CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203313Orig1s000
203314Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME MEMORANDUM

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:	September 1, 2015
Application Type and Number:	NDA 203313
Product Name and Strength:	Ryzodeg 70/30 (insulin degludec and insulin aspart) injection, 100 units/mL
Product Type:	Combination (Drug + Device)
Rx or OTC:	Rx
Applicant/Sponsor Name:	Novo Nordisk
Panorama #:	2015-1341036
DMEPA Primary Reviewer:	Sarah K. Vee, PharmD
DMEPA Team Leader:	Yelena Maslov, PharmD

1 INTRODUCTION

The Applicant submitted the proposed proprietary name, Ryzodeg on March 26, 2015 (b) (4) Division of Medication Error Prevention and Analysis (DMEPA) found the name conditionally acceptable in our previous review[1] .

On August 19, 2015, the Agency recommended that the Applicant consider including the modifier "70/30" to the proposed proprietary name to indicate the concentrations of the two insulins in the formulation. Since Ryzodeg is a mixed insulin formulation containing 70 % insulin degludec and 30 % insulin aspart, the addition of the modifier 70/30 would be consistent with current naming approach for mixed insulins.

Thus, the Applicant submitted the name, Ryzodeg 70/30, for review on August 21, 2015. We note that the product characteristics are the same. This memorandum is to communicate that DMEPA finds the proposed proprietary name, Ryzodeg 70/30 (b) (4) is acceptable from both a misbranding and safety perspective.

2 CONCLUSIONS

The proposed proprietary name is acceptable.

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

2.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Ryzodeg 70/30, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your August 21, 2015 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

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[1] . Vee, Sarah. Proprietary Name Review for Ryzodeg (NDA 203313). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2015 MAY 29. 32 p. OSE RCM No.: 2015-80127.

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

/s/

SARAH K VEE
09/01/2015

YELENA L MASLOV
09/02/2015

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)

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Date of This Review:	May 29, 2015
Application Type and Number:	NDA 203313
Product Name and Strength:	Ryzodeg (70 % insulin degludec and 30 % insulin aspart) injection, 100 units/mL
Product Type:	Combination (Drug + Device)
Rx or OTC:	Rx
Applicant/Sponsor Name:	Novo Nordisk
Panorama #:	2015-80127
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, Ryzodeg, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by Addison Whitney, for this product.

1.1 REGULATORY HISTORY

The Applicant submitted the proposed proprietary name, Ryzodeg on October 5, 2011 (b) (4) (b) (4) . Division of Medication Error Prevention and Analysis (DMEPA) found the name, conditionally acceptable in OSE Review #2011-3893, dated December 22, 2011. However, the application received a complete response.

Thus, the Applicant re-submitted the name, Ryzodeg, for review on March 26, 2015.

1.2 PRODUCT INFORMATION

The following product information is provided in the 3/26/2015 proprietary name submission.

- Intended Pronunciation: RY-zoh-deg
- Active Ingredient: 70% insulin degludec and 30% insulin aspart
- Indication of Use: (b) (4) insulin analog indicated to improve glycemic control in adults with diabetes mellitus
- Route of Administration: subcutaneous injection
- Dosage Form: solution for injection
- Strength: 100 units/mL
- Dose and Frequency: individualized dose once or twice daily
- How Supplied:

Ryzodeg	Total volume	Concentration	Total units available in presentation	NDC number	Max dose per injection *	Dose increment *
U-100 FlexTouch	3 mL	100 U/mL	300 U	0169-2770-15	80 U	1 U
(b) (4)						

- Storage:

	Not in-use (unopened) Refrigerated (2°C - 8°C [36°F - 46°F])	Not in-use (unopened) Room Temperature (below 30°C [86°F])	In-use (opened) Room Temperature (below 30°C[86°F])
3 mL Ryzodeg U100 FlexTouch (b) (4)	Until expiration date	28 days (4 weeks)	28 days (4 weeks) (b) (4)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Metabolism and Endocrinology (DMEP) concurred with the findings of OPDP's 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 name[1].

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Ryzodeg in their submission. This proprietary name is comprised of a single 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.

The Applicant submitted (b) (4) (b) (4) Thus, this review focuses on the Tresiba component of the proposed proprietary name.

[1]USAN stem search conducted on April 22, 2015.

2.2.4 FDA Name Simulation Studies

Seventy-six practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Most mis-interpretation occurred with "y" interpreted as an "i" and "g" misinterpreted as "x", "q", or "z". Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines at Initial Review

In response to the OSE, April 15, 2015 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.6 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of ≥50% retrieved from our POCA search[2] organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified from the or by (b) (4)

Table 1. POCA Search Results	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥50% to ≤ 69%	57
Low similarity name pair: combined match percentage score ≤49%	5

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

Our analysis of the 63 names contained in Table 1 determined 63 names will not pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Products (DMEP) via e-mail on May 1, 2015. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DMEP on May 12, 2015, they stated no additional concerns with the proposed proprietary name, Ryzodeg.

[2] POCA search conducted on April 3, 2015.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

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, Ryzodeg, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your March 26, 2015 submission are altered prior to approval of the marketing application, 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 evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). 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. [3]

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

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

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 ≥70%.
- Moderately similar pair: combined match percentage score ≥50% to ≤ 69%.
- Low similarity: combined match percentage score ≤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. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (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, and it 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 to mitigate confusion (e.g., route, frequency, dosage form, etc.) may be limited when the strength or dose overlaps. We review such 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 (See Table 5) 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.

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 ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of 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.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), 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 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 ≥50% to ≤69%).

Step 1	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 or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: o 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. o Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. o Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

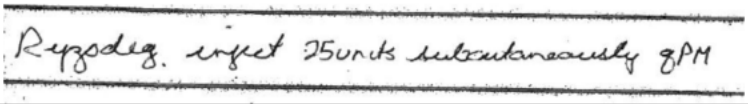
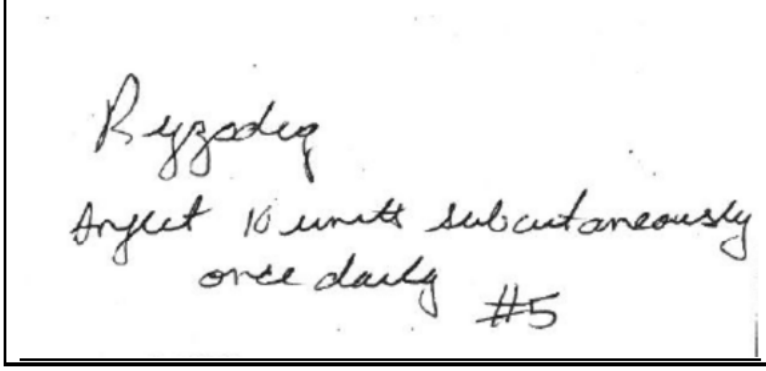
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), 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?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤49%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name 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. Ryzodeg Study (Conducted on 4/14/2015)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order:  Outpatient Prescription:  	Ryzodeg Inject 10 units sub-Q once daily #5

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

247 People Received Study
76 People Responded
Study Name: Ryzodeg

Total	**26**	**23**	**28**	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
BYZADEG	1	0	0	1
REYZODEG	0	0	1	1
RHIZODEK	0	1	0	1
RISADEG	0	1	0	1

RISODAY	0	1	0	1
RISODEG	0	4	0	4
RISODEX	0	1	0	1
RIZODED	0	1	0	1
RIZODEG	0	9	0	9
RIZODEK	0	1	0	1
RIZODIQ	1	0	0	1
RYOZDEG	0	0	1	1
RYZADEQ	2	0	0	2
RYZADIQ	2	0	0	2
RYZADIZ	1	0	0	1
RYZDEG	0	0	1	1
RYZEDEG	1	0	0	1
RYZODAG	0	1	0	1
RYZODEG	0	3	10	13
RYZODEQ	7	0	1	8
RYZODIG	3	0	5	8
RYZODIQ	6	0	0	6
RYZSDEG	0	0	4	4
RYZSDEQ	0	0	1	1
RYZSDIG	1	0	2	3
RYZSDIQ	1	0	0	1
RYZSKEQ	0	0	1	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name: Ryzodeg** **Established name: 70% insulin degludec and 30% insulin aspart** **Dosage form: solution for injectcion** **Strength: 100 units/mL** **Usual Dose: individualized dose once or twice daily**	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Ryzodeg***	100	Subject of Review

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Reno-Dip	60
2.	Ryzolt	60
3.	Rifadin	55
4.	Robitet/Robitet500	50

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name: Ryzodeg** **Established name: 70% insulin degludec and 30% insulin aspart** **Dosage form: solution for injectcion** **Strength: 100 units/mL** **Usual Dose: individualized dose once or twice daily**	**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.	Rezamid	61	Third syllable of this name pair has sufficient phonetic differences. Suffix of this name pair has sufficient orthographic differences.
2.	Ryanodex	61	The second syllable of this name pair has sufficient phonetic differences. The infix of this name pair has sufficient orthographic differences.
3.	Rilutek	56	The second syllable of this name pair has sufficient phonetic differences. The infix of this name pair has sufficient orthographic differences.
4.	Rx-Otic	54	The first and second syllables of this name pair have sufficient phonetic differences. The infix and suffix of this name pair have sufficient orthographic differences.
5.	Razadyne	53	Third syllable of this name pair have sufficient phonetic differences. The suffix of this name pair has sufficient orthographic differences.
6.	Trazodone	52	The first and third syllables of this name have sufficient phonetic differences. The prefix and suffix of this name pair have sufficient orthographic differences.
7.	Rotateq	52	The first and second syllables of this name have sufficient phonetic differences. The infix of this name pair has sufficient orthographic differences.

8.	Eryzole	50	The first, second, and third syllables of this name have sufficient phonetic differences. The suffix of this name pair has sufficient orthographic differences.
9.	Restone	50	This name has one less syllable. The name pair sounds different when spoken. The infix and suffix of this name have sufficient orthographic differences.
10.	Riluzole	50	The second and third syllables of this name pair have sufficient phonetic differences. The infix and suffix of this name pair have sufficient orthographic differences.
11.	Ritifed	50	The second and third syllables of this name pair have sufficient phonetic differences. The infix and suffix of this name pair have sufficient orthographic differences.
12.	Rosadan	50	The second and third syllables of this name pair have sufficient phonetic differences. The infix and suffix of this name pair have sufficient orthographic differences.
13.	(b) (4)	50	This name has one less syllable The second and third syllables of this name pair have sufficient phonetic differences. The infix and suffix of this name pair have sufficient orthographic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤49%)

No.	Name	POCA Score (%)
1.	Phisohex	26
2.	Pyridium	30
3.	Reyataz	44
4.	RibaTab	44
5.	Risperdal	40

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Renotec	62	NDA 17045 withdrawn FR effective 3/13/2009 no generics
2.	Ricobid/D	58	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
3.	(b) (4)	56	Proposed proprietary name for NDA 22442 withdrawn on 1/30/2009. Approved under Rezira.
4.			(b) (4)
5.	(b) (4)	56	Alternate proposed proprietary name for IND 9125/BLA 125476. Entyvio*** found acceptable for this application OSE Review #2013-590 on 8/19/2013.
6.	Ridafed	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
7.	Ridifed	55	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
8.	Rinatec	54	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
9.	Rondec	54	Name identified in RxNorm database. Unable to find

			product characteristics in commonly used drug databases.
10.	Renitec	53	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
11.	Rynatan	53	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
12.	Ramodar	52	Name found in RxNorm. Unable to find product characteristics in commonly used databases
13.	Rauzide	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
14.	Recofen	52	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
15.	Rondex	51	Name identified in Rx Norm database. Unable to find product characteristics in commonly used drug databases
16.	Sinodec	51	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
17.	Carbodec	50	Name identified in RxNorm database. Product characteristics found in Redbook, but product is no longer marketed and no generic alternatives are available.

18.	Radent	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
19.	Razoxane	50	Name identified in Rx Norm database. Unable to find product characteristics in commonly used drug databases
20.	Razoxin	50	Name identified in Rx Norm database. Unable to find product characteristics in commonly used drug databases
21.	Rezine	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
22.	Rezulin	50	NDA 20720 withdrawn FR effective 1/10/2003 no generics
23.	Ridenol	50	Name identified in Rx Norm database. Unable to find product characteristics in commonly used drug databases
24.	Robadex	50	Name identified in Rx Norm database. Unable to find product characteristics in commonly used drug databases
25.	Robalog	50	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
26.	Rusyde	50	Name identified in Rx Norm database. Unable to find product characteristics in commonly used drug databases
27.	(b) (4)	50	Dual Proposed Proprietary Name found unacceptable (b) (4)

			application [(b) (4)] withdrawn by the Applicant on [(b) (4)].

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Gris-Peg	56
2.	Vazobid	56
3.	Lysodren	54
4.	Zydelig	54
5.	Vazotab	53
6.	Lidodan	52
7.	Varizig	52
8.	Zomig	51
9.	Cytotec	50
10.	Oraltag***	50
11.	Vasotec	50
12.	Vetameg	50

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

/s/

SARAH K VEE
05/29/2015

YELENA L MASLOV
06/04/2015

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:	May 29, 2015
Application Type and Number:	NDA 203314
Product Name and Strength:	Tresiba (insulin degludec) injection, 100 units/mL & 200 units/mL
Product Type:	Combination (Drug + Device)
Rx or OTC:	Rx
Applicant/Sponsor Name:	Novo Nordisk
Panorama #:	2015-80128
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, Tresiba, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by (b) (4), for this product.

1.1 REGULATORY HISTORY

The Applicant submitted the proposed proprietary name, Tresiba on October 5, 2011 which (b) (4) (b) (4) Division of Medication Error Prevention and Analysis (DMEPA) found the name, conditionally acceptable in OSE Review #2011-3891, dated December 11, 2011 and OSE Reivew #2012-2497, dated February 7, 2013. However, the application received a complete response.

Thus, the Applicant re-submitted the name, Tresiba, for review on March 26, 2015.

1.2 PRODUCT INFORMATION

The following product information is provided in the March 26, 2015 proprietary name submission.

- Intended Pronunciation:
- Active Ingredient: insulin degludec
- Indication of Use: (b) (4) human insulin analog indicated to improve glycemic control in adults with diabetes mellitus
- Route of Administration: subcutaneous
- Dosage Form: solution for injection
- Strengths: 100 units/mL and 200 units/mL
- Dose and Frequency: Individualized once daily
- How Supplied:

Tresiba	Total volume	Concentration	Total units available in presentation	NDC number	Max dose per injection*	Dose increment*
U-100 FlexTouch	3 mL	100 U/mL	300 U	0169-2660-15	80 U	1 U
U-200 FlexTouch	3 mL	200 U/mL	600 U	0169-2550-13	160 U	2 U
(b) (4)						

- Storage:

	Not in-use (unopened) Refrigerated (2°C - 8°C[36°F - 46°F])	Not in-use (unopened) Room Temperature (below 30°C[86°F])	In-use (opened) Room Temperature (below 30°C[86°F])
3 mL Tresiba U100 FlexTouch (b) (4)	Until expiration date	56 days (8 weeks)	56 days (8 weeks) (b) (4)
3 mL Tresiba U200 FlexTouch	Until expiration date	56 days (8 weeks)	56 days (8 weeks) (b) (4)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Metabolic and Endocrinology Products (DMEP) concurred with the findings of OPDP's 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 name[1].

2.2.2 Components of the Proposed Proprietary Name

The Applicant did not provide a derivation or intended meaning for the proposed name, Tresiba 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.

The Applicant submitted (b) (4)

[1]USAN stem search conducted on 4/20/2015.

(b) (4) Thus, this review focuses on the Tresiba component of the proposed proprietary name.

2.2.4 FDA Name Simulation Studies

Forty-nine practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines at Initial Review

In response to the OSE, April 15, 2015 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.6 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Table 1 lists the number of names with the combined orthographic and phonetic score of ≥50% retrieved from our POCA search[2] organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified by (b) (4)

Table 1. POCA Search Results	**Number of Names**
Highly similar name pair: combined match percentage score ≥70%	5
Moderately similar name pair: combined match percentage score ≥50% to ≤ 69%	258
Low similarity name pair: combined match percentage score ≤49%	2

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

Our analysis of the 266 names contained in Table 1 determined 266 names will not pose a risk for confusion as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Product (DMEP) via e-mail on May 1, 2015. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DMEP on May 12, 2015, they stated no additional concerns with the proposed proprietary name, Tresiba.

[2] POCA search conducted on April 3, 2015.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

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, Tresiba, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your March 26, 2015 submission are altered prior to approval of the marketing application, 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 evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). 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. [3]

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

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

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

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 ≥70%.
- Moderately similar pair: combined match percentage score ≥50% to ≤ 69%.
- Low similarity: combined match percentage score ≤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. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (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, and it 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 to mitigate confusion (e.g., route, frequency, dosage form, etc.) may be limited when the strength or dose overlaps. We review such 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 (See Table 5) 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.

