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Title: No relevant drug-drug interaction between inhaled NVA237 and oral cimetidine

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Body: Introduction: NVA237 (glycopyrronium bromide) is a once-daily long-acting muscarinic antagonist for the treatment of COPD. Renal clearance is a major elimination pathway of NVA237 and active tubular secretion in the kidneys contributes to this process. This study investigated the effect of inhibition of the organic cation transport in the kidneys on NVA237 disposition. Cimetidine was used as a probe inhibitor. Methods: 20 healthy volunteers participated in this two-sequence crossover study. They inhaled a single 100 µg dose of NVA237 via the Breezhaler® device on two occasions, i.e. alone (Treatment A) and on the 4th day of a 6-day treatment regimen with cimetidine 800 mg twice-daily (Treatment B). Treatments were separated by a washout period of 7 to 10 days. Plasma concentrations and urinary excretion of NVA237 were determined after each NVA237 dose. The primary PK parameters were plasma peak concentration (Cmax), AUC up to the last measured concentration (AUClast) and renal clearance (CLr) of NVA237. Trough plasma concentrations of cimetidine were determined throughout cimetidine dosing. Results: Cimetidine trough concentrations indicated that the inhibitor drug had reached PK steady state prior to NVA237 inhalation in Treatment B. The concomitant administration of cimetidine resulted in an increase of total systemic exposure (AUClast) of NVA237 by 22%. This exposure increase correlated with a slight decrease of 23% in CLr. Cmax was not affected. Both treatments were safe and well tolerated. Conclusion: Based on the magnitude of the PK changes, no relevant drug interaction is expected when NVA237 is co-administered with cimetidine or other inhibitors of the organic cation transport in the kidneys.