CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
21-306

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:	June 4, 2010
To:	Bob Rappaport, MD, Director Division of Anesthesia and Analgesia Products
Through:	Denise Toyer, PharmD., Deputy Director Division of Medication Error Prevention and Analysis
From:	Zachary Oleszczuk, PharmD., Acting Team Leader Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Butrans (Buprenorphine) Transdermal System
Application Type/Number:	NDA 021306
Applicant:	Purdue Pharma L.P.
OSE RCM #:	2010-896

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1 INTRODUCTION

This re-assessment of the proprietary name is written in response to the anticipated approval of NDA 021306 within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Butrans, acceptable in OSE Review #2009-1990, dated January 7, 2010. The Division of Drug Marketing, Advertising and Communication (DDMAC) found the name acceptable from a promotional perspective on October 29, 2009.

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 used the same search criteria outlined in OSE Review #2009-1990, dated January 7, 2010, for the proposed proprietary name, Butrans. None of Butrans's product characteristics 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 4, 2010.

However, the searches of the databases listed in section 6 identified five additional names thought to look similar to Butrans and represent a potential source of drug name confusion. The five names thought to look similar to Butrans were: Betaxon, (b) (4) (b) (4) (b) (4) and Rituxan.

4 DISCUSSION

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

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment indicates that the proposed name, Butrans, 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, Butrans, 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 Anesthesia and Analgesia Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

6 REFERENCES

1. Oleszczuk, Z. OSE Review #2009-1990: Proprietary Name Review for Butrans. January 7, 2010.

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

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

3. USAN Stems (http://www.ama-assn.org/ama/pub/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.

APPENDICIES

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

Proprietary Name	Similarity to Butrans	Reason for Discard
(b) (4)		

Appendix B: Proposed proprietary names of drug products that are discontinued and no generic equivalent is available

Proprietary Name	Similarity to Butrans	Status
Betaxon	Look	Discontinued in Drugs@FDA and the Orange Book with no generic equivalents available.

<u>Appendix C:</u> Products with overlapping numerical strengths that have multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Butrans (Buprenorphine) Transdermal System		**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**	
(b) (4)				
Rituxan (Rituximab)	Look	Injection: 100 mg/10 mL and 500 mg/50 mL	**Non-Hodgkin's Lymphoma:** 375 mg/m^2 as an IV infusion according to the following schedules based on the state of the disease: Administer once weekly for 4 or 8 doses. Administer on Day 1 of each cycle of CVP chemotherapy, for up to 8 doses, then weekly for 4 doses at 6-month intervals to a maximum of 16 doses. **Chronic Lymphocytic Leukemia:** 375 mg/m^2 the day prior to the initiation of FC chemotherapy, then 500 mg/m2 on Day 1 of cycles 2-6 (every 28 days). **Recommended Dose as a Component of Zevalin®** 250 mg/m^2 within 4 hours prior to the administration of Zevalin. **Recommended Dose for Rheumatoid Arthritis** Two; 1000 mg intravenous infusions separated by 2 weeks.	Dosage form (transdermal system vs. injection) Dose (5 mcg/hour, 10 mcg/hour, and 20 mcg/hour vs. doses based on body surface area) Route (topical vs. intravenous)

<u>Appendix C:</u> Products with overlapping numerical strengths that have multiple differentiating product characteristics (continued)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Butrans (Buprenorphine) Transdermal System		**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**	
(b) (4)				

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21306	ORIG-1	PURDUE PHARMA LP	BuTrans (buprenorphine transdermal system)

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/s/

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06/04/2010

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06/04/2010

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:	January 7, 2010
To:	Bob Rappaport, MD, Director Division of Anesthesia, Analgesia, and Rheumatology Products
Through:	Kellie Taylor, Pharm D, MPH, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Zachary Oleszczuk, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Butrans (Buprenorphine) Transdermal System
Application Type/Number:	NDA 021306
Applicant/Applicant:	Purdue Pharma L.P.
OSE RCM #:	2009-1990

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CONTENTS

EXECUTIVE SUMMARY

Butrans is the proposed proprietary name for Buprenorphine Transdermal System. This proposed 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, Butrans, acceptable for this product.

If approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Anesthesia, Analgesia, and Rheumatology Products (DAARP) 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 resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from Purdue Pharma, L.P., on October 15, 2009, for an assessment of the proposed proprietary name, Butrans, regarding potential name confusion with other proprietary or established drug names in the usual practice settings. The Applicant submitted an external study conducted by (b) (4) in support of their proposed proprietary name. Purdue Pharma also submitted container labels, carton and package insert labeling for review, which will be reviewed in a separate review (OSE Review #2009-1861).

