

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

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PROPRIETARY NAME REVIEW(S)

**Department of Health and Human Services
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Office of Surveillance and Epidemiology**

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Through: Zachary Oleszczuk, Pharm.D., Team Leader
Carol Holquist, R.Ph, Director
Division of Medication Error Prevention and Analysis
From: Yelena Maslov, Pharm.D., Safety Evaluator
Division of Medication Error Prevention and Analysis
Subject: Proprietary Name Review
Drug Name(s): Tradjenta (Linagliptin) Tablets, 5 mg
Applicant/sponsor: Boehringer Ingelheim Pharmaceuticals, Inc.
OSE RCM #: 2010-2473

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EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of proposed proprietary name, Tradjenta for Linagliptin Tablets. Our evaluation did not identify concerns that would render the name unacceptable based on product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Tradjenta, acceptable for this product.

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 Metabolism and Endocrinology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be re-submitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to the request from Boehringer Ingelheim Pharmaceuticals, Inc., dated February 1, 2011, for an assessment of the proposed proprietary name, Tradjenta, regarding the promotional nature and potential name confusion with other proprietary or established drug names in the usual practice setting.

1.2 REGULATORY HISTORY

This is the third proposed proprietary name for this product. DMEPA found the first proposed proprietary name, Ondero, unacceptable in OSE Review #2010-1510, dated October 6, 2010 (b) (4)

DMEPA found the second proposed proprietary name, Trajenta, unacceptable (b) (4) and informed the Applicant of the unacceptability of the name via teleconference held on January 19, 2011.

1.3 PRODUCT INFORMATION

Tradjenta (Linagliptin) is a dipeptidyl peptidase-4 (DPP-4) inhibitor proposed as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. The recommended dose is 5 mg orally once daily. Tradjenta may be taken with or without food. No dose adjustment is recommended for patients with renal or hepatic impairment. Tradjenta will be available as 5 mg tablets in bottles containing 30, 90, or 1000 tablets and in physician samples packaged in blister packs of seven tablets each. The tablets should be stored at 25° C (77° F); excursions permitted to 15° to 30° C (59° to 86° F).

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 the proposed proprietary name, Tradjenta.

2.1 SEARCH CRITERIA

For this review, a particular consideration was given to drug names beginning with the letter 'T' 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.^{1,2}

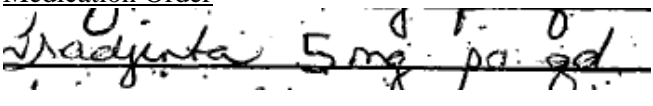
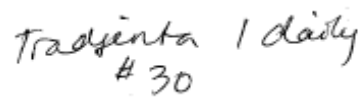
To identify drug names that may look similar to Tradjenta, the DMEPA safety evaluators also consider the orthographic appearance of the name on the lined and unlined orders. Specific attributes taken into the consideration include the length of the name (nine letters), upstrokes (three, the first capital letter 'T' and lower case letters 'd' and 't'), down strokes (one, lower case letter 'j'), cross-strokes (one, lower case letter 't'), and dotted letters (one, lower case letter 'j'). Additionally, several letters in the proposed name, Tradjenta, may be vulnerable to ambiguity when scripted (See Appendix B). As such, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Tradjenta.

When searching to identify potential names that may sound similar to Tradjenta, the DMEPA safety evaluators search for names with similar number of syllables (three), stresses (TRAD-jen-ta, trad-JEN-ta, or trad-jen-TA), and placement of vowel and consonant sounds. Additionally, DMEPA safety evaluators consider that pronunciation of part of the name can vary (see Appendix B). The Applicant's intended pronunciation [TRAD-gen-ta] was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced or spoken with regional accents and dialects, so other pronunciations of the names are considered.

2.2 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 and verbal orders were communicated during FDA prescription studies on February 11, 2011.

