CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211913Orig1s000

PROPRIETARY NAME REVIEW(S)

ADDENDUM

TO 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:	June 10, 2019
Application Type and Number:	NDA 211913
Product Name and Strength:	Absorica LD (isotretinoin) capsule, 8 mg, 16 mg, 20 mg, 24 mg, 28 mg, 32 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Sun Pharmaceutical Industries Limited
Panorama #:	2018- 26930007-1
DMEPA Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA

1 PURPOSE OF ADDENDUM

DMEPA previously completed a review which found the proposed proprietary name, Absorica LD, conditionally acceptable under NDA 211913 on January 14, 2019.[a] However, the Division of Dermatology and Dental Products (DDDP), based on additional review of the application, raised a potential misbranding concern after we completed our previous evaluation of the proposed proprietary name, Absorica LD.

This addendum to the DMEPA's previous proprietary name review for Absorica LD is to assess the DDDP's potential misbranding concerns.

1.1 MISBRANDING ASSESSMENT

On May 21, 2019, a meeting was held with DDDP and Office of Surveillance and Epidemiology (OSE), to discuss the new misbranding concern with the proposed proprietary name, Absorica LD. At the meeting, DDDP expressed concern that modifier 'LD' which has intended meaning for low dose, may be interpreted as lower risk or safer to use than the currently approved product Absorica which has different dosing and bioavailability. DDDP was concern that the Applicant may use modifier "LD" to have marketing advantage over other isotretinoin products.

In email communication dated May 21, 2019, DMEPA communicated DDDP's misbranding concerns to the Office of Prescription Drug Promotion (OPDP) and requested that OPDP reassess the name Absorica LD, taking into consideration the DDDP's concerns. In email communication dated May 29, 2019, OPDP stated that OPDP discussed the name Absorica LD and maintains their non-objection to the proposed proprietary name, Absorica LD. DDDP deferred to OPDP regarding acceptability of the proposed proprietary name from a misbranding perspective.

2 CONCLUSION

DMEPA maintains that the proposed proprietary name, Absorica LD, is acceptable. We have no additional concerns at this time.

If you have any questions or need clarifications, please contact Tri Minh Bui-Nguyen, OSE project manager, at 240-402-3726.

[a] Patel, M. Proprietary Name Review for Absorica LD (NDA 211913). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 JAN 14. Panorama No.: 2018-26930007.

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/s/

MADHURI R PATEL
06/10/2019 12:21:20 PM

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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:	January 14, 2019
Application Type and Number:	NDA 211913
Product Name and Strength:	Absorica LD (isotretinoin) capsules, 8 mg, 16 mg, 20 mg, 24 mg, 28 mg, 32 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Sun Pharmaceutical Industries Limited
Panorama #:	2018- 26930007
DMEPA Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA Team Leader (acting):	Teresa McMillan, PharmD
DMEPA Deputy Director	Irene Z. Chan, PharmD, BCPS

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Absorica LD, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Sun Pharmaceutical Industries Limited did not submit an external name study for this proposed proprietary name.

1.1 PRODUCT INFORMATION

The following product information for Absorica LD is provided in the proprietary name submission received on October 29, 2018. For comparison purposes, the product characteristics for the currently marketed Absorica are included in Table 1.

Table 1. Product Characteristics of Absorica LD and the Listed Drug

Product	**Absorica LD (NDA 211913)**	**Absorica (NDA 021951)**
Intended Pronunciation	ab sore' i kah (L-D)	ab sore' i kah
Initial Approval Date	N/A	May 25, 2012
Active Ingredient	isotretinoin	isotretinoin
Indication	treatment of severe recalcitrant nodular acne in patients 12 years of age and older.	treatment of severe recalcitrant nodular acne in patients 12 years of age and older.
Route of Administration	oral	oral
Dosage Form:	capsules	capsules
Strength:	8 mg, 16 mg, 20 mg, 24 mg, 28 mg, 32 mg	10 mg, 20 mg, 25 mg, 30 mg, 35 mg and 40 mg
Dose and Frequency	0.4 to 0.8 mg/kg/day given in two divided doses without regard to meals for 15 to 20 weeks. Adult patients whose disease is very severe with scarring or is primarily manifested on the trunk may require dose adjustments up to 1.6 mg/kg/day of Absorica LD, as tolerated.	0.5 to 1 mg/kg/day given in two divided doses without regard to meals for 15 to 20 weeks. Adult patients whose disease is very severe with scarring or is primarily manifested on the trunk may require dose adjustments up to 2 mg/kg/day, as tolerated

