Case Study

veeda clinical research.

Handling a complex liposomal molecule - **Amphotericin B**

Situational Analysis

A specialty pharmaceutical company based in USA that specializes in development, manufacturing, and Commercialization of complex injectable products was planning to conduct a Bioequivalence study of a complex liposomal drug i.e. Amphotericin and required a partner to develop and provide a robust analytical method for the precise quantitation of free and liposomal form of Amphotericin.

Amphotericin B is an antifungal medication used for serious fungal infections and leishmaniasis. The fungal infections it is used to treat include aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, and cryptococcosis.

Highlights of the Achievement

- Method Development of Free (F-AMP) and Liposomal Amphotericin (L-AMP) completed with highest standards
- Method validation for Free (F-AMP) and Liposomal Amphotericin (L-AMP) performed in-line with regulatory requirement
- Long term stability established for duration of about 135 days for both Free (F-AMP) and Liposomal Amphotericin (L-AMP) at -78°C
- Method demonstrated to be able to quantitate the Free and Liposomal Amphotericin with reproducibility in one patient exploratory study

The Liposomal Challenge

Liposomal drug delivery system for amphotericin is a true single bilayer and due to the nature and quantity of amphophilic substances used, and the lipophilic moiety in the amphotericin B molecule, the drug is an integral part of the overall structure of the AmBisome liposomes. This makes the handling of liposomal amphotericin even critical in terms of handling in biological matrix, exposure to ultra low temperatures during sample storage and shipment.

Challenges

The Development of reproducible and robust method was challenging in terms of defining a rugged procedure for handling of samples under the controlled buffering conditions, controlling the leaching effect on the liposome bound drug due to exogenous factors and instability of the liposomal and free amphotericin in biological matrix.

Analytical Challenges

- Handling of liposomes to prevent any leaching of free drug from the bound drug
- Stability of free and liposomal bound drug under the ultra-low temperature
- Long term stability of Amphotericin B due to long half-life
- Non-availability of labeled internal Standard

Action Plan

- Sponsor was well informed of the prerequisites and technical competency at Veeda
- Dedicated team of experienced bio-scientists was designated to handle such complex molecule where extensive method development strategy was established
- Sponsor was regularly informed about the method development proceedings

Outcome

- A robust & reproducible method was developed and validated providing resolution of challenges in terms of Stability and handling of Liposomes in Matrix
- Methods were tested in exploratory study which reflected the efficiency of the method and results were reproducible over the period
- 2/3rd of the analyzed exploratory study samples showed reproducibility over the several day of analysis