

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

200063Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	April 1, 2014
Application Type and Number:	NDA 200063
Product Name and Strength:	Contrave (naltrexone and bupropion) Extended-Release Tablets, 8 mg/90 mg
Product Type:	Multi-ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Orexigen
Submission Date:	January 27, 2014
Panorama #:	2014-16848
DMEPA Primary Reviewer:	Sarah K. Vee, PharmD
DMEPA Team Leader:	Yelena Maslov, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Contrave, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

The sponsor previously submitted the proposed proprietary name, Contrave, on August 5, 2009 and May 14, 2010. The proposed name was found acceptable in OSE Review #2009-1569, dated January 27, 2010 and OSE Review #2010-1080, dated July 30, 2010. The application received complete responses on dates January 31, 2011.

The Applicant re-submitted the name, Contrave, for review on January 27, 2014.

1.2 PRODUCT INFORMATION

The following product information is provided in the January 27, 2014 proprietary name submission.

- Intended Pronunciation: CON-trayv
- Active Ingredient: naltrexone HCl and bupropion HCl
- Indication of Use: a dual pro-opiomelanocortin cell [POMC] enhancer, is indicated for the management of obesity, including weight loss and maintenance of weight loss, and should be used in conjunction with lifestyle modification. CONTRAVE is recommended for patients with an initial body mass index ≥ 30 kg/m² or ≥ 27 kg/m² with one or more risk factors (e.g. diabetes, dyslipidemia, or hypertension).
- Route of Administration: oral
- Dosage Form: extended-release film-coated tablet
- Strength: 8 mg/90 mg
- Dose and Frequency: 2 tablets twice daily (morning and evening)

	Morning Dose	Evening Dose
Week 1	One CONTRAVE 8/90 tablet	–
Week 2	One CONTRAVE 8/90 tablet	One CONTRAVE 8/90 tablet
Week 3	Two CONTRAVE 8/90 tablets	One CONTRAVE 8/90 tablet
Week 4 – Onward (Maintenance Dose)	Two CONTRAVE 8/90 tablets	Two CONTRAVE 8/90 tablets

- How Supplied: Bottles of 120 tablets or 70 tablets

- Storage: Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].
- Container and Closure Systems: packaged in an opaque white high density polyethylene (HDPE) bottle, a (b) (4) cap with an induction seal, and an adsorbent packet.

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name.

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Metabolic and Endocrinology Products (DMEP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name¹.

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Contrave, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

One hundred twelve practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. Eighty-six participants interpreted the name correctly as "Contrave". Nine participants misinterpreted the "o" as an "a". Appendix B contains the results from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, February 5, 2014 e-mail, DMEP did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

¹USAN stem search conducted on February 10, 2014.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of $\geq 50\%$ retrieved from our POCA search organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified from previous reviews.

POCA Search Results	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	6
Moderately similar name pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$	280
Low similarity name pair: combined match percentage score $\leq 49\%$	10

2.2.6 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 296 names contained in Table 1 determined 296 names will not pose a risk for confusion as described in Appendices C through G.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to DMEP via e-mail on March 4, 2014. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DMEP on March 7, 2014, they stated no additional concerns with the proposed proprietary name, Contrave.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Terrolyn Thomas, OSE project manager, at 240-402-3981.

3.1 COMMENTS TO THE APPLICANT

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

If any of the proposed product characteristics as stated in your January 27, 2014 submission are altered, the name must be resubmitted for review.

4 REFERENCES

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

USAN Stems List contains all the recognized USAN stems.

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

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present.

Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (<http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#>).

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.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name.

1. **Promotional Assessment:** For prescription drug products, the promotional review of the proposed name is conducted by OPDP. For over-the-counter (OTC) drug products, the promotional review of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP or DNCE provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
 - a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. 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.²

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Affirmative answers to these questions indicate a potential area of concern.
Y/N	Does the name have obvious Similarities in Spelling and Pronunciation to other Names?
Y/N	Are there Manufacturing Characteristics in the Proprietary Name?
Y/N	Are there Medical and/or Coined Abbreviations in the Proprietary Name?
Y/N	Are there Inert or Inactive Ingredients referenced in the Proprietary Name?
Y/N	Does the Proprietary Name include combinations of Active Ingredients
Y/N	Is there a United States Adopted Name (USAN) Stem in the Proprietary Name?
Y/N	Is this the same Proprietary Name for Products containing Different Active Ingredients?
Y/N	Is this a Proprietary Name of a discontinued product?

² National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

- b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 50% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:
- Highly similar pair: combined match percentage score $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 49\%$.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. Based on our root cause analysis of post marketing experience errors, we find the expression of strength and dose, which is often located in close proximity to the drug name itself on prescriptions and medication orders, is an important factor in mitigating or potentiating confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion is limited (e.g., route, frequency, dosage form, etc.).

- For highly similar names, there is little that can mitigate a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are likely to be rejected by FDA. (See Table 3)
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics (e.g., route, frequency, dosage form, etc.) to mitigate confusion may be limited when the strength or dose overlaps. FDA will review these names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4)
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist (See Table 5).

- c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

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 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 record their interpretations of the orders which are recorded electronically.

- d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for 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 OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/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 provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is $\geq 70\%$).

Answer the questions in the checklist below. Affirmative answers to these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair do not share a common strength or dose (see Step 1 of the Moderately Similar Checklist).

<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
Y/N	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? <i>*FDA considers the length of names different if the names differ by two or more letters.</i>	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 50\%$ to $\leq 69\%$).