1.2 PRODUCT INFORMATION

Butrans (Buprenorphine) Transdermal system is being developed as a transdermal system providing systemic delivery of buprenorphine, a partial agonist opioid analgesic, continuously for up to 7 days. Butrans is indicated for the relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time. Butrans is available as patches of 5 mcg/hour, 10 mcg/hour and 20 mcg/hour and supplied in cartons containing 4 individually packaged patches and a pouch containing 4 patch disposal systems.

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, Butrans.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'B' 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]

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

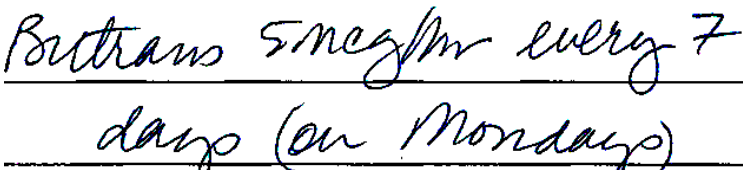
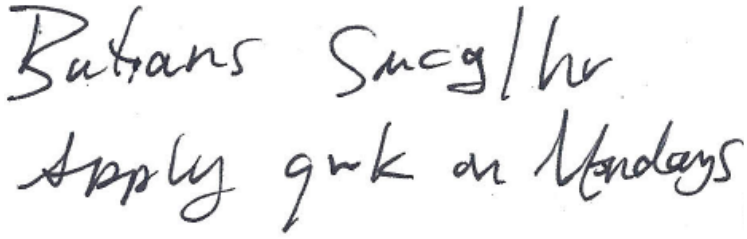
To identify drug names that may look similar to Butrans, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (7 letters), upstrokes (two, capital letter 'B' and lower case letter 't'), downstrokes (none), crosstrokes (one, lower case 't'), and dotted letters (none). Additionally, several letters in Butrans may be vulnerable to ambiguity when scripted (see Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Butrans.

When searching to identify potential names that may sound similar to Butrans, the DMEPA staff searches for names with similar number of syllables (two), stresses (BU-tranz and bu-TRANZ), and placement of vowel and consonant sounds. The Applicant's intended pronunciation is taken into consideration, as it was included in the Request for Proprietary Name Review. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (See Appendix B). Furthermore, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

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 medication order, outpatient medication order and verbal prescription was communicated during the FDA prescription studies.

Figure 1. Butrans Study (conducted on October 30, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order:  	Butrans 5 mcg/hour apply new patch every Monday dispense one box
Outpatient Medication Order:  	

[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. The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall findings 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 usual practice settings.

After the Safety Evaluator has determined the overall risk associated with the proposed name, the Safety Evaluator compares the findings of their overall risk 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

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 16 names as having some similarity to the name Butrans.

Fourteen of the names were thought to look like Butrans. These include Bactrim, Ben-Tann, Bitrex, Butalan, Butisol, Butramin, Dextran, (b) (4), (b) (4) Lutera, (b) (4) Pulmari, (b) (4) and Ultram. One name, Eutron was thought to sound similar to Butrans. The remaining name, Butrans, was thought to look and sound similar to Butrans.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of October 28, 2009.

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 Butrans.

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 twenty-five practitioners responded in the prescription analysis studies. Nine of the participants interpreted the name correctly as "Butrans," with most correct interpretations (n=7) occurring in the inpatient prescription study. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations in the written prescription studies occurred with the lower case letter 'n' being misinterpreted as a lower case letter 'm'. The lower case letter 'r' was also misinterpreted as a lower case letter 'i' and the lower case letter 'u' was misinterpreted as a lower case letter 'y'. In the verbal studies, the responses were misspelled phonetic variations of the proposed name, Butrans. The majority of misinterpretations in the verbal study occurred with the ending of the name '-ns' being misinterpreted as '-nz', '-n' or '-nd' and the first letter 'B-' being misinterpreted as the letter 'D-'. Additionally, one participant in the inpatient prescription study stated that the proposed proprietary name is "Too close to Bactrim". Bactrim was previously identified during DMEPA's database searches. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 EXTERNAL STUDY

The proposed name risk assessment conducted by (b) (4) identified and evaluated a total of 10 names thought to have some potential for confusion with the name Butrans: Buspar, Busulfan, Bumex, Subutex, Suboxone, Buprenorphine, Bupropion, Wellbutrin, Botox, and Rynatan. None of the 10 names were previously identified in DMEPA staff searches. All 10 names were evaluated in Section 3.6 below.

