

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**200533Orig1s000**

**PROPRIETARY NAME REVIEW(S)**

**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Surveillance and Epidemiology  
Office of Medication Error Prevention and Risk Management**

**Proprietary Name Review--Final**

Date: August 1, 2011

Reviewer(s): Jibril Abdus-Samad, PharmD, Safety Evaluator  
Division of Medication Error Prevention and Analysis (DMEPA)

Team Leader: Todd Bridges, RPh, Team Leader  
Division of Medication Error Prevention and Analysis (DMEPA)

Division Director: Carol Holquist, RPh, Director  
Division of Medication Error Prevention and Analysis (DMEPA)

Drug Name(s): Nucynta ER (Tapentadol) Extended-release Tablets  
50 mg, 100 mg, 150 mg, 200 mg, and 250 mg

Application Type/Number: NDA 200533

Applicant/sponsor: Ortho-McNeil-Janssen Pharmaceuticals, Inc.

OSE RCM #: 2011-926

\*\*\* This document contains proprietary and confidential information that should not be released to the public.\*\*\*

## CONTENTS

1	INTRODUCTION .....	3
2	METHODS AND DISCUSSION.....	3
3	CONCLUSIONS .....	3
4	REFERENCES .....	4

## 1 INTRODUCTION

This re-assessment of the proposed proprietary name, Nucynta ER is in response to the anticipated approval of this NDA 200533 within 90 days from the date of this review. DMEPA found the proposed name, *Nucynta ER*, acceptable in OSE Review 2009-2412 dated March 9, 2010.

## 2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review 2009-2412. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. The searches of the databases yielded five new names (Arcapta Neohaler, (b) (4) \*\*, Nuedexta, Prezista, and Twynsta), thought to look similar to *Nucynta ER* and represent a potential source of drug name confusion.

DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA)<sup>1</sup> of the proposed proprietary name, and focuses on the avoidance of medication errors. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with any of the five identified names and lead to medication errors. This analysis determined that the name similarity between Nucynta ER and the five identified names was unlikely to result in medication error for the reasons presented in Appendix A.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of July 8, 2011.

DDMAC reviewed the proposed name on June 9, 2011 and had no concerns regarding the proposed name from a promotional perspective.

## 3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Nucynta ER, did not identify any vulnerabilities that would result in medication errors with the additional names noted in this review. Thus, DMEPA has no objection to the proprietary name, *Nucynta ER*, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA 200533 is delayed beyond 90 days from the date of this review, the Division of Anesthesia, Analgesia and Addiction Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

If you have further questions or need clarifications, please contact Danyal Chaudhry, OSE project manager, at 301-796-3813.

---

\*\*\* This document contains proprietary and confidential information that should not be released to the public.

<sup>1</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

## 4 REFERENCES

### 1. OSE Review

Abdus-Samad, J. OSE Review # 2009-2412: Proprietary Name Review for Nucynta ER. March 9, 2010

### 2. *Drugs@FDA* (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

### 3. *USAN Stems* (<http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page>)

USAN Stems List contains all the recognized USAN stems.

### 4. *Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request*

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

**Appendix A:** FMEA Table

Product name with potential for confusion	Similarity to Nucynta ER	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
Nucynta ER (Tapentadol)		50 mg, 100 mg, 150 mg, 200 mg, 250 mg, Tablets, Extended-release	Take 1 tablet orally twice daily	<p><b>Dose: 1 tablets</b></p> <p><b>Dosage Form: tablet</b></p> <p><b>Route of Administration: oral</b></p> <p><b>Frequency of Administration: twice daily</b></p>
Arcapta Neohaler (Indacaterol)	Look	75 mcg per capsule, inhalation powder	Inhale 1 capsule (75 mcg) orally using the Neohaler once a day.	<p>Orthographic Differences: The modifiers, <i>Neohaler</i> and <i>ER</i>, will have to be omitted on a prescription for confusion to occur.</p> <p>Dose: 75 mcg vs. 50 mg, 100 mg, 150 mg, 200 mg, and 250 mg</p> <p>Frequency of Administration: once daily vs. twice daily</p> <p>Medication orders for Arcapta may include words such as <i>Inhale</i> and <i>puff</i>.</p>
(b) (4)				

\*\*\* This document contains proprietary and confidential information that should not be released to the public.