<p>Step 1</p>	<p>Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths have a higher potential for confusion and should be evaluated further (see Step 2).</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p> <p>For any combination drug products, consider whether the strength or dose may be expressed using only one of the components.</p> <p>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:</p> <ul style="list-style-type: none"> ○ Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. ○ Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. ○ Similar sounding doses: 15 mg is similar in sound to 50 mg
<p>Step 2</p>	<p>Answer the questions in the checklist below. Affirmative answers to these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion between moderately similar names with overlapping or similar strengths or doses.</p>

<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names begin with different first letters? <p>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</p> <ul style="list-style-type: none"> • Are the lengths of the names dissimilar* when scripted? <p>*FDA considers the length of names different if the names differ by two or more letters.</p> <ul style="list-style-type: none"> • Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted? 	<p>Phonetic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?
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Table 5: Low Similarity Name Pair Checklist (i.e., combined score is $\leq 49\%$).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where there are data that suggest a name with low similarity might be vulnerable to confusion with your proposed name (for example, misinterpretation of the proposed name as a marketed product in a prescription simulation study). In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Contrave Study (Conducted on February 6, 2014)

Handwritten Requisition Medication Order	Verbal Prescription
<p data-bbox="188 804 428 835"><u>Medication Order:</u></p> <p data-bbox="188 846 708 961">- 1 Contrave 1 po bid</p>	<p data-bbox="954 804 1377 888">Contrave 2 by mouth twice daily #120</p>
<p data-bbox="188 982 500 1014"><u>Outpatient Prescription:</u></p> <p data-bbox="240 1077 727 1224">Contrave 2 po BID #120</p>	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Contrace

274 People Received Study

112 People Responded

	37	38	37	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
CANTRANE	1	0	0	1
CANTRARE	1	0	0	1
CANTRAV	0	1	0	1
CANTRAVE	9	0	0	9
CENTRAVE	0	0	1	1
CONGRAVE	1	0	0	1
CONTRACE	0	1	0	1
CONTRAISE	0	2	0	2
CONTRAIZ	0	1	0	1
CONTRARE	4	0	0	4
CONTRAVE	19	31	34	84
CONTRAVE 2 BY MOUTH	0	1	0	1
CONTRAVE ONE ORALLY TWICE DAILY	0	0	1	1
CONTREAS	0	1	0	1
CONTSAVE	0	0	1	1
CONTVAVE	1	0	0	1
UNKNOWN	1	0	0	1

Appendix C: Highly Similar Names (i.e., combined POCA score is $\geq 70\%$)

No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Orthographic and/or phonetic differences in the names sufficient to prevent confusion
1.	Pedtrace-4	70	- 'Con' and 'Ped' appear different when scripted. They also sound different when spoken. - The modifier '4' in 'Pedtrace-4' would help further differentiate the two names
2.	(b) (4)		
3.	Contramid***	70	Proposed modifier for NDA 21745 (Tramadol Contramid OAD). Found unacceptable in OSE Review #2006-0050.
4.	Contrin	70	- 'ave' and 'in' appear different when scripted. They also sound different when spoken.

Appendix D: Moderately Similar Names (i.e., combined POCA score is $\geq 50\%$ to $\leq 69\%$) with no overlap in Strength and/or Dose

No.	Proposed Name	POCA Score
1.	Accutane	52
2.	Akpentolate	50
3.	Altoprev	51
4.	Antivert	50
5.	Anturane	68
6.	(b) (4)***	52
7.	Cankaid	54
8.	Canrenone	54

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9.	Carbatrol	50
10.	Cardrase	66
11.	Carnitine	50
12.	Cartrol	54
13.	Catapres	58
14.	Catarase	66
15.	Centrax	66
16.	Cetapred	54
17.	Cipro I.V.	50
18.	Clorpres	52
19.	Cobavite	50
20.	Codrix	50
21.	Combipres	54
22.	Cometriq	62
23.	Compazine	56
24.	Concerta	56
25.	Congess	53
26.	Conray	60
27.	Conray 280	60
28.	Conray 30	60
29.	Conray 325	60
30.	Conray 400	60
31.	Conray 43	60
32.	Contac	60
33.	Contac 12 Hour	52
34.	Copaxone	52
35.	Cordran	56
36.	Cortalone	59
37.	Cort-Dome	59
38.	Cortef	50
39.	Cortisone	53

40.	Cortizone-10	55
41.	Cortizone-5	55
42.	Cortone	59
43.	Cortril	60
44.	Cotolone	54
45.	Cutivate	56
46.	Dantrium	54
47.	Dantrolene	52
48.	Enpresse-21	54
49.	Enpresse-28	54
50.	Ergostrate	52
51.	Estrace	57
52.	Femtrace	66
53.	Gantrisin	54
54.	Gentran 40	57
55.	Gentran 70	57
56.	Humatrope	54
57.	Invirase	52
58.	Isentress	53
59.	Kantrex	65
60.	Kophane	50
61.	Novantrone	54
62.	Omnitrope	52
63.	Paltrase	61
64.	Pancrease	60
65.	Pancreaze	62
66.	Panokase	51
67.	Penetrex	52
68.	Pentacef	56
69.	Pentazine	53
70.	Pentetate	54

71.	Pertofrane	54
72.	Pontocaine	52
73.	Prochieve	50
74.	Sandril	50
75.	Sertraline	50
76.	Somatrem	60
77.	Sorbitrate	60
78.	Sotret	50
79.	Sterane	53
80.	Trandate	52
81.	Tranxene	52
82.	Ultrase	54
83.	Zenatane	50

