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ORIGINAL ARTICLES

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

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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/m^2, 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 (C_{max}) 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 C_{max} 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 $AUC_{(0–45\ min)}$ values of 491, 592, 1231, 1310, and 1894 µU/ml/min ($p < .0001$). Glucose $AUC_{(0–45\ min)}$ 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.

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Abbreviations: (AUC) area under the curve, (C_{max}) maximum concentration, (PD) pharmacodynamic, (PK) pharmacokinetic, (ORMC) Orlando Regional Medical Center, (T_{max}) time to maximum concentration

Keywords: intranasal insulin, CPE-215, cyclopentadecalactone, Nasulin, ultra-rapid time action profile

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