Comparison Pharmacokinetics of Two Concentrations (0.7% and 1.0%) of Nasulin™, an Ultra-Rapid-Acting Intranasal Insulin Formulation

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Abbreviations: (AUC) area under the curve, (Cmax) maximum concentration, (PD) pharmacodynamic, (PK) pharmacokinetic, (ORMC) Orlando Regional Medical Center, (Tmax) time to maximum concentration

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Abstract

Background:
This pharmacokinetic (PK) study was designed to characterize the dose response of two concentrations (0.7% and 1%) of a nasal spray of recombinant regular human insulin in combination with cyclopentadecalactone (CPE-215), a compound that enhances absorption of molecules across mucous membranes (Nasulin™, CPEX Pharmaceuticals). Nasulin has been effective in lowering blood glucose in both normal subjects and diabetes patients, and additional dosing options would allow greater titration flexibility.

Method:
A five-period crossover study of 24 healthy, nonsmoking subjects (ages 18–50, basal metabolic index <33 kg/m², weight >70 kg) were studied. Subjects were in a fasted state for 5 h before and 45 min after administration for PK assessment and were then given a meal. Each spray contained 100 µl. Doses tested were 25, 35, 50, 70, and 100 U. Maximum concentration (Cmax) and area under the curve (AUC) were estimated for each dose group. Glucose measurements were also performed.

Results:
A dose response (slope of the natural log response versus dose) was demonstrated by baseline-adjusted Cmax of 22, 27, 56, 62, and 84 µU/ml for the 25, 35, 50, 70, and 100 U doses (p < .0001), respectively, and by baseline-adjusted AUC0–45 min values of 491, 592, 1231, 1310, and 1894 µU/ml/min (p < .0001). Glucose AUC0–45 min determinations also demonstrated a pharmacodynamic (PD) dose response.

Conclusions:
Proportional and linear dose responses for both PK and PD parameters were demonstrated for the two concentrations, making multiple doses available for clinical development.