Appendix E: Moderately Similar Names (i.e., combined POCA score is $\geq 50\%$ to $\leq 69\%$)
with overlap in Strength and/or Dose

No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	Ak-Pentolate	50	The name pair has sufficient orthographic and phonetic differences
2.	Antrenyl	56	The name pair has sufficient orthographic and phonetic differences
3.	Beconase	51	The name pair has sufficient orthographic and phonetic differences
4.	Bepreve	53	The name pair has sufficient orthographic and phonetic differences
5.	Bontril	58	The name pair has sufficient orthographic and phonetic differences
6.	Cafetrate	62	The name pair has sufficient orthographic and phonetic differences
7.	Calcitrene	52	The name pair has sufficient orthographic and phonetic differences
8.	Caltrate	68	The name pair has sufficient orthographic and phonetic differences
9.	Cam-Metrazine	53	The name pair has sufficient orthographic and phonetic differences
10.	Campral	56	The name pair has sufficient orthographic and phonetic differences
11.	Candex	51	The name pair has sufficient orthographic and phonetic differences
12.	Cantharone	64	The name pair has sufficient orthographic and phonetic differences
13.	Cantil	52	The name pair has sufficient orthographic and phonetic differences
14.	Cartilade	60	The name pair has sufficient orthographic and phonetic differences
15.	Cenolate	52	The name pair has sufficient orthographic and phonetic differences

No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
16.	Cinryze	52	The name pair has sufficient orthographic and phonetic differences
17.	Centrum	56	- 'ave and 'um' appear different when scripted
18.	CereVe	58	The name pair has sufficient orthographic and phonetic differences
19.	(b) (4) ***	62	(b) (4)
20.	Citra Ph	50	The name pair has sufficient orthographic and phonetic differences
21.	Clindareach	50	The name pair has sufficient orthographic and phonetic differences
22.	Clindesse	52	The name pair has sufficient orthographic and phonetic differences
23.	Clofibrate	52	The name pair has sufficient orthographic and phonetic differences
24.	Codafed	50	The name pair has sufficient orthographic and phonetic differences
25.	Codar AR	50	The name pair has sufficient orthographic and phonetic differences
26.	Codeprex	53	The name pair has sufficient orthographic and phonetic differences
27.	Colace	58	The name pair has sufficient orthographic and phonetic differences
28.	Colcrys	50	The name pair has sufficient orthographic and phonetic differences

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No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
29.	Cold Cream	54	The name pair has sufficient orthographic and phonetic differences
30.	Colgate	50	The name pair has sufficient orthographic and phonetic differences
31.	Colytrol	52	The name pair has sufficient orthographic and phonetic differences
32.	Complera	55	The name pair has sufficient orthographic and phonetic differences
33.	Compro	54	The name pair has sufficient orthographic and phonetic differences
34.	Comtan	56	- 'rave' and 'an' appear different when scripted - Contrave appears longer in length when scripted because it contains eight letters whereas Comtan contains six
35.	Conate	60	The name pair has sufficient orthographic and phonetic differences
36.	Concentraid	58	The name pair has sufficient orthographic and phonetic differences
37.	Conceptrol	50	The name pair has sufficient orthographic and phonetic differences
38.	(b) (4) ***	60	Proposed proprietary name for IND (b) (4), withdrawn by Sponsor on 2/13/12
39.	(b) (4) ***	56	Proposed proprietary name for IND (b) (4) Found unacceptable in OSE Review #2012-302
40.	Constilac	54	The name pair has sufficient orthographic and phonetic differences
41.	Constulose	58	The name pair has sufficient orthographic and phonetic differences
42.	Contac Sinus	51	The name pair has sufficient orthographic and phonetic differences

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

No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
43.	Conte-Pak-4	58	The name pair has sufficient orthographic and phonetic differences
44.	Contragesic	60	The name pair has sufficient orthographic and phonetic differences
45.	Control Rx	60	The name pair has sufficient orthographic and phonetic differences
46.	Coraz	50	The name pair has sufficient orthographic and phonetic differences
47.	Cordarone	56	<ul style="list-style-type: none"> - ‘rave’ and ‘arone’ appear different when scripted - Contrave appears shorter in length when scripted because it contains eight letters whereas Cordarone contains ten - The cross-stroke of the letter “t” in Contrave vs. the letters “da” in Cordarone look different which helps to differentiate the names
48.	Cordran-N	54	NDA 50345 withdrawn FR effective 9/25/1998
49.	Cortaid	53	<ul style="list-style-type: none"> - ‘rave’ and ‘aid’ appear different when scripted - Cortaid ends with an upstroke provided by the letter ‘d.’ - Cortaid (family of names) may be written with a modifier to distinguish the product.
50.	Cortane	64	<ul style="list-style-type: none"> - ‘rave’ and ‘ane’ appear different when scripted - Dose (2 tablets vs. apply)
51.	Cortane-B	57	<ul style="list-style-type: none"> - ‘rave’ and ‘ane - B’ appear different when scripted - Dose (2 tablets vs. apply)
52.	Corticaine	50	The name pair has sufficient orthographic and phonetic differences
53.	Corticreme	60	The name pair has sufficient orthographic and phonetic differences
54.	Cortratigen	52	The name pair has sufficient orthographic and phonetic differences

