

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

200533Orig1s000

STATISTICAL REVIEW(S)



U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Science
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

NDA/Serial Number: 200-533

Drug Name: NUCYNTA ER

Indication(s): Management of moderate to severe chronic pain

Applicant: Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

Date(s): Letter date: Nov. 30, 2009
PDUFA date: Oct. 1, 2010

Review Priority: Standard

Biometrics Division: II

Statistical Reviewer: Yan Zhou, Ph.D.

Concurring Reviewers: Dionne Price, Ph.D.
Thomas Permutt, Ph.D.

Medical Division: Division of Anesthesia and Analgesia Products

Clinical Team: Eric Brodsky, M.D.

Project Manager: Dominic Chiapperino, Ph.D.

Keywords: NDA review, Clinical Studies, Missing data imputation

Table of Contents

STATISTICAL REVIEW AND EVALUATION	1
LIST OF TABLES.....	3
LIST OF FIGURES.....	4
1. EXECUTIVE SUMMARY	5
1.1 CONCLUSIONS AND RECOMMENDATIONS	5
1.2 BRIEF OVERVIEW OF CLINICAL STUDIES	5
1.3 STATISTICAL ISSUES AND FINDINGS	6
2. INTRODUCTION	8
2.1 OVERVIEW.....	8
2.2 DATA SOURCES	9
3. STATISTICAL EVALUATION	9
3.1 EVALUATION OF EFFICACY	9
3.1.1 <i>Study PAI-3011/KF23</i>	9
3.1.2 <i>Study PAI-3008/KF11</i>	13
3.1.3 <i>Study PAI-3015/KF36</i>	15
3.2 EVALUATION OF SAFETY	19
4. FINDINGS IN SPECIAL/SUBGROUP POPULATIONS	19
4.1 GENDER, RACE AND AGE	19
4.2 OTHER SPECIAL/SUBGROUP POPULATIONS	20
5. SUMMARY AND CONCLUSIONS	22
5.1 STATISTICAL ISSUES AND COLLECTIVE EVIDENCE	22
5.1.1 STATISTICAL ISSUES.....	22
5.1.2 COLLECTIVE EVIDENCE.....	23
5.2 CONCLUSIONS AND RECOMMENDATIONS	23
APPENDICES.....	30
SUMMARY OF DEMOGRAPHICS AND BASELINE CHARACTERISTICS.....	31
SIGNATURE/DISTRIBUTION LIST	34

LIST OF TABLES

Table 1: Subjects' Disposition of PAI-3011/KF23.....	10
Table 2: Primary Efficacy Results (Study PAI 3011/KF23).....	12
Table 3: Subjects' Disposition of PAI-3008/KF11.....	14
Table 4: Primary Efficacy Results (Study PAI 3008/KF11).....	14
Table 5: Subjects' Disposition of PAI-3015/KF36.....	16
Table 6: Primary Efficacy Results (Study PAI 3015/KF36).....	17
Table 7: Primary Efficacy Results by Subgroup (Study PAI-3011/KF23).....	19
Table 8: Primary Efficacy Results by Subgroup (Study PAI-3015/KF36).....	20
Table 9: Efficacy Results by Country (Study PAI-3011/KF23).....	21
Table 10: Efficacy Results by prior opioid use and baseline pain intensity (Study PAI-3011/KF23).....	21
Table 11: Efficacy Results by country, prior opioid use and baseline pain intensity (Study PAI-3015/KF36).....	22

LIST OF FIGURES

Figure 1: Percent Improvement in Pain from Baseline at Week 12 of the Maintenance Period (Study PAI-3011/KF23).....	12
Figure 2: Percent Improvement in Pain from Baseline at Week 12 of the Maintenance Period (Study PAI-3008/KF11).....	15
Figure 3: Percent Improvement in Pain from Baseline at Week 12 of the Maintenance Period (Study PAI-3015/KF36) including 21 subjects who didn't meet the randomization criterion.....	18
Figure 4: Percent Improvement in Pain from Baseline at Week 12 of the Maintenance Period (Study PAI-3015/KF36) excluding 21 subjects who didn't meet the randomization criterion.....	18

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.