CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022524Orig1s000

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

Date:	July 1, 2010
To:	Donna Griebel, MD, Director Division of Gastroenterology Products
Through:	Kristina A. Toliver, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Lori Cantin, RPh, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Zuplenz (Ondansetron) Oral Soluble Film 4 mg and 8 mg
Application Type/Number:	NDA 022524
Applicant:	Par Pharmaceuticals, Inc.
OSE RCM #:	2010-1033

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

1 INTRODUCTION

This re-assessment of the proprietary name responds to the anticipated approval of NDA 022524 within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Zuplenz, acceptable in OSE Reviews #2009-314 and #2009-1775, dated July 30, 2009, and December 30, 2009, respectively. The Division of Gastroenterology Products did not have any concerns with the proposed name, Zuplenz, during our initial review. Additionally, the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective on November 4, 2009, and May 20, 2010.

2 METHODS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see Section 6) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the completion of the previous OSE proprietary name review. We use the same search criteria outlined in OSE Review #2009-314, dated July 30, 2009, for the proposed proprietary name, Zuplenz. None of the product characteristics for Zuplenz have been altered since our previous review, thus we did not re-evaluate previous names of concern. Additionally, DMEPA searches the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

3 RESULTS

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

However, the searches of the databases listed in Section 5 identified four additional names thought to look similar to Zuplenz and represent a potential source of drug name confusion. The four names thought to look similar to Zuplenz were: (b) (4), (b) (4), Zyclara, and Zenpep.

Failure mode and effect analysis (FMEA) was applied to determine if the proposed name could potentially be confused with any of the four names and lead to medication errors. This analysis determined that the name similarity between Zuplenz and the four names identified was unlikely to result in medication errors for the reasons presented in Appendices A and B.

4 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment indicates that the proposed name, Zuplenz, is not vulnerable to name confusion that could lead to medication errors, nor is the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Zuplenz, for this product at this time.

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

5 REFERENCES

1. Cantin, L. OSE Review #2009-314: Proprietary Name Review for Zuplenz. July 30, 2009.

Cantin, L. OSE Review #2009-1775: Proprietary Name Review for Zuplenz (Pre-action). December 30, 2009

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/category/4782.html)

USAN Stems List contains all the recognized USAN stems.

4. Division of Medication Error Prevention and Analysis proprietary name 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.

APPENDICES

Appendix A: Proposed proprietary names that have never been marketed.

Proprietary Name	Similarity to Zuplenz	Reason for Discard
(b) (4) (b) (4) Dosage Form: Injection Strength: 5 mg/mL Usual Dose: 3 mg/kg intravenously over 90 minutes every 3 weeks for 4 doses	Look	(b) (4)
(b) (4) (b) (4) Dosage Form: Capsule Strength: 5 mg and 10 mg Usual Dose: 5 mg to 10 mg at once daily at bedtime	Look	(b) (4)

Appendix B: Product with Differences in Product Characteristics and No Overlap in Strength

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Zuplenz	**N/A**	**4mg and 8 mg**	**Usual dose:** 24 mg given successfully as three 8 mg strips, 30 minute prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Zyclara (Imiquimod) Topical cream NDA 022483 Approved March 25, 2010	Look	3.75%	**Usual Dosage Regimen for Zyclara:** Apply a thin film once daily at bedtime to affected area for 2 two week cycles separated by no a treatment period of two weeks. Wash skin with soap and water after 8 hours. **Orthographic Differences:** Zuplenz has three downstrokes when scripted ('Z', 'p' and 'z') vs. Zyclara which has two downstrokes when scripted ('Z' and 'y'). Additionally, the dowstroke 'p' in Zuplenz is in a different position than the 'y' in Zyclara, which helps to differentiate this name pair orthographically. **Product Characteristic Differences:** Zuplenz is available in two strengths (4 mg and 8 mg), thus strength and/or dose (4 mg, 8 mg, 16 mg, or 24 mg) must be specified on a prescription, which will differentiate Zuplenz from Zyclara. Additionally, characteristics such as frequency and duration of use can help to differentiate Zuplenz and Zyclara. Zuplenz is administered once, twice or thrice daily with chemotherapy for a limited duration, or one dose prior to anesthesia, whereas Zyclara is administered daily for 2 two week cycles, separated by no a treatment period of two weeks.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Zuplenz	**N/A**	**4mg and 8 mg**	**Usual dose:** 24 mg given successfully as three 8 mg strips, 30 minute prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Zenpep (Pancrelipase: Lipase/Protease Amylase/) NDA 022210	**Look**	20,000 USP units of lipase; 68,000 units of protease; 109,000 units of amylase.	**Usual Dosage Regimen for Zenpep:** Enzyme dosing should begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day. Half of the dose for a meal is prescribed for snacks. **Orthographic Differences:** Zuplenz has two upstrokes ('Z' and 'l'), while Zenpep has one upstroke when scripted ('Z'). The name Zuplenz appears longer than Zenpep when scripted. **Product Characteristic Differences:** Zuplenz is available in two strengths (4 mg and 8 mg), thus strength and/or dose (4 mg, 8 mg, 16 mg, or 24 mg) must be specified on a prescription, which will differentiate Zuplenz from Zenpep, which is a single strength product typically ordered as a number of capsules per meal and with snacks. Additionally, characteristics such as frequency can help to differentiate Zuplenz and Zenpep. Zuplenz is administered once, twice or thrice daily with chemotherapy for a limited duration, or one dose prior to anesthesia, whereas Zenpep is administered with meals and with snacks.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22524	ORIG-1	PAR PHARMACEUTICAL	ZUPLENZ (ONDASETRON) ORALLY-DISSOLVING F