No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
55.	Cortrosyn	54	The name pair has sufficient orthographic and phonetic differences
56.	Cosyntropin	51	The name pair has sufficient orthographic and phonetic differences
57.	Cotameth	50	The name pair has sufficient orthographic and phonetic differences
58.	Cotrim	55	The name pair has sufficient orthographic and phonetic differences
59.	Cotrim D.S.	51	The name pair has sufficient orthographic and phonetic differences
60.	Econopred	56	The name pair has sufficient orthographic and phonetic differences
61.	Econtra	66	The name pair has sufficient orthographic and phonetic differences
62.	Endrate	60	The name pair has sufficient orthographic and phonetic differences
63.	Entre-S	54	The name pair has sufficient orthographic and phonetic differences
64.	Entrocel	52	The name pair has sufficient orthographic and phonetic differences
65.	Foltrate	60	The name pair has sufficient orthographic and phonetic differences
66.	Introvale	56	The name pair has sufficient orthographic and phonetic differences
67.	Isoditrate	55	The name pair has sufficient orthographic and phonetic differences
68.	Isotrate	56	The name pair has sufficient orthographic and phonetic differences
69.	Kcentra	62	The name pair has sufficient orthographic and phonetic differences
70.	Kestrone 5	61	The name pair has sufficient orthographic and phonetic differences

No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
71.	Kinerase	62	The name pair has sufficient orthographic and phonetic differences
72.	Kutrase	68	The name pair has sufficient orthographic and phonetic differences
73.	Lactrase	56	- 'on' and 'ac' appear different when scripted
74.	Lodrane 24	56	The name pair has sufficient orthographic and phonetic differences
75.	Magtrate	54	The name pair has sufficient orthographic and phonetic differences
76.	Meta Trace	54	The name pair has sufficient orthographic and phonetic differences
77.	Neotrace-4	58	<p>- 'Con' and 'Neo' appear different when scripted. The modifier '4' in 'Neotrace-4' further helps differentiate the two names.</p> <p>- Contrave would be dosed in 1 or 2 tablets whereas Neotrace-4 would be dosed in mL.</p> <p>- Neotrace-4 is indicated for total parenteral nutrition and the trace elements should be monitored for dose adjustment.</p>
78.	Nitro Iv	50	The name pair has sufficient orthographic and phonetic differences
79.	Nora-Be	50	The name pair has sufficient orthographic and phonetic differences
80.	(b) (4) ***	58	Proposed proprietary name for IND (b) (4). Found unacceptable in OSE Review #2013-242.
81.	(b) (4) ***	58	Proposed proprietary name for NDA (b) (4), withdrawn by the Applicant on 6/28/2013
82.	Pentacel	52	The name pair has sufficient orthographic and phonetic differences

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No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
83.	Penthrane	66	The name pair has sufficient orthographic and phonetic differences
84.	Pentrax	62	The name pair has sufficient orthographic and phonetic differences
85.	Phentride	65	The name pair has sufficient orthographic and phonetic differences
86.	Phenurone	50	The name pair has sufficient orthographic and phonetic differences
87.	Pimtrea	50	The name pair has sufficient orthographic and phonetic differences
88.	(b) (4) ***	55	(b) (4)
89.	(b) (4) ***	56	Proposed proprietary name for IND (b) (4), withdrawn by sponsor on 3/15/2013
90.	(b) (4) ***	54	The name pair has sufficient orthographic and phonetic differences
91.	Procentra	50	The name pair has sufficient orthographic and phonetic differences
92.	(b) (4) ***	60	Alternate proposed proprietary name for NDA (b) (4). Never reviewed.
93.	Qinprezo	54	The name pair has sufficient orthographic and phonetic differences
94.	Scopace	54	The name pair has sufficient orthographic and phonetic differences
95.	Seb-Prev	52	The name pair has sufficient orthographic and phonetic differences

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No.	Proposed name: Contrave Strength: 8 mg/90 mg Usual Dose: 2 tablets BID	POCA Score	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
96.	(b) (4) ***	60	Alternate proposed proprietary name for BLA (b) (4) approved under (b) (4) ***
97.	Solaraze	54	The name pair has sufficient orthographic and phonetic differences
98.	Soolantra	54	The name pair has sufficient orthographic and phonetic differences
99.	Sudatrate	60	The name pair has sufficient orthographic and phonetic differences
100.	Suprane	56	The name pair has sufficient orthographic and phonetic differences
101.	Supreme	50	Not a drug. glucose test
102.	(b) (4) ***	54	Proposed proprietary name for IND (b) (4). Found unacceptable in OSE Review #2012-914. (b) (4) *** approved for BLA (b) (4)
103.	(b) (4) ***	54	Proposed proprietary name for IND (b) (4). Found unacceptable in OSE Review #2011-2846.
104.	Tetra-Ide	53	The name pair has sufficient orthographic and phonetic differences
105.	Tetramed	52	The name pair has sufficient orthographic and phonetic differences
106.	Tnkase	50	The name pair has sufficient orthographic and phonetic differences
107.	Vitraxe	52	The name pair has sufficient orthographic and phonetic differences
108.	Vontrol	54	The name pair has sufficient orthographic and phonetic differences
109.	Zorbtive	50	The name pair has sufficient orthographic and phonetic differences

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Appendix F: Low Similarity Names from Previous Reviews (i.e., combined POCA score is $\leq 49\%$)

No.	Name	POCA Score
1.	Antara	44
2.	Cardene	47
3.	Cardenz	38
4.	Centamin	46
5.	(b) (4) ***	36
6.	Congestac	41
7.	Cortan	47
8.	Lantus	33
9.	Oralone	36
10.	Questran	45