Product name with potential for confusion	Similarity to Nucynta ER	Strength, Dosage Form	Usual Dose	Differing product characteristics that minimize the risk of medication error
<b>Nucynta ER (Tapentadol)</b>		<b>50 mg, 100 mg, 150 mg, 200 mg, 250 mg, Tablets, Extended-release</b>	<b>Take 1 tablet orally twice daily</b>	<b>Dose: 1 tablets</b> <b>Dosage Form: tablet</b> <b>Route of Administration: oral</b> <b>Frequency of Administration: twice daily</b>
Nuedexta (Dextromethorphan Hydrobromide and Quinidine Sulfate)	Look	20 mg/10 mg	Take 1 capsule daily for 7 days, then 1 capsule twice daily	Orthographic Differences: Nuedexta contains an additional upstroke letter 'd' in the middle of the name and an additional crosstroke letter 'x'. Nucynta ER contains a downstroke letter 'y' and the letters 'ER' at the end.  Dose: 20 mg/10 mg vs. 50 mg, 100 mg, 150 mg, 200 mg, and 250 mg  No AERS reports of confusion between Nuedexta and approved Nucynta.
Prezista (Darunavir Ethanolate)	Look	75 mg, 150 mg, 400 mg, 600 mg tablets	Adults Treatment-naive: Take 800 mg (2 tablets) once daily with Ritonavir and food.  Treatment-experienced: 800 mg (2 tablets) once daily with Ritonavir and food or 600 mg twice daily with Ritonavir twice daily  Children 6 to 18 years old: Take 375 mg to 600 mg orally twice daily with Ritonavir twice daily with food	Orthographic differences: The initial letters ('P' vs. 'N') are orthographically different. Additionally, Nucynta ER contains the letters 'ER' at the end.  No AERS reports of confusion between Prezista and approved Nucynta.
Twynsta (Telmisartan and Amlodipine)	Look	40 mg/5 mg, 40 mg/10 mg, 80 mg/5 mg, 80 mg/10 mg tablets	Take 1 tablet orally once daily	Orthographic Differences: The initial letters ('T' vs. 'N') are orthographically different. Additionally, Nucynta ER contains the letters 'ER' at the end.  Dose: 40 mg/5 mg, 40 mg/10 mg, 80 mg/5 mg, 80 mg/10 mg vs. 50 mg, 100 mg, 150 mg, 200 mg, and 250 mg  Frequency of Administration: once daily vs. twice daily.  No AERS reports of confusion between Twynsta and approved Nucynta.

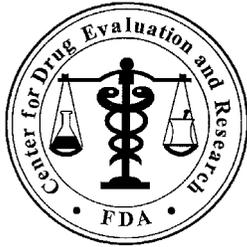
-----  
**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
-----

/s/  
-----

JIBRIL ABDUS-SAMAD  
08/01/2011

TODD D BRIDGES  
08/01/2011

CAROL A HOLQUIST  
08/01/2011



**Department of Health and Human Services**  
**Public Health Service**  
**Food and Drug Administration**  
**Center for Drug Evaluation and Research**  
**Office of Surveillance and Epidemiology**

Date: March 9, 2010

To: Bob Rappaport, MD  
Director, Division of Anesthesia, Analgesia, and Rheumatology  
Products (DAARP)

Through: Todd Bridges, RPh, Team Leader  
Kellie Taylor, PharmD, MPH, Associate Director  
Denise Toyer, PharmD, Deputy Director  
Carol Holquist, RPh, Director  
Division of Medication Error Prevention and Analysis (DMEPA)

From: Jibril Abdus-Samad, PharmD, Safety Evaluator  
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Nucynta ER (Tapentadol) Extended-release Tablets  
50 mg, 100 mg, 150 mg, 200 mg, and 250 mg

Application Type/Number: NDA# 200533

Applicant: Ortho-McNeil-Janssen Pharmaceuticals, Inc.

OSE RCM #: 2009-2412

**\*\*\* This document contains proprietary and confidential information that should not be released to the public.\*\*\***

## CONTENTS

EXECUTIVE SUMMARY .....	3
1 BACKGROUND .....	3
1.1 Introduction.....	3
1.2 Regulatory History.....	3
1.3 Product Information .....	3
2 METHODS AND MATERIALS.....	4
2.1 Search Criteria.....	4
2.2 FDA Adverse Event Reporting System (AERS) .....	5
2.3 FDA Prescription Analysis Studies.....	5
3 RESULTS .....	6
3.1 Database and Information Sources.....	6
3.2 Expert Panel Discussion.....	6
3.3 FDA Adverse Event Reporting System (AERS) Database.....	6
3.4 FDA Prescription Analysis Studies.....	6
3.5 Comments from the Division of Anesthesia, Analgesia, and Rheumatology Products (DAARP).....	7
3.6 Safety Evaluator Risk Assessment of Proposed Proprietary Name .....	7
4 DISCUSSION.....	7
4.1 Promotional Review.....	7
4.2 Safety Review .....	7
5 CONCLUSIONS AND RECOMMENDATIONS .....	9
5.1 Comments to the Applicant.....	10
6 REFERENCES .....	11
APPENDICES .....	12

## **EXECUTIVE SUMMARY**

Our analysis of the proposed proprietary name Nucynta ER indicates that confusion can occur between Nucynta and Nucynta ER. Although this finding would lead to DMEPA objecting to the proposed name, our FMEA determined the use of an alternate proprietary name can lead to concomitant therapy with Nucynta and the alternate name. The Applicant's proposal to add a modifier to the Nucynta root name is a recognized naming convention commonly used when an extended-release dosage form is added to a product line with an existing immediate-release product. Therefore, we will not object to the use of the name, Nucynta ER, for this product. However, we recommend at the time of product launch the Applicant inform healthcare practitioners about the differences between Nucynta ER and the currently marketed Nucynta product. Further enhancements to the labels and labeling will also minimize the confusion between Nucynta and Nucynta ER.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

## **1 BACKGROUND**

### **1.1 INTRODUCTION**

This review is in response to a request from Ortho-McNeil-Janssen Pharmaceuticals, Inc., dated December 11, 2009, for an assessment of the proposed proprietary name, Nucynta ER, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. Additionally, the Applicant submitted draft container labels, carton and insert labeling. The labels and labeling will be reviewed separately under OSE Review #2009-2413.

### **1.2 REGULATORY HISTORY**

Nucynta (Tapentadol Hydrochloride) is currently marketed in the United States. Nucynta tablets were approved by FDA on November 20, 2008, under NDA 022304. For this application, the Applicant is proposing an extended-release formulation of tapentadol to be marketed under the proprietary name, Nucynta ER.