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/s/

LORI G CANTIN
07/01/2010

KRISTINA C ARNWINE
07/01/2010

DENISE P TOYER
07/02/2010

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:	December 30, 2009
To:	Donna Griebel, MD, Director Division of Gastroenterology Products
Through:	Kristina Arnwine, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Lori Cantin, RPh,, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Zuplenz (Ondansetron) Oral Soluble Film 4 mg and 8 mg
Application Type/Number:	NDA 022524
Applicant:	Nycomed
OSE RCM #:	2009-1775

CONTENTS

1 INTRODUCTION

This re-assessment of the proprietary name is written in response to a notification that NDA 022254 may be approved within 90 days. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Zuplenz, acceptable in OSE Review #2009-314, dated July 20, 2009. The Division of Gastroenterology Products did not have any concerns with the proposed name, Zuplenz, and the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective on March 5, 2009, and November 4, 2009.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search 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. We used the same search criteria that were used in OSE Review #2009-314 for the proposed proprietary name, Zuplenz. None of the proposed product characteristics were altered, therefore, we did not re-evaluate previous names of concern. Additionally, DMEPA searches the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

The searches of the databases yielded two new names, Zipsor and Zirgan, thought to look similar to Zuplenz and represent a potential source of drug name confusion. These names were evaluated using FMEA. The findings of the FMEA indicate that the proposed name, Zuplenz, is not likely to result in name confusion with Zipsor and Zirgan for the reasons presented in Appendix A.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name Zuplenz, as of December 7, 2009.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Zuplenz, is not vulnerable to name confusion that could lead to medication errors nor is the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Zuplenz, for this product at this time.

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

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Nitin Patel, OSE Project Manager, at 301-796-5412.

4 REFERENCES

1. **OSE review #2009-314. Proprietary Name Review of Zuplenz: Cantin, Lori.**

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. ***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.

4. ***USAN Stems (***http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml***)***
   USAN Stems List contains all the recognized USAN stems.

5. ***Division of Medication Error Prevention and Analysis proprietary name 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.

Appendix A: Product with No Overlap in Strength

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Zuplenz	**N/A**	**4mg and 8 mg**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minute prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Zipsor (Diclofenac potassium) Oral Capsule NDA 022202 Approved June 16, 2009	Look	25 mg	**Usual Dose of Zipsor:** 25 mg orally four times a day **Orthographic Differences:** Zuplenz has two upstrokes ('Z' and 'l') Zipsor which has only one upstroke ('Z') Zuplenz has three downstrokes when scripted ('Z', 'p' and 'z') vs. Zipsor which has two downstrokes when scripted ('Z' and 'p') **Phonetic Differences:** The suffix "-plenz" does not sound like the suffix "-sor" **Product Characteristic Differences:** Zuplenz is available in two strengths (4 mg and 8 mg), thus strength and/or dose (4 mg, 8 mg, 16 mg, or 24 mg) must be specified on a prescription, which will differentiate Zuplenz from Zipsor. Additionally, characteristics such as frequency and duration of use can help to differentiate Zuplenz and Zipsor. Zuplenz is administered once, twice or thrice daily with chemotherapy for a limited duration, or one dose prior to anesthesia, whereas Zipsor is administered four times a day for an indefinite duration
Zirgan (Ganciclovir) Ophthalmic Gel NDA 022211 Approved September 15, 2009.	Look	0.15%	**Usual Dose of Zirgan:** 1 drop to affected eye(s) five times a day (every 3 hours while awake) until corneal ulcer heals, then 1 drop three times a day for seven days **Product Characteristic Differences:** The dose of Zuplenz and Zirgan may overlap (e.g., "1" soluble film vs. "1" drop), however, Zuplenz is available in two strengths (4 mg and 8 mg), thus strength and/or dose (4 mg, 8 mg, 16 mg, or 24 mg) must be specified on a prescription, which will help differentiate Zuplenz from Zirgan.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22524	ORIG-1	PAR PHARMACEUTICAL	ZUPLENZ (ONDASETRON) ORALLY-DISSOLVING F

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/s/

LORI G CANTIN
12/30/2009

DENISE P TOYER on behalf of KRISTINA C ARNWINE
12/31/2009

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12/31/2009

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:	July 20, 2009
To:	Donna Griebel, MD, Director Division of Gastroenterology Products
Through:	Kristina Arnwine, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Lori Cantin, RPh,, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Zuplenz (Ondansetron) Orally-Dissolving Film Strip 4 mg and 8 mg
Application Type/Number:	NDA 22-524
Applicant:	Nycomed
OSE RCM #:	2009-314

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

CONTENTS

EXECUTIVE SUMMARY

Zuplenz is the proposed proprietary name for Ondansetron Orally-Dissolving Film Strip. This proposed proprietary name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Zuplenz, conditionally acceptable for this product. The proposed proprietary name must be re-reviewed upon submission of the NDA and 90 days before approval of the NDA.

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.

Our evaluation noted the pharmaceutical dosage form for this product 'orally-dissolving film strip' appears to be a new dosage form and is not recognized by the United States Pharmacopeia (USP). The Office of New Drug Quality Assurance (ONDQA) is currently reviewing evaluating the nomenclature issue for this dosage form. A final decision as to their recommendation for the proper nomenclature may take several months. Therefore, we will not provide further comment on this issue at this time.

1 BACKGROUND

1.1 INTRODUCTION

This consult was written in response to a request from the Division of Gastroenterology Products for assessment of the proprietary name, Zuplenz, regarding potential name confusion with other proprietary or established drug names. Proposed draft labels and labeling were submitted with the NDA on the May 1, 2009, and will be reviewed under separate cover.