Appendix G: Names with unidentified product characteristics

No.	Name	POCA Score
1.	Centrine	72
2.	(b) (4) ***	70
3.	Aconitine	53
4.	ANTIROBE	64
5.	Benztrone	54
6.	C Complex	52
7.	Camphor Ice	54
8.	Carace	62
9.	Care-Creme	54
10.	Carprieve	64
11.	CATALASE	59
12.	Centex	50

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13.	Centovir	52
14.	Cetazone	50
15.	Cetrimide	50
16.	Chlorate	50
17.	Chlotride	53
18.	cinoxate	53
19.	citral	50
20.	Citrate	62
21.	Citravet	58
22.	ClindaRobe	59
23.	Cloburate	54
24.	cocoate	50
25.	Combantrin	52
26.	(b) (4) ***	50
27.	Comfortis	50
28.	Comtess	54
29.	Comtrex NT	56
30.	Conacetol	52
31.	Concordin	52
32.	Condasin	58
33.	Condrin	66
34.	Condylin	56
35.	coniine	52
36.	Conpec	53
37.	Contact Cold	52
38.	Contimin	56
39.	Contraflam	62
40.	Coro-Nitro	50
41.	Contuss	56
42.	Corrective	54

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43.	Cortilone	55
44.	Cortimed	53
45.	Cortinide	50
46.	Counteract IB	50
47.	Covace	57
48.	CURATREM	54
49.	Denti Care	52
50.	Denticare	52
51.	Depandrate	50
52.	Ecopace	52
53.	Ecosave	59
54.	Entre-B	54
55.	Estrate	52
56.	Fortral	50
57.	GentaVed	51
58.	Gentaved 100	51
59.	Gonabreed	56
60.	Kentace	68
61.	Kentiazem	54
62.	Kentovace	66
63.	Lodrane	56
64.	(b) (4) ***	58
65.	nydrane	54
66.	PanaKare	52
67.	Panaleve	54
68.	pentane	62
69.	Pentran	63
70.	picrate	50
71.	Point Relief	54
72.	Ponderax	54

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73.	prolintane	50
74.	PROMACE	50
75.	(b) (4) **	52
76.	Sandrena	50
77.	Santura	52
78.	(b) (4) ***	53
79.	SILODRATE	50
80.	Sinthrome	59
81.	Soft Care	54
82.	(b) (4) ***	51
83.	(b) (4) ***	58
84.	sometribove	62
85.	Sonapram	58
86.	Syntaris	51
87.	tartrate	61
88.	Trandide	50
89.	Tridrane	52
90.	Zentrip	50

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/s/

SARAH K VEE
04/01/2014

YELENA L MASLOV
04/01/2014

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

Date: July 30, 2010

Application Type/Number: NDA 200063

Through: Melina Griffis RPh, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis
(DMEPA)

From: Richard Abate, RPh, MS, Safety Evaluator
Division of Medication Error Prevention and Analysis
(DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Contrave
(Naltrexone Hydrochloride and Bupropion Hydrochloride)
Extended-Release Tablets, 4 mg/90 mg and 8 mg/90 mg

Applicant/sponsor: Orexigen Therapeutics, Inc.

OSE RCM #: RCM 2010-1080

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EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed proprietary name, Contrave for (Naltrexone Hydrochloride and Bupropion Hydrochloride) Extended-Release Tablets. Our evaluation identified no concerns from a safety and promotional perspective that would render the name unacceptable. Thus, DMEPA finds the proposed proprietary name, Contrave, acceptable for this product.

The proposed proprietary name, Contrave, must be re-reviewed 90 days before approval of the NDA. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review summarizes the Division of Medication Error Prevention and Analysis' risk assessment for the proposed proprietary name, Contrave (Naltrexone Hydrochloride and Bupropion Hydrochloride) Extended-Release Tablets. The Applicant, Orexigen Therapeutic, requested an assessment of the proposed proprietary name in a submission dated May 14, 2010. The Division of Medication Error Prevention and Analysis (DMEPA) assesses a proposed proprietary name regarding its potential for name confusion with other proprietary or established drug names in the usual practice settings. Additionally, DMEPA considers the Division of Drug Marketing, Advertising and Communications' (DDMAC's) promotional assessment of the name.

In addition, the Applicant submitted draft container labels and carton labeling which are evaluated in a separate review (OSE review # 2010-1081).

1.2 REGULATORY HISTORY

DMEPA previously reviewed the proposed proprietary name, Contrave, under IND 068858 in OSE review #2009-1569 dated January 27, 2010. We found the proposed proprietary name acceptable but raised concern with the Division of Metabolism and Endocrinology Products regarding the dosage form description, “(b) (4) (b) (4)” was found to be an unrecognized USP dosage form. Orexigen was notified that the proposed name, Contrave, was acceptable on February 2, 2010. Orexigen included a recognized dosage form “extended-release tablets” with the NDA submission.

1.3 PRODUCT INFORMATION

Contrave is the proposed proprietary name for Naltrexone Hydrochloride and Bupropion Hydrochloride Extended-Release Tablets. Contrave is indicated for the treatment of obesity and weight management, including weight loss and maintenance of weight loss, and should be used in conjunction with lifestyle modification. It is recommended for patients with an initial body mass index (BMI) $\geq 30 \text{ kg/m}^2$ or 27 kg/m^2 with one or more risk factors such as diabetes, dyslipidemia or hypertension. Contrave is available in two

strengths (4 mg/90 mg and 8 mg/90 mg). Contrave requires a dose escalation at the beginning of therapy which is described in Table 1 below.