Body Weight		Total Daily (mg)		
Kilograms	Pounds	0.4 mg/kg	0.8 mg/kg	1.6 mg/kg
40	(b) (4)	16	32	64
50		20	40	80
60		24	48	96
70		28	56	112
80		32	64	128
90		36	72	144
100		40	80	160

Body Weight		Total Daily (mg)		
Kilograms	Pounds	0.5 mg/kg	1 mg/kg	2 mg/kg
40	88	20	40	80
50	110	25	50	100
60	132	30	60	120
70	154	35	70	140
80	176	40	80	160
90	198	45	90	180
100	220	50	100	200

<table>
<tr>
<td></td>
<td>The below table represents the comparison of strengths between ABSORICA LD and ABSORICA and other generic products available in the market.
<table>
<tr><th>ABSORICA (strengths in mg)/ and other generic products available</th><th>ABSORICA LD (strengths in mg)</th></tr>
<tr><td>40 mg</td><td>32 mg</td></tr>
<tr><td>35 mg</td><td>28 mg</td></tr>
<tr><td>30 mg</td><td>24 mg</td></tr>
<tr><td>25 mg</td><td>20 mg</td></tr>
<tr><td>20 mg</td><td>16 mg</td></tr>
<tr><td>10 mg</td><td>8 mg</td></tr>
</table></td>
<td></td>
</tr>
<tr>
<td>How Supplied:</td>
<td>Box of 30 capsules (3 x 10 Prescription Packs)</td>
<td>Box of 30 capsules (3 x 10 Prescription Packs)</td>
</tr>
<tr>
<td>Storage:</td>
<td>Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature]. Protect from light.</td>
<td>Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature]. Protect from light.</td>
</tr>
<tr>
<td>Pharmacokinetics</td>
<td>Pharmacokinetic Parameters for Single 32 mg Dose of Absorica LD
<table>
<tr><th></th><th>C_{max} (ng/mL) Mean (±SD)</th><th>T_{max} (hr)# Median (Range)</th><th>AUC_{0-t} (ng•hr/mL) Mean (±SD)</th><th>$t_{1/2}$ (hr) Mean (±SD)</th></tr>
<tr><td>Fasting condition (N = 63)</td><td>611.33 ± 285.15</td><td>3.50 (1.25 to 12.00)</td><td>8466.26 ± 2458.22</td><td>25.50 ± 7.07</td></tr>
<tr><td>Fed condition (N = 65)</td><td>645.74 ± 275.18</td><td>5.00 (1.50 to 24.00)</td><td>10209.11 ± 1967.48</td><td>23.52 ± 6.60 *</td></tr>
</table>
Median (Range); *N = 64 for $t_{1/2}$</td>
<td>Pharmacokinetic Parameters of ABSORICA Mean (%CV) Following Administration of 40 mg Strength, N=14
<table>
<tr><th>ABSORICA (1 x 40 mg capsules)</th><th>AUC_{0-t} (ng x hr/mL)</th><th>C_{max} (ng/mL)</th><th>T_{max} (hr)</th><th>$T_{1/2}$ (hr)</th></tr>
<tr><td>Fed</td><td>6095 (26 %)</td><td>395 (39 %)</td><td>6.4 (47 %)</td><td>22 (25 %)</td></tr>
<tr><td>Fasted</td><td>4055 (20 %)</td><td>314 (26 %)</td><td>2.9 (34 %)</td><td>24 (28 %)</td></tr>
</table></td>
</tr>
</table>

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Absorica LD would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Dermatology and Dental Products (DDDP) concurred with the findings of OPDP's assessment for Absorica LD.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Absorica LD.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[a].