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 ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of 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.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), 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 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 ≥50% to ≤69%).

Step 1	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 or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: o 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. o Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. o Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

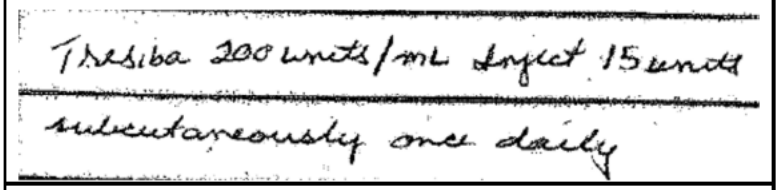
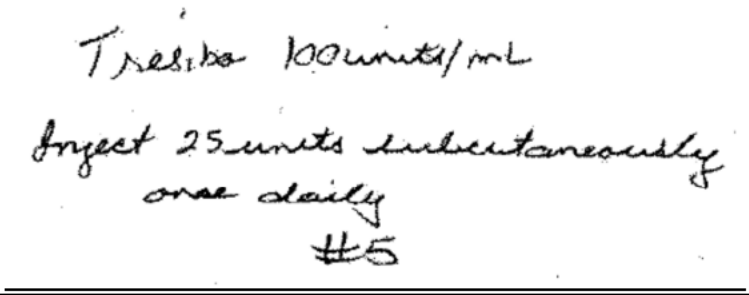
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), 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?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤49%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name 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. Tresiba Study (Conducted on April 14, 2015)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order:  Outpatient Prescription:  	Tresiba 100 units/mL Inject 25 units sub-Q once a day #5

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

247 People Received Study
49 People Responded
Study Name: Tresiba

Total	**19**	**14**	**16**	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
CRISIVA	0	1	0	1
PRESIBA	0	1	0	1
TRACIBA	0	1	0	1
TRASIVA	0	1	0	1
TRESIBA	19	1	15	35
TRESIVA	0	1	0	1
TREZYVA	0	1	0	1
TRICIDA	0	1	0	1
TRICIVA	0	1	0	1

TRICYVA	0	1	0	1
TRISEBA	0	0	1	1
TRISIBA	0	1	0	1
TRISYVA	0	3	0	3

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name: Tresiba** **Established name: insulin degludec** **Dosage form: solution for injection** **Strength: 100 units/mL or 200 units/mL** **Usual Dose: Individual Dose**	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Tresiba***	100	Subject of this review
2.	(b) (4)	78	Name identified in POCA in RxNorm. Unable to find product characteristics in internal databases and commonly used drug databases.
3.	Trivita	76	This is the product line or "family" name for nutritional supplements. As the product line includes more than twenty products, and each has a proprietary name, the proprietary name is needed for a complete order to order the product.
4.	Cresemba	72	First letters are different. "em" is longer when scripted then "i" Dosage form (oral capsules or powder for injection), strength, dose, and route of administration must be specified for Cresemba (oral or intravenous injection)
5.	(b) (4)	70	Strength and dose must be specified for Tresiba whereas (b) (4).

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Trinessa	68
2.	Tripedia	66
3.	Tri-Luma	65
4.	(b) (4)	64
5.	Tirofiban	64
6.	Truvada	64

7.	(b) (4)	62
8.	Tarceva	62
9.	Tasigna	62
10.	Treanda	62
11.	Trivora-21 Or -28	62
12.	Trumenba	62
13.	Trasicor	61
14.	Trezix	61
15.	Treximet	60
16.	Trizivir	60
17.	Trelstar	59
18.	Nesina	58
19.	Pitressin	58
20.	Tretten	58
21.	Trexall	58
22.	Triacet	58
23.	Triphasil-21 Or -28	58
24.	(b) (4)	58
25.	Terocin	56
26.	Terrasil	56
27.	Threda	56
28.	Trental	56
29.	Tricalm	56
30.	Triostat	56
31.	Ultresa	56
32.	Trecator	55
33.	Tretin X	55
34.	Triferic	55
35.	(b) (4)	54
36.	Tirosint	54
37.	Torisel	54
38.	Triesence	54
39.	Trilyte	54

40.	Trospium	54
41.	Travatan	53
42.	Trexbrom	53
43.	Triderm	53
44.	Trisenox	53
45.	Trusopt	53
46.	VITA-Respa	53
47.	(b) (4)	52
48.	Procysbi	52
49.	Trasylol	52
50.	Tretinoin	52
51.	Triacin C	52
52.	Triacin-C	52
53.	Trioxin	52
54.	Tri-Vi-Sol	52
55.	Tyzeka	52
56.	Crest	51
57.	Tri-Linyah	51
58.	Tysabri	51
59.	Crestor	50
60.	Feiba	50
61.	(b) (4)	50
62.	Rescula	50
63.	Tradjenta	50
64.	Trametinib	50
65.	Travasol 10, 2.75, 2.75/5, 3.5, 4.25/10, 4.25/25, 4.25/5, 5.5, 8.5	50
66.	Tru-Micin	50
67.	(b) (4)	50

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name: Tresiba** **Established name: insulin degludec** **Dosage form: solution for injection** **Strength: 100 units/mL or 200 units/mL** **Usual Dose: Individual Dose**	**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.	Trokendi	56	The second and last syllables of this name pair have sufficient phonetic differences. The infix of this name pair has sufficient orthographic differences ("ken" vs. "si").
2.	Trovan	56	This name contains fewer syllables. The second and last syllables of this name pair have sufficient phonetic differences. There are sufficient orthographic differences in the suffix of the name pair ("van" vs. "siba")
3.	(b) (4)		
4.			
5.	Entresto***	50	This name pair sounds different when spoken. The infix of this name pair have sufficient orthographic differences ("tres" vs. esi").

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤49%)

No.	Name	POCA Score (%)
1.	Sustiva	46
2.	Amitiza	42

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Tri-sudo	67	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
2.	Trest	64	NDA 13420; Withdrawn FR Effective 9.4.1991 with no generics
3.	Triam-A	64	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
4.	Triban	64	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
5.	(b) (4)		
6.	Prefrin-A	63	NDA 7953 withdrawn FR effective 1/21/1974 no generics
7.	(b) (4) ***	62	OSE Review # 2014-46035: (b) (4)
8.	Trypsin	62	Powder for compounding
9.	B-12 Resin	61	Name identified in RxNorm

			database, unable to identify product characteristics in commonly used databases
10.	(b) (4)		
11.	Refissa	60	Name identified in Rx Norm database. Name was found conditionally acceptable in OSE# 2008-1081, however, application ANDA 076498 appears to be marketed under the established name.
12.	Respa	60	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
13.	Traxam	60	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
14.	(b) (4)	60	(b) (4)
15.	Triafed	60	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
16.	Triphed	60	ANDA 88630 Withdrawn FR Effective 9/1/1994; no generics
17.	(b) (4)		
18.			

			(b) (4)
19.	T-Gesic	59	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
20.	(b) (4)	59	Alternate proposed proprietary name for NDA 206334 approved under Orbactiv on 8/6/2014
21.	Tremin	59	ANDA 080381 was withdrawn federal register effective on 12/10/1992. No therapeutic equivalents are available
22.	Ceresin	58	Product is not a drug- inactive ingredient
23.	Tresaderm	58	Veterinary Product
24.	Tussi-Bid	58	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
25.	Atosiban	57	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
26.	Trifed C	57	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
27.	Triofed	57	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
28.	Atreza	56	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
29.	(b) (4)		

			acceptable for IND (b) (4).
30.	Treagan	56	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
31.	Tridane	56	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
32.	Triotann	56	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
33.	Tri-Pseudo	56	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
34.	Triseptin	56	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
35.	Tri-Statin	56	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
36.	Tritop	56	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
37.	(b) (4)		
38.	Tussitab	56	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
39.	Torecan	55	NDA 12753, 12754, 13247 withdrawn FR Effective 6/18/2009 with no generics available
40.	Trapidil	55	Product identified in Rx Norm.

			Product characteristics could be found in commonly used databases.
41.	(b) (4)		
42.	Trisofed	55	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
43.	Trivase	55	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
44.	Triveen	55	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
45.	Pressimmune	54	Name found in RxNorm. Unable to find product characteristics in commonly used databases
46.	Respa-SA	54	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
47.	(b) (4)	54	Alternate proposed proprietary name for NDA 206334 approved under Orbactiv on 8/6/2014
48.	Travase	54	NDA 12828 Withdarwn FR Effective 8/29/2013 no generics
49.	Triad	54	ANDA 89023 Withdarwn FR Effective 8/16/1999
50.	Tri-Otic	54	Veterinary Product
51.	Tri-Pase	54	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
52.	Triposed	54	Name identified in RxNorm database, unable to identify product characteristics in

			commonly used databases
53.	(b) (4)	54	Proposed proprietary name for ANDA 90793 approved under Tri-Estarylla OSE Review # 2011-534
54.	Tritec	54	NDA 20559 Withdrawn FR Effective 9/13/2000 no generics
55.	Tropium	54	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
56.	Trosyl	54	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
57.	Tuss Da	54	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
58.	Pressair***	53	Name entered by SE. This is a device modifier for several proposed names, e.g., drug name "XXXX Pressair "
59.	Prosed	53	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
60.	Resinol	53	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
61.	Tolrestat	53	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
62.	(b) (4)	53	Alternate proposed proprietary name for IND 70345. Trilipix was approved for this IND in OSE Review #2007-(b) (4), (b) (4)
63.	Tri-Zel	53	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases

64.	Altresyn	52	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
65.	(b) (4)	52	Name identified in Names Entered by Safety Evaluator database. Unable to find product characteristics in internal databases.
66.	Cresatin	52	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
67.	Fresh UP	52	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
68.	Gastrese-LA	52	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
69.	Mytrex A	52	ANDA 62598/62609 withdrawn FR Effective 7/12/1999
70.	Perestan	52	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
71.	(b) (4)	52	Proposed proprietary name for ANDA 200494 found unacceptable in OSE Review# 2012 (b) (4) (b) (4).
72.	(b) (4)		
73.	Triacetin	52	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
74.	Triam	52	Name found in Rx norm. Product characteristics not found in commonly used drug databases.

75.	Tricosal	52	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
76.	Tridil	52	NDA 18537 Withdrawn FR Effective 3/13/2009
77.	Trifexis	52	Veterinary Product
78.	Tri-Med	52	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
79.	Trimo San	52	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
80.	(b) (4)	52	Alternate proposed proprietary name for NDA 20120 approved under (b) (4)
81.	Tri-Nasal	52	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
82.	(b) (4)	52	Alternate proposed proprietary name for ANDA 90793 approved under Tri-Estarylla OSE Review # 2011-534
83.	Trobicin	52	Product withdrawn from market and is available for veterinary use only. No available generics.
84.	Trysul	52	A 87887 withdrawn FR effective 11/1/2005 no generics
85.	Respigam	51	Product identified in Rx Norm, Cerner and CBER Biologics.
86.	(b) (4)	51	Proposed proprietary name for (b) (4) withdrawn. Ibrance found acceptable for this product OSE Review # 2013-16612, 4/24/2014
87.	Triaz	51	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases

88.	Tri-Dec	51	Name identified in RxNorm database. Unable to find product characteristics in internal databases.
89.	Tussi-12d	51	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
90.	(b) (4)		
91.	Etretinate	50	NDA 19369 withdrawn FR effective 9/10/2003 no generics
92.	Lypressin	50	NDA 16755 withdrawn FR effective 3/20/2000 no generics
93.	(b) (4)		
94.	Prascend	50	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
95.	Precef	50	NDA 50554 withdrawn pending FR notice 4/13/1990 no generics
96.	Prep-Hem	50	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
97.	Resaid	50	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
98.	Terfinax	50	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
99.	Trelstar LA	50	Name found in Rx norm. Product characteristics not

			found in commonly used drug databases.
100.	Treosulfan	50	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
101.	Trepibutone	50	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
102.	Triavil 2-10, 2-25, 4-10, 4-25, 4-50	50	NDA 14715 withdrawn FR effective 3/13/2009
103.	Trikof D	50	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
104.	Trilisate	50	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
105.	(b) (4)	50	ANDA 200494 name withdrawn 5/31/2011
106.	Trituss Er	50	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
107.	Trovan Iv	50	NDA 20760 withdrawn FR effective 6/16/2006 no generics
108.	Truxade	50	Product identified in Rx Norm. Product characteristics could be found in commonly used databases.
109.	Tussin Pe	50	Name identified in RxNorm database, unable to identify product characteristics in commonly used databases
110.	Tylosin	50	Name found in Rx norm. Product characteristics not found in commonly used drug databases.
111.	(b) (4)		

			(b) (4)

Appendix H: Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	(b) (4)	64
2.	Retin-A	61
3.	Pre Sed	60
4.	Prezista	60
5.	Revina	60
6.	Lessina	57
7.	Lessina-21	57
8.	Lessina-28	57
9.	Brexin L.A.	56
10.	Carisoma	56
11.	Certiva	56
12.	Pre-Sate	56
13.	Profasi	56
14.	Chrysin	55
15.	Frisium	55
16.	Rezira	55
17.	Brevital	54
18.	Corisin	54
19.	Dristan	54
20.	Etrafon-A	54
21.	Frusid	54
22.	Pepsin A	54
23.	Prascion Ra	54
24.	Prefrin	54
25.	(b) (4)	54
26.	Rezipas	54

27.	(b) (4)	53
28.	Provera	53
29.	Strattera	53
30.	Atripla	52
31.	Atrofed	52
32.	Carlesta	52
33.	(b) (4)	52
34.	Lexiva	52
35.	Narasin	52
36.	Natroba	52
37.	Otrivin	52
38.	Potaba	52
39.	Prascion	52
40.	Prefest	52
41.	Prevpac	52
42.	Prometa	52
43.	Prosaid	52
44.	Prostap 3	52
45.	Raptiva	52
46.	(b) (4)	52
47.	Cotab A	51
48.	Droxia	51
49.	Egrifta	51
50.	Pristiq	51
51.	Profen La	51
52.	Solesta	51
53.	Ubretid	51
54.	Brovana	50
55.	Crofab	50
56.	Curretab	50
57.	Disipal	50
58.	Fortesta	50
59.	Kronofed-A	50

60.	Motrin Ib	50
61.	Peroxin A	50
62.	Peroxin A 10	50
63.	Pet-Ema	50
64.	Prazepam	50
65.	Prenexa	50
66.	Prepidil	50
67.	Prevacid	50
68.	Prevacid	50
69.	Prevnar	50
70.	Prevnar 13	50
71.	Propecia	50
72.	Proscar	50
73.	Revia	50
74.	Strazepam	50
75.	Striverdi	50

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05/29/2015

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06/04/2015

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

Proprietary Name Review--Final

Date:	February 7, 2013
Reviewer(s):	Richard A Abate, RPh, MS, Safety Evaluator Division of Medication Error Prevention and Analysis
Deputy Director	Kellie Taylor, PharmD, MPH Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh, Division of Medication Error Prevention and Analysis
Drug Name(s) and Strengths:	Tresiba (Insulin Degludec [rDNA origin]) Injection, 100 units/mL (U-100) FlexTouch Pen (b) (4) and 200 units/mL (U-200) FlexTouch Pen
Application Type/Number:	NDA 203314
Sponsor:	Novo Nordisk
OSE RCM #:	2012-2497

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Tresiba is written in response to the anticipated action on this NDA within 90 days from the date of this review. DMEPA found the proposed name, Tresiba, acceptable in OSE Review 2011-3891 dated December 30, 2011.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review 2011-3891. We note that none of the proposed product characteristics were altered. However, we evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. The searches of the databases yielded two new names ((b) (4) and Luride), thought to look or sound similar to Tresiba and represent a potential source of drug name confusion. Additionally, two new names (Flector and Flex Power) were thought to look or sound similar to (b) (4), FlexTouch. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with (b) (4) and Luride and lead to medication errors. This analysis determined that the name similarity between Tresiba and Luride or FlexTouch and the identified names was unlikely to result in medication error for the reasons presented in Appendix A.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of November 5 2012. The Office of Prescription Drug Promotion OPDP re-reviewed the proposed name on November 2, 2012 and had no concerns regarding the proposed name from a promotional perspective.

2.1 FAILURE MODE AND EFFECTS ANALYSIS OF SIMILAR NAME (b) (4)

The root name, Tresiba, is being evaluated (b) (4) FlexTouch (b) (4). However, in our evaluation of the proposed name, we also consider that prescribers may not always (b) (4) when writing a prescription. (b) (4) have been omitted or overlooked in practice when prescribing drug products.