Table 1. Contrave dose escalation for the initiation of therapy.

	Morning Dose	Evening Dose
Week 1	One CONTRAVE 8/90 tablet	–
Week 2	One CONTRAVE 8/90 tablet	One CONTRAVE 8/90 tablet
Week 3	Two CONTRAVE 8/90 tablets	One CONTRAVE 8/90 tablet
Week 4 – Onward (Maintenance Dose)	Two CONTRAVE 8/90 tablets	Two CONTRAVE 8/90 tablets

The lower strength of Contrave (4 mg/90 mg) may be considered for initiation and escalation of therapy. But if the patient tolerates the 4 mg/90 mg tablets well, the dose should be switched to the 8 mg/90 mg tablets. The tablets should not be cut, chewed, or crushed. Both strengths are packaged in bottles containing 120 tablets or a one month supply. These bottles are stored at 25° C (room temperature).

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. Section 2.1 identifies specific information associated with the methodology for the proposed proprietary name, Contrave.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter ‘C’ 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 Contrave, the DMEPA safety evaluators also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (eight letters), upstrokes (two, capital letter C and lower case t), down strokes (none), cross strokes (one), and dotted (none). Additionally, several letters in Contrave 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 Contrave.

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)

When searching to identify potential names that may sound similar to Contrave, the DMEPA safety evaluators search for names with similar number of syllables (two), stresses (CON-treyv or con-TREYV), and placement of vowel and consonant sounds. (See Appendix B) The Sponsor's intended pronunciation (CON-trayv) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

3 RESULTS

The names identified from DMEPA's methods as potential sources for name confusion with Contrave are listed below.

3.1 DATABASE AND INFORMATION SOURCES

Our searches of database and DMEPA' information sources yielded a total of 21 names as having some similarity to the name Contrave.

Twenty of the names were thought to look like Contrave. These include: Anturane, Caltrate, Cardene, Cartrol, Centrax, Centrum, CereVe, Compro, Comtan, Contrin, Cordran, Cortaid, Cortane, Cortane-B, Cortef, Corticaine, Cortisone, Cortone, Lantus, and Questran. The remaining name, Contrave, was thought to look and sound similar to Contrave.

Additionally, DMEPA safety evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of July 30, 2010.

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 Contrave.

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

3.3.1 Initial Phase of Review

In response to a June 1, 2010 OSE e-mail, the Division of Metabolism and Endocrinology Products (DMEP) indicated they had no comments and/or concerns with the proposed proprietary name at the initial phase of the name review.

3.3.2 Midpoint of Review

DMEPA notified the Division of Metabolism and Endocrinology Products via e-mail that we had no concerns with the proposed proprietary name, Contrave, on July 1, 2010. Per e-mail correspondence from the Division of Metabolism and Endocrinology Products on July 12, 2010, they again noted no concerns with the proposed proprietary name, Contrave.

3.4 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary DMEPA safety evaluator resulted in the identification of one additional name which was thought to look or sound similar to Contrave and represent a potential source of drug name confusion. The name, Antara, was identified as having look-alike similarities

Eight of the 22 names identified above were evaluated in OSE review # 2009-1569. Although the Applicant included product characteristic changes in this submission, these described changes (i.e., the labeling describes the dose escalation of Contrave using only the 8 mg/90 mg strength tablets and dosage form description to Extended-Release Tablets) do not alter the conclusions in the previous review of the proposed proprietary name, Contrave, as the (b) (4)

(b) (4). These eight names include Anturane, Cartrol, Centrax, Centrum, Cortone, Cortane-B, Comtan, and Contrin.

Another of the 22 identified names, Contrave, is actually a name for this product, and the trademark is licensed to the Applicant and thus was not further evaluated. Thus, we identified a total 13 names as having some similarity to the proposed name, Contrave, and requiring further evaluation: one identified by the primary safety evaluator and 12 identified in section 3.1 above.

4 DISCUSSION

This proposed name, Contrave, was evaluated from a safety and promotional perspective. Furthermore, input from pertinent disciplines involved with the review of this application was considered accordingly.

4.1 PROMOTIONAL ASSESSMENT

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name. DMEPA and the Division of Metabolism and Endocrinology Products concurred with the findings of DDMAC's promotional assessment of the proposed proprietary name.

4.2 SAFETY ASSESSMENT

DMEPA evaluated 13 names for their potential similarity to the proposed name, Contrave. No other aspects of the name were determined to pose a different source for potential confusion with the name.

Four of the 13 names were eliminated for the reasons described in Appendix C and D. Appendix C lists proprietary names which lack sufficient orthographic similarity with Contrave to result in confusion. Appendix D describes proprietary names not found in usual clinical practice.

Failure modes and effects analysis (FMEA) was applied to determine if the proposed proprietary name could potentially be confused with the remaining nine names and lead to medication errors. This analysis determined that the name similarity between Contrave and all of the nine identified names was unlikely to result in medication error for the reasons presented in Appendix E.

5 CONCLUSIONS AND RECOMMENDATIONS

We have completed our review of the proposed proprietary name, Contrave, and it is not promotional nor is it vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis has no objections to the proprietary name, Contrave, at this time.