1.2 REGULATORY HISTORY

The original pre-Investigational New Drug (PIND) application for this drug product was submitted by the Applicant on April 28, 2008. A request for a review of the proprietary name, Zuplenz, was submitted on February 9, 2009, under the PIND application. The Applicant submitted a 505(b)(2) NDA on May 1, 2009, which references the listed drug, Zofran ODT. The Applicant dose not market Ondansetron in any other dosage form.

This NDA submission also contained a request for a proprietary name review, as well as the results of an external proprietary name review conducted by (b) (4).

1.3 PRODUCT INFORMATION

Zuplenz (Ondansetron) orally-dissolving film strip is for the treatment of the following indications:

1. Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, including Cisplatin > 50 mg/m^2. The recommended adult oral dosage is 24 mg given successively as three 8 mg strips administered 30 minutes before the start of single-day highly emetogenic chemotherapy.
2. Prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy. The recommended adult oral dosage is 8 mg given twice daily.

3. Prevention of nausea and vomiting associated with radiotherapy in patients receiving total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen. The recommended adult oral dosage is 8 mg given three times daily.
4. Prevention of postoperative nausea and/or vomiting. The recommended adult oral dosage is 16 mg given successively as two 8 mg strips administered 1 hour before the induction of anesthesia.

Zuplenz Orally-dissolving Strip is a thin, flexible, non-friable polymeric strip containing dispersed Ondansetron as the active ingredient. Zuplenz is intended to be placed on the tongue for rapid disintegration/dissolution in saliva prior to swallowing, for delivery into the gastrointestinal tract. This product will be available in 4 mg and 8 mg strengths. Each dose will be supplied in individual foil-foil sealed child-resistant pouches. Multiple pouches will be packaged in a carton. Each strip will feature printed alphanumeric identifiers using pharmaceutical grade edible ink.

Zuplenz is to be stored at controlled room temperature (b) (4) in the carton. The strip is to be kept in the foil-foil pouch until ready to use.

2 METHODS AND MATERIALS

This section describes the methods and materials used by DMEPA staff to conduct a proprietary name risk assessment. The primary focus for this assessment is to identify and remedy potential sources of medication error prior to drug approval. 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. [1]

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Zuplenz, 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 CDER.

For the proprietary name, Zuplenz, the DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Section 2.1.1.1) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see Section 2.1.1.2). DMEPA also conducts internal FDA prescription analysis studies (see Section 2.1.2).

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 (see Section 2.1.3). The overall risk assessment is based on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [2] FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or

[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

[2] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

patient harm while the medication is in the control of the health care professional, patient, or consumer. [1] DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting that the product is likely to be used in 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. As such, the staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since 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 drug name include, but are not limited to established name of the proposed product, the proposed indication, 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 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.[2]

2.1.1 Search Criteria

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'Z' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the United States Pharmacopeia-Institute of Medication Practices (USP-ISMP) Medication Error Reporting Program involve pairs beginning with the same letter.[3,4]

To identify drug names that may look similar to Zuplenz, the DMEPA staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (7 letters), upstrokes (two, capital letter 'Z' and 'l'), down strokes (two, 'p' and 'z'), cross-strokes (possibly two, 'Z' and 'z'), and dotted letters (none). Additionally, several letters in Zuplenz may be vulnerable to ambiguity when scripted (see Appendix B). As such, the staff also considers these alternate appearances when identifying drug names that may look similar to Zuplenz.

When searching to identify potential names that may sound similar to Zuplenz, the DMEPA staff searches for names with similar number of syllables (two), stresses (ZU-plenz or zu-PLENZ), 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

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[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

[2] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

[3] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

[4] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artifical Inteligence in Medicine (2005)

regional accents and dialects, so other potential pronunciations of the name are considered. The Applicant's intended pronunciation of the proprietary name (ZOO-plenz) was provided as part of the request for a proprietary name review submission, and is also taken into consideration.

The DMEPA staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, the DMEPA staff were provided with the following information about the proposed product: the proposed proprietary name (Zuplenz), the established name (Ondansetron), proposed indications (prevention nausea and vomiting), strength (4 mg and 8 mg), dose (8 mg, 16 mg, and 24 mg), frequency of administration (30 minutes prior to chemotherapy, twice daily, three times daily, and 1 hour before induction of anesthesia), route of administration (oral) and dosage form of the product (Orally-dissolving Strip). Appendix A provides a more detailed listing of the product characteristics the medication error staff generally takes into consideration.

Lastly, the DMEPA staff also considers the potential for the proposed 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. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Database and Information Sources

The proposed proprietary name, Zuplenz, was provided to the DMEPA staff to conduct a search 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 Zuplenz using the criteria outlined in Section 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the DMEPA staff uses 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, DMEPA staff reviews the United States Adopted Names (USAN) stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by DMEPA to gather CDER professional opinions on the safety of the product and the proprietary name, Zuplenz. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of DMEPA staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of DMEPA staff were presented 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 Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