### **1.3 PRODUCT INFORMATION**

Nucynta ER has a proposed indication of use for the management of moderate to severe chronic pain in patients 18 years of age or older when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. The recommended daily dose is 100 mg to 250 mg twice daily, taken approximately every 12 hours, with or without food. Patients currently not taking opioid analgesics should begin Nucynta ER therapy with 50 mg twice a day (approximately every 12 hours) and then be individually titrated to adjust to an optimal dose within the therapeutic range of 100 mg to 250 mg twice daily. Nucynta ER tablets will be available in five strengths: 50 mg, 100 mg, 150 mg, 200 mg, and 250 mg. All five strengths will be marketed in bottles of 60 tablets and unit-dose blister packs of 10 tablets.

Nucynta (Tapentadol Hydrochloride) tablets are approved for the relief of moderate to severe acute pain in patients 18 years of age or older. Nucynta tablets are available in 50 mg, 75 mg, and 100 mg strengths. The recommended dose is 50 mg, 75 mg, or 100 mg every 4 to 6 hours depending upon pain intensity. See Appendix J for the product characteristics of Nucynta and Nucynta ER.

## 2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for reviewing the proposed proprietary name, Nucynta ER.

### 2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter ‘N’ when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.<sup>1,2</sup> With regard to the modifier, the search criteria also took into consideration that the modifier could be misinterpreted as numbers, dosing instructions, or medical abbreviations. Additionally, since omission of a modifier is cited in the literature as a common cause of medication errors<sup>3</sup>, DMEPA considers ‘Nucynta ER’ as a complete name as well as ‘Nucynta’, the root term, omitting the modifying term ‘ER.’

DMEPA staff evaluates the appropriateness of the modifier “ER” for this product in addition to searching commonly used databases (see Section 6) for currently marketed product names that include “ER” and defining the meaning of “ER” for those products.

To identify drug names that may look similar to Nucynta ER, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the root name (9 letters), upstrokes (4, capital letter ‘N’, lower case letter ‘t’, and capital letters ‘ER’), downstrokes (1, lower case letter ‘y’), cross strokes (1, lower case ‘t’), dotted letters (none) and modifiers (ER). Additionally, several letters in Nucynta ER are vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Nucynta ER. DMEPA staff also considers how the exclusion of ‘ER’ may change the appearance of the name.

When searching to identify potential names that may sound similar to Nucynta ER, the DMEPA staff search for names with similar number of syllables (five), stresses (‘NU-cyn-ta E-R’ or ‘nu-CYN-ta E-R’), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (see Appendix B). Furthermore, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered. DMEPA staff also considers how the exclusion of ‘ER’ may change the sound of the name. The Applicant’s intended pronunciation of the proprietary name was not taken into consideration, as this was not provided with the Applicant’s submission.

---

<sup>1</sup> Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

<sup>2</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. *Artificial Intelligence in Medicine* (2005)

<sup>3</sup> Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

## 2.2 FDA ADVERSE EVENT REPORTING SYSTEM (AERS)

Since the root name 'Nucynta' has been marketed since November 20, 2008, DMEPA conducted a search of the FDA Adverse Event Reporting System (AERS) database to determine if there are any medication errors which may be indicative of potential name confusion with Nucynta ER. DMEPA conducted an AERS search on January 7, 2010, for medication errors involving Nucynta or tapentadol hydrochloride.

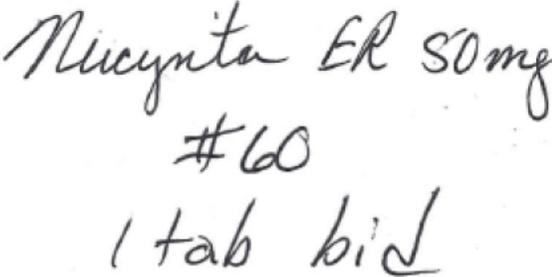
The MedRA High Level Group Terms (HLGT) "Medication Errors" and "Product Quality Issues" were used as search criteria for *Reactions*. The search criteria used for *Products* were active ingredients "tapentadol", trade name "Nucynta" and verbatim substance search "tapen%" and "Nucy %."

The reports were manually reviewed to determine if a medication error occurred. Duplicate reports were combined into cases. The cases that described a medication error were categorized by type of error. We reviewed the cases within each category to identify factors that contributed to the medication errors. If a root cause was associated with name confusion or look and/or sound alike similarity to Nucynta, the case was considered pertinent to this review. Those reports that did not describe a medication error or did not describe an error applicable to this review (e.g. errors related to accidental exposures, intentional overdoses, etc.) were excluded from further analysis.

## 2.3 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies.

**Figure 1. Nucynta ER Study (conducted on December 23, 2009)**

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p><u>Inpatient Medication Order:</u></p> 	<p>Nucynta ER 50 mg Dispense #60 1 tab bid</p>
<p><u>Outpatient Prescription:</u></p> 	

### **3 RESULTS**

#### **3.1 DATABASE AND INFORMATION SOURCES**

The searches yielded a total of 13 names having some similarity to the name Nucynta ER.

Nine names were thought to look like Nucynta ER. These include Indocin SR, Namenda, Natacyn, Nembutal, Neulasta, Neurelan, Niacin ER, Niacin SR, and Ucephan.