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

3.5.1 Initial Phase of Review

In response to the OSE October 29, 2009 e-mail, DAARP did not forward any comments and/or concerns on the proposed name at the initial phase of the name review.

3.5.2 Midpoint of Review

On November 20, 2009, DMEPA notified the Division of Anesthesia, Analgesia, and Rheumatology Products via e-mail that we had no objections to the proposed proprietary name, Butrans. The Division of Anesthesia, Analgesia, and Rheumatology Products stated via e-mail correspondence on January 5, 2010, that the division was concerned with the use of the route of administration in the name.

3.6 SAFETY EVALUATOR RISK ASSESSMENT

Although 26 names were identified by the DMEPA database searches and the external name assessment, one of the 26 names, Butrans, is the subject of this review and has been removed from further analysis. Independent searches by the primary Safety Evaluator did not identify any additional names which were thought to look similar to Butrans and represent a potential source of drug name confusion. Thus, we identified and evaluated a total of 25 names for their similarity to the proposed name.

4 DISCUSSION

Comments for pertinent disciplines were considered in the overall evaluation of the name. DDMAC did not have concerns with the proposed name Butrans. The Division of Anesthesia, Analgesia, and Rheumatology Products stated they were concerned with the use of the route of administration in the proposed name. Considering this we explored whether or not the letter string '-trans', which is also contained within the dosage form (transdermal patch) and the route of administration (transdermal or topical) for the proposed product, could be considered a route of administration. DMEPA was not able to verify that the letter string '-trans' is a recognized abbreviation for the word transdermal[3,4] and thus, DMEPA does not believe that the route of administration and dosage form are in the name. Additionally, DMEPA did not identify other factors besides names with potential similarity to Butrans that would render the name unacceptable.

A total of 25 names were identified and evaluated by DMEPA. Seven of the 25 names lacked convincing orthographic and/or phonetic similarity to the proposed proprietary name Butrans and were not evaluated further (see Appendix D).

[3] Davis, Neil M; Medical Abbreviations; Westminster, PA: 2009.

[4] Definition obtained from MediLexicon at: http://www.medilexicon.com/medicalabbreviations.php. Accessed on January 5, 2010.

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 18 names and lead to medication errors. This analysis determined that the name similarity between Butrans was unlikely to result in medication errors with any of the 18 products for the reasons presented in Appendices E through K. This finding was consistent with and supported by an independent risk assessment of the proprietary name submitted by the Applicant.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Butrans, 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, Butrans, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, 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 of the name are subject to change. If the approval of this application is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

5.1 COMMENTS TO THE DIVISION

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Chery Milburn, OSE project manager, at 301-796-2084.

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 Anesthesia, Analgesia, and Rheumatology Products (DAARP) should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

5.2 COMMENTS TO THE APPLICANT

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

If approval of the NDA is delayed beyond 90 days from the date of this review, the proprietary name must be re-reviewed prior to the new approval date.

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

REFERENCES

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

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

2. Phonetic and Orthographic Computer Analysis (POCA)

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

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

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

4. AMF Decision Support System [DSS]

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

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

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

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

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

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

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

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

USPTO provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

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. Stat!Ref (www.statref.com)

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

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

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

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

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

16. Medical Abbreviations Book

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

APPENDICES

Appendix A:

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

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

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

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. [6] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[7] 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 in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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

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

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

Type of similarity	**Considerations when searching the databases**		
	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 Upstrokes Down strokes Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
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

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.[8] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses 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?"***

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

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

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

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

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

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

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

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

Appendix B: Letters with Possible Orthographic or Phonetic misinterpretation

Letters in Name, Butrans	Scripted may appear as	Spoken may be interpreted as
Capital 'B'	'D' (block), 'R', or 'S'	'D' or 'V'
Lower case 'u'	'a', 'n', 'v', 're', or 'y'	'A', 'E' 'I', 'O', 'ALL', or 'Y'
Lower case 't'	'f', 'r', or 'x'	'D' or 'PT'
Lower case 'r'	'i', 'n', 'v', or 'x'	'WR'
Lower case 'a'	'c', 'ci', 'ce', 'el', 's', 'x' 'e', 'o', or 'u'	'E', 'I', 'ALL', 'U', 'O', or 'Y'
Lower case 'n'	'h', 'm', 'r', 's', or 'x'	'DN', 'GN', 'KN', 'MN', or 'PN'
Lower case 's'	'a', 'g', 'l', or 'n'	'S', 'PS', 'TS', 'X', or 'Z'

Appendix C: FDA Prescription Study Responses.