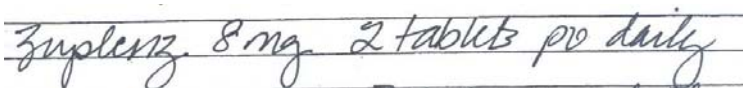
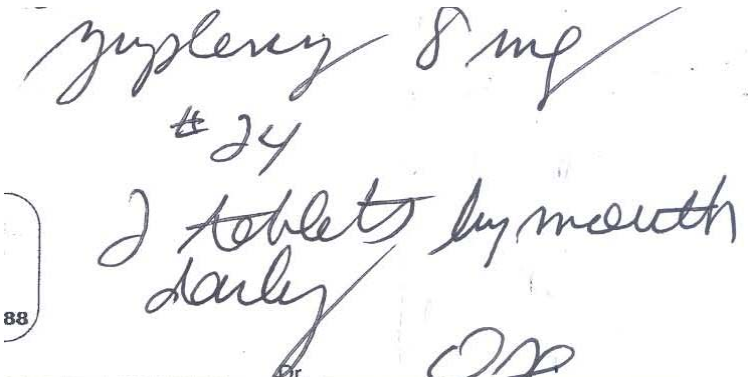
2.1.2 FDA Prescription Analysis Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Zuplenz 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 a total of 122 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Zuplenz in handwriting and verbal communication of the name, an inpatient medication order and outpatient prescription are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 122 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 the DMEPA staff.

Figure 1. Zuplenz Prescription Study (conducted April 9, 2009)

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDERS	VERBAL PRESCRIPTION
Inpatient Medication Order:  	Zuplenz 8mg #24 2 tablets by mouth daily
Outpatient Prescription:  	

2.1.3 Comments from the Division of Gastroenterology Products

DMEPA requests the regulatory division in the Office of New Drugs responsible for the application for their comments and/or clinical/other concerns on the proposed proprietary name at 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. Any comments or concerns are addressed in the safety evaluator's assessment.

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

2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Mode and Effects Analysis and provide an overall risk 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.[1] When applying FMEA to assess the risk of a proposed proprietary name, the Division of Medication Error Prevention and Analysis seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and 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 look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective then remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. 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 evaluation, and studies, and identifies potential failure modes by asking:

"Is the name Zuplenz convincing 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 Zuplenz 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 possesses similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated 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?"

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 ultimately not be a source of medication errors in the usual practice setting, the name is eliminated 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 that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an

[1] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMEPA will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. 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 trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. The Division of Medication Error Prevention and Analysis 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)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains a USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. DMEPA identifies a potential source of medication error within the proposed proprietary name. 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.

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 is awarded approval first has the right to the use the name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEPA will not object to the use of the proprietary name. If any of these conditions are met, then DMEPA will object to the use of the proprietary 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 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission for Healthcare Organizations (JCAHO), and Institute for Safe Medication Practices (ISMP), who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken 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 the 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 practitioner's vocabulary, and as such, 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 limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used 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, and so DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and Information Sources

Our search identified a total of twenty-seven (27) names as having some similarity to the name Zuplenz.

Sixteen (16) of the names were thought to look like Zuplenz including: Zublinox, Suplena, Xopenex, Zephrex, Zephiran, Lupron, (b) (4), Norplant, Nplate, Loprox, (b) (4), (b) (4), Zolinza, Zemplar, Zolpidem, and Zyprexa.

Four (4) of the names were thought to sound like Zuplenz including: Z-Clinz, Relenza, Supplin, and Suplentin

Seven (7) names were thought to both look and sound like Zuplenz including: Zaleplon, (b) (4), Zyban, Zypan, Aplenzin, Replens, and Replenz.

The Division of Medication Error Prevention and Analysis did not identify any United States Adopted Names (USAN) stems in the name Zuplenz as of May 8, 2009.

3.1.2 CDER Expert Panel Discussion

The Expert Panel reviewed the pool of names identified by DMEPA staff (see section 3.1 above), and noted no additional names thought to have orthographic or phonetic similarity to Zuplenz and have the potential for confusion.

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

3.1.3 FDA Prescription Analysis Studies

A total of 24 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About 42% of the participants (n=10) interpreted the name correctly as "Zuplenz", with correct interpretation occurring more frequently in the written studies. The remainder of the respondents (n= 14) misinterpreted the drug name. The majority of misinterpretations (n=11) occurred in the outpatient prescription study. Common misinterpretations in the outpatient study include 'z' being misinterpreted as 'y', and 'up' being misinterpreted as 'yp' or 'ys'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Comments from the Division of Gastroenterology Products

In response to the OSE March 6, 2009, e-mail, DGP did not forward any comments and/or clinical/other concerns on the proposed name at the initial phase of the name review.

DMEPA notified DGP via e-mail that we had found no objections to the proposed proprietary name, Zuplenz, on May 11, 2009. Per e-mail correspondence from the Division of Gastroenterology Products on June 10, 2009, they indicated they concur with our assessment of the proposed name, Zuplenz.

3.1.5 External Proprietary Name Risk Assessment

In the proposed name risk assessment submitted by the Applicant, the (b) (4) evaluated a total of thirteen names (13) thought to have some confusion with the name 'Zuplenz'.

Five (5) names of pharmaceutical products were thought to sound like 'Zuplenz'. They are: Replens, Suprax, Carraklenz, Sufentanyl, and Zosyn.

Six (6) names of pharmaceutical products were thought to sound like 'Zuplenz'. They are: Zyprexa, Mirapex, Zaleplon, Zanaflex, Zemplar, and Zyrtec.

Two (2) names of pharmaceutical products were thought to look and sound like 'Zuplenz'. They are: Zofran and Suplena.

Seven (7) of the thirteen names were not previously identified by the Division of Medication Error Prevention and Analysis as having potential for name confusion with any part of the proposed proprietary name, Zuplenz. They are: Suprax, Carraklenz, Sufentanil, Zosyn, Mirapex, Zanaflex, and Zyrtec.

The findings of the independent risk assessment support the name 'Zuplenz' for the proposed product.