One name, Lucentis, was thought to sound like Nucynta ER.

Three names were thought to both look and sound like Nucynta ER. These names are Nucenta, Nucenza, and Nucynta.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of March 9, 2010.

#### **3.2 EXPERT PANEL DISCUSSION**

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1 above) and added an additional name, Namenda XR<sup>\*\*\*</sup>, thought to have orthographic similarity to Nucynta ER.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

#### **3.3 FDA ADVERSE EVENT REPORTING SYSTEM (AERS) DATABASE**

The AERS search conducted on January 7, 2010, yielded 10 cases. All 10 of the following cases were excluded from further evaluation:

- Accidental and intentional overdoses (n=6)
- Incorrect schedule of drug administration (n=2)
- Accidental exposure (n=1)
- Adverse drug reaction (n=1)

These cases were not related to name confusion with Nucynta and will be considered in our review of the product labels and labeling.

#### **3.4 FDA PRESCRIPTION ANALYSIS STUDIES**

A total of 48 practitioners responded in the prescription analysis studies. Twenty (n=20, 42%) of the participants interpreted the name correctly as “Nucynta ER.” The outpatient study had the most correct responses (n=10). The verbal study had the most misinterpretations (n=12). Notable misinterpretations are listed below.

- Substitution of letter ‘N’ with ‘M’ (n=10)
- Substitution of the modifier ‘ER’ with ‘SR’ (n=5)
- Omission of the modifier (n=3)
- Misinterpretation similar to marketed products (n=2)
  - Metoprolol SR, similar to Metoprolol (will be included in Safety Evaluator Risk Assessment)

---

<sup>\*\*\*</sup> This document contains proprietary and confidential information that should not be released to the public.

- Lucenta ER, similar to Lucentis (already identified in database searches)

See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

### **3.5 COMMENTS FROM THE DIVISION OF ANESTHESIA, ANALGESIA, AND RHEUMATOLOGY PRODUCTS (DAARP)**

#### ***3.5.1 Initial Phase of Review***

In a response to the OSE January 15, 2010, e-mail, the Division of Analgesics, Anesthetics and Rheumatology Products (DAARP) did not object to the proposed proprietary name, Nucynta ER.

#### ***3.5.2 Midpoint of Review***

On January 26, 2010, DMEPA notified DAARP via e-mail that we had no objections to the proposed proprietary name Nucynta ER. Per e-mail correspondence from DAARP on March 5, 2010, they indicated that they did not have concerns with the proposed proprietary name, Nucynta ER.

### **3.6 SAFETY EVALUATOR RISK ASSESSMENT OF PROPOSED PROPRIETARY NAME**

Independent searches by the primary Safety Evaluator resulted in the identification of the following five additional names which were thought to look similar to Nucynta ER and represent a potential source of drug name confusion: Hemocyte F, Herceptin, Miraphen PE, Miraphen PSE, and Mucinex DM.

Thus, we evaluated a total of 20 names for their similarity to the proposed name: one identified at the Expert Panel Discussion, one identified in the Prescription Study, five identified by the primary safety evaluator and 13 identified in section 3.1.

The searches also confirmed that the modifier 'ER' is commonly used to identify extended-release formulations (e.g. Opana ER and VoSpire ER)

## **4 DISCUSSION**

### **4.1 PROMOTIONAL REVIEW**

DDMAC found no objection to the proposed name 'Nucynta ER' from a promotional perspective. DAARP and DMEPA concurred with this assessment.

### **4.2 SAFETY REVIEW**

#### ***4.2.1 Look-Alike and Sound-Alike Evaluation***

DAARP had no concerns with the proposed name Nucynta ER. DMEPA identified a total of 20 names that were thought to be similar to the proposed name Nucynta ER.

Ten of the 20 names were not evaluated further for the following reasons: Six of the 20 names lacked convincing orthographic and/or phonetic similarity to the proposed proprietary name Nucynta ER (see Appendix D), four other names did not undergo failure mode and effect analysis (FMEA) because they were either products withdrawn or not marketed in the US, or proposed proprietary names for products later approved under a different proprietary name (see Appendix E).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining ten names and lead to medication errors. This analysis determined that the name similarity between Nucynta ER was unlikely to result in medication errors with nine of the ten products for the reasons presented in Appendices F through I. The remaining name,

Nucynta, is the immediate-release formulation of the proposed product and as such represents a potential source of confusion.

#### 4.2.2 Modifier ‘ER’

Nucynta ER will represent an extension of the tapentadol product line. Currently, the only marketed Nucynta product is an immediate-release tablet available in strengths of 50 mg, 100 mg, (b) (4) that is administered every 4 to 6 hours (see Appendix K). The Applicant proposes to use the modifier ‘ER’ to differentiate the tapentadol extended-release formulation from the currently marketed immediate-release formulation. This naming convention is commonly used for product line extensions to distinguish an extended-release formulation from the immediate-release base brand (see Appendix J). The modifier ‘ER’ is typically used for extended-release products that are administered once or twice daily (see Appendix J). There are also two currently marketed extended-release products with the modifier ‘ER’ (Metadate ER, Methylin ER) that are administered three times daily (these were approved in June 1988 and May 2000). More recently, extended-release products containing the modifier ‘ER’ have been approved for those products that require once or twice daily administration. Based on the variability of the frequency of administration among these products, there does not appear to be a definitive linkage between the extended-release formulation and a specific frequency of administration. Rather, it appears as currently used, ‘ER’ indicates a change in formulation to decrease the frequency of administration compared to an immediate-release product in the same product line (see Appendix J). Currently, we are not aware of any medication error reports that describe wrong frequency errors resulting from misunderstanding of the ER modifier. Additionally, to our knowledge, there have been no reports of orthographic and/or phonetic misinterpretation of the modifier ‘ER’.

