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Effect of Concomitant Medications Affecting Gastric pH and Motility on Posaconazole Tablet Pharmacokinetics

Walter K. Kraft  
*Thomas Jefferson University, walter.kraft@jefferson.edu*

P. Chang  
*Thomas Jefferson University*

MLPS Van Iersel  
*MSD, Oss, Netherlands*

H. Waskin  
*Merck*

G. Krishna  
*Merck*

See next page for additional authors

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Effect of Concomitant Medications Affecting Gastric pH and Motility on Posaconazole Tablet Pharmacokinetics

WK Kraft,1 P Chang,1 MLPS van Jersel,2 H Waskin,3 G Krishna,2 W Kersemakers2

1Thomas Jefferson University, Philadelphia, PA, USA; 2NSD, Oss, Netherlands; 3Merck, Whitehouse Station, NJ, USA

*Current affiliation: Cubist, Lexington, MA, USA

ABSTRACT

Background: Posaconazole (POS) tablet coadministration with antifungal prophylaxis and treatment should be taken with food to maximize absorption6,7 and antacids to neutralize gastric pH.8,9 A new POS tablet formulation has been developed that results in substantially improved exposure compared with the oral suspension in healthy adults in the fasting state. This study evaluated the effect of concomitant medications altering gastric pH (ra nitidine, esomeprazole) and gastric motility (metoclopramide) on oral exposure and bioavailability of POS tablet in healthy volunteers.

METHODS

This was a prospective, open-label, 3-way crossover study in healthy volunteers, enrolled between June 19, 2011, and September 28, 2011. Each subject received 5 treatments in a 5-way crossover design; subjects were randomly assigned to 1 of 11 sequences. All 5 treatments were administered on separate occasions in an outpatient setting before the study. POS tablet alone or in combination with medications affecting gastric pH or gastric motility (ra nitidine, esomeprazole, or metoclopramide) was administered to healthy adults in the fasting state. POS tablet alone or with medications affecting gastric pH and gastric motility were administered in a 5-way crossover design; subjects were randomly assigned to 1 of 11 sequences. All 5 treatments were administered on separate occasions in an outpatient setting before the study. POS tablet alone or in combination with medications affecting gastric pH or gastric motility (ra nitidine, esomeprazole, or metoclopramide) was administered to healthy adults in the fasting state.

RESULTS: Posaconazole AUC0–last and Cmax were similar whether POS was administered alone or with medications affecting gastric pH and gastric motility (Table 2). In an attempt to optimize absorption and bioavailability without regard to food intake, a new POS tablet formulation has been developed that results in substantially improved exposure compared with the oral suspension in healthy adults in the fasting state. This study evaluated the effect of concomitant medications altering gastric pH (ranitidine, esomeprazole) and gastric motility (metoclopramide) on oral exposure and bioavailability of POS tablet in healthy volunteers.

CONCLUSIONS: The PK of POS tablet when administered alone or with medications affecting gastric pH or gastric motility in healthy volunteers was similar to that seen with POS tablet administered alone. The PK of POS tablet when administered alone or with medications affecting gastric pH or gastric motility in healthy volunteers was similar to that seen with POS tablet administered alone. The PK of POS tablet when administered alone or with medications affecting gastric pH or gastric motility in healthy volunteers was similar to that seen with POS tablet administered alone. The PK of POS tablet when administered alone or with medications affecting gastric pH or gastric motility in healthy volunteers was similar to that seen with POS tablet administered alone.

SUPPORTING INFORMATION: Information available from the journal website includes the following:

• Table 1. Demographic Characteristics
• Figure 1. Study design
• Figure 2. Blood concentration-time profiles of POS tablet administered alone or in combination with concomitant medications for 480 mg dose
• Figure 3. Individual ratios, GMR (POS tablet + ranitidine/POS tablet) and 90% CI of AUC0–last and Cmax for 400 mg dose of POS tablet administered alone or in combination with concomitant medications
• Figure 4. Individual ratios, GMR (POS tablet + esomeprazole/POS tablet) and 90% CI of AUC0–last and Cmax for 400 mg dose of POS tablet administered alone or in combination with concomitant medications
• Figure 5. Individual ratios, GMR (POS tablet + metoclopramide/POS tablet) and 90% CI of AUC0–last and Cmax for 400 mg dose of POS tablet administered alone or in combination with concomitant medications
• Table 2. POS tablet PK parameters for 400 mg dose

REFERENCES