3.1.5 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator identified one (1) additional name: Zofran, which was thought to look similar to Zuplenz and represent a potential source of drug name confusion. This name was also identified in the external proprietary name risk assessment conducted by (b) (4) As such, a total of thirty-five (35) names were analyzed to determine if the drug names could be confused with Zuplenz, and if the drug name confusion would likely result in a medication error.

Eight (8) of the thirty-five names lacked orthographic and/or phonetic similarities and were not evaluated further (see Appendix D).

The remaining twently-seven (27) names were determined to have some orthographic and/or phonetic similarity to Zuplenz, and thus determined to present some risk for confusion. Failure Mode and Effect Analysis (FMEA) was then applied to determine if the proposed name, Zuplenz, could potentially be confused with any of the twenty-seven (27) names and lead to medication error. This analysis determined that the name similarity between Zuplenz and the identified names was unlikely to result in a medication error with the twenty-seven (27) products identified for the reasons presented in Appendices E through K.

3.2 DOSAGE FORM

The pharmaceutical dosage form for this product 'orally-dissolving film strip' appears to be a new dosage form and is not recognized by the United States Pharmacopeia (USP). The Office of New Drug Quality Assurance (ONDQA) is currently evaluating the nomenclature issue for this dosage form. A final decision as to their recommendation for the proper nomenclature may take several months.

4 DISCUSSION

DMEPA identified and evaluated thirty-five (35) names for their potential similarity to the proposed name, Zuplenz. The FMEA indicates that the proposed name, Zuplenz is not likely to result in name confusion that could lead to medication errors.

Neither DDMAC nor DGP had concerns with the proposed name, Zuplenz.

DMEPA noted that the proposed proprietary name, Zuplenz, for the proposed product does not make reference to the orally-dissolving film strip dosage form. The proposed product will be the first orally-dissolving film strip dosage form for this drug product and currently, the Applicant does not manufacture any other formulation of Ondansetron. A sample of the proposed dosage form was submitted and it is clearly a "strip". It does not resemble a tablet or other any other dosage form, so this minimizes our concerns regarding the potential for confusion in the marketplace if the Applicant were to introduce any other dosage forms. Therefore, the orally-dissolving film strip and any other dosage forms that the Applicant may introduce in the future could be managed under the same proprietary name.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate the proposed name, Zuplenz, is not vulnerable to confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis has no objection to the use of the proprietary name, Zuplenz, for this product. Our findings were consistent with, and supported by, an independent risk assessment of the proprietary name submitted by the Applicant.

If **any** of the proposed product characteristics are altered prior to approval of the marketing application; DMEPA rescinds this Risk Assessment finding, and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment and, as such, the conclusions on re-review are subject to change. Additionally, if the product approval is delayed beyond 90 day from the date of this review, the proposed name must be resubmitted for evaluation.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

The pharmaceutical dosage form for this product 'orally-dissolving film strip' appears to be a new dosage form and is not recognized by the United States Pharmacopeia (USP). The Office of New Drug Quality Assurance (ONDQA) is currently evaluating the nomenclature issue for this dosage form. A final decision as to their recommendation for the proper nomenclature for this dosage form may take several months.

We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Phuong (Nina) Ton, OSE Project Manager, at 301-796-1648.

6.2 COMMENTS TO THE APPLICANT

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

The proposed proprietary name, Zuplenz, 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.

7 REFERENCES

1. Micromedex Integrated Index (http://weblern/)

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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. This is a database which was created for DMETS, FDA.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://weblern/)

Drug Facts and Comparisons is a compendium organized by therapeutic Course; 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 Error Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by DMEPA 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 and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and "Chemical Type 6" approvals.

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

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. U. S. Patent and Trademark Office website http://www.uspto.gov.

Provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (http://weblern/)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

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

11. Natural Medicines Comprehensive Databases (http://weblern/)

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

12. Stat!Ref (http://weblern/)

Contains full-text information from approximately 30 texts. 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)

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

15. Lexi-Comp (www.pharmacist.com)

A web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The medication error staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compare 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. The medication error 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* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The medication error staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the medication error staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, DMEPA also considers a variety of pronunciations that could occur in the English language.

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		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstokes Downstrokes Cross-stokes	• Names may look similar when scripted, and lead to drug name confusion in written communication

		Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
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	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name: Zuplenz	**Scripted may appear as**	**Spoken may be interpreted as**
Capital letter 'Z'	'T' or 'F'	"S" or "X"
Lower case 'u'	'a', 'e', 'i', or 'ei'	Any vowel
Lower case 'p'	'yn'	"b"
Lower case 'up'	'ys'	"oop"
Lower case 'l'	'e'	
Lower case 'e'	'a', 'i', 'o', 'u'	Any vowel
Lower case 'n'	'm' 'r', 's', 'u' 'v'	"m"
Lower case 'z'	'm', 'r', 'y'	"s"

Appendix C:

FDA Prescription Study Responses

Inpatient	Outpatient	Voice
Zuplenz	Zuplenz	Zuplens
Zuplenz	Zyslenz	
Zuplenz	Zupleny	
Zuplenz	Zypleny	
Zuplenz	Zypleny	
Zuplenz	Zupleny	
Zuplenz	Zuysleny	
Zuplenz	Zuplenz	
?	Zysleny	
	Zerplenz	
	Zupleny	
	Zuplenz	
	Zupleny	
	Zupleny	

Appendix D: Proprietary names discarded because they are not convincingly similar in look or sound to the proposed name	
Proprietary Name	**Similarity to Zuplenz**
Suplentin	Sound
Zolpidem	Look
Xopenex	Look
Lupron	Look
Norplant	Look
Nplate	Look
Loprox	Look
Sufentanil	Sound

Appendix E: Proprietary names identified only in Foreign Countries.		
Proprietary name	**Similarity to Zuplenz**	**Country**
(b) (4)		
Supplin (Metronidazole)	SA	Multiple Countries

Appendix F: Natural Ingredients/Herbal Medicines not likely to be written as a prescription

Proprietary Name	Similarity to Zuplenz	Description
Zypan	LA/SA	Proprietary Blend 700 mg: Betaine Hydrochloride, Pancreas extract (Cytosol), Pancreatin (3X), Fatty Acid, Pepsin (1:10,000), Ammonium Chloride, Bovine Spleen, Ovine Spleen.