The orthographic similarity of (b) (4) and Tresiba stems from the fact that both names (b) (4)), (b) (4) within the name ((b) (4) vs. 'resiba'). (b) (4)

In addition to the orthographic similarities, (b) (4) and Tresiba share overlapping product characteristics that increase the likelihood for a medication error to occur in the usual practice setting. The dose of (b) (4) has numeric overlap with an achievable dose of Tresiba (i.e. (b) (4) vs. 1 unit or 2 units). Furthermore, in some cases, a decimal point may be overlooked. Thus the dose of

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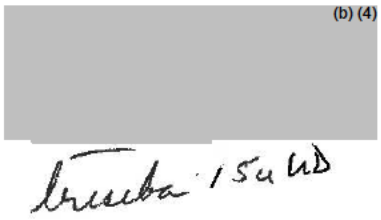
(b) (4) can also have numerical similarity to doses of Tresiba (i.e. (b) (4) vs. 15 units or 25 units). We acknowledge that the unit of measure differs for these products (b) (4) vs. unit); however, when taken in the context of a prescription, 'u' may not be sufficiently distinguishable from (b) (4) and thus may not prevent an error from occurring.

The strengths between the two products differ. (b) (4) is proposed with (b) (4) . Tresiba is proposed with two strengths, U-100 (100 units/mL) and U-200 (200 units/mL). However, providers do not always include a designation of strength for insulin prescriptions since U-100 is the most common strength of insulin prescribed and may be considered an implied strength in practice. Therefore, a prescription for (b) (4) or Tresiba could be written with the dose alone and still be filled.

The two products have differing frequencies of administration. (b) (4) is administered (b) (4) (b) (4) whereas Tresiba will be administered once daily. However, prescriptions for either of these products may be written with "use as directed" or "UD" for simplicity since (b) (4) is a product that requires a (b) (4) and Tresiba is a self-injectable product with dosing based upon individual blood glucose levels that can vary. Therefore, a prescriber may provide specific dosing instructions directly to the patient instead of writing it on the prescription. In addition, both of these products are available in a single dosage form and given by only one route of administration, so these potential sources of differentiation may be omitted on a prescription. As a result, a prescription written for (b) (4)** (b) (4) may be misinterpreted as "Tresiba 15 u UD or as directed" and vice versa as the following writing sample demonstrates:



However, the Sponsor for (b) (4)* withdrew this proposed proprietary name on January 31, 2013. Thus, we no longer have concerns with the potential for confusion between these products.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Tresiba, did not identify any vulnerability that would result in medication errors with any additional name(s) noted in this review. Thus, DMEPA has no objection to the proprietary name, Tresiba, 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 Metabolism and Endocrinology should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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

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REFERENCES

1. **OSE Reviews**

   OSE Review 2011-3891; Proprietary Name Review of Tresiba, December 30, 2011, Abate, R.

   OSE Review 2012 (b) (4) Proprietary Name Review for (b) (4), Defronzo, K.

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

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

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

   USAN Stems List contains all the recognized USAN stems.

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

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

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Appendix A: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

No.	**Proposed name: Tresiba (insulin degludec) (b) (4) FlexTouch and (b) (4) (b) (4) U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4) U-200 (200 units/mL) in a 3 mL disposable pen. Usual dose (U-100): Inject 1 unit to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)**	**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.	Luride (sodium fluoride) 0.25 mg, 0.5 mg and 1 mg chewable tablets 0.5 mg/mL oral solution Usual dose: Dosing is age based: 0-3 years- 0.25 mg (one tablet or 0.5 mL), 3-6 years 0.5 mg (one tablet or 1 mL), 6-16 years (one tablet or two mL) by mouth once daily	**Orthographic similarity:** Both names include a similar number of letters (six vs. seven), appear to have a similar length and shape when scripted, begin with a letter grouping (Lur-Tre-) that may appear similar when scripted, include letter providing an upstroke towards the end of the name (d vs. b) which is proceeded by the letter 'i,' and end with a	Luride is an oral product which is available in two dosage forms (chewable tablets and oral solution). In addition, the chewable tablets are available in three strengths (0.25 mg, 0.5 mg and 1 mg) which differ from those of Tresiba (100 units/mL and 200 units/mL). As the two oral dosage forms include overlapping doses (0.25 mg - 1 mg), prescriptions for Luride must include either the dosage form, strength or a more complete dose description (milliliters/dropper or tablets) to communicate the correct product. Tresiba is available in (b) (4) injectable presentations, FlexTouch pen injector (b) (4) (b) (4) which if included may provide some orthographic differentiation.

		letter that may appear similar when scripted (e vs. a). Similar product characteristics: both have a frequency of use of once daily.	
2.	Flector (diclofenac epolamine) 1.3% patch Usual dose: Apply patch to most painful area and replace after 12 hours. (Apply twice a day)	**Orthographic similarity to Flex Touch:** Both names begin with the same three letters (Fle-) and include the letters 't' and 'o' in the fifth and sixth positions, respectively (b) (4) Flex Touch, may be inadvertently written alone as a product name. This often occurs when (b) (4) is used for the first time in the market.	Orthographic difference: Flex Touch includes two additional letters and may be scripted as two words (b) (4). Flex Touch also ends with the letter 'h' providing an upstroke at the end of the name. Flex Touch is the Pen Injector presentation of Tresiba and will likely be launched with the mixed insulin, Ryzodeg. Thus, prescribers will need to specify the insulin product needed when writing for Flex Touch.
3.	Flex-Power (trolamine salicylate) 10 % cream Flex-Power Active Women Homeopathic cream Usual dose: apply three to four times daily, as needed.	**Orthographic similarity to Flex Touch:** Both names share the same first word (Flex).	Orthographic difference: The second part of Flex Touch (Touch) begins with a 'T" which appears different from the 'P' in Power and also ends with the letter 'h' providing an upstroke at the end of the name.

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/s/

RICHARD A ABATE
02/07/2013

KELLIE A TAYLOR
02/07/2013

CAROL A HOLQUIST
02/07/2013

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

Proprietary Name Review

Date:	December 30, 2011
Reviewer(s):	Richard A Abate, RPh, MS, Safety Evaluator Division of Medication Error Prevention and Analysis
Team Leader:	Carlos Mena-Grillasca, RPh, Team Leader Division of Medication Error Prevention and Analysis
Acting Division Director:	Irene Chan, Pharm D, BCPS, Team Leader Division of Medication Error Prevention and Analysis
Drug Name(s) and Strengths:	Tresiba (Insulin Degludec [rDNA origin]) Injection, 100 units/mL (U-100) FlexTouch Pen (b) (4) and 200 units/mL (U-200) FlexTouch Pen
Application Type/Number:	NDA 203314
Sponsor:	Novo Nordisk
OSE RCM #:	2011-3891

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Tresiba, 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 also submitted labels, labeling, and a use validation study for the Flex Touch pen injector that will be reviewed under separate cover (OSE 2011-3892).

1.1 REGULATORY HISTORY

DMEPA previously reviewed the proposed proprietary name, [redacted] (b) (4) for this product under IND 076496 in OSE review # 2011 [redacted] (b) (4) dated August 4, 2011. DMEPA found the name unacceptable due to its orthographic similarity to and overlapping product characteristics with the marketed products, [redacted] (b) (4). The Applicant submitted the proposed proprietary name, Tresiba on October 5, 2011 [redacted] (b) (4) (b) (4)

1.2 PRODUCT INFORMATION

The following product characteristics were obtained from the Request for Proprietary Name Review submitted October 5, 2011 and the draft insert labeling submitted September 29, 2011:

- Established Name: insulin degludec [rDNA origin] injection
- Indication of Use: To improve glycemic control in adults with diabetes mellitus.
- Route of administration: Subcutaneously
- Strength: 100 units/mL(U-100) and 200 units/mL (U-200)
- Dosage form: injection
- Dose: The dose for insulins varies based on the patients needs but usual starting dose is 10 units for insulin naïve patients. The dose with the U-100 FlexTouch device [redacted] (b) (4) ranges from 1 unit to 80 units in one unit increments. The dose of the U-200 FlexTouch device ranges from 2 units to 160 units in two unit increments. The dose is administered once daily, and the dose may be administered any time of the day.
- How Supplied: 100 units/ml (U-100) in 3 mL FlexTouch disposable pen injector packaged as five pens per carton [redacted] (b) (4). The 200 units/mL (U-200) in 3 mL FlexTouch disposable pen injector is packaged as three pens per carton.
- Storage: The pens [redacted] (b) (4) are stored between 2° and 8° C (36° and 46° F). Do not freeze. After initial use, the product in any configuration may be stored at room temperature, below 30° C (86° F) for up to [redacted] (b) (4).

- Container and Closure systems: The disposable pen-injector is the PDS290 device. (b) (4)

2 RESULTS

The following sections provide the information obtained and considered in the 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 Metabolism and Endocrinology Products (DMEP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following sections are considered in the overall safety evaluation of the proposed name, Tresiba.

2.2.1 United States Adopted Names (USAN) SEARCH

On December 14, 2011, the primary safety evaluator's United States Adopted Name (USAN) stem search identified that a USAN stem is not present in the proposed proprietary name.

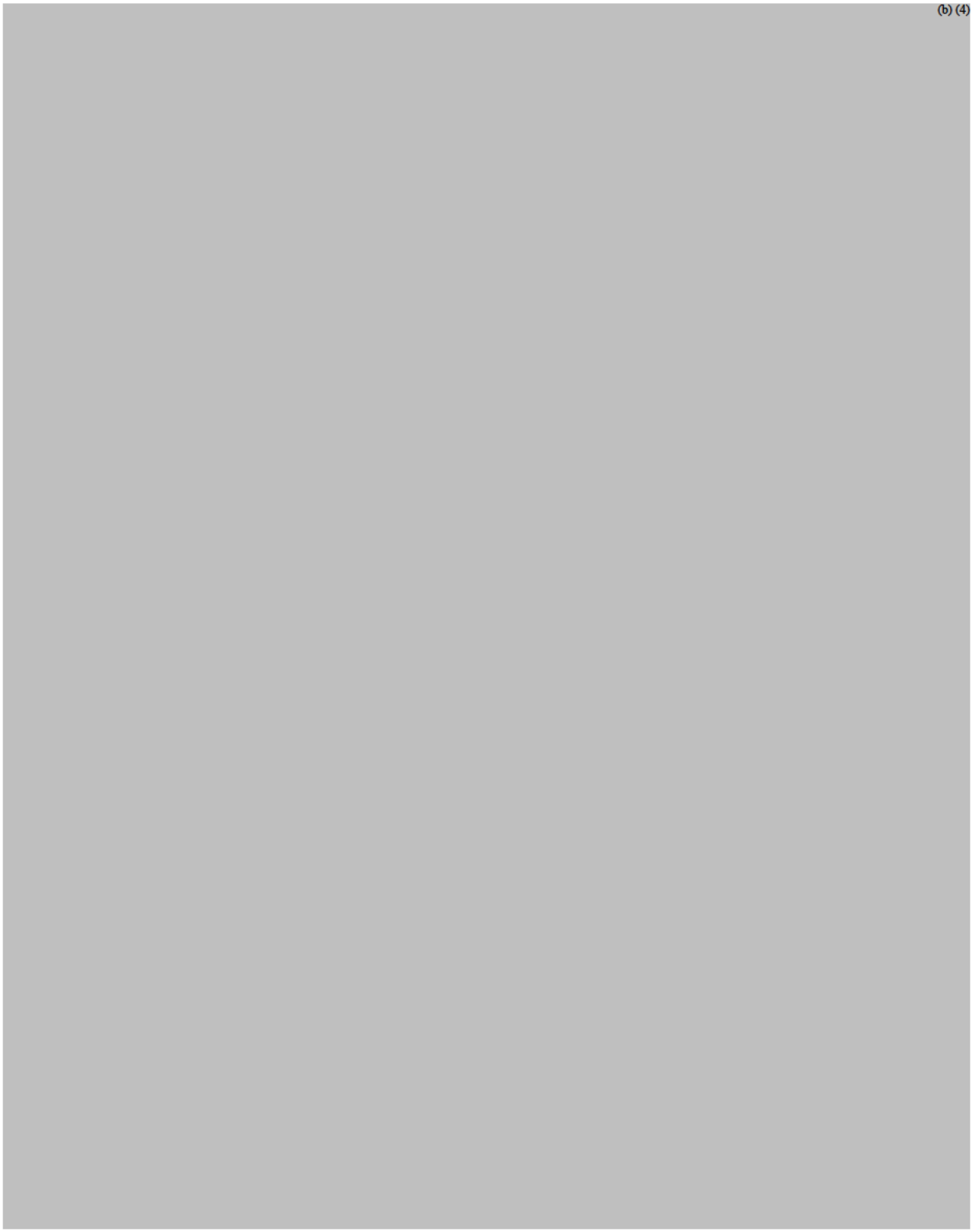
2.2.2 Components of the Proposed Proprietary Name

The Applicant , Novo Nordisk, noted that the name, Tresiba, was not derived form one particular concept.

This submitted proprietary name (b) (4) (b) (4) Names similar to (b) (4) FlexTouch (b) (4), are identified in Section 2.2.6 and evaluated in Appendices D and E.

2.2.3 Medication Error Data

(b) (4)



2.2.4 FDA Name Simulation Studies

Thirty-nine practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed

products. Of note, 23 out of 25 respondents interpreted the name correctly in the written studies (15 in the inpatient and eight in the outpatient). The two misinterpretations began with the respondent reporting an 'l' for the letter 'b.' The verbal responses were all phonetic variations on the proposed name, Tresiba. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines

In response to the OSE, November 3, 2011 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in Tresiba, FlexTouch, (b) (4). Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Tresiba, FlexTouch, (b) (4), Tresiba FlexTouch, (b) (4). These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names not previously identified by DMEPA but identified by (b) (4), a third party vendor, who completed an external name assessment for the proposed proprietary name for the Applicant.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines or (b) (4)

Look Similar to Tresiba		Sound Similar to Tresiba		Look and Sound Similar to Tresiba	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Feiba	FDA	Amitiza	(b) (4)	Prezista	(b) (4)
Fusilev	FDA	Droxia	FDA	Tarceva	FDA and (b) (4)
Levitra	FDA	Lessina	FDA	(b) (4)	FDA
Lusedra	FDA	Sustiva	(b) (4)	Tresiba	FDA
Tasigna	FDA and (b) (4)	Trizivir	FDA and (b) (4)	(b) (4)	FDA
(b) (4)	FDA	Trospium	(b) (4)	Tri-sudo	FDA
Tetrex	FDA			Truvada	FDA and (b) (4)

*** **This is proprietary and confidential information that should not be released to the public*****

(b) (4)	FDA
Look Similar to Tresiba	
Tradjenta	FDA
Trasicor	FDA
Trasylol	FDA
Treanda	FDA and (b) (4)
Trecator	FDA and (b) (4)
Trelstar	FDA
Tremin	FDA
Trental	FDA and (b) (4)
Trisenox	FDA
Testred	FDA
Tretinoin	FDA
Trexall	FDA
Treximet	FDA and DSI
Trezix	FDA
Triacet	FDA
Tri-Luma	FDA and (b) (4)
Trinate	FDA
Tripedia	FDA and (b) (4)
Trisudex	FDA
Trivora	FDA
Trihexiphenidyl	(b) (4)
Trivita	
Trusopt	

Tysabri	FDA and (b) (4)
Look and Sound Similar to Tresiba	
Trinessa	(b) (4)

Look and Sound Similar to Tresiba FlexTouch		Look and Sound Similar to (b) (4)		Look Similar to FlexTouch (b) (4)	
Levemir FlexTouch***	FDA	(b) (4)	FDA	Flextra	FDA
Look and Sound Similar to Tresiba FlexTouch				**Look Similar to FlexTouch (b) (4)**	
Novolog FlexTouch***	FDA			Hextend	FDA
(b) (4)	FDA				
Look Similar to (b) (4) (b) (4))		**Sound Similar to (b) (4) (b) (4))**		**Look and Sound Similar to (b) (4) ((b) (4) (b) (4)**	
(b) (4)	FDA	(b) (4)	FDA	(b) (4)	FDA
	FDA		FDA		FDA
	FDA				

Our analysis of the 59 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics for these names. We determined the 59 names will not pose a risk for confusion as described in Appendices D and E.

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated these midpoint review findings to the Division of Metabolism and Endocrinology Products (DMEP) via e-mail on December 28, 2011. At that time we requested DMEP provide any information or concerns that could inform our review. Per e-mail correspondence from the Division of Metabolism and Endocrinology Products on December 28, 2011, they stated no additional concerns with the proposed proprietary name, Tresiba.

3 CONCLUSIONS

The proposed proprietary name, Tresiba, is acceptable from both a promotional and safety perspective. In addition, (b) (4), FlexTouch (b) (4), are (b) (4) acceptable from a promotional and safety perspective.

