

A Novel Extended-Release Formulation of Oxycodone/Acetaminophen with Abuse Deterrent Properties

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Purpose

A significant problem with the use of opioids is the increasing rate of unintentional deaths due to overdose from misuse or abuse of these products. An extended-release formulation of oxycodone/acetaminophen (DDS-08B) has been developed in an attempt to minimize misuse potential. This novel twice-daily formulation is designed to be less easily defeated than other extended-release opioid products (e.g., less susceptible to dose dumping if the tablet is bisected, crushed, or chewed, or following co-ingestion with alcohol).

Method

A clinical study was performed in 24 healthy volunteers to evaluate the pharmacokinetic profile, safety, and tolerability of intact and crushed orally administered DDS 08B extended-release tablets. The proposed 20 mg oxycodone hydrochloride (HCl) /650 mg acetaminophen extended-release formulation was compared to the approved immediate-release (IR) reference product, Percocet[®] 10 mg oxycodone HCl/325 mg acetaminophen tablet (Endo Pharmaceuticals) taken orally. The test product was administered as a single dose and the reference product was administered twice, 6 hours apart. For pharmacokinetic evaluations, blood samples were collected over 36 hours following dosing. Plasma concentrations of oxycodone and acetaminophen were determined using a validated HPLC with MS/MS detection method.

Results

DDS 08B intact followed the expected temporal pattern characteristic for extended-release products with a gradual increase in mean plasma concentrations. Peak concentrations for oxycodone occurred at approximately 6 hours post dose, and peak concentrations for acetaminophen occurred at approximately 4 hours post dose. Oral administration of DDS-08B crushed showed a more rapid rise to mean plasma concentrations of oxycodone and acetaminophen. The pharmacokinetic profile of crushed DDS-08B differed from both Percocet[®] and DDS-08B intact, suggesting that the formulation was modified by crushing but still retained some of its extended-release properties.

A single dose administration of DDS 08B intact was shown to have equivalent systemic exposure (AUCs) of oxycodone and acetaminophen to a single dose administration of DDS-08B crushed and to two doses of Percocet[®] administered 6 hours apart. However, consistent with its extended-release properties, C_{max} of DDS 08B intact was lower than DDS-08B crushed and than Percocet[®] for both oxycodone and acetaminophen.

A single dose administration of DDS 08B crushed was shown to have equivalent systemic exposure (AUCs) of oxycodone and acetaminophen to two doses of Percocet[®] administered 6 hours apart. Moreover, oxycodone C_{max} of DDS-08B crushed was also equivalent to Percocet[®], indicating that crushing of DDS-08B tablets does not result in massive dose-dumping of oxycodone.

Conclusions

A novel twice-daily extended-release formulation of oxycodone/acetaminophen has been developed and was shown to have equivalent systemic exposure, with respect to AUCs, to two doses of Percocet[®]

administered 6 hours apart. DDS-08B tablets also demonstrated to retain some of their extended-release properties when crushed, indicating that crushing of the tablets does not result in massive dose-dumping.