The proposed proprietary name, Contrave, must be re-reviewed 90 days before approval of the NDA. Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

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

5.1 COMMENTS TO THE APPLICANT

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

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

If any of the proposed product characteristics as stated in your May 14, 2010 submission are altered, the proprietary name should be resubmitted for review.

6 REFERENCES

6.1 REVIEWS

1. OSE Review # 2009-1569, Proprietary Name Review Contrave(Naltrexone Hydrochloride and Bupropion Hydrochloride) Sustained-Release Tablets, Holmes, L. January 27,2010

6.2 DATABASES

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. FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]

DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the 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/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)

USAN Stems List contains all the recognized USAN stems.

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.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.

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

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

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 drug 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.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.

⁵ 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	<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 Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> 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	<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. 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.

4. 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 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.

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

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: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Contrave	Scripted may appear as	Spoken may be interpreted as
Capital 'C'	A, E, G, L, and O	'K'
lower case 'c'	a, e, i, and o	'k'
lower case 'o'	a, c, and u	any vowel
lower case 'n'	h, m, r, u, or v	'm'
lower case 't'	f or l	'd'
lower case 'r'	n, s, t, or v	'w'
lower case 'a'	'ce,' 'ci,' e, o, or u	any vowel
lower case 'v'	n, o, r, s , or u	'b' or 'f'
lower case 'e'	c, i, or l	Although silent in this name, any vowel

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

Proprietary Name	Similarity to Contrave
CereVe	Look
Compro	Look

Appendix D: Proprietary names not used in usual practice settings for the reasons described.

Proprietary Name	Active Ingredient	Similarity to Contrave	Failure preventions
Cortane	Hydrocortisone	Look	Unable to identify product on the searched databases and information sources. Identified on Google only as a topical hydrocortisone product.
Corticaine	Hydrocortisone and Dibucaine	Look	Noted on Micromedex that discontinued by manufacturer in 1987.

Appendix E: Risk of name confusion minimized by preventions listed. (Potential contributing causes highlighted by *italics*)

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
<p>Contrave (Naltrexone Hydrochloride and Bupropion)</p>		<p>4 mg/90 mg and 8 mg/90 mg extended-release tablets</p>	<p>Week 1: One 8 mg/ 90 mg tablet every morning. Week 2: One 8 mg/90 mg tablet twice daily. Week 3: Two 8 mg/90 mg tablets every morning and one 8 mg/ 90 mg tablet every evening Week 4 and onward as maintenance dose two 8 mg/ 90 mg tablets twice daily.</p> <p>The lower strength (4 mg/90 mg) may be used if patient is not able to tolerate 8 mg/90 mg strength.</p>	
<p>Caltrate (product family name which include) Caltrate 600 (Calcium Carbonate) Caltrate + D (Calcium Carbonate and Cholecalciferol) Caltrate + D plus minerals (Calcium Carbonate, Cholecalciferol, Magnesium Oxide, Manganese Sulfate, Zinc Oxide, Sodium Borate and Copper Sulfate)</p>	Look	<p>600 mg (calcium) tablet 600 mg/400 IU tablet 600 mg/400 IU/50 mg/1.8 mg/7.5 mg/250 mcg/1 mg tablet</p>	<p><i>One tablet by mouth twice daily</i></p>	<p>Orthographic difference: Caltrate includes four upstrokes and two cross strokes compared to the two upstrokes and single cross stroke in Contrave. Caltrate may be written with a modifier.</p> <p>Strength: Caltrate may be written with the 600 mg strength vs. Contrave which requires a strength to be written for a complete prescription. 4 mg/ 90 mg and 8 mg/90 mg. There is no numerical overlap.</p>
<p>Cordran (Flurandrenolide)</p>	Look	<p>0.025% cream, 0.05% lotion and 4 mcg/cm² tape Single strength in each formulation, thus may be omitted</p>	<p>Apply a small amount of lotion or cream to affected area <i>twice daily</i> or three times daily. Apply appropriate size of tape over affected area every 12 to 24 hours.</p>	<p>Strength: 0.025%, 0.05%, and 4 mcg/cm² vs. 4 mg/90 mg and 8 mg/90 mg. Cordran Tape may have a numerically similar strength (4 mcg/cm² vs. 4 mg/90 mg), but Cordran Tape is a single strength, thus strength may be omitted. Contrave's strength includes two numbers, one for each active ingredient.</p> <p>Dosage form and Route of administration: Cream, lotion or topical tape applied topically vs. oral extended-release tablets.</p>