*** **This is proprietary and confidential information that should not be released to the public*****

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Tresiba, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your September 29, 2011 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review. Additionally, this proprietary name must be re-evaluated 90 days prior to the approval of the application. The conclusions upon re-review are subject to change.

4 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. ***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. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

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.

17. ***Adverse Event Reporting System (AERS)***

    AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly

from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential post-marketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP 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 provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, 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.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. 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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product 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.

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

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2] The product characteristics considered for this review appears in Appendix B1 of this review.

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. 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. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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 2 below for details).

Table 2. 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*
	Similar spelling	Identical prefix Identical infix Identical suffix	• Names may appear similar in print or electronic media and lead to drug name

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

Look-alike		Length of the name Overlapping product characteristics	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/Similar shape Upstrokes Down strokes Cross-strokes 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, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the

trademark being evaluated. Lastly, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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 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.

4. 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.

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, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.[3] 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 Appendix B1 of this review. 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? And Are there any components of the name that may function as a source of error beyond sound/look-alike"***

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

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 or because of some other component of the name. 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?"***

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.

Moreover, 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 Overall Risk Assessment:

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP'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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for 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 Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above 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, confusing, or misleading 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 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.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Tresiba	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'T'	F, J, or T	'D'
lower case 't'	A, f, r, or x	'd'
lower case 'r'	n, s, t, or v	'w' or 'wr'
lower case 'e'	a, c, i, or l	any monophthong vowel
lower case 's'	a, n, or r	'c' or 'z'
lower case 'i'	c, e, or l	any monophthong vowel
lower case 'b'	h, k, l, 'le,' or 'li'	'p'
lower case 'a'	c, 'ce,' 'ci,' 'cl,' d, e, o or u	any monophthong vowel
Letters (b) (4), FlexTouch	**Scripted May Appear as**	**Spoken May Be Interpreted as**
Capital 'F'	J, T or Z	'Pf' 'Ph' or 'V'
lower case 'f'	b, l, or t	'pf,' 'ph,' or 'v'
lower case 'l'	A, b, e, i, P, or s	'n' 'r' or 'w'
lower case 'x'	a, d, skinny f, k, n, p, r, t, v, or y	'cks,' 'ks,' s, or z
lower case 'o'	a, c, e, or u	any vowel
lower case 'u'	a, ee, ei, ie, n, o, v, w, or y	any vowel
lower case 'c'	a, e, i, or l	see below
lower case 'h' in combination 'ch'	b, k, l, or n none	- 'j' or 'sh'
Letters (b) (4), (b) (4)	**Scripted May Appear as**	**Spoken May Be Interpreted as**
		(b) (4)

Appendix C: Prescription Simulation Samples and Results

Figure 1. Tresiba Study (Conducted on November 2, 2011)

Handwritten Requisition Medication Order	Verbal Prescription
(b) (4)	

FDA Prescription Simulation Responses.

INPATIENT	STRENGTH	VOICE	STRENGTH	OUTPATIENT	STRENGTH
TRESIBA	(b) (4)	CHESEBA	(b) (4)	TRESIBA	
(b) (4)					


(b) (4)

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

Proprietary Name	Active Ingredient	Similarity to Tresiba	Failure preventions
Amitiza	Lubiprostone	Sound	Amitiza lack sufficient phonetic similarity as Amitiza has an additional syllable and the first two syllables (/æ/ and /mɪ/) are not heard in Tresiba.
Santura	**Trospium** chloride	Sound	Trospium lacks sufficient phonetic similarity as the second syllable begins with the consonant sound /p/ and the third includes no beginning consonant sound yet ends with the consonant sound /m/.
Sustiva	Efanirenz	Sound	Sustiva lacks sufficient phonetic similarity as it includes the consonant sound /s/ in the first syllable at the beginning and the ending, and the second syllable begins with the consonant sound /t/ which is plosive alveolar.
(b) (4)		Look	Alternative proprietary name for the product now marketed as Dexilant.
(b) (4)		Look and Sound	Proposed proprietary name which DMEPA found unacceptable. The product is currently marketed under the established name.
Tetrex	Tetracycline Phosphate Complex	Look	Discontinued product with no generic equivalents, Application was withdrawn and Federal Register notice was published September 1990.
(b) (4)		Look	A proposed proprietary name which DMEPA found unacceptable. The application received a Complete Response by the Agency. Subsequently, the application was withdrawn by the Applicant.
Tradjenta	Linagliptin	Look	Tradjenta lacks sufficient orthographic similarity as it includes two additional letters, includes an additional upstroke and the letter 'j' providing a down stroke.
Trasicor	Oxprenolol HCl	Look	Discontinued product with no generic equivalents. The application withdrawn and Federal Register notice published September 1995.
Trasylol	Aprotinin bovine	Look	Removed from the market November 2007 for safety concerns.

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

Proprietary Name	Active Ingredient	Similarity to Tresiba	Failure preventions
Tremin *(discontinued product with generic equivalents)*	**Trihexyphenidyl** HCl	Look	Tremin lacks sufficient orthographic similarity as it includes no letters providing an upstroke. Trihexyphenidyl lacks sufficient orthographic similarity as it includes 15 letters and is twice as long as Tresiba when scripted.
Tresiba	Insulin degludec	Look and Sound	Trademark licensed to this Applicant and only associated with this product.
Tretinoin	established name for Atralin, Avita, Retin-A, Renova and Refissa	Look	Tretinoin lacks sufficient orthographic similarity as it includes two additional letters, and the letter providing the upstroke appear in the first half of the name and also may provide an cross stroke.
(b) (4)		Look and Sound	Proposed proprietary name to which DMEPA objected. The product is currently marketed under the proprietary name, Treximet.
Trivita	multiple products	Look	This is the product line or "family" name for nutritional supplements. As the product line includes more than twenty products, and each has a proprietary name, the proprietary name is needed for a complete order or to order the product.
Proprietary Name	**Active Ingredient**	**Similarity to Tresiba FlexTouch** (b) (4)	**Failure preventions**
Levemir FlexTouch***	Insulin detemir	Look and Sound	Proposed name for the presentation of Levemir in this device. The drug's proprietary name, Levemir, provides sufficient orthographic and phonetic differentiation.
Novolog FlexTouch*** (b) (4)	Insulin aspart	Look and Sound	Proposed name for the presentation of Novolog in the FlexTouch device. The drug's proprietary name, Novolog, provides sufficient orthographic and phonetic differentiation.
			(b) (4)

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

Proprietary Name	Active Ingredient	Similarity to (b) (4) (b) (4)	Failure preventions (b) (4)

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

Appendix E: Risk of medication errors due to product confusion minimized by the dissimilarity of the names and/ or use in clinical practice for the reasons described.

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch (b) (4) (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion **Causes (could be multiple)**	**Prevention of Failure Mode (name confusion)**
Feiba (Anti-inhibitor coagulant complex) 500 unit, 1000 unit, and 2500 unit vials Usual dose: 25 units/kg to 100 units/kg intravenously one time.	**Orthographic similarity to Tresiba:** Both names begin with a letter that appears similar when scripted (F vs. T), and share four letter including the last three letters (e and -iba). Both are injectable products, available in a numerically similar strength (1000 units vs. 100 units/mL) and utilize the same units of measure in dosing (units).	Orthographic difference stems from the fact that Tresiba has two additional letters (r and s) which provide added length to the name when scripted. Fieba is dosed based on the patients weight (units/kg) and will not overlap with an achievable dose of Tresiba. Fieba is used in the clinic or emergency room settings. Tresiba is available in two dosage form presentations in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4): FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Fusilev (Levoleucovorin calcium) 50 mg vial and 175 mg/17.5 mL and 250 mg/5 mL vials Usual dose: Following methotrexate for osteosarcoma: 7.5 mg intravenously every six hours for 10 doses. With 5-Fluorouracil for advanced colorectal cancer: 10 mg/m^2 or 100 mg/m^2 intravenously daily for five daily.	**Orthographic similarity to Tresiba:** Both names have seven letters and a similar length when scripted, begin with a letter that appears similar when scripted (F vs. T), and shares a letter grouping at the end with shared letters and similar appearance when scripted (-silev vs. siba). Both are injectable products which may be administered daily. Both share numeric achievable doses that overlap numerically (16 mg to 22 mg based on 10 mg/m^2 vs. 10 units to 160 units).	Fusilev is available in three strength presentations, none of which overlap with those of Tresiba. In addition, Fusilev is administered as an adjunct to or rescue agent for chemotherapy drugs and is thus treated similarly as a high alert medication in the inpatient or clinic settings often with a separate order form. Tresiba is available in two strength presentations and also in two dosage form presentations in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Levitra (Vardenafil HCl) 2.5 mg, 5 mg, 10 mg, and 20 mg Usual dose: One tablet by mouth once daily or as needed no more than once daily.	**Orthographic similarity with Tresiba:** Both names have seven letters and a similar length when scripted, begin with a letter that may appear similar when scripted (L vs. T), include the letter 'r,' include one letter providing an upstroke in a similar position (t vs. b), and share the same vowels in same order and similar positions in each name (e, i, and a). Both products share numerically achievable doses (10 mg or 20 mg vs. 10 units or 20 units) and are available in numerically similar strengths which are exacerbated by the use of trailing zeroes (10.0 mg or 20.0 mg vs. 100 units/mL or 200 units/mL)	Orthographic difference may be provided by the fact that the letter 'r' appears in differing positions in each name. In Tresiba, the letter 'r' appears after the beginning letter 'T' which provides some additional separation between the letters 'T' and 'b.' In Levitra, the letter 'r' appears in the sixth position after the letter 't' which may provide added length following the upstroke. Finally, the letter 't' in Levitra may be scripted with a cross stroke. Levitra is an oral tablet. Levitra would not be used in the inpatient setting. Tresiba is a subcutaneous injection. It is available in two strengths which may be written U-100 and U-200 and is available in (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4) .

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Lusedra (fospropofol disodium) 1050 mg/30 mL vials Usual dose: 6.5 mg/kg intravenously to initiate anesthesia. Repeat a dose of 1.6 mg/kg intravenous bolus to maintain anesthesia.	**Orthographic similarity to Tresiba:** Both names have seven letters and a similar length when scripted, begin with a letter that may appear similar when scripted (L vs. T), include the letter 'r,' include one letter providing an upstroke in a similar position (d vs. b) and end with the same letter (a). Both are injectable products.	Lusedra is available in one strength presentations which does not overlap with those of Tresiba. It is limited to use in the operating room or procedure areas that requires anesthesia. Tresiba is dosed as a daily subcutaneous injection. It is available in two strengths which may be written U-100 and U-200 and is available in (b) (4) the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4): FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Testred (Methyltestosterone) 10 mg capsules Usual dose: One to five capsules (10 mg to 50 mg) by mouth daily.	**Orthographic similarity to Tresiba:** Both names have seven letters and have a similar length when scripted, begin with the same letter (T), include the letter pair (es) and include a letter providing an upstroke in a similar position (t vs. b). The products share achievable doses (10 mg to 50 mg vs. 10 units to 50 units) which are administered daily and numerically similar strengths (10 mg vs. 100 units/mL)	Orthographic difference stems from the fact that Testred ends with the letter 'd' which provides an upstroke. In addition, Tresiba includes a four letter grouping which separates the letter 'T' from the upstroke provided by the letter 'b.' Testred is an oral tablet. Tresiba is a subcutaneous injection. It is available in two strengths which may be written U-100 and U-200 and is also available (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4): FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Treanda (Bendamustine HCl) 25 mg and 100 mg vials Usual dose: CLL-100 mg/m^2 intravenously over 30 minutes on days 1 and 2 of a 28 day cycle. NHL-120 mg/m^2 intravenously over 30 minutes on days 1 and 2 of a 21 day cycle.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the same three letters (Tre-), end with the same letter (a) and include a letter in the sixth position providing an upstroke (d vs. b). Both are injectable products available in same numeric strength (100 mg vs. 100 units/mL)	Orthographic differences may be provided by the fact that the letter pair (an) and the preceding loop of the letter 'd' in Treanda provide additional separation between the letter T and the upstroke. Treanda is a chemotherapy agent that is a high alert medication in the inpatient or clinic settings often with a separate order form or prescription process from other medications. Tresiba is dosed as a daily subcutaneous injection and is available in (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)
Trecator (Ethionamide) 250 mg tablets Usual dose: One tablet (250 mg) three or four times daily.	**Orthographic similarity to Tresiba:** Both names have a similar length when scripted, begin with the same three letters (Tre) and include a letter providing an upstroke in a similar position. Both products may be written with a frequency of use that appear similar when scripted and have been confused (four times daily or **QID** vs. once daily or **QD**).	Orthographic difference may be provided by the letter 't' when scripted with a cross stroke. In addition , Trecator includes two letters (or) following the 't' which provides additional length to the name after the upstroke. Trecator is a tablet in a single strength presentation which is not similar to those of Tresiba. Trecator is dosed as one tablet. Tresiba is dosed in number of units as a subcutaneous injection and a 250 units dose is not achievable. Tresiba is available (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4): FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Trelstar (Triptorelin pamoate) 3.75 mg, 11.25 mg, and 22.5 mg vials Usual dose: One vial intramuscularly one time. 3.75 mg is repeated every four weeks. 11.25 mg is repeated every 12 weeks. 22.5 mg is repeated every 24 weeks.	**Orthographic similarity to Tresiba:** Both names have similar length when scripted, begin with the same three letters (Tre) and include a letter providing an upstroke in the sixth position (t vs. b). Both products are injectable.	Orthographic difference stem from the fact that Trelstar includes the letter 'l' which provides an additional upstroke in the name. In addition, a letter pair (ar) follows the letter 't' which provides some additional length after the last upstroke in Trelstar. Trelstar is available in three strength presentations which do not overlap with those of Tresiba or are these strengths/doses achievable with any of the presentations of Tresiba.
Trental (Pentoxifilline) 400 mg tablets Usual dose: One tablet (400 mg) by mouth three times daily.	**Orthographic similarity with Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the same three letters (Tre-), and include a letter providing an upstroke in a similar position (t vs. b). The numeric dose of each may appear similar, This is exacerbated by the use of trailing zeroes or the abbreviation 'U' for units (400 mg vs. 40.0 units or 40U).	Orthographic difference stems from the fact that Trental ends with the letter 'l' which provides an additional upstroke to the name appearing at the end. Trental is an oral tablet in a single strength presentation which does not overlap with those of Tresiba. Tresiba is a daily subcutaneous injection. It is available in two strengths which may be written U-100 and U-200 and is available (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4).