Appendix G: Nonprescription product name or general term not likely to be written as a prescription

Proprietary Name	Similarity to Zuplenz	Description
Suplena	LA	Enteral nutrition product; not likely to be prescribed as a drug
Replens	LA/SA	Vaginal lubricant; 1 applicatorful every 2 to 3 days
Replenz	LA/SA	Dietary supplement (identified in SAEGIS, can not find in any other commonly used professional references).
Carra-Klenz (Acemannan hydrogel)	SA	Wound and skin cleanser Pump spray bottle Listed on OTC section of Red Book

Appendix H: Proprietary Names of Drug Products that are no Longer Marketed, are Discontinued, or are Withdrawn by the FDA Commissioner, and there are no Generic Equivalent Products Available

Proprietary name	Similarity to Zuplenz	Status
		(b) (4)

Appendix I: Proposed Proprietary Name for Product that has never been Marketed

Proprietary name	Similarity to Zuplenz	Status
		(b) (4)

Appendix J: Drug Products with no Numerical Overlap in Strength or Dose			
Zuplenz **(Ondansetron)**		**4 mg and 8 mg orally dissolving strip**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minute prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Zephrex (guaifenesin 400 mg + pseudoephedrine 60 mg)	LA	400 mg/60 mg ('1 tablet')	1 tablet orally every 6 hours Off-market per Clinical Pharmacology Online
Zephiran (benzalkonium chloride)	LA	**Solution, aqueous**: 1:750 — In 240 ml and gal. **Disinfectant concentrate**: 17% — In 120 ml and gal. **Tincture**: 1:750 — In gal. **Tissue**: 1:750. With chlorothymol, isopropyl alcohol and alcohol (20%) — In individual single use packets.	Antisepsis of skin, mucous membranes, and wounds; Usual dose not applicable.
Zaleplon (established name for Sonata)	LA/SA	5 mg and 10 mg oral capsules	5 mg or 10 mg immediately before bedtime
Zyban (bupropion hydrochloride)	LA/SA	150 mg extended-release tablet	150 mg orally once daily or twice daily
Aplenzin (bupropion hydrobromide)	LA/SA	174 mg, 348 mg, and 522 mg extended-release tablets	174 mg to 522 mg orally once daily

Appendix J: Drug Products with no Numerical Overlap in Strength or Dose			
Zuplenz (Ondansetron)		**4 mg and 8 mg orally dissolving strip**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minute prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Z-Clinz (benzoyl peroxide and clindamyicn)	SA	5%/1% 10%/1%	Apply topically to affected areas twice daily, morning and evening. Listed on onlinedrugtest.com. medicinenet.com and misc other sites, but not in any commonly used references such as Clinical Pharmacology, Facts and Comparisons, Orange Book, LexiComp, Drugs @FDA Appears to be a generic of Benzaclin, but no information found to support that it's approved.
Relenza (Zanamivir)	SA	5 mg Powder for Oral Inhalation	Oral Inhalation: 10 mg (2 inhalations) twice daily for 5 days, or 10 mg once daily for 10 days or 28 days
Zolinza (Vorinostat)	LA	100 mg oral capsule	300 mg to 400 mg orally once daily 300 mg orally once daily on five consecutive days a week
Zyprexa (Olanzapine)	LA	**Tablets:** 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, and 20 mg **Injection:** 10 mg vial, lyophilized powder	5 mg to 20 mg orally once daily 2.5 mg to 10 mg intramuscularly; subsequent dose of up to 10 mg may be given

Appendix J: Drug Products with no Numerical Overlap in Strength or Dose			
Zuplenz **(Ondansetron)**		**4 mg and 8 mg orally dissolving strip**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minute prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose** **(if applicable)**
Zosyn (Piperacillin and Tazobactam)	SA	**Powder for Injection:** 40.5 g bulk vial; 2.25 g, 3.375 g, and 4.5 g single-dose vial; 2.25 g, 3.375 g, and 4.5 g ADD-Vantage vial. **Injection (frozen solution):** 2.25 g, 3.375 g, and 4.5 gm in Galaxy Container	3.375 g to 4.5 g intravenously every 6 hours For reduced renal function: 2.25 g intravenously every 6 hours, every 8 hours or every 12 hours, depending on creatinine clearance.
Suprax (Cefixime)	SA	**Powder for Suspension:** 100 mg/5 mL 200 mg/5 mL	Adults and children (> 12 years old): 400 mg orally once daily or as a single dose Children (12 years of age and under): 8 mg/kg/day as a once daily dose, or 4 mg/kg/day every 12 hours.
Sufentanil	SA	**Injection:** 50 mcg/mL in 1 mL, 2 mL, and 5 mL ampules.	Slow intravenous injection of infusion: Up to 8 mcg/kg as an analgesic adjunct to anesthesia; $\geq$ 8 mcg/kg as a primary anesthetic agent for induction and maintenance of anesthesia. For children < 12 years of age: 10 mcg to 25 mcg as an anesthetic dose with 100% oxygen; supplemental doses of up to 25 mcg to 50 mcg are recommended for maintenance based on response to initial dose.

