Hot Melt Extruded Aprepitant-Soluplus® Solid Dispersion: Preformulation Considerations
S. Penumetcha 1, L. Gutta 1, S. Rudraraju 2, S. Yamili 1, V. Rudraraju 1
1 Aizant Drug Research Solutions Pvt., Ltd, 2 University of Texas at Dallas

Purpose
To investigate the miscibility and moisture sorption properties of Aprepitant and Soluplus® for hot melt extrusion (HME) and to assess In-Vitro release.

Methods
Soluplus® was selected as a carrier for Aprepitant from group contribution solubility parameters. Differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) was performed to determine optimum HME temperature based on melting point depression of drug in drug polymer physical mixtures and glass forming ability of drug. Melt extrusion temperature range from 170-185°C and screw speed of 180rpm was used for extruding a 1:4 drug polymer mixture in a co-rotating 12mm twin screw extruder (Steer Omicron 12P). Moisture sorption isotherms of hot melt physical mixture and amorphous drug both prepared from heat cool DSC scans as well as crystalline drug and polymer were collected using a dynamic vapor sorption (DVS) analyzer at 25°C from 0-90-0% RH. In-Vitro release from crystalline drug, physical mixture and extrudate was assessed in fasted state simulated intestinal fluid (FaSSIF) with 0.25% SLS, wherein Lecithin and Sodiumtaurocholate were replaced with SLS.

Results
Aprepitant was classified as a glass II former exhibiting re-crystallization upon reheating in a heat cool heat DSC scan. Physical mixture with a melting point depression at 170°C showed amorphization of drug upon reheating in DSC. Transparent hot melt extrudates were obtained within a temperature range from 170-185°C with HME. In-Vitro release of hot melt extrudates showed a seven fold increase in % release compared to crystalline drug. The % moisture uptake of polymer, physical mixture and crystalline drug were 25%, 21% and 0.06% respectively at 90%RH indicating hygroscopicity of polymer and non hygroscopic nature of drug. Amorphous drug and hot melt physical mixture showed greater % moisture uptake than crystalline drug with a significant hysteresis loop indicating hygroscopicity. Amorphous drug did not however recrystallize at the end of desorption step. Correlation of shape of hysteresis loop to In-vitro release was evident.

Conclusion
Optimum temperature for HME of Aprepitant and Soluplus® was ascertained from thermal analysis. Moisture sorption isotherms can help qualitatively predict solubilization and stability of hot melt extrudates.