Proposed name: Tresiba (insulin degludec) **(b) (4): FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Trexall (Methotrexate) 5 mg, 7.5 mg, 10 mg, and 15 mg tablets Usual dose: for rheumatoid arthritis, 7.5 mg by mouth once weekly, may be given 2.5 mg every 12 hours for three doses. For psoriasis, 10 mg to 25 mg by mouth once weekly, may be divided over 36 hours as above, for juvenile rheumatoid arthritis: 10 mg/m^2 by mouth once a week.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the same three letters (Tre-), and include a letter providing an upstroke in a similar position (l vs. b). Both share numeric achievable doses (10 mg or 15 mg vs. 10 units or 15 units). Both have a numerically similar strength (10 mg vs. 100 units/mL)	Orthographic difference stems from the fact that Trexall includes a double letter pair (ll) at the end of the name providing a pair of upstrokes. Trexall is an oral tablet which are taken once a week. Preliminary drug use data suggest that prescribers use a frequency of use when prescribing this product. Tresiba is a daily subcutaneous injection. It is available in (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4): FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Treximet (Sumatriptan succinate and Naproxen sodium) 85 mg/500 mg tablets Usual dose: One tablet by mouth one time, may repeat after two hours. No more than two tablets in 24 hours.	**Orthographic similarity to Tresiba:** Both names include a similar number of letters (8 vs. 7), begin with the same three letters (Tre-) and include one letter providing an upstroke (t vs. b). Both may be written "use as directed."	Orthographic difference stems from the fact that Treximet ends with the letter 't' which provides for the upstroke to appear as the final stroke in the name and at a greater distance from beginning letter 'T.' In addition, the final letter 't' may be scripted with a cross stroke. Treximet is an oral tablet with a single strength presentation that is likely to be omitted and does not overlap with those of Tresiba. Treximet is dosed in terms of the number of tablets. Tresiba is available in two strengths which may be written U-100 or U-200. A strength is necessary for a complete prescription when written "use as directed." It is available (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)
Trezix (Acetaminophen, Caffeine, and Dihydrocodeine bitartrate) 320.5 mg/30 mg/16 mg capsules Usual dose: Two capsules by mouth every four hours as needed, maximum of 10 capsules in 24 hours.	**Orthographic similarity to Tresiba:** Both names include a similar number of letters (6 vs. 7), begin with the same three letters (Tre-) followed by a letter pair that may appear similar when scripted (zi vs. si), and end with a letter that may appear similar when scripted (x vs. a).	Orthographic difference stems from the fact that Tresiba includes the letter 'b' which provides an upstroke. Trezix is an oral capsule with a single strength presentation that is likely to be omitted and does not overlap with those of Tresiba. Tresiba is available in two strengths. It is available (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **[redacted]: FlexTouch and [redacted]** **U-100 (100 units/mL) in a 3 mL disposable pen and a [redacted]** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or [redacted]) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Triacet (Triamciniolone acetonide) 0.1% cream Usual dose: Apply to affected area twice or three times daily.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the same letter pair (Tr-), include a letter grouping that appear similar (iac vs. esi) and include one letter providing an upstroke.	Orthographic difference stems from the fact that Triacet ends with the letter 't' which provides for the upstroke to appear as the final stroke in the name. Tresiba includes the letter 'a' after the upstroke provided by the letter 'b.' Triacet is a topical cream in a single strength presentation that is likely to be omitted and does not overlap with those of Tresiba. It is available in two sizes (15 g and 80 g tubes) which must be specified if written "use as directed." Tresiba is available in two strengths. A strength is needed if written "use as directed." [redacted] in the 100 unit/mL strength (FlexTouch and [redacted]) which is necessary information for a complete prescription or to order the medication. [redacted]

Proposed name: Tresiba (insulin degludec) **(b) (4): FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Tri-Luma (Fluocinolone acetonide, Hydroquinone and Tretinoin) 0.01%/4%/0.05% cream Usual dose: Apply topically to face once daily at bedtime.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the similar letter grouping (Tri- vs. Tre-) include a letter providing an upstroke (l vs. b) and end with the same letter (a). Both products have a frequency of use of once daily and may have a dispense quantity of one (one tube or one carton).	Orthographic difference stems from the fact that Tri-Luma presents the letter 'L' or 'l' in the fourth position which is followed by three letters (uma) and additional length compared to the single letter 'a' which follows the letter 'b' in Tresiba. Tri-Luma is a topical cream in a single strength presentation that is likely to be omitted and does not overlap with those of Tresiba. Tresiba is available in two strengths. (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)
Trinate (Prenatal vitamin supplement) Usual dose: One tablet by mouth daily.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the similar letter grouping (Tri- vs. Tre-) and include a letter providing an upstroke in the sixth position (t vs. b). Both products are administered once daily, may be written, "use as directed," and may have a dispense quantity of one (one tube or one carton).	Trinate is an oral tablet in a single strength presentation that is likely to be omitted. Tresiba is available in two strength presentations. A strength is needed for complete prescription when written "use as directed." (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Tripedia (Diptheria/Pertussis/Tetanus vaccine) 5 mL vials Usual dose: 0.5 mL intramuscularly every four to eight weeks for a total of three injections. The doses should start to be administered from the age o six weeks to up to 7 years old.	**Orthographic similarity to Tresiba:** Both names include a similar number of letters (8 vs. 7) and have a similar length when scripted, begin with the similar letter grouping (Tri- vs. Tre-) include a letter providing an upstroke in the sixth position (d vs. b) and end with the same letter (a). Both are injectable products.	Orthographic difference stems from the fact that Tripedia includes the letter 'p' which provides a down stoke. Tripedia is available in a single strength presentation (vial) and the strength likely to be omitted. It is administered to pediatric patients in a physician's office or clinic. Tresiba is available in two strength presentations and is (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)
Trisenox (Arsenic trioxide) 10 mg/10 mL ampule Usual dose: 0.15 mg/kg infused intravenously over one to two hours daily up to 25 doses for consolidation treatment or 60 doses for induction of bone marrow remission.	**Orthographic similarity to Tresiba:** Both names begin with a five letter grouping that includes the same letters (Trise- vs. Tresi-) and end with a letter that may appear similar when scripted (x vs. a). Both are injectable products that are administered daily. Both have numerically similar strengths (10 mg/mL vs. 100 units/mL)	Orthographic difference stems from the fact that Tresiba includes the letter 'b' which provides and upstroke. Trisenox is a chemotherapy agent that is dosed based on weight. It is a high alert medication in the inpatient or clinic settings often with a separate order form or prescribing process in these settings. Tresiba is available (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Trisudex **Tri-sudo** (Pseudoephedrine HCl and Triprolidine HCl) 60 mg/2.5 mg tablets Usual dose: One tablet by mouth every four to six hours as needed, no more than four tablets in 24 hours.	**Trisudex orthographic similarity to Tresiba:** Both names include a similar number of letters (8 vs. 7) and have a similar length when scripted, begin with the similar letter grouping (Tris- vs. Tres-) include a letter providing an upstroke in the sixth position (d vs. b) and end with a letter that may appear similar (x vs. a). **Tri-sudo orthographic similarity to Tresiba:** Both names include the same number of letters (7) and have a similar length when scripted, begin with the similar letter grouping (Tris- vs. Tres-) include a letter providing an upstroke in the sixth position (d vs. b) and end with a letter that may appear similar (o vs. a). Both may be written "use as directed."	Trisudex is an oral tablet available in a single combination strength presentation, and the strength likely to be omitted and does not overlap with those of Tresiba. Tri-sudo is an oral tablet available in a single combination strength presentation, and the strength likely to be omitted and does not overlap with those of Tresiba. Tresiba available in two strength presentations which may be written U-100 or U-200. A strength is necessary for a complete prescription when written "use as directed." (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4) .

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Trivora (Levonorgestrel and Ethinyl estradiol) 0.05 mg/0.03 mg (6 tablets), 0.075 mg/0.04 mg (5 tablets), 0.125 mg/0.03 mg (10 tablets), plus 7 inert tablets Usual dose: One tablet by mouth once daily.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the similar letter grouping (Tri- vs. Tre-) and end with the same letter (a). Both products are administered once daily, may be prescribed "use as directed," and may have a dispense quantity of one (one month or one pack vs. one carton)	Orthographic difference stems from the fact that Tresiba includes the letter 'b' which provides an upstroke. Trivora is an oral tablet available in a single strength presentation and the strength likely to be omitted and does not overlap with those of Tresiba. Tresiba available in two strength presentations. A strength is needed for a complete prescription if written "use as directed." (b) (4) in the 100 unit/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)
Trusopt (Dorzolamide HCl) 2% ophthalmic solution Usual dose: One drop to each eye three times daily.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the same letter pair (Tr), include a letter providing an upstroke (t vs. b). May be prescribed "use as directed" and may have a dispense quantity of one (one bottle vs. one carton)	Orthographic difference stems from the fact that Trusopt includes the letter 'p' in the sixth position which provides a down stroke and the letter 't' appears in the seventh and final position which may be scripted with a cross stroke. Trusopt is available in one strength presentation which is likely to be omitted and does not overlap with those of Tresiba. Tresiba is available in two strength presentations. A strength is needed for a complete prescription if written "use as directed." Also the 100 unit/mL strength is available (b) (4) (FlexTouch and (b) (4)) which are likely to be included with a prescription. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Droxia (Hydroxyurea) 200 mg, 300 mg, and 400 mg capsules Usual dose: 15 mg/kg/day with a 5 mg/kg/day increase every 12 weeks to a maximum of 35 mg/kg/day. The dose is one to three capsules by mouth once daily, twice daily, or three times daily.	**Phonetic similarity to Tresiba:** Both names include three syllables, the first syllable begins with a mixed consonant sound which include a plosive alveolar sound followed by the same/r/ (/dr/ vs. /tr/) and the vowel sounds in the second and third syllables are the same monophthong vowels (/i/ and /a/). Both share a numeric strength (200 mg vs. 200 units/mL)	Phonetic difference stems from the fact the names are stressed differently, Droxia in the first syllable and Tresiba in the second syllable. The consonant sounds heard in the second and third syllables also differ in Tresiba. The second syllable begins with /s/ compared to the mixed sound /ks/ heard in Droxia which starts with a plosive velar sound. Finally, the third syllable in Tresiba starts with /b/ while Droxia include no beginning consonant sound in the third syllable. Droxia is an oral capsule. The dose is weight based and is divided to up to three times daily. The dose is expressed in term of milligrams or capsules which sound different when spoken from the units to dose Tresiba (units). Tresiba is available in (b) (4) (FlexTouch and (b) (4)) which are likely to be included with a prescription. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Lessina (Levonorgestrel and Ethinyl estradiol) 0.1 mg/0.02 mg tablets Usual dose: One tablet by mouth daily.	**Phonetic similarity to Tresiba:** Both names include three syllables with the same monophthong vowel sounds (/ɜ/, /i/, and /a/) and the second and stressed syllable in both names begins with the same consonant sound (/s/). Both products are administered once daily, may be prescribed "use as directed," and may have a dispense quantity of one (one month or one pack vs. one carton)	Phonetic difference stems from the fact that Tresiba begins with a mixed consonant sound /tr/ that starts plosive alveolar while Lessina begins with a single consonant sound /l/ which is lateral alveolar. In addition, the third syllable in Tresiba begins with the consonant /b/ which is plosive bilabial compared to the /n/ that begins the third syllable in Lessina which is nasal alveolar. Lessina is an oral tablet available in one strength presentation which is likely to be omitted and does not overlap with those of Tresiba. Tresiba is available in two strength presentations which are needed for a complete prescription if written "use as directed." Also the 100 unit/mL strength is available (b) (4) (FlexTouch and (b) (4)) which are likely to be included with a prescription. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Tarceva (Erlotinib HCl) 25 mg, 100 mg and 150 mg tablets Usual dose: One tablet (100 mg or 150 mg) by mouth once daily.	**Orthographic Similarity to Tresiba:** Both names have seven letters and a similar length when scripted, and begin and end with the same letters (T and A, respectively). **Phonetic similarity to Tresiba:** Both names include three syllables with the same monophthong vowel sounds in the second and third syllables (/i/ and /a/, respectively), include the beginning consonant sound /t/, and the second syllable begins with the same consonant, /s/. Both share a numeric strength and achievable dose (100 mg or 150 mg vs. 100 units/ml or 100 units or 150 units) and are administered once daily.	Orthographic difference stems from the fact that Tresiba includes the letter 'b' which provides an upstroke. Phonetic difference stems from the fact that although the names both start with the letter 'T', Tresiba begins with the mixed consonant sound /tr/. In addition, the vowel sound in the first syllable of Tarceva is a heavy /ar/. Tarceva is an oral tablet. The dose is expressed in term of milligrams or tablets which sound different when spoken from the units to dose Tresiba (units). Tresiba is available (b) (4) in the 100 units/mL strength (FlexTouch and (b) (4)) which is necessary information for a complete prescription or to order the medication. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a 3 mL cartridge.** **U-200 (200 units/mL) in a (b) (4)** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Trizivir (Abacavir/Lamivudine/Zidovudine) 300 mg/150 mg/300 mg tablets Usual dose: One tablet by mouth once daily.	**Phonetic similarity to Tresiba:** Both names include three syllables, the first syllable begins with the same mixed consonant sound, /tr/, and the second syllable begins with an affricate alveolar consonant sound (/z/ vs. /s/). Both products are taken once daily and may have a dispensing quantity of one (one bottle vs. one carton.)	Phonetic difference stems from the fact that the third syllable in Trizivir begins with the consonant sound /v/ which is fricative labio-dental compared to the same syllable in Tresiba which begins with /b/ with is plosive-bilabial. Finally, the vowel sound in the third syllable of Trizivir is /ɪr/ which is a Tense-R vowel. Trizivir is an oral tablet available in one strength presentation which is likely to be omitted and does not overlap those of Tresiba. Tresiba prescribed in number of units and is available in two strength presentations. A strength is needed for a complete prescription if written "use as directed." Also the 100 unit/mL strength is available (b) (4) (FlexTouch and (b) (4)) which are likely to be included with a prescription. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Prezista (Darunavir) 75 mg, 150 mg, and 400 mg capsules 600 mg tablets Usual dose in adults: One tablet (600 mg) or two capsules (800 mg) by mouth once daily	**Orthographic similarity to Tresiba:** Both names have a similar number of letters (8 vs. 7) and a similar length when scripted, have five letters in common including the final letter (r, e, i, s, and the final letter, a) and include a letter which provides an upstroke in a similar position (t vs. b). **Phonetic similarity to Tresiba:** Both names include three syllables with the same monophthong vowel sounds (/ɜ/, /i/, and /a/) and the second syllable begin with a affricate alveolar consonant sound (/z/ vs. /s/). Both products are administered once daily and have a numerically similar achievable dose exacerbated by the use of trailing zeroes or the abbreviation 'U' for units (600 mg and 800 mg vs. 60.0 units or 60U and 80.0 units or 80U).	Orthographic difference stems from the fact that Prezista begins with the letter 'P,' includes an additional letter 'z' between the beginning letter and the letter providing the up stroke (t). The letter 'z' may be scripted with a down stroke, and the letter 't' may be scripted with a cross stroke. Phonetic difference stems from the fact that the beginning consonant sound of Prezista is /pr/. The second syllable of Prezista includes the shared affricate alveolar consonant sound of /z/ and /s/ at the ending of the second syllable as well as the beginning. Prezista's last syllable begins with /t/. Prezista is available as oral tablets or as oral capsules in three strength presentation which is needed for a complete prescription. In addition, these strengths do not overlap with those of Tresiba. Tresiba is available in two strength presentations which are needed for a complete prescription if written "use as directed." Also the 100 unit/mL strength is available (b) (4) (FlexTouch and (b) (4)) which are likely to be included with a prescription. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a 3 mL cartridge.** **U-200 (200 units/mL) in a (b) (4)** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Tasigna (nilotinib) 150 mg and 200 mg capsules Usual dose: Two capsules (300 mg or 400 mg) twice daily.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the same letter (T) and end with the same letter (a). **Phonetic similarity to Tresiba:** Both names include three syllables with the same monophthong vowel sounds in the second and third syllables (/i/ and /a/, respectively), include the beginning consonant sound /t/ in the first syllable, and the second syllable begins with the same consonant, /s/. Both products share a numeric strength (200 mg and 200 units/mL). Visually, the dose may appear similar which is exacerbated by the use of trailing zeroes or the abbreviation 'U' for units (300 mg or 400 mg vs. 30.0 units , 30U, 40.0 units, or 40U).	Orthographic difference stems form the fact that Tresiba includes the letter 'b' which provides an upstroke. In addition, Tasigna includes the letter 'g' which provides a down stroke. Phonetic difference stems from the fact that although the names both start with the letter 'T', Tresiba begins with the mixed consonant sound, /tr/. Tasigna has a second syllable which includes an ending consonant sound /g/ and the third syllable begins with /n/. Tasigna is an oral capsule which is dosed in number of capsules and administered twice a day. Tresiba is available (b) (4) in the 100 units/mL strength (FlexTouch and (b) (4)) which are likely to be included with a prescription. The (b) (4) .

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a 3 mL cartridge.** **U-200 (200 units/mL) in a (b) (4)** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Trinessa (norgestimate and ethinyl estradiol) 0.18mg/0.035 mg (7 tablets), 0.215 mg/0.035 mg (7 tablets), 0.25 mg/0.035 mg (7 tablets), and 7 inert tablets Usual dose: on tablet by mouth daily.	**Orthographic similarity to Tresiba:** Both names include a similar number of letters (8 vs. 7) and have a similar length when scripted, begin with the similar letter grouping (Tri- vs. Tre-) and end with the same letter (a). **Phonetic similarity to Tresiba:** Both names include three syllables with the same monophthong vowel sounds (/ɜ/, /i/, and /a/) and begin with the same mixed consonant sound /tr/. Both products are administered once daily, may be prescribed "use as directed," and may have a dispense quantity of one (one month or one pack vs. one carton)	Orthographic difference stems from the fact that Tresiba includes the letter 'b' which provides an upstroke. Phonetic difference stems form the fact that includes the same vowel sound in a different sequence compare to Tresiba. In addition, the second syllable of Trinessa begins with the consonant sound /n/ which is nasal compared to the /s/ in Tresiba which is affricate. Finally, the third syllable in Tresiba begins with the consonant sound /b/ which is not heard in Trinessa. Trinessa is an oral tablet available in one strength presentation which is likely to be omitted and does not overlap with those of Tresiba. Tresiba is available in two strength presentations which are needed for a complete prescription if written "use as directed." Also the 100 unit/mL strength is available (b) (4) (FlexTouch and (b) (4)) which are likely to be included with a prescription. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Truvada (emtricitabine and tenofovir disoproxil fumarate) 200 mg/300 mg tablet Usual dose: One tablet by mouth once daily.	**Orthographic similarity to Tresiba:** Both names include seven letters and have a similar length when scripted, begin with the same letter pair (Tr), end with the same letter (a) and include a letter in the sixth position providing an upstroke (d vs. b). **Phonetic similarity to Tresiba:** Both names include three syllables, the first syllable begins with the same mixed consonant sound, /tr/ and the last syllable includes the same monophthong vowels sound (/a/). Both products share a numerically similar strength (200 mg/300 mg vs. 200 units/mL) and both are administered once daily.	Orthographic differences may be provided by the fact that the letter grouping (uva) and the preceding loop of the letter 'd' in Treanda provide additional separation between the letter T and the upstroke when scripted. Phonetic difference stems from the fact that the consonants heard in the second and third syllable sound different. The second syllable of Truvada begins with /v/ which is fricative labio-dental sound compared to the /s/ in Tresiba which is an affricate alveolar sound. The last syllable in each name include a plosive consonant (/d/ vs. /b/) ,but the placement in the mouth differentiates them. /d/ is alveolar while /b/ is bilabial. Truvada is an oral tablet that is available in one strength presentation which likely to be omitted. Tresiba is available in (b) (4) (FlexTouch and (b) (4)) which are likely to be included with a prescription. (b) (4) .