We considered whether the modifiers used with extended-release products such as CR, XR, SR, etc. might better communicate both the extended-release formulation and the twice daily administration requirement. However, in our review of some currently marketed products, we did not identify a modifier that is more likely to clearly communicate both meanings since the other modifiers are more often used with other frequencies of administration (i.e. XR is often used for once daily) or, like ‘ER’, the modifiers were associated with a variety of administration frequencies. Therefore, since the proposed product, Nucynta ER, is extended-release and will be dosed less frequently than Nucynta immediate-release tablets, the use of the ‘ER’ modifier is suitable for this product.

However, since healthcare practitioners may not recognize the dosing frequency differences between Nucynta and Nucynta ER based on the inclusion of the ‘ER’ modifier alone, DMEPA recommends that the Applicant alert practitioners and patients on the proper use of these products and clearly communicate the available strengths and dosing frequency for both product formulations. Furthermore, enhancements to the labels and labeling will also help minimize confusion, which will be addressed separately under OSE Review #2009-2413.

Additionally, based on postmarketing experience with other product line extensions where Applicants have used the same proprietary name plus a modifier, we have concern that the naming convention of adding a modifier to the existing name Nucynta could lead to errors<sup>4</sup>. For example, the potential exists for prescribers to omit the modifier when prescribing the product, overlook the modifier, or mistakenly select the wrong product on electronic computer menus when prescribing medicines electronically. Additionally, similar computer selection errors may occur in the pharmacy when dispensing the product if the modifier is overlooked, particularly since the strengths of the immediate and extended-release tapentadol overlap (50 mg and 100 mg). If the modifier ‘ER’ is omitted or overlooked from a medication order of Nucynta ER 50 mg or 100 mg, it is highly probable that the immediate-release Nucynta Tablets will be dispensed since Nucynta has overlapping 50 mg and 100 mg product strengths with Nucynta ER.

---

<sup>4</sup> Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

Thus, patients will receive an immediate-release product with the dosing frequency (i.e. every 12 hours) of the extended-release product, possibly resulting in inadequate pain relief.

Lastly, selection errors may occur if the products are stored side-by-side in pharmacies, but the potential for such errors may be mitigated through well-differentiated container labels and carton labeling. This risk will be considered further in our forthcoming labeling review. With any of these errors involving confusion between the immediate and extended-release tapentadol, the potential exists for patients to be underdosed (immediate-release product dosed twice daily) or overdosed (extended-release formulation dosed every 4 to 6 hours).

In summary, post-marketing experience has shown that the introduction of product line extensions result in medication errors if the modifier is omitted and product characteristics are similar or overlap. Nucynta and Nucynta ER have overlapping product characteristics (see Appendix K). By choosing to develop an extended-release formulation of tapentadol with product strengths that overlap with those of the currently marketed Tapentadol Hydrochloride Immediate-release tablets, the Applicant has eliminated a potentially valuable error-reduction strategy that has been employed in other product line extensions. The Applicant should have chosen product strengths slightly different than available strengths of immediate-release Nucynta Tablets. If the modifier 'ER' is omitted or overlooked, the difference in strength would offer the opportunity for an error to be caught before it reaches the patient, provided it is a dose that could not be achieved with the current product strengths. These concerns were addressed at the Pre-NDA Meeting on June 5, 2007. However, since the Applicant has completed their clinical trials and submitted their new drug application, DMEPA acknowledges it is unlikely that the product strengths will be changed at this time.

#### **4.2.3 Use of an Alternate Name**

To decrease the potential risk of confusion between Nucynta and Nucynta ER, another option to consider is the use of alternate names. However, there are also risks associated with using dual proprietary names. With the use of a new proprietary name for the extended-release tapentadol, there is a risk of concomitant therapy of tapentadol if practitioners and patients fail to recognize that both products contain tapentadol. This could lead to concomitant therapy, thus increasing the likelihood of severe adverse reactions from exceeding the maximum daily dose (e.g., cardiovascular collapse and respiratory arrest).

These findings indicate there may be risk of medication errors in both scenarios, but the risk of harm and likelihood of error may be slightly less than if the product were marketed as Nucynta ER. Therefore, given the precedent for using this naming convention, and that the modifier 'ER' complies with the more recent criteria for acceptability (i.e. frequency of administration is less than Nucynta); Nucynta ER is an acceptable proprietary name for extended-release tapentadol.

Regardless of the proprietary name used, errors still may occur when prescribers order either product using the established name. Because we anticipate that medication errors will occur regardless of the proprietary name used, DMEPA plans to monitor for such errors after approval of Nucynta ER.