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Contrave (Naltrexone Hydrochloride and Bupropion)		4 mg/90 mg and 8 mg/90 mg extended-release tablets	Week 1: One 8 mg/ 90 mg tablet every morning. Week 2: One 8 mg/90 mg tablet twice daily. Week 3: Two 8 mg/90 mg tablets every morning and one 8 mg/ 90 mg tablet every evening Week 4 and onward as maintenance dose two 8 mg/ 90 mg tablets twice daily. The lower strength (4 mg/90 mg) may be used if patient is not able to tolerate 8 mg/90 mg strength.	
Cortaid (Family name of products) Cortaid Advanced (Hydrocortisone) Cortaid Intensive Therapy Moisturizing Cream (Hydrocortisone) Cortaid Intensive Therapy Cooling Spray (Hydrocortisone) Cortaid Maximum Strength (Hydrocortisone) Cortaid Poison Ivy Care a kit which includes a spray containing active ingredients (Pramoxine Hydrochloride and Zinc Acetate)		1% cream 1% cream 1% spray 1% cream and ointment 1%/0/12% spray kit also contains cleansing solution. Separately packaged cleansing clothes.	Apply a small amount topically to affected area three to four times daily. Apply a small amount topically to affected area three to four times daily. One spray to affected area three to four times daily. Apply a small amount topically to affected area three to four times daily. Cleanse site after exposure to poison ivy and rinse. Apply spray to affected area three to four times daily. Use cloth to cleanse exposed area and rinse.	Orthographic difference: Cortaid ends with an upstroke provided by the letter 'd.' Cortaid may be written with a modifier to distinguish the product. Strength: 1% or 15/0.12% vs. 4 mg/90 mg and 8 mg/90 mg Dosage form and route of administration: Topically applied creams, ointments, and sprays vs. oral extended-release tablets. Frequency of use: three to four times daily vs. daily or twice daily.
Cortef (Hydrocortisone tablets, USP)	Look	5 mg, 10 mg, and 20 mg tablets	5 mg to 60 mg (<i>one to three tablets</i>) by mouth daily, twice daily, or three times daily up to total of 240 mg daily.	Orthographic difference: Cortef includes fewer letters and appears shorter and ends with an 'f' providing an upstroke at the end of the name. Strength: 5 mg, 10 mg and 20 mg vs. 4 mg/90 mg, and 8 mg/90 mg

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Contrave (Naltrexone Hydrochloride and Bupropion)		4 mg/90 mg and 8 mg/90 mg extended-release tablets	Week 1: One 8 mg/ 90 mg tablet every morning. Week 2: One 8 mg/90 mg tablet twice daily. Week 3: Two 8 mg/90 mg tablets every morning and one 8 mg/ 90 mg tablet every evening Week 4 and onward as maintenance dose two 8 mg/ 90 mg tablets twice daily. The lower strength (4 mg/90 mg) may be used if patient is not able to tolerate 8 mg/90 mg strength.	
Cardene (Nicardipine Hydrochloride)	Look	20 mg and 30 mg IR capsules 30 mg, 45 mg and 60 mg ER capsules 25 mg/10 mL vials 20 mg/200 mL and 40 mg/ 400 mL premixed bags	<i>One</i> capsule (20 mg or 30 mg) by mouth three times daily/ <i>One</i> extended release capsule (30 mg to 60 mg) <i>by mouth twice daily</i> . Infuse 5 mg/hour intravenously to control blood pressure. May increase by 2.5 mg/hr up to a maximum of 15 mg/hr for a 15 minute duration.	Strength of oral solids: 20 mg, 30 mg, 45 mg, and 60 mg vs. 4 mg/90 mg and 8 mg/ 90 mg. Numerically similar strengths (40 mg/ 400 mL vs. 4 mg/90 mg) appear in differing dosage forms (premixed bag vs. extended-release) likely preventing this failure.
Lantus (Insulin Glargine)	Look	100 units/mL 10 mL vial and 3 mL prefilled cartridge (single strength may be omitted)	Inject 10 to 60 units subcutaneously once daily. (the same time each day.)	Orthographic difference: Lantus includes fewer letters and appears shorter when scripted. Strength: 100 units/mL (a single strength which may be omitted) vs. 4 mg/90 mg vs. 8 mg/90 mg. Dosage forms and route of administration: injection given subcutaneously vs. oral extended-release tablets. The numeric doses of may overlap partially (16 units vs. 16 mg/180 mg) but the dosage form and route of administration likely prevents this failure.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)	Failure Mode of name confusion prevented by the combination of stated product characteristics as well as orthographic and/or phonetic differences as described.
Contrave (Naltrexone Hydrochloride and Bupropion)		4 mg/90 mg and 8 mg/90 mg extended-release tablets	Week 1: One 8 mg/ 90 mg tablet every morning. Week 2: One 8 mg/90 mg tablet twice daily. Week 3: Two 8 mg/90 mg tablets every morning and one 8 mg/ 90 mg tablet every evening Week 4 and onward as maintenance dose two 8 mg/ 90 mg tablets twice daily. The lower strength (4 mg/90 mg) may be used if patient is not able to tolerate 8 mg/90 mg strength.	
Cardenz (Multivitamin and mineral supplement)	Look	No strength specified. (includes twelve Vitamins and minerals)	<i>One tablet by mouth daily</i>	Orthographic difference: Cardenz includes the letter 'z' which may provide a down stroke at the end of the name when scripted. Strength: No strength vs. 4 mg/90 mg and 8 mg/90 mg Cardenz is an over-the-counter vitamin and mineral supplement. Preliminary drug use data shows no prescriptions filled or written for this product.
Questran (Cholestyramine)	Look	4 g/packet (single strength may be omitted)	4 g (one packet or scoopful) mixed in 8 ounces of fluid <i>by mouth daily or twice daily.</i>	Orthographic difference: The first half of the name, Questran, (Ques-) appears differently when compared to Contrave (Con-). The letter 'e' provides added length between the beginning letter and the 't' in Questran. Dosage form: powder for oral suspension vs. extended release tablets
Antara (Fenofibrate)	Look	34 mg and 130 mg capsules (micronized)	<i>One capsule (34 mg or 130 mg) by mouth daily.</i> Lower dose for renally impaired patients.	Orthographic difference: Antara contains only six letters and appears shorter when scripted. Strength: 34 mg and 130 mg vs. 4 mg/90 mg and 8 mg/90 mg

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200063	ORIG-1	OREXIGEN THERAPEUTICS INC	CONTRAVE® (Naltrexone HCl and Bupropion HCl)

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/s/

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