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Tysabri (natalizumab) 300 mg/15 mL vial Usual dose: 300 mg intravenously as a one hour infusion one time every four weeks.	**Orthographic similarity to Tresiba:** Both names have seven letters and have a similar length when scripted, begin with the same letter (T), and include the letter 'b' in a similar position. **Phonetic similarity to Tresiba:** Both names include three syllables, include the beginning consonant sound /t/ in the first syllable, the second syllable begins with the same consonant, /s/ and includes the consonant sound /b/ at the beginning of the third syllable. Both products are injectable.	Orthographic difference stems from the fact that Tysabri includes the letter 'y' which provides a down stroke. Phonetic difference stems from the fact that although the names both start with the letter 'T', Tresiba begins with the mixed consonant sound, /tr/. Tysabri include the diphthong vowel sound /aɪ/ rather than a monophthong vowel and ends with a close front vowel /i/ rather than an open back vowel /a/. Tysabri is available as a single strength presentation that does not overlap with those of Tresiba. In addition, Tysabri has a risk of PML which is mitigated with a REMS that includes a restricted distribution program. Tresiba is available in two strength presentations. Also the 100 unit/mL strength is available (b) (4) (FlexTouch and (b) (4)) which are likely to be included with a prescription. (b) (4)

Proposed name: Tresiba (insulin degludec) **(b) (4) FlexTouch and (b) (4)** **U-100 (100 units/mL) in a 3 mL disposable pen and a (b) (4)** **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Flextra (Acetaminophen, Caffeine, and Phenyltoloxamine Citrate) 425 mg/35 mg/45 mg capsules Flextra DS (Acetaminophen and Phenyltoloxamine Citrate) 500 mg/50 mg tablets Flextra 650 (Acetaminophen and Phenyltoloxamine Citrate) 650 mg/60 mg capsules	(b) (4) Both names share the first five letters (Flext-). (b) (4), FlexTouch, may be inadvertently written alone as the product name by prescribers. This often occurs when (b) (4) is used for the first time in the market.	Orthographic difference: FlexTouch includes two additional letters which make the name appear longer. FlexTouch also end with the letter 'h' providing an upstroke at the end of the name. Flextra is the root name for three different oral Acetaminophen combination products. Two of the formulations have a modifier (DS and 650) which provide additional orthographic differentiation.

Proposed name: Tresiba (insulin degludec) [(b) (4)] **FlexTouch and** [(b) (4)] **U-100 (100 units/mL) in a 3 mL disposable pen and a** [(b) (4)] **U-200 (200 units/mL) in a 3 mL disposable pen.** **Usual dose (U-100): Inject 10 units to 80 units subcutaneously once daily. (U-200) 2 units to 160 units subcutaneously once daily.**		**Other Failures to Consider with this product** • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (FlexTouch or* [(b) (4)] *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Hextend (Hetastarch) 6% injection in 500 mL and 1000 mL bags of lactated electrolyte injection Usual dose: One bag infused intravenously over several hours to replace blood loss.	**Orthographic similarity to** [(b) (4)]**, FlexTouch:** Both names begin with similar appearing letter grouping when scripted (He vs. Fle), followed by the same letter in the middle of the name (x), and the letter grouping at the end appear similar (tend vs. touch) when scripted. [(b) (4)], FlexTouch, may be inadvertently written alone as the product name by prescribers. This often occurs when [(b) (4)] is used for the first time in the market.	Hextend is a plasma expander which is limited to use in the operating room or the trauma area of an emergency department. The dose is determined by the number of bags or the rate of infusion (ml/hour). FlexTouch is a pen device that is used to administer insulin products. Dose is determined in the hospital setting by patient's diet.

Appendix F: ISR numbers of reports retrieved from AERS search in Section 2.2.3

3668852	4049237	4377955	5127116	5719407	6143158	6497904	7116188
3676468	4057851	4435088	5136242	5719411	6155278	6516701	7137831
3870311	4084876	4447484	5157252	5729262	6183109	6527025	7150324
3882150	4174494	4501087	5164374	5738677	6282525	6529451	7156156
3896483	4223263	4501946	5176419	5951716	6332717	6546004	7210235
3964482	4240621	4536061	5182581	5974974	6335015	6568034	7323100
3970990	4285415	4559142	5427273	5999698	6335018	6595974	7488304
4002003	4307754	4689710	5513702	6047244	6341691	6640345	7553707
4003611	4317456	4748923	5566530	6075057	6399938	6745675	7686382
4011334	4326401	4765785	5719403	6099439	6444477	6942304	7884960
4025784	4330478	4804925	5719404	6110961	6466358	7093802	7917020
4026936	4362147	4884356	5719405	6121037	6480162	7101785	

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/s/

CARLOS M MENA-GRILLASCA
12/30/2011

IRENE Z CHAN
12/30/2011

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

Proprietary Name Review

Date:	December 22, 2011
Reviewer(s):	Richard A Abate, RPh, MS, Safety Evaluator Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
Drug Name(s) and Strengths:	Ryzodeg (70% Insulin Degludec and 30% Insulin Aspart [rDNA origin]), 100 units/mL (U-100) Flex Touch Pen (b) (4)
Application Type/Number:	NDA 203313
Sponsor:	Novo Nordisk
OSE RCM #:	2011-3893

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Ryzodeg, 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.

1.1 REGULATORY HISTORY

DMEPA previously reviewed the proposed proprietary name, [redacted] for this product under IND 073198 in OSE review # 2010[redacted]. DMEPA found the name, [redacted] unacceptable do to its similarity to and overlapping product characteristics with [redacted]. However, [redacted], Flex Touch, was found to be acceptable. The Applicant submitted the proposed proprietary name, Ryzodeg on October 5, 2011 which [redacted]

1.2 PRODUCT INFORMATION

The following product characteristics were obtained from Request for Proprietary Name Review submitted October 5, 2011 and the draft insert labeling submitted September 29, 2011

- Established Name: 70% insulin degludec and 30% insulin aspart [rDNA origin] injection
- Indication of Use: To improve glycemic control in patients with diabetes mellitus.
- Route of administration: Subcutaneously
- Dosage form: injection in a prefilled disposable syringe [redacted].
- Dose: The dose for insulins varies based on the patients needs but usual starting dose is 10 units for insulin naïve patients. The dose with the Flex Touch device ranges from 1 unit to 80 units. The dose is administered once daily before a meal or may be divided and administered twice daily before a meal.
- How Supplied: 100 units/ml (U-100) in 3 mL Flex Touch disposable pen injector. The pens are packaged five pens per carton. [redacted]
- Storage: The pens [redacted] are stored between 2° and 8° C (36° and 46° F). Do not freeze. After initial use, the product in either configuration may be stored at room temperature, below 30° C (86° F) for up to four weeks.
- Container and Closure systems: The disposable pen-injector is the PDS290 device which a use validation study was included with the Application. [redacted]

2 RESULTS

The following sections provide the information obtained and considered in the 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 Metabolism and Endocrinology Products (DMEP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following sections are considered in the overall safety evaluation of the proposed name, Ryzodeg.

2.2.1 United States Adopted Names (USAN) SEARCH

On December 6, 2011, the primary safety evaluator's United States Adopted Name (USAN) stem search identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant stated the derivation of the proposed proprietary name, Ryzodeg, was from the previously submitted name, (b) (4) to address the similarities found to (b) (4) and to alleviate the FDA's concerns of name confusion.

(b) (4), Flex Touch (b) (4) (b) (4), which are evaluated in conjunction with the proposed proprietary name, Ryzodeg, as well as separately for vulnerabilities for confusion that could lead to medication errors. (b) (4) Flex Touch, will be new to the market and used to identify the disposable prefilled pen-injector presentation. (b) (4) An AERS search for medication errors involving the (b) (4) of marketed products is discussed in Section 2.2.4. Names similar (b) (4), Flex Touch and (b) (4), are identified in Section 2.2.7 and evaluated in Appendices E and F.

2.2.3 Components of the Established Name

The Applicant proposes the established name, 70% insulin degludec and 30% insulin aspart [rDNA origin]. The strength of the product is 100 units/mL which is a single strength and does not represent the dose of each component of this product as required by 21 CFR 201.100. The CMC reviewer noted this at the filing meeting. Comments regarding this issue were provided to the Applicant in the Filing letter on November 30, 2011. Historically, the proprietary name of insulin products containing a mixture of two insulins has included a modifier that represents the percentage of each component (e.g. 50/50, 70/30, or 75/25). The proprietary names of the products that have included the modifier, 70/30, appear in Appendix D. As this presentation of the ratio of insulin

components as a modifier has historical precedence for use and is currently used in clinical practice, DMEPA will assess the proposed proprietary name, Ryzodeg, with the potential for the addition of the modifier, 70/30. (See Appendix F). This assessment will evaluate if inclusion of this modifier could contribute to medication errors.

2.2.4 Medication Error Data

(b) (4)

(b) (4)

2.2.5 FDA Name Simulation Studies

Thirty-nine practitioners participated in DMEPA's prescription studies. See Appendix D for the complete listing of interpretations from the verbal and written prescription studies. Of note, seventeen respondents interpreted the name correctly as "Ryzodeg" in the written studies (15 in the inpatient and two in the outpatient). In addition, all nine respondents to the outpatient study understood (b) (4) correctly as "Flex Touch." The letter 'g' was misinterpreted as the letter 'q' or the letter 'd' was misinterpreted as the letter 'l' preceded by another letter. The verbal responses were all phonetic variations on the name "Ryzodeg."

2.2.6 Comments from Other Review Disciplines

In response to the OSE, November 3, 2011 e-mail, the Division of Metabolism and Endocrinology Products did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.7 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in Ryzodeg, Flex Touch, or (b) (4). Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Ryzodeg, Flex Touch, (b) (4), Ryzodeg Flex Touch, or (b) (4). These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names not previously identified by DMEPA but identified by (b) (4) a third party vendor, who completed an external name assessment of the proposed proprietary name for the Applicant.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines and (b) (4)

Look Similar to Ryzodeg		Sound Similar to Ryzodeg		Look and Sound Similar to Ryzodeg	
Name	***Source***	***Name***	***Source***	***Name***	***Source***
(b) (4)	FDA	Cytotec	FDA	Rilutek	FDA and (b) (4)
Erycette	FDA	Digitek	FDA	Ryzodeg	FDA
Eryzole	FDA	Dynafed	FDA	Ryzolt	FDA and (b) (4)
Kytril	FDA	Phisohex	(b) (4)	Razadyne	FDA and (b) (4)
Lusedra	FDA	Rezira	FDA		
Lysodren	FDA	Vasotec	FDA and (b) (4)		
Nystop	FDA	Rezulin			
Penecort	FDA	RibaTab			
Penetrex	FDA	Rifadin			
Pyopen	FDA				
Pyridium	FDA and (b) (4)				
Reyataz	FDA and (b) (4)				
Refludan	FDA				
Renotec	FDA				
Repronex	FDA				
Rymed	FDA				
Rynex DM	FDA				
Rynex PE	FDA				
Rynex PSE	FDA				
Rynatan	FDA and (b) (4)				

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Look Similar to Ryzodeg	
Risperdal	(b) (4)
Rvnatuss	FDA
(b) (4)	FDA
Vytorin	FDA
Vyvanse	FDA

Look Similar to Ryzodeg Flex Touch		Sound Similar to Ryzodeg Flex Touch		Look and Sound Similar to Ryzodeg Flex Touch	
Rizatriptan Benzoate	FDA	(b) (4)	FDA	Novolog Flex Touch***	FDA
Levemir Flex Touch***	FDA			(b) (4)	FDA
Novolog Flex Pen	FDA				
Novolog Mix 70/30 Flex Pen	FDA				

Look Similar to Flex Touch (b) (4))		Look and Sound Similar to (b) (4)	
Flextra	FDA	(b) (4)	FDA
Hextend	FDA		

Look Similar to (b) (4) (b) (4))		Sound Similar to (b) (4) ((b) (4))		Look and Sound Similar to (b) (4) ((b) (4)	
(b) (4)	FDA	(b) (4)	FDA	(b) (4)	FDA
	FDA		FDA		FDA
	FDA				

Our analysis of the fifty-six names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics for these names.

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We determined the fifty-six names will not pose a risk for confusion as described in Appendix E and F.

2.2.8 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated these midpoint review findings to the Division of Metabolism and Endocrinology Products via e-mail on December 14, 2011. At that time we requested DMEP provide any information or concerns that could inform our review. Per e-mail correspondence from the DMEP on December 16, 2011, they stated no additional concerns with the proposed proprietary name, Ryzodeg.

3 DISCUSSION

The proposed proprietary name, Ryzodeg was submitted (b) (4), Flex Touch (b) (4) (b) (4). However, the fact that this is a product containing a mixture of two different insulins, insulin degludec and insulin aspart. provides the potential for the use a modifier to identify the ratio of the insulins in Ryzodeg.

3.1 Consideration of the Addition of a Modifier, 70/30

The modifier, 70/30, is currently marketed for other insulin mixtures. We note that should the modifier, 70/30, be included with this proprietary name, Ryzodeg, it is consistent with those products in which this modifier currently appears (i.e., the longer acting insulin is presented first, 70%, followed by the rapid acting insulin, 30%). None of the medication errors identified for this review noted confusion related to the modifier, specifically 70/30. In addition, DMEPA similarly noted in OSE review 2009-2424 Novolog Mix 70/30 Flex Touch*** proprietary name review dated March 10, 2010 that the medication errors involving insulin products with percentage modifiers resulted from confusion between the root name of the product rather than the modifiers. Furthermore, DMEPA notes that NovoNordisk proposes a completely different proprietary name for the insulin degludec product that is not similar to Ryzodeg. Additionally, the risk of medication errors resulting from the omission of the modifier, 70/30, would be minimal because no other product uses the proprietary name, Ryzodeg. Finally, our Failure Mode and Effect Analysis of the proposed name, Ryzodeg, considered the inclusion the modifier, 70/30, and no failures resulted in medication errors due to name confusion.

4 CONCLUSIONS

The proposed proprietary name, Ryzodeg, is acceptable from both a promotional and safety perspective. In addition, (b) (4), Flex Touch (b) (4) (b) (4), (b) (4) acceptable from a promotional and safety perspective. Furthermore, should it be determined that the modifier, 70/30, be included as part of the name of this product, DMEPA would still find this name acceptable.

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4.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Ryzodeg, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your September 29, 2011 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review. Additionally, this proprietary name must be re-evaluated 90 days prior to the approval of the application. The conclusions upon re-review are subject to change.

5 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. ***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. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

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.

17. ***Adverse Event Reporting System (AERS)***

    AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly

from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential post-marketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by DDMAC. DDMAC 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. DDMAC provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, 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.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. 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. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product 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.

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

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[2] The product characteristics considered for this review appears in Appendix B1 of this review.

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. 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. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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 2 below for details).

Table 2. 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*
	Similar spelling	Identical prefix Identical infix Identical suffix	• Names may appear similar in print or electronic media and lead to drug name

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

Look-alike		Length of the name Overlapping product characteristics	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/Similar shape Upstrokes Down strokes Cross-strokes 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, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the

trademark being evaluated. Lastly, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). 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). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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 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.

4. 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 DDMAC'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.

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, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.[3] 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 Appendix B1 of this review. 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? And Are there any components of the name that may function as a source of error beyond sound/look-alike"***

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

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 or because of some other component of the name. 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?"***

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.