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Butram	Butaris	Butran
Butrams	Butians	Butran
Butrams	Butians	Butrand
Butrans	Butians	Butrans
Butrans	Butians	Butrans
Butrans	Butram	Butranz
Butrans		Butron
Butrans		Dutrans Patch
Butrans		
Butrans		
Bytrans		

Appendix D: Proprietary names that lack convincing orthographic and/or phonetic similarities

Proprietary Name
Subutex
Buprenorphine
Bupropion
Wellbutrin
Botox
Rynatan
Ultram

Appendix E: Proprietary names that are internationally registered

Proprietary Name	Similarity to Butrans	Active Ingredient	Country
Butramin	Look	Sibutramine	Bangladesh and Columbia

<u>Appendix F:</u> Proposed proprietary names that have never been marketed and are associated with an inactive application, a withdrawn application, or the proposed name has been withdrawn.

Proprietary Name	Similarity to Butrans	Reason for Discard
		(b) (4)

<u>Appendix G:</u> Proposed proprietary names of drug products that are discontinued and no generic equivalent is available

Proprietary Name	Similarity to Butrans	Status and Date
Eutron (Pargyline and methyclothiazide)	Sound	NDA 016047 Application Withdrawn November 5, 1992

Appendix H: Products that are not used as Drug Products

Proprietary Name	Active Ingredient	Description	Similarity to Butrans
Bitrex	(denatonium benzoate)	This is the most biter compound known. This compound is added to Bath foam, Soap, Perfume, after shave, Nail polish remover, Shampoo, Shower gel, Body scrub, Conditioner, Anti nail biting preparations, household cleaning products, industrial products, and automobile products to deter consumption of these products. This product can also be used to denature alcohol.	Look

Appendix I: Products with no numerical overlap in strength

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose
Butrans (Buprenorphine) Transdermal System		**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**
Bactrim (Trimethoprim and Sulfamethoxazole)	Look	Tablets: 80 mg trimethoprim and 400 mg sulfamethoxazole 160 mg trimethoprim and 800 mg sulfamethoxazole Oral suspension: 40 mg Trimethoprim and 200 mg Sulfamethoxazole per 5 mL Injection: 80 mg Trimethoprim and 400 mg Sulfamethoxazole per 5 mL	Tablets and Oral Suspension: Trimethoprim 160 mg and Sulfamethoxazole 800 mg orally every 12 hours for 14 days Intravenous injection: 10 mg/kg/day (Trimethoprim component) intravenous in 3 to 4 equally divided doses for up to 14 days