Figure 1: Tradjenta study samples

Handwritten Requisition Medication Order	Verbal Prescription
<u>Medication Order</u> 	Tradjenta 5 mg po qd
<u>Outpatient Prescription</u> 	

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

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

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant submitted an external evaluation of the proposed proprietary name conducted by Pharmaceutical Nomenclature Consultant. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall finding of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in the usual practice settings.

After the Safety Evaluator has determined the overall risk associated with the proposed name, the Safety Evaluator compares the findings to their overall assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

The following sections describe findings from our database searches, expert panel discussion, prescription analysis study, external name study, and safety evaluator search results.

3.1 DATA BASE AND INFORMATION SOURCES

The DMEPA safety evaluator searches yielded a total of twelve names (n=12) as having some similarity to the name, Tradjenta.

Nine (n=9) of the twelve names were thought to look like Tradjenta by the safety evaluators. These names are Trandate, Trental, Trionate, Twynsta, Trileptal, TriLyte, Truvada, Travatan, and (b) (4)

The remaining three names (n=3), Trajenta***, Sufenta, and Alfenta were thought to look like and sound like Tradjenta by safety evaluators.

3.2 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 Tradjenta.

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 PRESCRIPTION ANALYSIS STUDIES

A total of forty-three practitioners responded to the prescription analysis studies. None of the responses overlapped with currently marketed products. Twenty-one practitioners interpreted the proposed name correctly as 'Tradjenta' with correct interpretation occurring with inpatient (n=8) and outpatient prescription studies (n=13). The remaining twenty-two participants misinterpreted the name. The most common misinterpretation of the outpatient orders has letter 'd' being omitted from the name (n=15) and letter 'j' misinterpreted as the letter 'g' (n=11). Additionally, the most common misinterpretation in the inpatient and outpatient orders occurred with letter 'e'

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misinterpreted as the letter 'i' (n=5). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

The proposed name risk assessment submitted by the Applicant and conducted by Pharmaceutical Nomenclature Consultant found the proposed proprietary name, Tradjenta, acceptable.

Pharmaceutical Nomenclature Consultant evaluated seven names for their potential similarity to the name, Tradjenta. Two of these names, Travatan and Trental, were also identified by DMEPA's safety evaluators as look-alike and sound-alike names. The remaining five names, Tracleer, Trazadone, Trientine, Cogentin, and Gentamicin, were thought to look-like and sound-like Tradjenta by the Consultant. These names were added to the proprietary name risk assessment by the primary safety evaluator.

3.5 COMMENTS FROM THE DIVISION OF METABOLISM AND ENDOCRINOLOGY PRODUCTS (DMEP)

3.5.1 Initial Phase of Review

DMEP did not have any comments or concerns regarding the proposed proprietary name, Tradjenta, at the initial point of review.

3.5.2 Mid-Point of Review

In response to DMEPA's email on March 31, 2010, DMEP indicated that the name Tradjenta is acceptable to them.

3.6 SAFETY EVALUATOR SEARCH RESULTS

The primary safety evaluator identified an additional seven names (n=7) which were thought to look similar to Tradjenta and represent a potential source of drug confusion. These names are Treagan, Tagamet, Trilafon, Tripedia, Fragmin, (b) (4) and Triglide.

Thus, twenty four names (n=24) were identified as having some similarity to the proposed name, Tradjenta (12 names from DMEPA searches, 5 names from external study, and 7 names were identified by the primary safety evaluator).

4 DISCUSSION

The proposed proprietary name, Tradjenta, 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.

4.1 PROMOTIONAL ASSESSMENT

DDMAC did not find the name Tradjenta promotional on February 10, 2011. DMEPA and DMEP concurred with this finding.

4.2 SAFETY ASSESSMENT

The safety assessment considered the orthographic and phonetic similarity of the proposed proprietary name to the currently marketed drugs, the results of the prescription studies, and other aspects of the name that might be a source of confusion.

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A total of 24 names were identified and evaluated as being potentially similar to the proposed proprietary name, Tradjenta.