Moreover, 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 Overall 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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for 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 Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above 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, confusing, or misleading 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 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.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Ryzodeg	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'R'	B, K, Pr, or Z	'W' 'Wr'
lower case 'r'	e, n, s or v	'w'
lower case 'y'	'ej,' g, 'ij,' q, u, or z	any diphthong vowel
lower case 'z'	c, e, g, n, m, q, r, s, v or y	c, s, or x
lower case 'o'	a, c, e, or u	any vowel
Lower case 'd'	'cl' or t	'b' or 't'
lower case 'e'	a, c, i, or l	any vowel
lower case 'g'	q, s, y or z	'k'
Letters (b) (4), Flex Touch	**Scripted May Appear as**	**Spoken May Be Interpreted as**
Capital 'F'	T or Z	'Pf' 'Ph' or 'V'
lower case 'f'	b, l, or t	'pf,' 'ph,' or 'v'
lower case 'l'	A, b, e, i, P, or s	'n' or 'w'
lower case 'x'	a, d, skinny f, k, n, p, r, t, v, or y	'cks,' 'ks,' s, or z
Capital 'T'	F, J, or T	'D'
lower case 't'	A, f, r, or x	'd'
lower case 'u'	a, ee, ei, ie, n, o, v, w, or y	any vowel
lower case 'h' in combination 'ch'	b, k, l, or n none	- 'j' or 'sh'

Appendix C: Prescription Simulation Samples and Results

Figure 1. Ryzodeg Study (Conducted on November 2, 2011)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Ryzodeg 20 units sub-q daily with breakfast	Ryzodeg 20 units Subcutaneously daily with breakfast.
Outpatient Prescription: ℞ Ryzodeg Flex-Touch #5 Use as directed	

FDA Prescription Simulation Responses.

INPATIENT	STRENGTH	VOICE	STRENGTH	OUTPATIENT	STRENGTH
RYZODEG	20 units	RAZODEC		RYZOBLOQ FLEX-TOUCH	
RYZODEG	20 units	RHYZADEC	20 units	RYZODEG FLEX TOUCH	
RYZODEG	20 units	RISADEG	20 u	RYZODEG FLEX-TOUCH	
RYZODEG	20units	RISADEG		RYZODEQ FLEX TOUCH	
RYZODEG	20 U	RISADEG	20 units	RYZOLEG FLEX TOUCH	
RYZODEG		RISADEG	20 U SQ	RYZOOLEG FLEX-TOUCH	
RYZODEG	20 units	RISIDEC	20u	RYZOTLEG FLEX TOUCH	
RYZODEG	20units	RISODEG	20 units	RYZOTLEG FLEX TOUCH	
RYZODEG		RISODEX	20 units	URYZOLEG FLEX TOUCH	

RYZODEG	20 units	RIZADEG	20 units
RYZODEG	20 units	RIZODEC	20units
RYZODEG	20units	RIZODEG	20 units
RYZODEG	20 units	RYZADEK	
RYZODEG	20 unites	ZYRODEX	
RYZODEG	20 units		
RYZODES	20 units		

Appendix D: Marketed insulin products using the 70/30 modifier

Proprietary names	**included insulin the product**
Humulin 70/30	70% human insulin isophane suspension and 30% human insulin injection [rDNA origin]
Humulin 70/30 Pen	70% human insulin isophane suspension and 30% human insulin injection [rDNA origin]
Mixtard Human 70/30	discontinued product 1999
	(b) (4)
Novolog Mix 70/30	70% insulin aspart protamine suspension and 30% insulin aspart injection [rDNA origin]

Appendix E: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

Proprietary Name	Active Ingredient	Similarity to Ryzodeg	Failure preventions
(b) (4)	sumatriptan	Look	An alternate proposed name, which was never evaluated, for an NDA which DMEPA found the primary name, Zecuity***, acceptable. The NDA received a complete response secondary to CMC and CDRH deficiencies.
Cytotec	misoprostol	Sound	Lacks sufficient phonetic similarity to lead to name confusion based on the following aspects of the name, Cytotec: begins with /s/ consonant sound, the second syllable begins with /t/ sound and the last consonant sound heard is /k/ which is not voiced.
Digitek	digoxin	Sound	Lacks sufficient phonetic similarity to lead to name confusion based on the following aspects of the name, Digitek: begins with a consonant sound /d/, the second syllable begins with the consonant sound /dj/ and the last consonant sound heard is /k/ which is not voiced.
Dynafed	chlorpheniramine maleate and pseudoephedrine HCl	Sound	Lacks sufficient phonetic similarity to lead to name confusion based on the following aspects of the name, Dynafed: begins with a consonant sound /d/, the second syllable begins with the consonant sound, /n/, and the last consonant sound heard is /d/.
Erycette	erythromycin	Look	Lacks sufficient orthographic similarity to lead to confusion based on the following aspects of the name, Erycette: Begins with the letter 'E,' includes two of the letter 't,' and the last letter 'e' is scripted without a down stroke.
Eryzole	erythromycin ethylsuccinate and sulfisoxazole acetyl	Look	Lacks sufficient orthographic similarity to lead to confusion based on the following aspects of the name, Eryzole: appears shorter when scripted , begins with the letter 'E,' and the last letter 'e' is scripted without a down stroke.

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

Kytril	granisetron	Look	Lacks sufficient orthographic similarity to lead to confusion based on the following aspects of the name, Kytril; Appears shorter when scripted, includes the letter 't' in the third position which may provide and upstroke, and ends with the letter 'l' which provides an upstroke at the end of the name.
Lusedra	fospropofol	Look	Lacks sufficient orthographic similarity to lead to confusion based on the following aspects of the name, Lusedra: begins with the letter 'L' and includes no letters providing down strokes when scripted.
Penecort	hydrocortisone	Look	Lacks sufficient orthographic similarity to lead to confusion based on the following aspects of the name, Penecort: includes no letters providing down strokes when scripted and ends with the letter 't' which provides an upstroke and a cross stroke.
Penetrex	enoxacin	Look	A discontinued product with no generic equivalents. The application has been withdrawn and Federal Register posted notice April 2005.
Pyopen	carbenicillin disodium	Look	A discontinued product with no generic equivalents. This Application was withdrawn November 1997. Also, lacks sufficient orthographic similarity to lead to confusion based on the following aspects of the name, Pyopen: appears shorter when scripted, includes no letters providing upstrokes and ends with the letter 'n' which provides no down stroke.
Renotec	technitium TC-99M ferpantate kit	Look	Discontinued radiologic agent with no generic equivalents. The Application was withdrawn from the Agency with a Federal Register notice in March 2009.
Rezulin	troglidazone	Sound	Withdrawn from the market due to safety concerns related to liver toxicities,
Ryzodeg	insulin degludec and insulin aspart	Look and sound	Identified as a trademark to NovoNordisk and only associated with the product in this NDA.

Proprietary Name	Active Ingredient	Similarity to Ryzodeg Flex Touch	Failure preventions
Levemir Flex Touch[***]	insulin detemir	Look and Sound	Proposed name for the presentation of Levemir in this device. The drug's proprietary name, Levemir, provides sufficient orthographic and phonetic differentiation.
Maxalt	**Rizatriptan Benzoate**		Lack of sufficient orthographic and phonetic similarity due to the following: Rizatriptan benzoate is longer when scripted and include two additional syllables when spoken.
(b) (4)		Look and Sound	Proposed name to this product (b) (4) to which DMEPA objected.
Proprietary Name	**Active Ingredient**	**Similarity to** (b) (4)	**Failure preventions**
			(b) (4)
			(b) (4)

[***] **This is proprietary and confidential information that should not be released to the public. ***

(b) (4)

Proprietary Name	Active Ingredient	Similarity to (b) (4) (b) (4)	Failure preventions (b) (4)

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

Appendix F: Risk of medication errors due to product confusion minimized by the dissimilarity of the names and/ or use in clinical practice for the reasons described.

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion **Causes (could be multiple)**	**Prevention of Failure Mode (name confusion)**
Lysodren (mitotane) 500 mg tablet Usual dose: 2 g to 4 g daily divided. One to two tablets (500 mg to 1000 mg) by mouth three times or four times daily. (Maximum daily dose is 6 g.)	**Orthographic similarity to Ryzodeg:** Both names have a similar length when scripted and include a letter groupings that share many letters and appear similar when scripted (-ysod- vs. –yzod-). Both products are single strength products. The products have a numerically similar achievable dose in adult populations which can be exacerbated by the use of trailing zeros (500 mg vs. 50.0 units).	Orthographic difference stems from the fact that Lysodren begins with the letter 'L' rather than an 'R' in Ryzodeg and ends with an 'n' which provides no down stroke. Lysodren in an oral tablet. Ryzodeg is available (b) (4) (Flex Touch disposable pen and (b) (4) (b) (4)).

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Nystop (nystatin) topical powder 100,000 USP units per gram Usual dose: Apply topically to affected area twice or three times daily.	**Orthographic similarity to Ryzodeg:** Both names have a similar shape, begin with a letter grouping that may appear similar when scripted (Nys- vs. Ryz-) and also end with a letter grouping that may appear similar when scripted (-top vs. -deg). Both are single strength products that may be administered twice a day.	Orthographic difference stems from the fact that Ryzodeg includes an additional letter (o) which not only adds to the length of the name when scripted but provides separation of the two similar letter groupings. The letter 't' in Nystop may be scripted with a cross stroke. The letter 'z' in Ryzodeg may be scripted with a down stroke. Nystop is a topical powder. Ryzodeg is available (b) (4) (b) (4) (Flex Touch disposable pen and) (b) (4) .
Pyridium (phenazopyridine) 100 mg and 200 mg tablets Usual dose: one or two tablets (200 mg) by mouth three times daily after meals for 3 days. *(Discontinued products with multiple generic products available)*	**Orthographic similarity to Ryzodeg:** Both names begin with similar appearing letters (P vs. R) followed by the letter 'y' and include the letter 'd' in the fifth position. Both products share a numeric strength (100 mg vs. U100 or 100 units/mL)	Orthographic difference stems from the fact the Pyridium appears longer when scripted and ends with the letter 'm' which is scripted without a down stroke. Pyridium is an oral tablet. Ryzodeg is available in (b) (4) (b) (4) (Flex Touch disposable pen and (b) (4) .

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Razadyne (Galantamine HBr) 4 mg/mL oral solution; 4 mg, 8 mg, and 12 mg tablets; Razadyne ER 8 mg, 16 mg and 24 mg capsules Usual dose: One tablet (4 mg to 12 mg) or one mL to three mL by mouth twice daily. Usual dose (ER); One capsule (8 mg to 24 mg) by mouth once daily.	**Orthographic similarity to Ryzodeg:** Both names begin with the same letter R, include the letters 'z' and 'd' in the third and fifth positions respectively which are separated by a similar appearing letter (a vs. o). **Phonetic similarity to Ryzodeg:** Both names include three syllables, each syllable begins with the same consonant sound (/r/, /z/, and /d/) and both share the diphthong vowel sound /aɪ/ provided by the letter 'y.' Both products share numeric achievable doses (4 mg to 24 mg vs. 4 units to 24 units) which may be taken one or twice daily.	Orthographic difference stems from the fact that Ryzodeg includes the letter 'y' in the second position providing a down stroke as well as a down stroke provided by the letter 'g' at the end of the name. In Razadyne, the down stroke from the letter 'y' appears immediately following the 'd' and is in turn followed by a letter pair 'ne.' Phonetic difference may be provided by the fact that the third and final syllable in Ryzodeg includes a monophthong vowel /ɛ/ and ends with the plosive velar consonant sound /g/. The shared diphthong vowel sound, /aɪ/, is heard in the first syllable in Ryzodeg while it is heard in the third of Razadyne. Razadyne ends with the nasal alveolar consonant sound /n/. Razadyne is available in three oral dosage forms tablets, capsules (with a modifier, ER) and solution. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4)) (b) (4) .

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Refludan (lepirudin) 50 mg vial Usual dose: 0.4 mg/kg intravenous loading dose followed by a continuous intravenous infusion of 0.15 mg/kg/hour.	**Orthographic similarity to Ryzodeg:** Both names have a similar length, begin with the same letter (R), include a letter grouping that appear similar when scripted (-uda- vs. -ode-) and a letter that may be scripted with a down stroke in the first half of the name (f vs. y). Both are single strength, injectable products.	Orthographic difference stems from the fact that Refludan includes the letters 'f' and 'l' which provide additional upstrokes when scripted. These upstrokes appear together in the name. Finally, Ryzodeg ends with the letter 'g' which provides a down stroke. Ryzodeg is available (b) (4) (Flex Touch disposable pen and (b) (4) (b) (4))

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Repronex (menotropins) 75 IU and 150 IU vials Usual dose: 150 IU to 450 IU (one to six vials) subcutaneously once daily up to 12 days.	**Orthographic similarity to Ryzodeg:** Both names begin with the same letter (R), have a similar length and include a letter providing down stroke (p vs. y) in the first half of the name. Both are injectable products administered subcutaneously once daily. The products have a numerically similar achievable dose in adult populations which can be exacerbated by the use of trailing zeros. (150 units to 450 units vs. 15.0 units to 45.0 units)	Orthographic difference stems from the fact that Ryzodeg includes the letters 'd' which provides an upstroke and 'g' which provides an additional and final down stroke at the end of the name. Ryzodeg also includes the letter 'z' which may be scripted with a cross stroke or a down stroke. Repronex is available in two strength presentations, 75 IU and 150 IU. A strength must be specified for a complete prescription or to order the medication. Ryzodeg is only available in one strength presentation, 100 units/ml (U-100) which does not overlap with those of Repronex. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4) (b) (4)

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4). **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4)*) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Reyataz (Atazanavir Sulfate) 100 mg, 150 mg, 200 mg, and 300 mg capsules Usual dose in adults: 400 mg (two capsules) by mouth daily when used alone, or 300 mg (one capsule) by mouth once daily when used with concomitant medications. Usual dose in pediatrics with ritonavir: 15 kg to less than 25 kg: 150 mg (one capsule) by mouth daily; 25 kg to less than 32 kg: 200 mg (one capsule) by mouth daily; 32 kg to less than 39 kg: 250 mg (one 100 mg capsule plus one 150 mg capsule) by mouth daily. 39 kg or more; 300 mg (one capsule) by mouth daily.	**Orthographic similarity to Ryzodeg:** Both names contain seven letters and have similar length; begin with the same letter (R), include a 'y' which provides a down stroke, and include a letter providing an upstroke in a similar position ('t' vs. 'd'). Both share a numerically similar strength/ concentration (100 mg and 300 mg vs. 100 units/mL or 300 units/3 mL) Both may be administered once a day. The products have a numerically similar achievable dose in adult populations which can be exacerbated by the use of trailing zeros (300 mg and 400 mg vs. 30.0 units and 40.0 units).	Orthographic difference: Reyataz includes the letter 'e' which separated the 'R' from the 'y' and includes the letter 't' which provides a cross stoke and ends with a 'z' which may be scripted without any down stroke. (b) (4) Reyataz is available as oral capsules. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4) (b) (4).

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Rilutek (Riluzole) 50 mg tablets Usual dose: One tablet (50 mg) by mouth every 12 hours.	**Orthographic similarity to Ryzodeg:** Both names contain seven letters and have similar length and with the same letter (R) and include a letter providing an upstroke in the fifth position (t vs. d). **Phonetic similarity to Ryzodeg:** Both names contain three syllables; the names share the first syllable (/raɪ/) and the third syllables sound similar (/tɛk/ vs. dɛg") as both /g/ and /k/ sounds are made using the mouth placement (velar and plosive.) Both are single strength products and include a numeric achievable dose (50 mg vs. 50 units).	Orthographic difference stems from the fact that Rilutek includes a total of four letters providing upstrokes in the names (R, l, t, and k) while Ryzodeg only has two (R and d). In addition, Ryzodeg includes letters (y and g) scripted with a down stroke as well as the letter 'z' which may be scripted with a cross stroke or a down stroke. Phonetic difference stems from the second syllable in Rilutek which sounds different when pronounced (/lu/ vs. /zo/) . Rilutek is an oral tablet. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4) (b) (4) .

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Risperdal (Risperidone) 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg tablets and orally disintegrating tablets 1 mg/ ml oral solution Usual dose: One tablet (any strength) by mouth once daily or twice daily (to a maximum of 8 mg per day). Consta: 12.5 mg, 25 mg and 50 mg kit for injection Usual dose: one kit (12.5 mg to 50 mg) intramuscularly every two weeks.	**Orthographic similarity to Ryzodeg:** Both names begin with the same letter (R), include a letter providing a down stroke (p vs. y) in the first half of the name and include the letter 'd.' Both may be administered daily. Both are have injectable formulations that may have numeric overlap in dose (25 mg and 50 mg vs. 25 units and 50 units).	Orthographic difference stems from the fact that Risperdal contains nine letters and appears longer when scripted. In addition, Risperdal ends with the letter 'l' which provides an additional upstroke in the name. Ryzodeg ends with the letter 'g' which provides a down stroke. Risperdal is available in multiple strengths and formulations which do not overlap with (b) (4). Although the dose of an injectable formulation may overlap, Risperdal Consta has a modifier and is administered by a healthcare provider in a physician's office every two weeks. Ryzodeg will be administered by the patient or caregiver. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4)) (b) (4)
Rymed (dexchlorpheniramine maleate and phenylephrine HCl) 2 mg/10 mg tablets Usual dose: One tablet by mouth every four to six hours as needed.	**Orthographic similarity:** Both names begin with the same letter pair (Ry) and include the letter 'd' in the fifth position. Both are single strength products.	Orthographic difference stems form the fact that Rymed appears shorter when scripted as it only includes five letters. In addition, Ryzodeg includes the letter pair 'eg" following the 'd' which provides an additional down stroke as well as the added length. Rymed is an oral tablet. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4)) (b) (4) .

