

2002 Fall A36

EN3231, AN NMDA-ENHANCED ANALGESIC, PROVIDES EFFECTIVE ANALGESIA, IS OPIOID-SPARING, AND DOES NOT INCREASE THE INCIDENCE OF ADVERSE EVENTS IN ARTHRITIS PATIENTS

Schlagheck, T.; Galer, B.; Gammaitoni, A.; Nagle, B.; Caruso, F.

1. Endo Pharmaceuticals Inc., Chadds Ford, PA

The objective of this study was to compare the efficacy and safety of treatment with EN3231 [a 1:1 (mg:mg) combination of morphine sulfate and dextromethorphan] to morphine sulfate (MS) alone, each administered orally every 4-8 hours, in patients with pain due to arthritis.

A multicenter, randomized, double-blind, 2-way crossover study was conducted with 77 patients suffering chronic pain who required treatment with at least 60 mg/day oral morphine (MS). Patients were initially entered into an open-label run-in period where MS was titrated to achieve satisfactory pain relief. Patients were then blindly randomized to EN3231 (15mg:15mg tablets) or MS (30mg tablets) for the first 2-week treatment period and dosages were self-titrated to maintain satisfactory pain relief. After the first treatment period, patients were crossed over to receive the alternate treatment for 2 weeks and again instructed to self-titrate to maintain satisfactory pain relief. The primary outcome measure was the mean daily opioid dose of the 2 drugs. Adverse events (AEs) were assessed throughout the study.

From this trial of patients with a variety of nonmalignant pain, a subgroup analysis was performed on 9 patients with pain due to arthritis. The mean daily opioid dose in this cohort was significantly lower in the EN3231 treatment group compared to the MS group with means of 75.1 mg and 153.5 mg, respectively ($p < 0.001$). As expected, mean daily pain scores were similar between treatment groups with means of 1.89 and 1.92, respectively, using a 0-3 categorical scale. Common opioid-related AEs were noted for both treatment groups. No increase in any side effects was noted with the combination therapy.

In conclusion, the addition of the NMDA-receptor antagonist, dextromethorphan, to MS in a 1:1 ratio (EN3231) resulted in equianalgesia at one-half the MS dose compared to MS alone ($p < 0.001$) in arthritis patients. No difference in incidence of AEs was noted between the 2 treatments. EN3231, an NMDA-enhanced analgesic, provides effective pain relief to arthritis patients at a significantly lower MS dose and with an acceptable safety profile.

EN3231-013 Clinical Study Report