Six (n=6) of the 24 names were eliminated from the further analysis for the following reasons: five names (n=5) lack orthographic or phonetic similarity to Tradjenta and one name (n=1) has never been marketed (See Appendices D and E).

Failure Mode and Effect Analysis (FMEA) was then applied to determine whether the proposed proprietary name could potentially be confused with the remaining 18 names; and thereby, lead to medication errors. This analysis determined that the name similarity between Tradjenta was unlikely to result in medication errors with all 18 of the remaining products for the reasons presented in Appendices F and G.

5 CONCLUSIONS AND RECOMMENDATIONS

Our assessment of the proposed proprietary name indicates that the proposed name, Tradjenta, is not vulnerable to name confusion that could lead to medication errors, nor is the name considered promotional. Thus, DMEPA has no objection to the proposed name, Tradjenta, for this product at this time.

Additionally, DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review or 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. The Applicant will be notified via letter.

If you have further questions or need clarifications, please contact Margarita Tossa, project manager, at 301-796-4053.

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. The Document Archiving, Reporting, and Regulatory Tracking System (DARRTS)

DARRTS 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)

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)

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)

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

12. Access Medicine Database (<http://www.accessmedicine.com/drugs.aspx>)

Access Medicine contains full-text information from approximately 60 medical titles: it includes tables and references. Among the database titles are: Goodman and Gilman's The Pharmacological Basis of Therapeutics, Current Medical Diagnosis and Treatment, Tintinalli's Emergency Medicine, and Hurst's the Heart.

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)

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.

17. LabelDataPlus Database (<http://www.labeldataplus.com/index.php?ns=1>)

LabelDataPlus database covers a total of 36773 drug labels. This includes Human prescription drug labels as well as Active Pharmaceutical Ingredients (APIs), OTC (Application and Monograph) drugs, Homeopathic drugs, Unapproved drugs, and Veterinary drugs.

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.³

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.

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.⁴ 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

³ National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

⁴ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

monitoring the impact of the medication.⁵ 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 Sponsor’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice.

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"> 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 Upstrokes Down strokes	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

⁵ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

		Cross-strokes 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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/or 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.⁶ 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

⁶ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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?”

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 Sponsor 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 Sponsor 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 Sponsor. 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), the 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 Sponsor 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. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Sponsor 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 Sponsors' 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).

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 Sponsor 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 Sponsor 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

Appendix B:

Table 1: Letters with possible orthographic or phonetic misinterpretation

Letters in the name, Tradjenta	Scripted may appear as	Spoken may be interpreted as
Capital 'T'	'F', 'Z', 'J', 'G', 'L', 'S'	'D'
Lower case 't'	'f', 'd', 'r', 'x', 'a'	'd'
Lower case 'r'	'c', 'n', 's', 'v', 'z'	wr
Lower case 'a'	'ci', 'ce', 'd', 'e', 'o', 'n', 'u'	any vowel
Lower case 'd'	'cl', 't', 'a'	't'
Letter string 'j'	'g', 'p', 'y'	'g'
Lower case 'e'	'a', 'c', 'i', 'l', 'o'	Any vowel
Lower case 'n'	'a', 'm', 'u', 'r', 'h', 's'	'm', 'dn', 'kn', 'mn', 'pn'

Appendix C: FDA Prescription study for Evotion from 02/11/2011

Figure 1: Tradjenta study samples

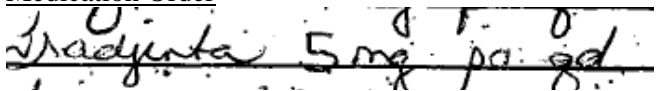
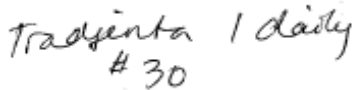
Handwritten Requisition Medication Order	Verbal Prescription
<u>Medication Order</u> 	Tradjenta 5 mg po qd
<u>Outpatient Prescription</u> 	