## **5 CONCLUSIONS AND RECOMMENDATIONS**

Our analysis of the proposed proprietary name Nucynta ER indicates that confusion can occur between Nucynta and Nucynta ER. Although this finding would lead to DMEPA objecting to the proposed name, our FMEA determined the use of an alternate proprietary name can lead to concomitant therapy with Nucynta and the alternate name. The Applicant's proposal to add a modifier to the Nucynta root name is a recognized naming convention commonly used when an extended-release dosage form is added to a product line with an existing immediate-release product. Therefore, we do not object to the use of the name, Nucynta ER, for this product. However, we recommend at the time of product launch the Applicant inform healthcare practitioners about the differences between Nucynta ER and the currently marketed Nucynta immediate-release tablets, and clearly communicate the available strengths and dosing

frequency for both products. Further enhancements to the labels and labeling will also minimize the confusion between Nucynta and Nucynta ER.

## **5.1 COMMENTS TO THE APPLICANT**

We have completed our review of the proposed proprietary name, Nucynta ER, and have concluded that it is acceptable.

The proprietary name, Nucynta ER, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

We recommend at the time of product launch you inform healthcare practitioners about the differences between Nucynta ER and currently marketed Nucynta product, and clearly communicate the available strengths and dosing frequency for both products.

## 6 REFERENCES

1. ***Micromedex Integrated Index*** (<http://csi.micromedex.com>)

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. ***Drug Facts and Comparisons, online version, St. Louis, MO*** (<http://factsandcomparisons.com>)

Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. ***AMF Decision Support System [DSS]***

DSS is a government database used to track individual submissions and assignments in review divisions.

5. ***Division of Medication Errors Prevention and Analysis proprietary name consultation requests***

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. ***Drugs@FDA*** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved [brand name](#), [generic drugs](#), [therapeutic biological products](#), [prescription](#) and [over-the-counter](#) human drugs and [discontinued drugs](#) and “[Chemical Type 6](#)” approvals.

7. ***Electronic online version of the FDA Orange Book*** (<http://www.fda.gov/cder/ob/default.htm>)

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. ***U.S. Patent and Trademark Office*** (<http://www.uspto.gov>)

USPTO provides information regarding patent and trademarks.

9. ***Clinical Pharmacology Online*** ([www.clinicalpharmacology-ip.com](http://www.clinicalpharmacology-ip.com))

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

**10. Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at ([www.thomson-thomson.com](http://www.thomson-thomson.com))**

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

**11. Natural Medicines Comprehensive Databases ([www.naturaldatabase.com](http://www.naturaldatabase.com))**

Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

**12. Stat!Ref ([www.statref.com](http://www.statref.com))**

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

**13. USAN Stems (<http://www.ama-assn.org/ama/pub/category/4782.html>)**

USAN Stems List contains all the recognized USAN stems.

**14. Red Book Pharmacy's Fundamental Reference**

Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

**15. Lexi-Comp ([www.lexi.com](http://www.lexi.com))**

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

**16. Medical Abbreviations Book**

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

## **APPENDICES**

### **Appendix A:**

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.<sup>5</sup>

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

---

<sup>5</sup> National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>6</sup> DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.<sup>7</sup> DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g. “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

---

<sup>6</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

<sup>7</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

**Table 1.** Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	Considerations when searching the databases		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

## **1. Database and Information Sources**

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

## **2. CDER Expert Panel Discussion**

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

## **3. FDA Prescription Analysis Studies**

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

#### **4. Comments from the OND review Division or Generic drugs**

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

#### **5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name**

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>8</sup> When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

***“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

***“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”***

---

<sup>8</sup> Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are

low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency’s credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants’ have changed a product’s proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners’ vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see Section 4 for limitations of the process).

**Appendix B:** Potential orthographic or phonetic misinterpretation of the letters in the name Nucynta ER

Letters in Name, Nucynta ER	Scripted may appear as	Spoken may be interpreted as
Capital ‘N’	M, H, Z	N, M
lowercase ‘u’	n, a, o, re, y	any vowel
lowercase ‘c’	e, i, r	k, c
lowercase ‘y’	g, u	a, i, e
lowercase ‘n’	m, u, x, r, h, s	m
lowercase ‘t’	f, r, x	
lowercase ‘a’	c, ci, ce, o, u	any vowel
Capital ‘E’	F	any vowel
Capital ‘R’	H, K, P	

**Appendix C: FDA Prescription Study Responses (December 23, 2009)**

<b>Outpatient Prescription</b>	<b>Inpatient Medication Order</b>	<b>Voice Prescription</b>
Nucynta ER	Nucynta SR	Newsenta ER
Nucynta	Nucynta ER	Nucenta ER
Nucynta ER	Nucynta	Nucynta ER
Nucynta Extended Release	Magenta SR	Nusenta ER
Nucynta ER	Macrynta ER	Newcenta ER
Nucynta ER	Mucynta ER	Nucynta ER
Nucynta ER	metoprolol SR	Nucenta ER
Nucynta ER	Nuaprt a ER	Nucynta ER
Mucynta ER	Nucrynta ER	Nucynta ER
Nucynta ER	Mincynta SR	Mucynta ER
Nucynta Extended Release	Magn ta SR	Nucenta ER
Mucynta		Neucenta ER
Mucynta, Extended Release		Nucynta ER
Nucynta ER		Lucenta ER
Nucynta ER		Nucynta ER
Nucynta ER		Nucyenta ER
		Nucynta ER
		Nucynta ER
		Nucynta ER
		Nucenta ER
		Nucenta ER

**Appendix D:** Names lacking significant orthographic or phonetic similarities to Nucynta ER

Proprietary Name	Similarity to Nucynta ER	Source
Indocin SR	Look	EPD
Natacyn	Look	EPD
Nembutal	Look	EPD
Niacin ER	Look	EPD
Niacin SR	Look	EPD
Metoprolol	Look	Rx Study

**Appendix E:** Proprietary name for discontinued product which has no generics available and products approved with a different name

Proprietary Name	Similarity to Nucynta ER	Status
(b) (4)		
Ucephan (Sodium Benzoate and Sodium Phenylacetate)	Look	Product no longer marketed per Drugs @ FDA, Orange Book, and Clinical Pharmacology; not available in Redbook
(b) (4)		

\*\*\* This document contains proprietary and confidential information that should not be released to the public.