Appendix J: Drug Products with no Numerical Overlap in Strength or Dose			
Zuplenz (Ondansetron)		**4 mg and 8 mg orally dissolving strip**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minute prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Product name with potential for confusion	**Similarity to Proposed Proprietary Name**	**Strength**	**Usual Dose (if applicable)**
Mirapex (Pramiprexole)	LA	**Tablets:** 0.125 mg, 0.25 mg, 0.5 mg, 0.75 mg, 1 mg, and 1.5 mg	0.125 mg to 1.5 mg orally three times a day.
Zyrtec (Cetirizine)	LA	**Tablets:** 5 mg and 10 mg **Tablets, chewable:** 5 mg and 10 mg **Oral Syrup:** 1 mg/mL	2.5 mg, 5 mg, or 10 mg once daily

Appendix K: Potential for name confusion with overlap in dose, achievable dose, or strength but with phonetic, orthographic, and/or product characteristic differences

Zuplenz **(Ondansetron)**	**Strength** **4 mg and 8 mg**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minutes prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Failure Mode: (Name confusion)	**Causes (could be multiple)**	**Effects**
Zofran (Ondansetron) Injection: 32 mg/50 mL D5W, 2 mg/mL (2 mL single-dose vial and 20 mL multidose vial) Solution: 5 mg/5 mL Tablets: 4 mg and 8 mg Orally Disintegrating Tablets: 4 mg and 8 mg **Parenteral dose (**intravenously, intramuscularly) ***Adults:*** **Dose range:** 0.15 mg/kg, 32 mg, 4 mg, 8 mg **Frequency:** Single dose 15 minutes to 30 minutes prior to chemotherapy, then repeated 4 hours and 8 hours after the first dose, over 15 minutes for 1 dose 30 minutes prior to chemotherapy, 1 to 2 hours prior to radiotherapy, immediately preoperatively ***Pediatrics (1 month to 12 years old)*** Dose: 0.1 to 0.3 mg/kg, 4 mg Frequency: Single dose over 15 minutes 30 minutes prior to chemotherapy, then repeat 4 hours and 8 hours; Single dose preoperatively or for	**Orthographic Similarity:** First letter similarity (both begin with 'Z') Similar length of names (7 vs. 6 letters) Prefix looks similar when scripted ('Zup' vs. 'Zof') Both names contain 2 upstrokes ('Z' and 'l' vs. 'Z' and 'f')) Both names contain a downstroke ('p' vs. 'f') in the 3rd position. **Phonetic Similarity:** The prefix of Zuplenz ('Zup') sounds like the prefix of Zofran ('Zof') **Similar Product Characteristics:** *Numerical overlap in strength* (4 mg and 8 mg vs. 4 mg and 8 mg) *Same frequency of administration* (Single dose prior to chemotherapy or anesthesia, twice daily, three times daily) *Similar dosage form* (Orally dissolving strips vs. oral tablets and orally disintegrating tablets) *Same active ingredient*	Orthographic and phonetic differences in the names minimize the likelihood of medication error in the usual practice setting. *Rationale:* **Orthographic Differences:** Zuplenz has three downstrokes ('Z', 'p', and 'z') while Zofran has two downstrokes ('Z' and 'f'). Additionally, the last letter of Zuplenz is and downstroke ('z') while the last letter of Zofran is not an downstroke, which helps to differentiate these two names when scripted Zuplenz contains potentially two cross-stroke ('Z' and 'z') while Zofran contains potentially two cross-stroke ('Z' and 'f'); if cross-strokes are used for the 'Z' and 'z', the second cross-stroke occurs in a different position (7th position vs. 3rd position). The suffix of Zuplenz (-lenz) does not look like the suffix of Zofran (-fran) when scripted. **Phonetic Differences:** The suffix of Zuplenz (-lenz) do not sound similar to the infix and suffix of Zofran (-fran)

Appendix K: Potential for name confusion with overlap in dose, achievable dose, or strength but with phonetic, orthographic, and/or product characteristic differences

Zuplenz **(Ondansetron)**	**Strength** **4 mg and 8 mg**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minutes prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Failure Mode: (Name confusion)	**Causes (could be multiple)**	**Effects**
nausea/vomiting. **Oral dosage** ***Adults and children ≥ 12 years*** Dose: 4 mg, 8 mg, 16 mg, 24 mg Frequency: three times per day, twice daily, single dose, once daily, single dose followed by two subsequent doses four hours and eight hours after the initial dose ***Pediatrics*** Dose: 4 mg, 3.2 mg,1.6 mg Frequency: every 8 hours; 1 dose 15 to 30 minutes prior to chemotherapy, then 1 dose 4 hours and 8 hours after the initial dose	(Ondansetron) *Same route of administration* (oral)	

Appendix K: Potential for name confusion with overlap in dose, achievable dose, or strength but with phonetic, orthographic, and/or product characteristic differences