Table 1: Responses to prescription study

Inpatient Medication Order	Outpatient Prescription Order	Voice Prescription
Fradjinta	Tradjenta	Trajenta
Tradjenta	Tradjenta	Tragenta
Tradjenta	Tradjenta	Tragenta
Tradjinta	Tradjenta	Tragenta
Tradjenta	Tradjinta	Tragenta
Tradjenta	Tradjenta	Trajenta
Tradjenta	Tradjenta	Trigenta
Tradjinta	Tradjenta	Trajenta
Tradjenta	Tradjenta	Tragenta
Lradjenta	Tradjenta	Tragenta
Tradjenta	Tradjenta	Tragenta
Tradjenta	Tradjenta	Trajenta
Fradjenta	Tradjinta	Trygenta
	Tradjenta	Tragenta
	Tradjenta	Trigenta

Appendix D: Names of products that lack convincing orthographic and/or phonetic similarity

Drug Product Name	Drug Product Name
Trientine	Gentamicin
Cogentin	Trionate
Tripedia	

Appendix E: Name of the product that has never been marketed

Proprietary Name	Similarity to Tradjenta	Status of a Product Name
Trajenta ^{***}	Look alike and sound alike	Trajenta ^{***} was a primary name for Linagliptin Tablets (NDA 201280) that was found unacceptable by DMEPA (b) (4). The Applicant was notified via teleconference on January 19, 2011.

Appendix F: Names of the products with no overlap in dose and/or strength

Product name with potential for confusion	Similarity to Tradjenta	Dosage Form and Strength	Usual Dose (If applicable)
Tradjenta (Linagliptin)	N/A	Tablets: 5 mg	Take 1 tablet orally once daily
Tagamet (Cimetidine)	Look alike	Tablet: 100 mg, 200 mg, 300 mg, 400 mg, and 800 mg	<u>For GERD</u> 800 mg orally twice daily or 400 mg orally four times daily <u>For Self-Medication of Heartburn</u> 200 mg orally once to twice daily up to 400 mg per day.
Trilafon* (Perphenazine) *Although proprietary name is discontinued, generic products are available Trilafon and its generic product Perphenazine Injection and Oral Solutions are no longer marketed.	Look alike	Tablet: 2 mg, 4 mg, 8 mg, and 16 mg	<u>Treatment of Psychotic Disorders</u> Adults: Take 4 mg to 8 mg three times daily Geriatric patients: 2 mg to 4 mg orally daily or 1 mg to 2 mg twice daily. <u>Treatment of Nausea/Vomiting</u> Take 8 mg to 16 mg in divided doses

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

Fragmin (Dalteparin)	Look alike	Injection: 2500units/0.2 mL; 5000 units/0.2 mL; 7500 units/0.3 mL; 10,000 units/mL; 12,500 units/0.5 mL; 15,000 units/0.6 mL; 18,000 units/0.72 mL 25,000 units/mL	Inject 200 units/kg subcutaneously once daily up to 18,000 units during the first month of treatment, then 150 units/kg subcutaneously once daily up to 18,000 units during months 2 through 6.
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(b) (4)

Tracleer (Bosentan)	Look alike and sound alike	Tablet: 62.5 mg and 125 mg	62.5 mg to 125 mg orally twice daily
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Appendix G: Potentially confusing names with overlap in strength, but analysis indicates low potential for confusion

