PriCara
Unit of Ortho-McNeil, Inc.

PriCara, Unit of Ortho-McNeil, Inc.

Clinical Study Synoptic Report

A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of ULTRACET® (Tramadol HCl/Acetaminophen) for the Treatment of Acute Low Back Pain

Protocol CAPSS-341; Phase IV

RWJ-26898/RWJ 03465

PRINCIPAL INVESTIGATOR:
Multicenter Study

DATE STUDY INITIATED:
29 March 2005

DATE STUDY COMPLETED:
13 May 2005

Issue/Report Date:	March 3, 2006
Department:	Clinical Affairs
Document No.:	EDMS-USRA-9767633:2.0

Compliance: The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

SYNOPSIS

NAME OF SPONSOR/COMPANY: PriCara, Unit of Ortho-McNeil, Inc. **NAME OF FINISHED PRODUCT:** ULTRACET® **NAME OF ACTIVE INGREDIENT(S):** Tramadol HCl/Acetaminophen	**INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(FOR NATIONAL AUTHORITY USE ONLY)**

Protocol No.: CAPSS-341

Title of Study: A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of ULTRACET® (Tramadol HCl/Acetaminophen) for the Treatment of Acute Low Back Pain

Investigator: Multicenter Study

Publication (Reference): None

Study Initiation/Date of Termination: The study was initiated on 29 March 2005 and was completed on 13 May 2005. The study was discontinued due to an administrative business decision.	**Phase of development:** IV

Objectives: The objective of the study was to compare the efficacy and safety of ULTRACET® (tramadol HCl/acetaminophen) versus placebo for the treatment of acute low back pain.

Methodology: This was a multicenter, randomized, double-blind, placebo-controlled, parallel group study which consisted of two phases: Screening and Double-Blind. During the Screening Phase, subjects with symptomatic acute low back pain were identified and evaluated for eligibility. A Brief Pain Inventory (BPI) and the Roland and Morris Disability Questionnaire (RDQ) were completed. Subjects who met the entry criteria for the study entered the Double-Blind Phase and were randomized to treatment with either ULTRACET® or matching placebo for up to 5 days. Subjects were instructed to call an Interactive Voice Response (IVR) system to complete a pain assessment prior to taking the first dose of study medication and every night at bedtime for the remainder of the study. Two tablets of study medication were self-administered by mouth every 4 to 6 hours while awake, as needed for back pain. The use of rescue medication was allowed; however, subjects who took rescue medication were considered discontinued from the study due to lack of efficacy. The Final Visit occurred on Day 6 (± 1 day) and subjects were asked to complete the BPI, RDQ and the Subject Global Impression of Change (SGIC). Other Final Visit procedures included a physical examination and vital signs as well as review of adverse events and concomitant medications. Subjects who discontinued from the study prior to Day 6 were asked to complete the BPI, RDQ and SGIC at the time of discontinuation and return on Day 6 for the remaining procedures. A Follow-Up Telephone Contact was completed by the study staff approximately 2 weeks after the Final Visit to evaluate the subject's post-study back pain and analgesic use.

Number of Subjects (planned and analyzed): The study was designed to enroll approximately 400 subjects. A total of 39 investigators in the United States were recruited to participate in this study. Ten investigators enrolled 22 subjects before the study was discontinued. This report presents the safety data of the 22 subjects who were enrolled.

Diagnosis and Main Criteria for Inclusion: Male and female subjects 18-65 years of age with symptomatic acute low back pain were enrolled in this study. Acute low back pain was defined as acute lumbar or lumbosacral back pain (with or without radiation no lower than the knee) with a duration between 2 and 10 days. Subjects had to be an appropriate candidate for pain management with an oral analgesic, and at the time of randomization, have an average acute low back pain score in the last 24 hours of ≥5 on an 11-point rating scale where 0=no pain and 10=pain as bad as you can imagine.

Test Product, Dose, and Mode of Administration, Batch No.: Study medication was packaged in child-resistant bottles containing 60 tablets. Subjects randomized to ULTRACET® were to self-administer 2 tablets of study medication (total dose: 75 mg tramadol HCl/650 mg acetaminophen) by mouth every 4 to 6 hours while awake as needed for low back pain, not to exceed 8 tablets per 24 hour period, or their maximum tolerated dose, whichever was less (Batch No. R12990).

SYNOPSIS (CONTINUED)

NAME OF SPONSOR/COMPANY: PriCara, Unit of Ortho-McNeil, Inc. **NAME OF FINISHED PRODUCT:** ULTRACET® **NAME OF ACTIVE INGREDIENT(S):** Tramadol HCl/Acetaminophen	**INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(FOR NATIONAL AUTHORITY USE ONLY)**

Reference Therapy, Dose, and Mode of Administration, Batch No.: Color-matched placebo tablets were identically packaged in child-resistant bottles. Subjects were to self-administer 2 tablets of study medication (placebo) by mouth every 4 to 6 hours while awake as needed for low back pain, not to exceed 8 tablets per 24 hour period, or their maximum tolerated dose, whichever was less (Batch No. R12991).

Duration of Treatment: Subjects were to take study medication for approximately 5 days or until the subject determined there was no further need for pain medication, whichever time point was less.

Criteria for Evaluation:

Safety: Safety evaluations included adverse event reports, physical examination (including a back examination) results and vital signs. In addition, urine pregnancy tests were performed at Screening for all women of child-bearing potential.

Statistical Methods: No efficacy analyses were performed. The safety data presented in this report were based on the 22 subjects who were enrolled in the study (i.e., randomized, received at least one dose of study medication and contributed safety data). The overall incidence of adverse events was determined by treatment group and classified by body system and preferred term.

SAFETY RESULTS: The number and percentage of subjects who experienced adverse events was similar between the two treatment groups: 2 (20.0%) ULTRACET® subjects had adverse events and 2 (16.7%) subjects in the placebo group. A total of 11 adverse events were reported between the 4 subjects. The 2 subjects in the ULTRACET® treatment group experienced adverse events in the central nervous, gastrointestinal and skin body systems (dizziness, vomiting [2 events], nausea, and pruritus) while the 2 placebo subjects experienced adverse events related to general body, gastrointestinal and psychiatric body systems (injury [3 events - skin abrasions and laceration], abdominal pain [2 events] and anxiety). There were no deaths or serious adverse events reported during the study. Two subjects in the ULTRACET® group were withdrawn from the study due to adverse events (dizziness and nausea/vomiting/pruritus).

Table 1: Adverse Events

	No. (%) of Subjects	
	ULTRACET® (N=10)	Placebo (N=12)
One or more adverse events	2 (20.0%)	2 (16.7%)
Deaths	0 (0.0%)	0 (0.0%)
One or more serious adverse events	0 (0.0%)	0 (0.0%)
Withdrawals due to adverse events	2 (20.0%)	0 (0.0%)

No clinically significant changes in vital signs or physical examination findings were observed during the study.

SUMMARY - CONCLUSIONS

CONCLUSION: The study was discontinued due to an administrative business decision. The adverse event profile of ULTRACET® in this study raised no new safety concerns and is consistent with the profile observed in previous clinical trials.

Date of the report: 03 March 2006

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