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

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ABSTRACT

BACKGROUND: Posaconazole (POS) oral suspension is an extended-spectrum triazole that should be taken with food to enhance exposure. In healthy subjects, POS tablets are administered twice daily (QD) without food. However, in patients at risk for invasive fungal infection, POS tablets are administered with a high-fat meal approximately 4 hours post dose on day 1. In patients, POS exposure, Tmax, and t½ were similar when administered alone or with medications affecting gastric pH and motility.

OBJECTIVES: To evaluate the effect of concomitant medications altering gastric pH and motility on the pharmacokinetics of POS tablets (400 mg) in healthy volunteers.

METHODS: This was a prospective, open-label, 5-way crossover study in 20 healthy volunteers. In each treatment period, a single 400-mg (100 mg x 4) dose of POS tablets was administered alone or with medications affecting gastric pH and motility. Subjects received all 5 treatments in a randomly assigned order according to a predefined treatment schedule with a washout period between treatments.

RESULTS: POS tablets administered alone or with medications affecting gastric pH and motility had no effect on exposure, Tmax, or t½ of POS. Geometric mean ratios (GMRs) of AUC0–last and Cmax were within 0.80 to 1.25 across all treatment sequences and were similar to the reference treatment (POS alone).

SUMMARY AND CONCLUSIONS: POS tablets are administered with a high-fat meal on day 1 only. In patients, POS exposure, Tmax, and t½ were similar when administered alone or with medications affecting gastric pH and motility. Geometric mean ratios of AUC0–last and Cmax of POS tablets administered alone or with medications affecting gastric pH and motility were within 0.80 to 1.25 across all treatment sequences and were similar to the reference treatment (POS alone). The PK of a single 400-mg dose of POS tablet is similar when the drug is administered alone or with medications affecting gastric pH and motility.