Failure Mode: Name Confusion	Causes (can be multiple)	Rationale for Failure Mode Prevention
Tradjenta (Linagliptin) Tablets, 5 mg	N/A	Take 1 tablet orally once daily
<p>Trandate (Labetalol) Tablets: 100 mg, 200 mg, and 300 mg</p> <p>Injection*: 20 mg/4 mL; 40 mg/8 mL; 100 mg/20 mL; 200 mg/40 mL (5 mg/mL)</p> <p>NOTE: No strength or dose overlap with tablets. However, there is a numerical overlap in strength and dose with Injection.</p> <p>*Proprietary name is no longer marketed, but generic products are still available.</p> <p><u>Usual Dose:</u> Oral: 100 mg to 400 mg orally twice daily Intravenous: 20 mg intravenously over 2 minutes. Additional injections of 40 mg or 80 mg may be administered in 10 minute intervals until the desired supine blood pressure is achieved or a total of 300 mg have been administered</p>	<p><u>Orthographic</u> Both names share the first letter string 'Tra-'. Additionally, letters 'd' and 't' are located in similar positions</p> <p><u>Dosage Form</u> Both products may be available as tablets</p> <p><u>Numerical Overlap in Strength/Dose</u> Tradjenta is dosed at the strength of 5 mg, which overlaps with the strength of Trandate Injection 5 mg/mL, if the volume is omitted (e.g., Trandate 5 mg)</p> <p><u>Route of Administration</u> Both products may be administered orally as tablets.</p>	<p><u>Orthographic</u> The name Tradjenta contains a down stroke whereas the name Trandate does not. Additionally, the letter string '-jenta' in Tradjenta lacks orthographic similarity to the letter string '-ate' in Trandate when scripted.</p> <p><u>Frequency of Administration</u> Once daily vs. twice daily (oral) or every 10 minutes (intravenous)</p>

<p>Trental (Pentoxifylline) Extended-release Tablets, 400 mg</p> <p><u>Usual Dose</u> 400 mg orally three times daily with meals</p>	<p><u>Orthographic</u> Both names start with the letter ‘T’ and share letter string ‘-ta-’ (although indifferent positions). Additionally, the letter string ‘Tra-’ in Tradjenta may be scripted to appear similar to the letter string ‘Tre-’ in Trental</p> <p><u>Dosage Form</u> Both products may be available as tablets</p> <p><u>Numerical Overlap in Strength</u> Both products are available as single strength products. Thus, strength may be omitted.</p> <p><u>Usual Dose</u> 1 tablet</p> <p><u>Route of Administration</u> Both products may be administered orally as tablets.</p>	<p><u>Orthographic</u> The name Tradjenta contains 9 letters and appears to be longer whereas the name Trental contains 7 letters and appears to be shorter. Additionally, the letter string ‘-djenta’ in Tradjenta lacks orthographic similarity to the letter string ‘-ntal’ when scripted.</p> <p><u>Frequency of Administration</u> Once daily vs. three times daily</p>
<p>Twynsta (Telmisartan and Amlodipine) Tablets: 40 mg/5 mg; 40 mg/10 mg,; 80 mg/5 mg; 80 mg/10 mg</p> <p><u>Usual Dose</u> 40 mg/5 mg to 80 mg/10 mg orally once daily</p>	<p><u>Orthographic</u> Both names start with the letter ‘T’ and end with the letter string ‘-ta-’. Additionally, the letter string ‘Tra-’ in Tradjenta may be scripted to appear similar to the letter string ‘Tw-’ in Twynsta if the letter ‘a’ is left open.</p> <p><u>Dosage Form</u> Both products may be available as tablets</p> <p><u>Partial Numerical Overlap in Strength/Dose</u> Tradjenta is dosed at the strength of 5 mg, which overlaps with the Amlodipine strength and dose of Twynsta (i.e., 40 mg/5 mg and 80 mg/5 mg).</p> <p><u>Route of Administration</u> Both products may be administered orally as tablets.</p> <p><u>Frequency of Administration</u> Both products should be administered once daily</p>	<p><u>Orthographic</u> The name Tradjenta contains an upstroke (letter ‘d’) in the middle of the name whereas Twynsta does not. Additionally, the letter string ‘-djen-’ in Tradjenta lacks orthographic similarity to the letter string ‘-yns-’ in Twynsta when scripted.</p> <p><u>Strength/Dose</u> Although Tradjenta’s strength/dose overlaps with Amlodipine active ingredient of Twynsta (5 mg), the entire strength of Twynsta must be scripted because the strengths of Telmisartan are different; and thus, cannot be omitted. (40 mg/5 mg and 80 mg/5 mg)</p>

