rizatriptan is approximately 30% higher in females than in males. No accumulation occurred on multiple dosing.

Following a single dose of 10mg RizaFilm, the mean C_{max} and AUC_{inf} of rizatriptan were 23.79 (± 8.36) ng/mL and 84.54 (± 18.65) ng·hr/mL, respectively; the maximum peak plasma concentrations were achieved in 1.4 hours.

Distribution

The mean volume of distribution is approximately 140 liters in male subjects and 110 liters in female subjects. Rizatriptan is minimally bound (14%) to plasma proteins.

Metabolism

The primary route of rizatriptan metabolism is via oxidative deamination by monoamine oxidase-A (MAO-A) to the indole acetic acid metabolite, which is not active at the 5-$HT_{1B/1D}$ receptor. N-monodesmethyl-rizatriptan, a metabolite with activity similar to that of parent compound at the 5-$HT_{1B/1D}$ receptor, is formed to a minor degree. Plasma concentrations of N-monodesmethyl-rizatriptan are approximately 14% of those of parent compound, and it is eliminated at a similar rate. Other minor metabolites, the N-oxide, the 6-hydroxy compound, and the sulfate conjugate of the 6-hydroxy metabolite are not active at the 5-$HT_{1B/1D}$ receptor.

Elimination

The total radioactivity of the administered dose recovered over 120 hours in urine and feces was 82% and 12%, respectively, following a single 10-mg oral administration of ^{14}C-rizatriptan. Following oral administration of ^{14}C-rizatriptan, rizatriptan accounted for about 17% of circulating plasma radioactivity. Approximately 14% of an oral dose is excreted in urine as unchanged rizatriptan while 51% is excreted as indole acetic acid metabolite, indicating substantial first-pass metabolism.

Following administration of RizaFilm, the mean plasma half-life of rizatriptan is 2 hours.

Cytochrome P450 Isoforms

Rizatriptan is not an inhibitor of the activities of human liver cytochrome P450 isoforms 3A4/5, 1A2, 2C9, 2C19, or 2E1; rizatriptan is a competitive inhibitor (Ki =1400 nM) of cytochrome P450 2D6, but only at high, clinically irrelevant concentrations.

Specific Populations

Geriatric: Rizatriptan pharmacokinetics in healthy elderly non-migraineur volunteers (age 65-77 years) were similar to those in younger non-migraineur volunteers (age 18-45 years).

Pediatric: The pharmacokinetics of rizatriptan was determined in pediatric migraineurs 12 to 17 years of age. Exposures following single-dose administration of 10 mg rizatriptan benzoate orally disintegrating tablets to pediatric patients weighing ≥40 kg (88 lbs.) were similar to those observed following single-dose administration of 10 mg rizatriptan benzoate orally disintegrating tablets to adults.

Gender: The mean $AUC_{0-\infty}$ and C_{max} of rizatriptan (10 mg orally) were about 30% and 11% higher in females as compared to males, respectively, while T_{max} occurred at approximately the same time.

Patients with Hepatic Impairment: Following oral administration in patients with hepatic impairment caused by mild to moderate alcoholic cirrhosis of the liver, plasma concentrations of rizatriptan were similar in patients with mild hepatic insufficiency compared to a control group of subjects with normal hepatic function; plasma concentrations of rizatriptan were approximately 30% greater in patients with moderate hepatic insufficiency.

Patients with Renal Impairment: In patients with renal impairment (creatinine clearance 10-60 mL/min/1.73 m^2), the $AUC_{0-\infty}$ of rizatriptan was not significantly different from that in subjects with normal renal function. In hemodialysis patients, (creatinine clearance <2 mL/min/1.73 m^2), however, the AUC for rizatriptan was
approximately 44% greater than that in patients with normal renal function.

Race: Pharmacokinetic data revealed no significant differences between African American and Caucasian subjects.

Drug Interactions

Monoamine Oxidase Inhibitors: In a drug interaction study, when rizatriptan benzoate 10 mg tablets were administered to subjects (n=12) receiving concomitant therapy with the selective, reversible MAO-A