Study Number: EN3225-001

Title of Study: Open-Label Pilot Study Assessing the Efficacy and Safety of New Formulations of Percocet® in the Treatment of Low Back Pain

Investigators: 4 investigators

Study Center(s): 4 centers in the United States

Publications (reference): None

Studied period (years): 22 October 2001 to 14 March 2002 | **Phase of development**: Phase 4

Objectives:

Primary: To demonstrate the analgesic effectiveness and safety of Percocet® in low back pain (LBP) patients who are sub-optimally responsive to non-steroidal anti-inflammatory drugs (NSAIDs), muscle relaxants, tramadol, and/or cyclo-oxygenase-2 (COX_2) drugs.

Secondary: To evaluate the mean daily dose and daily dose range of Percocet® reported by LBP patients as providing clinically-meaningful pain relief; to assess the change in pain interference with quality of life (QOL) from Baseline to Week 4; to assess the changes in the intensities of different pain qualities as measured by the Neuropathy Pain Scale (NPS); and to assess the change in functionality from Baseline to Week 4 using the Lumbar Spine Questionnaire.

Methodology: Prospective, open-label, non-randomized, multicenter, pilot study to determine the effectiveness and safety of Percocet® in the management of LBP.

Number of Subjects (Planned and Analyzed):

Planned: 25	Analyzed for Effectiveness (intent-to-treat [ITT] population): 33
Enrolled and Treated: 33	Analyzed for Safety (all treated patients population): 33
Completed: 28	

Diagnosis and Main Criteria for Inclusion: Males and females with moderate to severe chronic LBP who have been sub-optimally responsive to NSAIDs, muscle relaxants, tramadol and/or COX_2 inhibitors due to poor pain relief and/or intolerable side effects. Patients may not currently be taking or have in the past taken time-contingent opioids 'around-the-clock' for more than 2 weeks; patients may currently or in the past have taken 'PRN' opioids.

Test Product, Dose and Mode of Administration, Batch Number(s): Percocet® administered at an initial dose of 2.5 mg oxycodone/325 mg acetaminophen three times a day (t.i.d.) and titrated until clinically meaningful pain relief was obtained (i.e., an average daily pain intensity rating of ≤4/10). Tablets for oral administration contained 2.5 mg oxycodone/325 mg acetaminophen (Lot SD426A), 5 mg oxycodone/325 mg acetaminophen (Lot EPE129A), 7.5 mg oxycodone/325 mg acetaminophen (Lot RO049B), or 10 mg oxycodone/325 mg acetaminophen (Lot RO050B).

Duration of Treatment: 4 weeks

Reference Therapy, Dose and Mode of Administration, Batch Number(s): Not applicable

Criteria for Evaluation:

- Change in average daily pain intensity from Baseline to Week 4 using the Brief Pain Inventory (BPI)
- Pain interference with QOL measures using the BPI, both individual domains and sum score
- Changes in the intensities of different neuropathic pain qualities NPS

- Functional disability assessed using the North American Spine Society (NASS) Lumbar Spine Questionnaire
- Sleep quality using the NASS Lumbar Spine Questionnaire
- Pain duration and frequency
- Incidence of adverse events (AEs) and discontinuations due to AEs, laboratory tests, vital signs, and physical examinations

Statistical Methods: All effectiveness analyses were based on the ITT population, and all safety analyses included all treated patients. The primary effectiveness endpoint was the change in average daily pain intensity between Baseline and Week 4 as assessed with Question 5 of the BPI. A paired t-test was used for the analysis. The secondary pain parameters were analyzed in the same way as the average daily pain intensity. Summary tables and data listings were provided for all effectiveness parameters. The number and percent of patients experiencing at least 1 AE were summarized as overall, by body system, and by preferred term as well as by relationship to study medication and severity. Serious adverse events (SAEs) and discontinuations due to AEs were summarized separately. Results and changes from baseline were summarized for laboratory tests and vital signs by treatment group and study visit and for physical examinations by treatment group and body system.

SUMMARY:

Effectiveness Results:

There was a statistically significant decrease in average daily pain intensity from Baseline to Week 2 and Baseline to Week 4 as assessed by Question 5 of the BPI. The decrease in pain was greater at Week 4 than at Week 2.

Statistically significant improvements were seen for most variables between Baseline and Week 2 and Baseline and Week 4 in the secondary endpoints including:

- All BPI pain interference variables, except relations with people at Week 2
- NPS scores for sharp, unpleasant, and deep pain both at Week 2 and at Week 4, and intense and surface pain scores at Week 4
- All NASS Lumbar Spine Questionnaire Neurologic Symptoms Scale variables except for the bothersome rating for numbness and tingling in the leg and/or foot at Week 2
- All NASS Lumbar Spine Questionnaire Pain/Disability Scale variables (including sleep quality) except lifting, sitting, standing, travel, and sex life at Week 2 and all variables except travel at Week 4.

Most patients experienced pain every day during the past week both at Week 2 (26/33 patients; 78.8%) and Week 4/end of study (25/33 patients; 75.8%). Patients most frequently indicated that they experienced pain that lasted most of the day or several minutes to an hour both at Week 2 and Week 4/end of study.

Safety Results:

Overall, the mean daily dose for all treated patients was 24.4 mg oxycodone (range: 5-61.33 mg) and 1145.2 mg acetaminophen (range: 529.63-2860 mg).

No deaths or SAEs occurred during the study period. Overall, 20/33 treated patients (60.6%) experienced treatment emergent AEs during the study. The most frequently-reported AEs were those associated with the gastrointestinal disorders (13/33 patients; 39.4%) and nervous system disorders (8/33 patients; 24.2%) body systems. The most frequent individual events were nausea and constipation, both of which were reported in 8/33 (24.2%) patients and are expected side effects that may occur with Percocet®. Four patients discontinued due to AEs. The AEs that most frequently led to discontinuation were associated with Nervous System Disorders (insomnia, paresthesia, and sedation).

Changes from Screening values were generally small and clinically insignificant for all chemistry, hematology, and urinalysis test results, except for segmented neutrophils and white blood cell count (WBC) for which statistically significant increases from Screening were seen at the Week 4/end of the study visit.

No statistically significant or clinically significant changes were seen in any vital signs, and the patients' physical examination results remained generally stable throughout the study.