<p>Trileptal (Oxcarbazepine) Tablet: 150 mg, 300 mg, and 600 mg</p> <p>Oral Suspension: 300 mg/5 mL</p> <p>NOTE: No strength or dose overlap with tablets. However, there is a numerical overlap in strength and dose with Oral Suspension</p> <p><u>Usual Dose</u> 150 mg to 600 mg orally twice daily to a maximum of 2400 mg per day</p>	<p><u>Orthographic</u> Both names share the letter string ‘-ta’ in similar locations. Additionally, the letter string ‘Trad-’ in Tradjenta may be scripted to appear similar to the letter string ‘Tril-’ in Trileptal</p> <p><u>Dosage Form</u> Both products may be available as tablets</p> <p><u>Partial Numerical Overlap in Strength/Dose</u> Tradjenta is dosed at the strength of 5 mg, which overlaps with Trileptal strength or dose in milliliters (e.g., Trileptal 5 mL)</p> <p><u>Route of Administration</u> Both products may be administered orally</p>	<p><u>Orthographic</u> The name Tradjenta contains 3 upstrokes vs. the name Trileptal contains 4 upstrokes. Additionally, the name Trileptal ends with an upstroke ‘l’ whereas Tradjenta does not. Furthermore, the letter string ‘-jen-’ in Trajenta lacks orthographic similarity to the letter string ‘-ep-’ in Trileptal when scripted.</p> <p><u>Frequency of Administration</u> Once daily vs. twice daily</p>
<p>Trilyte (Sodium Bicarbonate, Sodium Chloride, Polyethylene Glycol 3350, Potassium Chloride) Powder for Oral Solution</p> <p><u>Usual Dose</u> Drink 240 mL orally every 10 minutes until 4 liters are consumed or the rectal effluent is clear.</p>	<p><u>Orthographic</u> The letter string ‘Tradj-’ in Tradjenta may be scripted to appear similar to the letter string ‘Trily-’ in Trilyte</p> <p><u>Numerical Overlap in Strength</u> Both products are available as single strength products. Thus, strength may be omitted.</p> <p><u>Route of Administration</u> Both products may be administered orally</p>	<p><u>Orthographic</u> The name Tradjenta appears to be longer than Trilyte (9 letters vs. 7 letters) when scripted</p> <p><u>Usual Dose</u> 1 tablet vs. 240 mL every 10 minutes</p> <p><u>Frequency of Administration</u> Once daily vs. every 10 minutes</p>

<p>Triglide (Fenofibrate) Tablet 50 mg and 160 mg</p> <p><u>Usual Dose</u> 50 mg to 160 mg orally one daily</p>	<p><u>Orthographic</u> The letter strings ‘Tra-’ and ‘-ta’ in Tradjenta may be scripted to appear similar to the letter strings ‘Tri-’ and ‘-de’ in Triglide</p> <p><u>Dosage Form</u> Both products are tablets</p> <p><u>Strength/Dose</u> Tradjenta will be dosed at the strength of 5 mg, which overlaps with Triglide’s strength and dose of 50 mg, especially if Tradjenta is scripted with a trailing zero (5.0 mg)</p> <p><u>Route of Administration</u> Orally</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> Tradjenta appears longer than Triglide it contains wider letters such as ‘a’, ‘d’, and ‘e’ vs. Triglide contains narrow letters ‘i’. Additionally, the letter string ‘-djen-’ lacks orthographic similarity with the letter string ‘-gli-’ when scripted.</p>
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*** This document contains proprietary and confidential information that should not be released to the public. ***