**Appendix F:** Products with no overlap in strength

<b>Product name with potential for confusion</b>	<b>Similarity to Proposed Proprietary Name</b>	<b>Strength, dosage form</b>	<b>Usual Dose (if applicable)</b>
<b>Nucynta ER (Tapentadol)</b>		<b>50 mg, 100 mg, 150 mg, 200 mg, 250 mg, Extended-release Tablets</b>	<b>Take 1 tablet orally 2 times daily</b>
Hemocyte F (Ferrous Fumarate, Folic Acid)	Look	324 mg/1 mg tablet	Take 1 tablet orally once daily
Namenda XR*** (Memantine Hydrochloride)	Look	7 mg, 14 mg, 21 mg, 28 mg extended-release capsules	Take 1 tablet orally once daily
Miraphen PE (Guaifenesin and Phenylephrine HCl)	Look	300 mg/20 mg extended-release Tablets	Take 1 tablet orally 2 times daily
Miraphen PSE (Guaifenesin and Pseudoephedrine)	Look	600 mg/120 mg extended-release tablets	Take 1 tablet orally 2 times daily
Mucinex DM (Dextromethorphan Hydrobromide, Guaifenesin)	Look	600 mg/30 mg extended-release tablets	Take 1 tablet orally 2 times daily

---

\*\*\* This document contains proprietary and confidential information that should not be released to the public.

**Appendix G:** Products with numerical overlap or overlapping achievable dose but different product characteristics.

<b>Failure Mode: Name confusion</b>	<b>Causes: (could be multiple)</b>	<b>Rationale why medications errors are unlikely to occur in usual practice setting</b>
<b>Nucynta ER (Tapentadol)</b>	<b>50 mg, 100 mg, 150 mg, 200 mg, 250 mg, Tablets, Extended-release</b>	<b>Usual Dose: Take 1 tablet orally 2 times daily</b>
<p>Herceptin (Trastuzumab)</p> <p>400 mg kit</p> <p>Usual Dose: Inject 4 mg/kg intravenous infusion over 90 minutes, then 2 mg/kg over 30 minutes weekly.</p> <p>Inject 8 mg/kg intravenous infusion over 90 minutes, then 6 mg/kg over 30 minutes</p>	<p>Achievable Dose: 250 mg (62.5 kg patient receiving Herceptin)</p>	<p>The product characteristics of these products will prevent medication errors.</p> <p><i>Dosage Form:</i> injection vs. tablet</p> <p><i>Route of Administration:</i> intravenous vs. oral</p> <p><i>Frequency of administration:</i> once weekly versus twice daily</p> <p><i>Practice Setting:</i> Chemotherapy Clinic vs. Inpatient/Outpatient</p> <p>Since Herceptin will be used in an oncology setting, and as an adjuvant to chemotherapy, orders may appear on a Chemotherapy Medication Order which will most likely require the route of administration and infusion rate.</p>
<p>Neulasta (Pegfilgrastim)</p> <p>6 mg injection</p> <p>Usual Dose: Inject 6 mg subcutaneously per chemotherapy cycle</p>	<p>Achievable Dose: 50 mg</p>	<p>The product characteristics of these products will prevent medication errors.</p> <p><i>Dosage Form:</i> injection vs. tablet</p> <p><i>Route of Administration:</i> subcutaneously vs. oral</p> <p><i>Frequency of administration:</i> per chemotherapy cycle versus twice daily</p> <p><i>Practice Setting:</i> Chemotherapy Clinic vs. Inpatient/Outpatient</p> <p>Since Neulasta will be used in an oncology setting, and as an adjuvant to chemotherapy, orders may appear on a Chemotherapy Medication Order which will most likely require the route of administration and infusion rate.</p> <p>A 50 mg dose of Neulasta is achievable however it is less likely multiple syringes will be dispensed per dose since a Neulasta is prefilled syringe with a dose of 6 mg.</p>