Zuplenz **(Ondansetron)**	**Strength** **4 mg and 8 mg**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minutes prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Failure Mode: (Name confusion)	**Causes (could be multiple)**	**Effects**
Zanaflex (Tizanidine) 2 mg, 4 mg, and 6 mg oral capsules Usual dose: 4 to 8mg for a single-dose; may repeat at 6 to 8 hour intervals for a maximum of three doses per day.	**Orthographic Similarity:** Both names begin with the letter 'Z' Similar length of names (7 letters vs. eight letters) 'pl' and 'fl' look similar when scripted **Phonetic Similarity:** Both begin with the letter 'Z' which sounds the same when spoken **Similar Product Characteristics:** Same route of administration: oral Overlap in dosage: 8 mg Overlap in strength: 4 mg Overlap in frequency of administration: three times per day	Orthographic and phonetic differences in the names minimize the likelihood of medication error in the usual practice setting. **Orthographic Difference:** Zuplenz has 3 downstrokes vs. two downstrokes in Zanaflex **Phonetic Differences:** Number of syllables (two in Zuplenz vs. three in Zanaflex) 'Zu' does not sound like 'Zan' **Product Characteristic Differences:** Dosage form: Strip vs. Oral Capsule; typically, the Rx would specify the dosage form or would provide instructions to 'dissolve on tongue'

Appendix K: Potential for name confusion with overlap in dose, achievable dose, or strength but with phonetic, orthographic, and/or product characteristic differences

Zuplenz **(Ondansetron)**	**Strength** **4 mg and 8 mg**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minutes prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Failure Mode: (Name confusion)	**Causes (could be multiple)**	**Effects**
Suplena (low protein enteral nutrition product for patients with acute and chronic renal failure who are pre-dialysis) Available in 8 ounce cans/24 cans per case	**Orthographic Similarity:** First letter similarity ('Z' can look like 'S' when scripted) Same length of names (7 letters) Both names contain the same 5 letters 'uplen' in the same position Prefix looks similar when scripted ('Zup' vs. 'Sup') Suffix looks similar when scripted ('lenz' vs. 'lena') especially if 'z' is not scripted as a lower case letter. Both names contain 2 upstrokes ('Z' and 'l' vs. 'S' and '1) Both names contain a downstroke ('p') in the 3rd position. **Phonetic Similarity:** The name Zuplenz ('Zup') sounds like the prefix and infix of Suplena ('Suplen') **Similar Product Characteristics:** *Potential for the same frequency of administration* (e.g., twice a day or three times a day) *Same route of administration* (Oral) *Potential for overlap in strength* (4 mg or 8 mg vs. 4 ounces or 8 ounces)	Differences in product characteristics between the two products, as well as orthographic and phonetic differences in the names, minimize the likelihood of medication error in the usual practice setting. *Rationale:* **Orthographic Differences:** Zuplenz has three downstrokes ('Z', 'p' and 'z') while Suplena has one downstroke ('p') when scripted. Additionally, the last letter of Zuplenz is and downstroke ('z') while the last letter of Zofran is not an downstroke, which helps to differentiate these two names when scripted Zuplenz contains potentially two cross-stroke ('Z' and 'z') while Suplena has zero cross-strokes.. **Phonetic Differences:** The suffix of Zuplenz (-plenz) do not sound similar to the suffix of Su-plen-a (-a) **Product characteristics:** *Units of measure* (mg vs. ounce or 'can') *Dosage form* (lingual strip vs. liquid); typically, the Rx would specify the dosage form of Zuplenz ('strip') or the method of administration ('on top of tongue').

Appendix K: Potential for name confusion with overlap in dose, achievable dose, or strength but with phonetic, orthographic, and/or product characteristic differences

Zuplenz **(Ondansetron)**	**Strength** **4 mg and 8 mg**	**Usual dose:** 24 mg given successfully as three 8 mg strips 30 minutes prior to chemo 8 mg strip twice daily 8 mg strip three times a day 16 mg given successfully as two 8 mg strips 1 hour before induction of anesthesia
Failure Mode: (Name confusion)	**Causes (could be multiple)**	**Effects**
Zemplar (Paricalcitol) **Oral Capsules:** 1 mcg, 2 mcg, 4 mcg capsules **Injection:** 2 mcg/mL (1 mL & 2 mL sizes) and 5 mcg/mL (1 mL) Oral: 1 mg to 2 mg once daily or 2 mg to 4 mg three times per week. IV bolus: 0.04 to 0.1 mcg/kg (2.8 to 7 mcg) administered as a bolus dose no more than three times per week	**Orthographic Similarity:** Both names begin with the letter 'Z' Same length of names (7 letters letters) Both names contain 'pl' in similar positions Lower case 'u' and 'e' in Zuplenz may look like lower case 'e' and 'a' in Zemplar, respectively Lower case 'z' in Zuplenz may be misinterpreted as lower case 'r' in Zemplar if printed, rather than scripted **Phonetic Similarity:** Both begin with the letter 'Z' which sounds the same when spoken The suffixes of both names begin with 'pl' **Similar Product Characteristics:** Same route of administration: oral Overlap in strength: 4 mg Overlap in achievable dose: 8 mg, 16 mg and 24 mg doses of Zuplenz are achievable with 4 mg dose of Zemplar	Orthographic and phonetic differences in the names, in conjunction with differences in product characteristics, minimize the likelihood of medication error in the usual practice setting. **Orthographic Difference:** When scripted, Zuplenz has two downstrokes ('p' and 'z' vs. one downstrokes in Zemplar ('p) **Phonetic Differences:** "Zu" does not sound like "Zem" The suffix endin "enz" in does not sound like the suffix ending "ar" **Product Characteristic Differences:** *Dosage form:* Orally-dissolving Film Strip vs. Oral Capsule; typically, the Rx would specify the dosage form or would provide instructions to 'dissolve on tongue' *Frequency of administration:* 30 minutes prior to chemo, twice daily, three times a day, or 1 hour before induction of anesthesia vs. once daily or three times per week

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/s/

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