<p>Truvada (Emtricitabine and Tenofovir) Tablet: 200 mg/300 mg</p> <p><u>Usual Dose</u> Take 1 tablet orally once daily with or without food</p>	<p><u>Orthographic</u> The letter string ‘Tra-’ and ‘-ta’ in Tradjenta may be scripted to appear similar to the letter strings ‘Tru-’ and ‘-da’ in Truvada</p> <p><u>Dosage Form</u> Both products may be available as tablets</p> <p><u>Numerical Overlap in Strength</u> Both products are available as single strength products. Thus, strength may be omitted.</p> <p><u>Usual Dose</u> 1 tablet</p> <p><u>Route of Administration</u> Both products may be administered orally</p> <p><u>Frequency of Administration</u> Both products should be administered once daily</p>	<p><u>Orthographic</u> Tradjenta contains an upstroke immediately next to the down stroke in the middle of the name (letters ‘d’ and ‘j’) whereas Truvada does not. Additionally, the letter string ‘-djen-’ in Tradjenta lacks orthographic similarity to the letter string ‘-va-’ in Truvada.</p>
<p>Travatan Z (Travoprost) Ophthalmic Solution 0.004%</p> <p><u>Usual Dose</u> Take 1 drop to affected eye once daily</p>	<p><u>Orthographic</u> Both names start with the letter string ‘Tra’ and contain the letter string ‘-ta-’ in similar positions.</p> <p><u>Numerical Overlap in Strength</u> Both products are available as single strength products. Thus, strength may be omitted.</p> <p><u>Frequency of Administration</u> Both products should be administered once daily</p>	<p><u>Orthographic</u> Tradjenta contains an upstroke immediately next to the down stroke in the middle of the name (letters ‘d’ and ‘j’) whereas Travatan does not. Additionally, the letter string ‘-djen-’ in Tradjenta lacks orthographic similarity to the letter string ‘-va-’ in Travatan</p> <p><u>Route of Administration</u> Orally vs. ophthalmically</p>

<p>Treagan (Antipyrine, Benzocaine, u-Polycosanol 410) Otic Solution: 5.4%/1.4%/0.0097%</p> <p><u>Usual Dose</u> Instill 1 to 2 drops to the ear every 1 to 2 hours until pain and congestion are relieved</p>	<p><u>Orthographic</u> The letter string 'Tra-' in Tradjenta may be scripted to appear similar to the letter string 'Tre-' in Treagan</p> <p><u>Numerical Overlap in Strength</u> Both products are available as single strength products. Thus, strength may be omitted.</p>	<p><u>Orthographic</u> The name Tradjenta appears to be longer than Treagan (9 letters vs. 7 letters). Additionally, the name Tradjenta contains 3 upstrokes and the name Treagan contains 1 upstroke.</p> <p><u>Route of Administration</u> Oral vs. otic</p> <p><u>Frequency of Administration</u> Once daily vs. every 1 to 2 hours until pain and congestion are relieved</p>
<p>Sufenta (Sufentanil Citrate) Injection 50 mcg/mL, 100 mcg/2 mL, 2.5 mg/5 mL</p> <p><u>Usual Dose</u> <u>For General Anesthesia</u> Start at the doses of 1 mcg/kg to 30 mcg/kg intravenously, maintenance dose is 0.5 mcg/kg to 10 mcg/kg</p> <p><u>Epidural Dosage During Labor and Delivery</u> 10 mcg to 15 mcg epidurally in combination with bupivacaine</p>	<p><u>Orthographic</u> The letter 'T' and letter string '-jenta' in Tradjenta may be scripted to appear similar to the letter 'S' and letter string '-fenta' in Sufenta</p> <p><u>Phonetic</u> Both names share letter string '-enta'</p> <p><u>Partial Numerical Overlap in Strength/Dose</u> Tradjenta is dosed at the strength of 5 mg which partially overlaps with Sufenta's strength of 50 mcg/2 mL and 2.5 mg/5 mL, if the volume or the strength were omitted (e.g., Sufenta 500 mcg or Sufenta 5 mL)</p>	<p><u>Orthographic</u> The name Tradjenta appears to be longer than Sufenta (9 letters vs. 7 letters). Additionally, the letter string '-rad-' in Tradjenta lacks orthographic similarity to the letter 'u' in Sufenta when scripted.</p> <p><u>Phonetic</u> The letter string 'Tradj-' in Tradjenta lacks phonetic similarity to the letter string 'Suf-' in Sufenta.</p> <p><u>Frequency of Administration</u> Once daily vs. continuous infusion or one time.</p>

