

Dose-proportionality, relative bioavailability, and effects of food on bioavailability of an immediate-release oxycodone HCl tablet designed to discourage tampering

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Purpose

An immediate-release oxycodone HCl product for management of moderate-to-severe pain was developed to deter intranasal and intravenous abuse (IRO-A; OXECTATM). This study evaluated dose-proportionality, food effect on pharmacokinetics of oxycodone from IRO-A, and relative bioavailability vs an immediate-release, commercially available oxycodone HCl tablet (IRO).

Method

An open-label, single-dose, randomized, 5-way crossover study with a ≥ 7 -day washout period between consecutive treatments was conducted in healthy subjects aged 18 to 55 years. Subjects received oral doses of 1x5 mg, 2x5 mg, and 2x7.5 mg IRO-A after an overnight fast, and 2x7.5 mg IRO-A and 1x15 mg IRO following a high-calorie/high-fat breakfast. Subjects received naltrexone 50 mg ~ 12 hours and \sim one hour before dosing to minimize opioid-associated adverse events. Peak plasma oxycodone concentration (C_{max}), time to C_{max} (T_{max}), and area under the concentration-time curve (AUC) from time zero to last quantifiable concentration (AUC_{last}) were determined. The dose-proportionality of oxycodone was assessed on data dose-normalized to 5 mg, using a 90% confidence interval (CI) criterion of 80% to 125%. The 90% CI was also used to assess food interaction.

Results

Of 35 subjects (mean [\pm SD] age 32.6 [± 11.1] years), 33 were included in the pharmacokinetic analysis. Oxycodone exposure (C_{max} , AUC_{last}) increased proportionately to dose between 5-mg and 15-mg IRO-A. Concomitant food intake with IRO-A resulted in a 14% reduction in oxycodone C_{max} (90% CI: 79%-94%), a 21% increase in AUC_{last} (90% CI: 113%-129%), and a delay in T_{max} from 1.25 hours to 3.00 hours. IRO-A and IRO in the fed state had equivalent AUC_{last} (90% CI: 94%-104%), but slightly reduced C_{max} (90% CI: 77%-91%). Adverse events following IRO-A and IRO administration were similar.

Conclusions

Dose-proportionality of oxycodone pharmacokinetics in a fasted state was observed between 5-mg and 15-mg IRO-A. Administration of IRO-A with food resulted in small changes in oxycodone pharmacokinetics that are not expected to be clinically significant. Oxycodone AUC_{last} was equivalent, and C_{max} slightly lower for IRO-A compared with IRO when administered with food. Tolerability of IRO-A and IRO was similar.