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) [redacted] **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Rynatan (Phenylephrine tannate and Chlorpheniramine tannate) 25 mg/9 mg tablets Usual dose: one or two tablets by mouth every 12 hours	**Orthographic similarity to Ryzodeg:** Both names contain seven letters and have similar length; begin with the same letter pair (Ry); and include a letter providing an upstroke the fifth position ('t' vs. 'd'). Both are single strength products.	Orthographic difference stems from the fact that Ryzodeg ends with the letter 'g' which provides a down stroke. Rynatan includes the letter 't' which may provide a cross stroke when scripted. The letter 'z' in Ryzodeg may be scripted with a down stoke. Rynatan is an oral tablet which is dosed as one or two tablets. Ryzodeg is an injection dosed as 10 to 80 units. In addition, Ryzodeg is available in (b) (4) [redacted] (Flex Touch disposable pen and (b) (4) [redacted]
Rynatuss (carbetapentane tannate, chlorpheniramine tannate, ephedrine tannate, and phenylephrine tannate) 60 mg/5 mg/10 mg/10 mg tablets Usual dose: one to two tablets by mouth every twelve hours.	**Orthographic similarity:** Both names have a similar length when scripted, begin with the same letter pair (Ry), include a letter providing an upstroke in the fifth position and end with a letter that may appear similar when scripted (s vs. g). Both are single strength products which may be taken twice a day (every 12 hours vs. twice daily).	Orthographic difference stems from the fact that Rynatuss ends with a double letter 's' (or ss) and includes the letter 't' which may be scripted with a cross stroke. The double letter 's' provides difference when compared to the single 'g' in Ryzodeg. In addition, Ryzodeg includes the letter 'z' which may be scripted with a down stroke. Rynatuss is an oral tablet dosed as one or two tablets. Ryzodeg is an injection dosed as 10 to 80 units. In addition, Ryzodeg is available in (b) (4) [redacted] Flex Touch disposable pen and (b) (4) [redacted])

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Rynex DM (brompheniramine maleate, dextromethorphan HBr, and phenylephrine HCl) 1 mg/5 mg and 2.5 mg per 5 mL **Rynex PE** (brompheniramine maleate and phenylephrine HCl) 1 mg/2.5 mg per 5 mL **Rynex PSE** (brompheniramine maleate and pseudoephedrine HCl) 1 mg/15 mg per 5 mL Usual dose: pediatric 2 years to under 6 years- one teaspoon (5 mL) by mouth every 4 hour to six hours as needed. pediatric 6 years to under twelve years: two teaspoons (10 mL) by mouth every four to six hour as needed Adult 12 years and older: four teaspoons (20 mL) by mouth every four to six hours as needed.	**Orthographic similarity between Rynex and Ryzodeg:** Both names begin with the same letter pair (Ry) and (b) (4) have a similar length.	Orthographic difference stems from the fact that Ryzodeg includes the letter 'g' at the end that provides a down stroke. In addition, the Rynex products are all over the could cough and cold products that use the modifiers (DM, PE and PSE) to distinguish themselves from each other. These modifiers also provide orthographic differences as they are in upper case which provides additional upstrokes. Rynex products are oral liquids. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4)) (b) (4)

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) **e.** (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*

(b) (4)

*** **This is proprietary and confidential information that cannot be release to the public. ***

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) [redacted] (b) (4) [redacted] **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Ryzolt (tramadol HCl) 100 mg, 200 mg, and 300 mg extended-release tablets Usual dose: One tablet (any strength) by mouth once daily.	**Orthographic similarity:** Both names begin with the same letter grouping (Ryzo-). **Phonetic similarity:** The first syllable in each name is pronounced the same (/raɪ/) and the second syllable share the same beginning consonant sound /z/ and vowel sound ("uh"). Both product share a numeric strength (100 mg vs. 100 units/mL or U-100) and are administered once daily. The products also have a numerically similar achievable dose in adult populations which can be exacerbated by the use of trailing zeros or the abbreviation 'u' for units (100 mg, 200 mg or 300 mg vs. 10.0 units, 20.0 units, or 30.0 units).	Orthographic difference stems from the fact that Ryzolt includes tow letters providing upstrokes ate the end ('l' and 't') while Ryzodeg ends with the letter 'g' which provides a down stroke. Phonetic difference stems from the fact that Ryzodeg includes a third syllable /dɛg/. In addition, Ryzolt ends with a mixed consonant sound /lt/. Ryzolt is an oral tablet. Ryzodeg is available in (b) (4) [redacted] (b) (4) [redacted] (Flex Touch disposable pen and (b) (4) [redacted]) (b) (4) [redacted] .

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4). **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Vytorin (ezetimibe and simvastatin) 10 mg/10 mg, 10 mg/ 20 mg, 10 mg/40 mg and 10 mg/80 mg tablets Usual dose: One tablet (any strength) by mouth once daily.	**Orthographic similarity:** Both names have a similar length when scripted, begin with a similar appearing letter when scripted (V vs. R), include the same letter (y) in the second position and have one letter providing an upstroke (t vs. d). Both products may be taken once daily.	Orthographic difference stems from the fact that Ryzodeg includes an upstroke which appears in the fifth position rather than the third as seen in Vytorin and ends with the letter 'g' which provides an additional down stroke. Vytorin is an oral tablet. Ryzodeg is available (b) (4) (b) (4) (b) (4) (Flex Touch disposable pen and).

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4). **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or (b) (4)) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Vyvanse (lisdecamfetamine dimesylate) 20 mg, 30 mg, 40 mg, 50 mg, 60 mg and 70 mg capsules Usual dose: One capsule (any strength) by mouth once daily.	**Orthographic similarity:** Both names include seven letters, have a similar length when scripted, and begin with a similar appearing letter grouping when scripted (Vyva vs. Ryzo). Products share an achievable dose (20 mg to 70 mg vs. 20 units to 70 units) which is administered once daily. If the modifier 70/30 is included, these products share numeric strength (70 mg vs. 70/30).	Orthographic difference stems from the fact that Ryzodeg includes an upstroke which appears in the fifth position and ends with the letter 'g' which provides an additional down stroke. Vyvanse in an oral capsule. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4) (b) (4)).

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4). **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Phisohex (Hexachlorophene) 3% Usual dose: Wet hands with water, Apply 5 mLs to hands and work into a lather and scrub , rinse thoroughly.	**Phonetic similarity to Ryzodeg:** Both names have three syllables with all sharing the same vowel sounds, the second syllable in each name begins with a similar sounding consonant (/s/ vs. /z/). Both are single strength products. Shared numerical achievable dose (5 mL vs. 5 units).	Phonetic difference stems from the fact that each name begins with a different consonant sound (/r/ which is approximant, alveolar vs. /f/ which is fricative, labio-dental) when spoken. The third syllables begin with different consonant sounds (/d/ which is plosive, alveolar, and voiced vs. /h/ affricate, glottal and voiceless). Phisohex is a topical scrub. The usual starting dose of insulin for an adult patient is 10 units. Ryzodeg is available (b) (4) (b) (4) (b) (4) (Flex Touch disposable pen and)
Rezira (Hydrocodone Bitartrate and Pseudoephedrine HCl) 5 mg/60 mg per 5 mL Usual dose: One teaspoon (5 mL) by mouth every four to six hours as needed.	**Phonetic similarity to Ryzodeg:** Both names include three syllables and include the same beginning consonant sounds for the first (/r/) and second (/z/) syllables. Both products have a single strength presentation.	Phonetic difference stems from the fact that third and final syllable sound different when spoken (/rah/ vs. /dɛg/). In addition the vowel sound in the first syllable of Ryzodeg is a diphthong (/aɪ/) compared to monophthong vowel (/ɛ/) heard in Rezira. Rezira is an oral liquid dosed in teaspoons or mL. Ryzodeg is available in (b) (4) (b) (4) (b) (4) (Flex Touch disposable pen and).

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4). **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
RibaTab (ribavirin) 400 mg and 600 mg tablets in a 28 day blister pack based on the daily dose (800 mg, 1000 mg, or 1200 mg) Usual dose: One tablet by mouth twice daily.	**Phonetic similarity to Ryzodeg:** Both names include three syllables, the first syllable is the same (/raɪ/), and the third syllable begins with a plosive alveolar consonant (/t/ vs. /d/). Both may be ordered as number of packages with direction for use as "use as directed."	Phonetic difference stems from the fact that the second and third syllables in each name sound different when spoken. The second syllable in RibaTab /bɑ/ begins with a plosive bilabial consonant when compared to the same syllable in Ryzodeg /zo/ which begins with a affricate, alveolar consonant. RibaTab is available in two strengths (400 mg and 600 mg tablets) which are packaged in 4 week blister card configurations. The strength or packaging configuration is needed for a complete prescription or to order the medication. Ryzodeg is available as one strength (100 units/mL or U-100) in (b) (4) (Flex Touch disposable pen and (b) (4)) (b) (4)

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) **e.** (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Rifadin (rifampin) 150 mg and 300 mg capsules and 600 mg vial Usual dose: 10 mg/kg (usually 600 mg) by mouth or intravenously once daily.	**Phonetic similarity to Ryzodeg:** Both names include three syllables, and have the same beginning consonant sound for the first (/r/) and third (/d/) syllables. Both products are available as injectable formulations (for injection in a vial vs. injection in a pen or cartridge).	Phonetic difference stems from the fact that the second syllable of Rifadin is pronounced /fɑ/ compared to the second syllable of Ryzodeg, /zo/. In addition, the third syllable of Rifadin , /din/, ends with a the /n/ sound which is nasal alveolar compared to the /g/ in Ryzodeg which is a plosive velar consonant. Rifadin is available in two dosage forms (capsules and for injection in vials) which is dosed 600 mg in adults. Ryzodeg is dosed 10 units to 80 units which dose not sound similar to that of Rifadin. Ryzodeg is available as one strength (100 units/mL or U-100) in (b) (4) (Flex Touch disposable pen and (b) (4)) (b) (4)

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4). **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4) *) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Vasotec (Enalapril maleate) 2.5 mg, 5 mg, 10 mg and 20 mg tablets Usual dose: One tablet (2.5 mg to 20 mg) by mouth once daily. (Enalaprilat) 1.25 mg/ml and 2.5 mg/2 mL injection in vials Usual dose: One vial (1.25 mg or 2.5 mg) intravenously every six hours.	**Phonetic similarity to Ryzodeg:** Both name include three syllables. The second and third are pronounced similarly making the names almost rhyme (-zoh dehg vs. –soh tehk) as both /g/ and /k/ sounds are made using the mouth placement (velar and plosive). Numerically achievable doses (10 mg and 20 mg vs. 10 units and 20 units) Both are available in injectable dosage forms. Both may be prescribed once daily.	Phonetic difference stems from the fact that each name begins with different sounding consonants. Vasotec begins with /v/ which is a voiced fricative consonant compared to Ryzodeg which begins with /r/ which is a voiceless and approximant consonant. The final consonant sound in each name differs as the /g/ is voiced and the /k/ is voiceless. Vasotec is administered orally or intravenously. Ryzodeg is available in (b) (4) (Flex Touch disposable pen and (b) (4) (b) (4)).

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4) **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4)*) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Novolog Flex Pen **Novolog Flex Touch***** **Novolog PenFill** (Insulin aspart) (U-100) 100 units/mL vial, pen device and cartridge Usual dose: 1-80 units subcutaneously before each meal. **Novolog Mix 70/30 Flex Pen** (b) (4) (70% insulin aspart protamine suspension and 30% insulin apart injection) (U-100) 100 units/mL vials and pen device Usual dose: 1-80 units subcutaneously before a meal twice daily.	**Orthographic similarity between Novolog and Ryzodeg:** Both names have seven letters and a similar length when scripted and include a letter grouping that shares letters and appears similar when scripted (volog vs. zoleg). The beginning letter in each name may appear similar when written in the lower case (n vs. r). These products contain insulin aspart, (b) (4) and are dosed before meals (three times daily vs. twice daily.) Ryzodeg is also a 70%/30% ratio combination formulation of two active ingredients. (b) (4)	Orthographic difference stems the fact that Ryzodeg includes the letter 'y' which provides a down stroke in the second position. In addition, Ryzodeg includes the letter 'z' which also may be scripted with a down stroke and the letter 'd' which when scripted includes a loop preceding the upstroke which adds separation between the first letter of the name and the upstroke.

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4). **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4)*) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Flextra (Acetaminophen, Caffeine, and Phenyltoloxamine Citrate) 425 mg/35 mg/45 mg capsules Flextra DS (Acetaminophen and Phenyltoloxamine Citrate) 500 mg/50 mg tablets Flextra 650 (Acetaminophen and Phenyltoloxamine Citrate) 650 mg/60 mg capsules	**Orthographic similarity to** (b) (4)**, Flex Touch:** Both names share the first five letters (Flext-). (b) (4), Flex Touch, may be inadvertently written alone as the product name by prescribers. This often occurs when (b) (4) is used for the first time in the market.	Orthographic difference: Flex Touch includes two additional letters and is intended as two words which make the name appear longer. Flex Touch also end with the letter 'h' providing an upstroke at the end of the name. Flextra is the root name for three different oral Acetaminophen combination products. Two of the formulations have a modifier (DS and 650) which provide additional orthographic differentiation.

Proposed name: **Ryzodeg** **(insulin degludec and insulin aspart)** **U-100 (100 units/mL) in a 3 mL disposable Flex Touch pen device** (b) (4) (b) (4). **Usual dose: Inject 1 unit to 80 units subcutaneously once daily or twice daily before a meal.**		**Other failures considered with this product** • ***Ryzodeg is a product with two active ingredients in a 70%/30% ratio. A modifier (i.e. 70/30) could be utilized to describe this ratio. (Included the use of the modifier 70/30 in the risk assessment.)*** • *This is a product available in one strength presentation. Thus, the strength may be omitted and the prescription may still be filled or the product may be ordered.* • *Preliminary drug use data demonstrates that prescribers write "use as directed" on prescriptions for insulin pens.* • *Products with a single route of administration may have the route omitted as the route may be implied by the product in the outpatient setting.* • *In the inpatient setting, the dosage form presentation (Flex Touch or* (b) (4)*) may not be used based on the fact that the formulary may carry only one presentation. However, a route of administration is necessary for a complete inpatient medication prescription.*
Hextend (Hetastarch) 6% injection in 500 mL and 1000 mL bags of lactated electrolyte injection Usual dose: One bag infused intravenously over several hours to replace blood loss.	**Orthographic similarity to** (b) (4)**, Flex Touch:** Both names begin with similar appearing letter grouping when scripted (He vs. Fle), followed by the same letter in the middle of the name (x), and the letter grouping at the end appear similar (tend vs. touch) when scripted. (b) (4), Flex Touch, may be inadvertently written alone as the product name by prescribers. This often occurs when (b) (4) is used for the first time in the market.	Hextend is a plasma expander which is limited to use in the operating room or the trauma area of an emergency department. The dose is determined by the number of bags or the rate of infusion (ml/hour). Flex Touch is a pen device that is used to administer insulin products. Dose is determined in the hospital setting by patient's diet and limited to 10 to 80 units per dose before meals.

Appendix G: ISR numbers of reports retrieved from AERS search in Section 2.2.4

3668852	4049237	4377955	5127116	5719407	6143158	6497904	7116188
3676468	4057851	4435088	5136242	5719411	6155278	6516701	7137831
3870311	4084876	4447484	5157252	5729262	6183109	6527025	7150324
3882150	4174494	4501087	5164374	5738677	6282525	6529451	7156156
3896483	4223263	4501946	5176419	5951716	6332717	6546004	7210235
3964482	4240621	4536061	5182581	5974974	6335015	6568034	7323100
3970990	4285415	4559142	5427273	5999698	6335018	6595974	7488304
4002003	4307754	4689710	5513702	6047244	6341691	6640345	7553707
4003611	4317456	4748923	5566530	6075057	6399938	6745675	7686382
4011334	4326401	4765785	5719403	6099439	6444477	6942304	7884960
4025784	4330478	4804925	5719404	6110961	6466358	7093802	7917020
4026936	4362147	4884356	5719405	6121037	6480162	7101785	

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/s/

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12/22/2011

CAROL A HOLQUIST
12/22/2011