<p>Alfenta (Alfentanil)Injection: 1 mg/2 mL and 2.5 mg/5mL (500 mcg/mL)</p> <p><u>Usual Dose</u> <u>For General Anesthesia</u> 50 mcg/kg to 245 mcg/kg intravenously over 3 minutes as induction. Maintenance doses of 0.5 mcg/kg/min to 1.5 mcg/kg/min</p> <p><u>For Conscious Sedation</u> 3 mcg/kg to 8 mcg/kg intravenously over 3 minutes. Maintenance doses should be 3 mcg/kg to 5 mcg/kg intravenously every 5 minutes to 20 minutes or continuous infusions of 0.25 mcg/kg/min to 1 mcg/kg/min. Total dose ranges 3 mcg/kg to 40 mcg/kg until the end of the procedure</p>	<p><u>Orthographic</u> The letter ‘T’ and letter string ‘-jenta’ in Tradjenta may be scripted to appear similar to the letter ‘A’ and letter string ‘-fenta’ in Alfenta, if both names are scripted with a lower case letters ‘t’ and ‘a’</p> <p><u>Phonetic</u> Both names share letter string ‘-enta’</p> <p><u>Partial Numerical Overlap in Strength/Dose</u> Tradjenta is dosed at the strength of 5 mg which partially overlaps with Alfenta’s strength of 500 mcg/mL and 2.5 mg/5 mL, if the volume or the strength were omitted (e.g., Alfenta 500 mcg or Alfenta 5 mL)</p>	<p><u>Orthographic</u> The name Tradjenta appears to be longer than Alfenta (9 letters vs. 7 letters). Additionally, the letter string ‘-rad-’ in Tradjenta lacks orthographic similarity to the letter ‘l’ in Alfenta when scripted.</p> <p><u>Phonetic</u> The letter string ‘Tradj-’ in Tradjenta lacks phonetic similarity to the letter string ‘Alf-’ in Alfenta.</p> <p><u>Frequency of Administration</u> Once daily vs. over 3 minutes, or every 5 to 20 minutes, or continuous infusion.</p>
<p>Trazodone Tablet: 50 mg, 100 mg, 150 mg, and 300 mg</p> <p><u>Usual Dose</u> 150 mg orally per day in two to three divided doses up to 400 mg (outpatient) and 600 mg (inpatient) in two to three divided doses.</p>	<p><u>Orthographic</u> Both names share the letter string ‘Tra-’</p> <p><u>Phonetic</u> Both names share the letter string ‘Tra-’</p> <p><u>Dosage Form</u> Both products may be available as tablets</p> <p><u>Numerical Overlap in Strength</u> Tradjenta is dosed at the strength of 5 mg, which overlaps with Trazodone strength of 50 mg.</p> <p><u>Route of Administration</u> Both products may be administered orally</p>	<p><u>Orthographic</u> Tradjenta contains 3 upstrokes vs. Trazodone contains 2 upstrokes. Additionally, the upstrokes ‘t’ in Tradjenta and ‘d’ in Trazodone appear to be in different positions.</p> <p><u>Phonetic</u> The letter string ‘-djenta’ in Tradjenta lacks phonetic similarity to the letter string ‘-zodone’ in Trazodone.</p> <p><u>Frequency of Administration</u> Once daily vs. two to three times daily</p>

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/s/

YELENA L MASLOV
04/08/2011

ZACHARY A OLESZCZUK
04/08/2011

CAROL A HOLQUIST
04/08/2011