2.2.2 Components of the Proposed Proprietary Name

The proprietary name is comprised of the root name, Absorica, and the modifier 'LD'. Sun Pharmaceutical Industries Limited stated the intended meaning of the modifier 'LD' is low dose. Our evaluation of the root name, Absorica, is provided in Section 2.2.5. Our evaluation of the appropriateness of the modifier, LD, is provided in Section 2.2.6.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, November 20, 2018 e-mail, the Division of Dermatology and Dental Products (DDDP) did not forward any comments or concerns relating to Absorica LD at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Sixty-seven practitioners participated in DMEPA's prescription studies for Absorica LD. The responses did overlap with the root name of the proposed product 'Absorica'. Four (outpatient n=1, inpatient =3) participants in the prescription study only listed 'Absorica', without the modifier 'LD'. In the inpatient study where the modifier was written in lower case letters, we note 1 participant misinterpreted the modifier 'LD' as 'ED' and 2 participants misinterpreted it as 'ID'. We discuss the omission of the modifier in Section 2.2.6. Appendix B contains the results from the verbal and written prescription studies.

2.2.5 Medication Error Data Selection of Cases

We searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 and Table 3 (see Appendix A1 for a description of FAERS database) for name confusion errors involving ***Absorica*** or the modifier LD that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	November 5, 2018

[a] USAN stem search conducted on November 30, 2018.

Table 2. FAERS Search Strategy	
Drug Name	Absorica [product name]
Event (MedDRA Terms)	**DMEPA Official PNR Name Confusion Search Terms Event List:** Preferred Terms: CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR DRUG ADMINISTRATION ERROR DRUG DISPENSING ERROR DRUG PRESCRIBING ERROR INTERCEPTED DRUG DISPENSING ERROR INTERCEPTED DRUG PRESCRIBING ERROR INTERCEPTED MEDICATION ERROR MEDICATION ERROR PRODUCT NAME CONFUSION TRANSCRIPTION MEDICATION ERROR Lower Level Terms: INTERCEPTED PRODUCT SELECTION ERROR INTERCEPTED WRONG DRUG PRODUCT SELECTED INTERCEPTED WRONG DRUG SELECTED PRODUCT SELECTION ERROR WRONG DEVICE DISPENSED WRONG DRUG ADMINISTERED WRONG DRUG DISPENSED WRONG DRUG PRESCRIBED WRONG DRUG PRODUCT SELECTED WRONG DRUG SELECTED WRONG PRODUCT SELECTED
Date Limits	May 25, 2012 to November 1, 2018

Each report was reviewed for relevancy and duplication. Duplicates were merged into a single case. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

After individual review, 130 reports were not included in the final analysis for the following reasons: Wrong quantity (n=42), Inappropriate schedule of drug administration (n=22), Wrong strength (n=17), Wrong dose ((n=15), Not enough information (n=13), Incorrect product storage (n=10), Adverse event (n=5), Wrong technique (n=3), Dose omission (n=2), Deteriorated drug error (n=1).

Following exclusions, the search yielded 1 relevant case.

The case described wrong drug dispensed error where the patient was prescribed Claravis, but the pharmacy processed for Absorica. The report does not provide information on root causes and contributing factors in order for us to determine why this error occurred. We considered

confusion with the name pair Claravis and Absorica. Claravis and Absorica may be located next to one another in the pharmacy if stored alphabetically by established name. However, we find that the two proprietary names have sufficient orthographic and phonetic differences.