**Appendix H:** Products with numerical overlap but with orthographic differences

<b>Failure Mode: Name confusion</b>	<b>Causes: (could be multiple)</b>	<b>Rationale why medications errors are unlikely to occur in usual practice setting</b>
<b>Nucynta ER (Tapentadol)</b>	<b>50 mg, 100 mg, 150 mg, 200 mg, 250 mg, extended-release tablets</b>	<b>Usual dose: Take 1 tablet orally 2 times daily</b>
<p>Namenda (Memantine Hydrochloride) 5 mg, 10 mg tablets Usual Dose: Take 1 tablet orally 1 to 2 times daily</p>	<p>Orthographic Similarity: Both names share 3 letters in same position ('N', 'n', 'a'), have an upstroke in the 6<sup>th</sup> letter position ('d' vs. 't'), share a letter that appears similar when scripted ('a' vs. 'u')</p>	<p>Orthographic differences: Nucynta contains an additional downstroke ('y'). Although both names have an upstroke in the 6<sup>th</sup> letter position, in the name Nucynta, the upstroke ( 't') is also a cross-stroke.</p> <p>It is unlikely for errors to occur with Nucynta and the Namenda Titration Pak and oral solution. Any prescription written for Nucynta ER must contain a strength which will differentiate it from Namenda Titration Pak or Oral Solution. Additional, a medication ordered for the Titration Pak may have some indication of the product packaging (i.e. Pak), while the oral solution will contain information to specify the liquid is requested (e.g. solution, liquid, mL, tsp).</p> <p>The addition of the modifier 'ER' will help further differentiate Nucynta ER from Namenda.</p>
<p>Titration Pak (tablets) Usual Dose: Use as directed</p>	<p>Numerical overlap: 5 mg vs. 50 mg 10 mg vs. 100 mg</p>	
<p>2 mg/mL oral solution Usual Dose: Take 2.5 mL to 5 mL (0.5 tsp to 1 tsp ) orally 1 to 2 times daily</p>	<p>Frequency of Administration: Both products can be prescribed twice daily</p>	

**Appendix I:** Products with phonetic differences and different product characteristics

<b>Failure Mode: Name confusion</b>	<b>Causes: (could be multiple)</b>	<b>Rationale why medications errors are unlikely to occur in usual practice setting</b>
<p><b>Nucynta ER (Tapentadol)</b></p>	<p><b>50 mg, 100 mg, 150 mg, 200 mg, 250 mg, extended-release tablets</b></p>	<p><b>Usual dose: Take 1 tablet orally 2 times daily</b></p>
<p>Lucentis (Ranibizumab) 0.5 mg/0.5 mL Usual Dose: Inject 0.5 mg intravitreally once a month</p>	<p>Phonetic Similarity: the beginning two syllables have sound similar ('Lu' vs. 'Nu', 'cen' vs. 'cyn')</p> <p>Numerical Overlap: 0.5 mg vs. 50 mg</p>	<p>Phonetic differences: Although the third syllables begin with a 't' sound, the ending of the syllables sound different ('tis' vs. 'ta'). Additionally Nucynta ER contains two additional syllables ('ER').</p> <p>It is unlikely that '0.5 mg' will be confused with '50 mg' during communication of a verbal prescription.</p> <p>The product characteristics of these products will prevent medication errors when communicated through a verbal prescription order.</p> <p><i>Dosage Form:</i> injection vs. tablet</p> <p><i>Route of Administration:</i> intravitreal vs. oral</p> <p><i>Frequency of administration:</i> once monthly vs. twice daily</p> <p><i>Practice Setting:</i> Ophthalmology Clinic or vs. Inpatient/Outpatient</p> <p>The addition of the modifier 'ER' will help further differentiate Nucynta ER from Lucentis. Additionally, there are no errors reported in AERS between approved Nucynta and Lucentis.</p>

**Appendix J:** Currently marketed products with ‘ER’ modifier and their corresponding immediate-release products with frequency of administration

Immediate-release product	Frequency	Extended-release product	Frequency
Depakote	two to three times daily	Depakote ER	once daily
Flagyl	three times daily	Flagyl ER	once daily
Razadyne	twice daily	Razadyne ER <sup>8</sup> (formerly Reminyl ER)	once daily
Ultram	four times daily	Ultram ER <sup>9</sup>	once daily
Dynahist ER does not have a corresponding immediate-release product		Dynahist ER	twice daily
Entex ER does not have a corresponding immediate-release product		Entex ER	twice daily
TriTuss ER does not have a corresponding immediate-release product		TriTuss ER	twice daily
Opana	every 4 to 6 hours	Opana ER <sup>8</sup>	twice daily
Albuterol tablets	three to four times daily	VoSpire ER <sup>8</sup>	twice daily
Methylphenidate tablets	two to three times daily	Metadate ER	three times daily
Methylphenidate tablets	two to three times daily	Methylin ER <sup>8</sup>	three times daily

<sup>9</sup> Proprietary name approved by DMEPA

**Appendix K:** Nucynta and Nucynta ER Product Characteristics

<b>Proprietary name</b>	Nucynta	Nucynta ER
<b>Established name</b>	Tapentadol Hydrochloride	Tapentadol
<b>Dosage Form</b>	Immediate-release tablets	Extended-release tablets
<b>Indication</b>	Relief of moderate to severe acute pain in patients 18 years of age or older	Management of moderate to severe chronic pain in patients 18 years of age or older when a continuous, around-the-clock opioid analgesic is needed for an extended period of time
<b>Route of Administration</b>	Oral	Oral
<b>Strength</b>	50 mg, 75 mg, 100 mg	50 mg, 100 mg, 150 mg, 200 mg, 250 mg
<b>Frequency</b>	every 4 to 6 hours	every 12 hours
<b>Dose</b>	50 mg, 75 mg, or 100 mg every 4 to 6 hours	50 mg to 250 mg twice daily
<b>Maximum daily dose</b>	600 mg/day	500 mg/day

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200533	ORIG-1	ORTHO MCNEIL JANSSEN PHARMACEUTICA LS INC	TAPENTADOL

---

**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

---

/s/

---

JIBRIL ABDUS-SAMAD  
03/09/2010

TODD D BRIDGES  
03/09/2010

KELLIE A TAYLOR  
03/09/2010

CAROL A HOLQUIST  
03/09/2010