<u>Appendix J:</u> Products with overlapping numerical strengths that have multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Butrans (Buprenorphine) Transdermal System		**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**	
Busulfan	Sound	Injection: 6 mg/mL Tablet: 2 mg	<u>Injection:</u> 0.8 mg/kg of ideal body weight or actual body weight, whichever is lower, administered every six hours for four days. <u>Tablets:</u> 60 mcg/kg of body weight or 1.8 mg/m^2 per day	Dosage form (transdermal system vs. tablets or injection) Frequency (once a week vs. every six hours or once daily) Route (topical vs. oral or intravenous)
Bumex (Bumetanide)	Look and Sound	Injection: 0.25 mg/mL Tablets: 0.5 mg, 1 mg, and 2 mg	<u>Injection:</u> 0.5 to 1 mg intravenous or intramuscular times one dose. If the response to an initial dose is deemed insufficient, subsequent doses may be given at intervals of 2 to 3 hours up to a daily maximum dose of 10 mg <u>Tablets:</u> 0.5 mg to 2 mg orally once daily. If the diuretic response to an initial dose is not adequate, a subsequent dose may be given at 4 to 5 hour intervals up to a maximum daily dose of 10 mg.	Dosage form (transdermal system vs. tablets or injection) Frequency (once a week vs. every six hours or once daily or every 2 to 5 hours) Route (topical vs. oral or intravenous)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Butrans (Buprenorphine) Transdermal System		**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**	
Benn-Tann (Diphenhydramine)	Look	Oral Suspension: 25 mg/mL	25 mg to 50 mg orally every 4 to 8 hours.	Dosage form (transdermal system vs. oral suspension) Frequency (once a week vs. every four hours to eight hours) Route (topical vs. oral)
Dextran	Look	Injection: 150 mg/mL Solution for Intravenous Infusion: 6%, 10%, and 32%	Injection: 3 grams (20 mL) given by intravenous push, 1 minutes to 2 minutes before intravenous infusion of clinical dextran. Solution for Intravenous Infusion: 10 mL/kg/day to 20 mL/kg/day	Dosage form (transdermal system vs. injection or intravenous infusion) Frequency (once a week vs. continuous infusion) Route (topical vs. intravenous injection or infusion)
Lutera (Ethinyl Estradiol and Levonorgestrel)	Look	Tablets: 20 mcg Ethinyl Estradiol and 0.1 mg Levonorgestrel	1 tablet orally once daily	Dosage form (transdermal system vs. tablets) Frequency (once a week vs. once daily) Route (topical vs. oral)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Differentiating product characteristics
Butrans (Buprenorphine) Transdermal System		**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**	
Pulmari (Brompheniramine Tannate, Carbetapentane Tannate, and Phenylephrine Tannate)	Look	Oral suspension: Brompheniramine Tannate 4mg, Carbetapentane Tannate 30 mg, and Phenylephrine Tannate 7.5 mg per 5 mL	5 mL to 10 mL orally every 12 hours	Dosage form (transdermal system vs. oral suspension) Frequency (once a week vs. every four hours to eight hours) Route (topical vs. oral)
				(b) (4)

Appendix K: Products with numerical overlap in strength or dose.

Failure Mode: **Name confusion**	**Causes** **(could be multiple)**	**Rationale**
Butrans (Buprenorphine) Transdermal System	**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**
Suboxone (Buprenorphine and Naloxone) Dosage From: Sublingual Tablets Strength: 2 mg of Buprenorphine and 0.5 mg Naloxone And 8 mg of Buprenorphine and 2 mg Naloxone Usual Dose: 12 mg to 16 mg of Buprenorphine sublingually once daily.	Phonetic similarity (the '-an-' in Butrans may sound similar to '-on-' in Suboxone) Orthographic similarity (both names contain a similar number of letters (7 vs. 8), both contain the same number of upstrokes (2, capital 'B' and lower case 't' vs. capital 'S' and lower case 'b') located in the same position (1st letter and 3rd letters), both contain the same number of crosstrokes (1, lower case 't' vs. lower case 'x'), the 1st letter of each name ('B-' vs. 'S-') may appear similar when scripted, both contain the same 2nd letter ('u'), the 5th and 6th letter of Butrans ('-an-') may appear similar to the 6th and 7th letter of Suboxone ('-on-')) Both products share and achievable numerical dose (15 mcg vs. 15 mg) if the naloxone ingredient is omitted from a prescription for Suboxone.	Phonetic and orthographic differences in addition to the different dosage form, route of administration and frequency of administration of each product will help minimize the likelihood of medication error in the usual practice setting. *Rationale:* The risk for medication error is minimized by the phonetic differences in the names. Each name has a different number of syllables (2 vs. 3). The beginning of each name ('Butr-' vs. 'Subox-') sound different when spoken. These differences will help to minimize the risk between these two products. The risk for medication error is also minimized by the orthographic differences in the names. The middle of each name ('-r-' vs. '-ox-') appears different when scripted. This difference will help to minimize the risk of error between the two products. Additionally, the difference in dosage form (transdermal system vs. sublingual tablet), route of administration (topical vs. sublingual), and frequency of administration (once every week vs. once daily) will help to differentiate the two products since dosage form, route of administration and frequency of administration are typically included on a prescription.

