

Clinical Trial Results Summary
Study EN3220-006

Study Number: EN3220-006	
Title of Study: Open-label Study Assessing the Efficacy of Topical Lidocaine Patch in Treatment of Low Back Pain, EN3220-006.	
Investigators: 6 investigators	
Study Centers: 6 study centers located in the United States	
Publication (reference): none	
Study Period (years): Date of First Enrollment: March 11, 2002 Date of Last Enrollment: October 24, 2002	Phase of Development: Phase IV
Objectives: The primary objective was to assess the effectiveness of Lidoderm [®] administered once daily (q24h) after 2 weeks in the treatment of acute and chronic lower back pain (LBP). The secondary objectives were: to assess the effectiveness of Lidoderm administered q24h after 6 weeks in the treatment of LBP; to assess the safety and tolerability of Lidoderm patches applied q24h; to assess the effect of Lidoderm on Quality of Life (QOL) in patients with LBP; and to assess the pharmacoeconomic impact of Lidoderm when added to a LBP patient's analgesic drug regimen by comparing the average wholesale price (AWP) per day from baseline to the end of the study (6 weeks).	
Methodology: At the screening evaluation (Day -7), patients with moderate to severe LBP were enrolled in the study after providing informed consent and completing all screening evaluations. Thereafter, patients recorded average daily pain intensity in a diary, provided at the screening visit, for 1 week prior to the baseline visit (Day 0). To meet the primary objective, a sufficient number of patients were to be enrolled in the study to ensure that 120 completed at least 2 weeks of treatment. At the time of enrollment, patients were stratified according to the duration of LBP prior to the study: acute (< 6 weeks), subacute (6 weeks to <3 months), short-term chronic (3 months to 12 months, inclusive), and long-term chronic (>12 months). Approximately 30 patients were to be enrolled into each group. During the 6-week treatment period, patients used up to four Lidoderm patches applied q24h. Patients returned to the study site on Days 7, 14, and 28 for study assessments. Site personnel contacted patients by telephone on Days 21 and 35 to assess concomitant medication use, adverse events (AEs), and average daily pain intensity. Beginning at the Day 14 visit (after completion of efficacy assessments), patients began tapering concomitant analgesic medications as instructed by the Investigator. All patients returned to the study site on Day 42 for the end-of-study assessments. Blood samples were collected just prior to patch application on Days 7, 14, and 42 for determination of plasma lidocaine concentrations.	
Number of Subjects Planned and Analyzed: Planned: 120 patients completing at least 2 weeks of treatment; Enrolled: 131 patients (Acute Group: N=21; Short-term Chronic Group: N=33; Long-term Chronic Group: N=77).	
Diagnosis and Main Criteria for Inclusion: Patients were males and females with non-radicular LBP for <3 months (Acute Group), 3-12 months (Short-term Chronic Group), or >1 year (Long-term Chronic Group).	
Test Product, Dose and Mode of Administration, Batch Number(s): Commercially available Lidoderm (lidocaine patch 5%), up to four patches applied topically once daily (q24h) to the area of maximal peripheral pain; Lot number: 1026.	
Duration of Treatment: 6 weeks	

Criteria for Evaluation:

Efficacy: The primary efficacy endpoint was the mean change in average daily pain intensity (Question 5 of Brief Pain Inventory [BPI] Questionnaire) from baseline to Week 2. Secondary efficacy endpoints included 1) mean change from baseline to Week 6 in average pain intensity (Question 5 of the BPI); 2) mean change from baseline to Week 2 and to Week 6 in Neuropathic Pain Scale (NPS) composite scores; 3) QOL: change from baseline to Week 2 and to Week 6 in Question 9 of the BPI, in Beck Depression Inventory questionnaire, and in the Patient and Investigator Global Assessments of Patch Satisfaction and Pain Relief.

Safety: Safety assessments included AEs, clinical laboratory tests, vital signs, physical/neurological examinations, and dermal/sensory assessments.

Statistical Methods: All efficacy and safety analyses were based on the treated population.

Efficacy: This was an uncontrolled, open-label study, and hypothesis testing was not conducted. The results of the BPI, NPS, and QOL measures in the BPI were displayed using appropriate descriptive statistics, and were summarized appropriately by visit. Mean change from baseline, assessed by paired t-tests, was the only formal statistical analysis performed in this study for designated efficacy endpoints.

Safety: The frequency of AEs, new-onset AEs, and treatment-related new-onset AEs was tabulated by MedDRA[®] term and body system. The incidence of AEs was summarized using appropriate descriptive statistics. Serious adverse events (SAEs) and discontinuations due to AEs were summarized. All clinical laboratory measurements were summarized by mean values, changes from baseline, and shift changes. Vital signs, physical examinations, and dermal/sensory assessments were summarized.

SUMMARY:

Efficacy Results: The comparison of mean change in average daily pain intensity from Baseline to Week 2 showed statistically significant decreases (improvements) within each patient group and overall. Mean baseline average daily pain intensity values were similar across patient groups (range: 5.9 to 6.2). Mean changes from baseline at Week 2 ranged from -1.2 (Short-term Chronic Group) to -2.2 (Acute Group). Statistically significant decreases in the comparison of mean change in average daily pain intensity from Baseline to Week 6 (End-of-Study) were observed within each patient group and overall. Mean changes from baseline were slightly more negative (showing greater improvement) in the Week 6 versus the Week 2 comparison to baseline. Statistically significant decreases (improvements) in mean change from Baseline to Week 2 and Week 6 (End-of-Study) in the NPS scores were found within each patient group and overall for the majority of individual items and composite scores. In general, the average change from Baseline to Week 2 and to Week 6 were similar. Overall, the majority of patients and investigators rated pain relief as moderate to complete both at Week 2 (56.9% and 59.6%, respectively) and Week 6 (End-of-Study) (54.4% each). Overall, the majority of patients and investigators were satisfied or very satisfied with Lidoderm both at Week 2 (67.9% and 74.3%, respectively) and Week 6 (End-of-Study) (58.4% and 60.0%, respectively). The majority of the BPI Question 9 sub-items showed statistically significant decreases (improvements) in the mean change from Baseline to Week 2 and Week 6 for each patient group and overall. At Baseline, the mean Beck Depression Inventory score for all groups and overall was less than 10 (normal); this overall rating prevailed throughout the study.

Pharmacokinetic Results: Mean plasma lidocaine concentrations at Week 6 (End-of-Study) (35.5 ± 72.8 ng/mL) were maintained well below those levels associated with cardiac activity (1500 ng/mL) or toxicity (5000 ng/mL).

Safety Results: Overall, 61 (46.5%) of 131 patients reported at least one treatment-emergent adverse event (TEAE); however, less than half of these (25/131, or 19.1%) were considered to be treatment related. The percentages were similar across treatment groups. The most frequently reported AEs by body system were: skin and subcutaneous tissue disorders (15 of 131 patients, or 11.5%), nervous system (18 of 131 patients, or 13.7%); infections and infestations (14 of 131 patients, or 10.7%), general

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disorders and administrative site conditions (12 of 131 patients; 9.2%), and gastrointestinal disorders (14 of 131 patients, or 10.7%). No deaths occurred in this study. One unrelated serious AE (concussion) was reported. Eighteen (13.7%) of the 131 patients discontinued due to an AE. No trends or clinically important changes in laboratory tests, vital signs, or physical/neurological examinations were observed over the course of the study. The majority of patients had no erythema, edema, papules, and/or vesicles at Baseline and throughout the study. The majority of patients had no changes in sensory assessments throughout the study.