablets 2 mg with IMODIUM® A-D (Loperamide) Tablets 2 mg and IMODIUM® Quick Dissolve Tablet 2 mg. The study aims to determine if the test formulation of Loperamide Hydrochloride Orally Disintegrating Tablets 2 mg is bioequivalent to the reference formulations of IMODIUM® A-D (Loperamide) Tablets 2 mg and IMODIUM® Quick Dissolve Tablet 2 mg, when administered as a single oral 8 mg dose (4 tablets x 2 mg) to healthy adult human subjects under fasting conditions.

Objective

To assess the bioequivalence and safety of the test product as compared to the reference product in healthy volunteers.

The reference products are approved for use in acute diarrhea and diarrhea associated with Irritable Bowel Syndrome (IBS).

Situational Analysis

An Indian multinational pharmaceutical company sought market approval via the 505(b)(2) pathway for a generic product with two innovators indicated for diarrhea and diarrhea associated with IBS. Veeda was tasked with delivering comprehensive services, encompassing: regulatory liaison, ethics committee submission, contract management, project oversight, subject recruitment and retention, investigational medicinal product management, data management, biostatistics, protocol writing, lab logistics & comprehensive report preparation.

Molecule Overview

Loperamide Hydrochloride is indicated for adults, adolescents, and children aged 12 years and older for the symptomatic treatment of acute diarrhoea and acute episodes of diarrhoea associated with IBS. It is also used to reduce the volume of discharge in ileostomies, colostomies, and other intestinal resections.

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

- Study Design & Execution
- Investigational Product Management (IMP) & Administration
- Volunteer Recruitment & Retention
- Local Regulatory Applications & Ethics Committee Submissions
- PK Blood Sample Management
- Data Analysis and Reporting

Highlights of Results Delivered

- **24** Subjects were enrolled and **23** Subjects completed the Study
- Average Retention Rate: **96%**

Safety Assessment parameters assessed throughout the study as below

- Subjects throughout the study were monitored, and safety and preventive measures were ensured to minimize the risk of AEs
- Safety parameter assessments such as Medical History, Vital Signs, Clinical Examinations, Clinical Laboratory Tests, Chest X-Ray, and 12-lead electrocardiogram (ECG) were conducted

Major Study Challenges & Actions

Challenges	Action Plan
Ensuring all subjects remain in a sitting posture and conducting thorough mouth checks immediately after dosing, increases the compliance complexity of the study protocol. Any deviation in the product administration process could affect the study outcomes.	Careful observation of the dosing activity to prevent any potential challenges associated with dosing and all the dosing procedure wa followed as per study protocol to avoid any kind of error.
Critical nature of the trial demanded rigorous screening tests to identify suitable candidates, posing a significant challenge in the recruitment process.	The team conducted screening based Medical History, Vital Signs, Clinical Examinations, Clinical Laboratory Tests, Chest X-Ray, and 12-lead electrocardiogram (ECG) ultimately enrolling 24 subjects for the study.
Cardiac events, including QT prolongation and torsades de pointes, had been reported. These risks necessitated careful monitoring of subjects to manage and mitigate potential adverse effects.	Subjects having clinically acceptable 12-lead electrocardiogram (ECG) were enrolled in the study and ECG recording was done at 04 hour after dosing.

Conclusion

Within the designated timeline, the study was successfully concluded, meeting the requirements for submission to the USFDA.

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