Pharmacokinetics and Abuse Potential of Benzhydrocodone, a Novel Prodrug of Hydrocodone, After Intranasal Administration in Drug Users

Introduction

Immediate-release opioids are commonly abused via alternative routes as enticement (β) and intravenous administration (γ). Benzhydrocodone (also known as P200) is a hydrocodone produg designed to deliver novel forms of abuse on a molecular level, rather than through formulation. Benzhydrocodone is the opioid active pharmaceutical ingredient in a novel, immediate-release hydrocodone formulation.

Objective

To compare the pharmacokinetics (PK) and abuse potential of benzhydrocodone to those of hydrocodone bitartrate (HB) following its administration to non-dependent, recreational opioid users.

Methods

This was a randomized, double-blind, two-way crossover study.

Study Participants:
Study participants included experienced opioid users, male or female, 18 to 55 years of age, inclusive, who were not currently physically dependent on opioids.

Qualification Phases:
Each part of the study began with an in-clinic Qualification Phase consisting of a NAS (narcotic addiction score) test to confirm the absence of opioid physical dependence.

In contrast to most human abuse potential studies, there was no drug washout period before infusion. In these analyses, participants died more likely to demonstrate differences in Drug Liking between the two treatments.

Study Design:
Following the nasoal result and a washout period of at least 12 hours, subjects were randomized to one of two treatment sequences: (1) IN benzhydrocodone followed by IN HB (PK Population, N=24) or (2) IN HB followed by IN benzhydrocodone (PK Population, N=24).

Pharmacokinetic Analyses:
The primary objective of the study was to compare the rate and extent of hydrocodone absorption from benzhydrocodone and HB.

For each treatment, plasma hydrocodone concentration was assessed in blood collected pretreatment and at 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, and 8 hours post dose.

Descriptive statistics were calculated for parameters including peak hydrocodone plasma concentration (Cmax), area under the plasma hydrocodone concentration-time curve (AUCinf) and terminal half-life (t1/2). Ratios between LSMeans (%)

Conclusions

• In recreational opioid abusers, benzhydrocodone produced a substantially lower peak and cumulative hydrocodone exposure compared with HB.

• Drug Liking mirrored the PK findings: lower and earlier peak Drug Liking during benzhydrocodone administration than with lower Drug Liking early in the time course and with a lower Drug Liking recovery.

• There were differences in Drug Liking were observed despite lack of a Discrimination Test typically included to enrich the population with subjects that can differentiate active drug from placebo.

• Benzhydrocodone was more difficult to insufflate than HB.

• The findings suggest that the produg benzhydrocodone may provide a deterrent to intranasal abuse.

References


Disclosures

Thara McBe and LeAnn Guettler are employees of KemPharm, Inc. Kathryn Rhooper and Lynn Webster have received consulting fees, honorarium, and/or travel fees from Astramchon, Cephalon, Teva, and Shionogi. Travis Mickle has received consulting fees, honorarium, and/or travel fees from Travus Mickle, Trevena, Scilex, and Shionogi. Sven Guenther is an employee of KemPharm, Inc. Kathryn Rhooper has received consulting fees, honorarium, and/or travel fees from Astramchon, Cephalon, Teva, and Shionogi.

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