Failure Mode: **Name confusion**	**Causes** **(could be multiple)**	**Rationale**
Butrans (Buprenorphine) Transdermal System	**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**
Buspar (Buspirone Hydrochloride) <u>Dosage From:</u> Tablets <u>Strength:</u> 5 mg, 7.5 mg, 10 mg, 15 mg, and 30 mg <u>Usual Dose</u>: 7.5 mg to 30 mg orally twice daily	Phonetic similarity (both names contain the same number of syllables (2), and the beginning of each name (‘Bu-’) is the same)) Orthographic similarity (both names contain a similar number of letters (8 vs. 7), both contain the same 1st and 2nd letters (‘Bu-’), both names contain the letter (‘a’) in the fifth position, and the sixth letter of each name (‘n’ vs. ‘r’) may appear similar when scripted) Both products share a numerical strengths (5 mcg/hour and 10 mcg/hour vs. 5 mg and 10 mg) and numerical doses (5 mcg/hour, 10 mcg/hour and 20 mcg/hour vs. 5 mg, 10 mg, and 20 mg).	Phonetic and orthographic differences in addition to the different dosage form, route of administration and frequency of administration of each product will help minimize the likelihood of medication error in the usual practice setting. *Rationale:* The risk for medication error is minimized by the phonetic differences in the names. The ending of each name (‘-trans’ vs. ‘-spar’) sound different when spoken. This difference will help to minimize the risk of error between the two products. The risk for medication error is also minimized by the orthographic differences in the names. Each names contains a different number of upstrokes (2, Capital ‘B’ and lower case ‘t’ vs. 1 Capital ‘B’), a different number of downstrokes (none vs. 1, lower case ‘p’), and a different number of crosstrokes (1, lower case ‘t’ vs. none). These differences will help to minimize the risk between these two products. Additionally, the difference in dosage form (transdermal system vs. tablet), route of administration (topical vs. oral), and frequency of administration (once every week vs. twice daily) will help to differentiate the two products since dosage form, route of administration and frequency of administration are typically included on a prescription.

Failure Mode: **Name confusion**	**Causes** **(could be multiple)**	**Rationale**
Butrans (Buprenorphine) Transdermal System	**Transdermal System:** **5 mcg/hour, 10 mcg/hour, and 20 mcg/hour**	**Usual dose:** **Apply one patch every week**
Butalan (Butabarbital Sodium) <u>Dosage From:</u> Elixir <u>Strength:</u> 30 mg/ 5 mL <u>Usual Dose</u>: 15 mg to 100 mg orally once daily to 4 times daily.	Orthographic similarity (both names contain the same number of letters (7), both contain the same first 3 letters (‘But-’), have the same number of crosstrokes (1, lower case ‘t’) located in the same position (3rd letter), and both names contain the letter combination (‘an’) in similar positions (5^{th} and 6^{th} letter vs. 6^{th} and 7^{th} letter)) Both products share a numerical dose (20 mcg/hour vs. 20 mg).	Orthographic differences in addition to the different dosage form, route of administration and frequency of administration of each product will help minimize the likelihood of medication error in the usual practice setting. *Rationale:* The risk for medication error is minimized by the orthographic differences in the names. Each names contains a different number of upstrokes (2, Capital ‘B’ and lower case ‘t’ vs. 3 Capital ‘B’, lower case ‘t’, and lower case ‘l’),. This difference will help to minimize the risk between these two products. Additionally, the difference in dosage form (transdermal system vs. elixir), route of administration (topical vs. oral), and frequency of administration (once every week vs. once to four times daily) will help to differentiate the two products since dosage form, route of administration and frequency of administration are typically included on a prescription.
Butisol (Butabarbital Sodium) <u>Dosage From:</u> Elixir and Tablets <u>Strength:</u> Elixir 30 mg/ 5 mL Tablets 30 mg and 50 mg <u>Usual Dose</u>: 15 mg to 100 mg orally once daily to 4 times daily.	Orthographic similarity (both names contain the same number of letters (7), both contain the same first 3 letters (‘But-’), have the same number of crosstrokes (1. lower case ‘t’ located in the same position (3rd letter), and the 5^{th} letter of Butrans (‘a’) may appear similar to the 6^{th} letter of Butisol (‘o’) when scripted) Both products share a numerical dose (20 mcg/hour vs. 20 mg).	Orthographic differences in addition to the different dosage form, route of administration and frequency of administration of each product will help minimize the likelihood of medication error in the usual practice setting. *Rationale:* The risk for medication error is minimized by the orthographic differences in the names. Each name contains a different number of upstrokes (2, Capital ‘B’ and lower case ‘t’ vs. 3 Capital ‘B’, lower case ‘t’, and lower case ‘l’),. This difference will help to minimize the risk between these two products. Additionally, the difference in dosage form (transdermal system vs. elixir or tablet), route of administration (topical vs. oral), and frequency of administration (once every week vs. once to four times daily) will help to differentiate the two products since dosage form, route of administration and frequency of administration are typically included on a prescription.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21306	ORIG-1	PURDUE PHARMA LP	BUPRENORPHINE TRANSDERMAL SYSTEM

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