Table 3. FAERS Search Strategy for Modifier	
Search Date	December 18, 2018
Drug Name	LD [product verbatim]
Event (MedDRA Terms)	**DMEPA Official PNR Name Confusion Search Terms Event List:** Preferred Terms: CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR DRUG ADMINISTRATION ERROR) DRUG DISPENSING ERROR DRUG PRESCRIBING ERROR INTERCEPTED DRUG DISPENSING ERROR INTERCEPTED DRUG PRESCRIBING ERROR INTERCEPTED MEDICATION ERROR MEDICATION ERROR PRODUCT NAME CONFUSION TRANSCRIPTION MEDICATION ERROR Lower Level Terms: INTERCEPTED PRODUCT SELECTION ERROR INTERCEPTED WRONG DRUG PRODUCT SELECTED INTERCEPTED WRONG DRUG SELECTED PRODUCT SELECTION ERROR WRONG DEVICE DISPENSED WRONG DRUG ADMINISTERED WRONG DRUG DISPENSED WRONG DRUG PRESCRIBED WRONG DRUG PRODUCT SELECTED WRONG DRUG SELECTED WRONG PRODUCT SELECTED
Date Limits	Up to December 1, 2018

The search yielded zero cases.

2.2.6 Safety Assessment of the Modifier

Sun Pharmaceutical Industries Limited proposes oral capsules for isotretinoin (NDA 211913) in strengths of 8 mg, 16 mg, 20 mg, 24 mg, 28 mg, and 32 mg, to be marketed under the same root name as the currently approved product, Absorica (NDA 021951), with the modifier, LD. Both products share the same active ingredient, dosage form, and indication, however, due to the

higher bioavailability of the proposed product, a lower dose is needed when compared with Absorica (See Section 1.1 Product Information Table 1).

We considered whether 'LD' is a suitable modifier from a safety perspective. We found that LD is a medical abbreviation representing low dose. For the proposed product currently under review, the 'LD' medical abbreviation is consistent with Absorica LD dosing requiring a lower dose than Absorica. Other definitions of 'LD' listed in MediLexicon include L-Dopa, Learning Disability, Lactate Dehydrogenase, Licensed Dietitian, Living Donor, Last Dose, Lethal Dose, Levodopa, Loading Dose, and Low Dosage[b]. L-Dopa/Levodopa is commonly available in combination with Carbidopa for the treatment of Parkinson's disease and syndrome as an oral tablet or liquid/suspension, whereas the proposed product is a capsule used for the treatment of acne and there is no overlap in strength (10 mg/100 mg, 25 mg/100 mg, 25 mg/250 mg, 50 mg/200 mg vs. 8 mg, 16 mg, 20 mg, 24 mg, 28 mg, 32 mg). We also note the availability of homeopathic L-Dopa liquid for the temporary relief of symptoms such as stiff muscles, tremors, weakness, and fatigue; however, due to the difference in dosage form (liquid vs capsule) and inconsistent strength of the L-Dopa liquid it is unlikely to pose a risk for name confusion with Absorica LD. Additionally, due to the weight-based dosing for the proposed product, it is unlikely for the abbreviation 'LD' to be misinterpreted as loading dose.

Furthermore, we note the 'LD' modifier has been used in the past for unapproved products (b) (4) [redacted] although none of these products are currently on the market and no generic equivalents are available[c]. A FAERS search performed on December 18, 2018 did not reveal any medication error cases related to the use of 'LD' (See Section 2.2.5). We also note 'LD' is not on ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations[d], is not a USAN Stem, and does not appear to present any overt safety concerns from a look-alike or sound-alike perspective.

We also considered whether the use of a modifier is appropriate to differentiate this product from the marketed product. It is not uncommon for modifiers to be used to denote a specific formulation or packaging configuration as part of a product line extension. The addition of a modifier to Absorica may help to differentiate the proposed product from the currently marketed capsules. However, we also note that omission and oversight of a modifier is cited in literature as a common cause of medication error[e]. Postmarketing experience shows that the introduction of product line extensions results in medication errors if the modifier is omitted and the product characteristics are similar or overlap. Both oral dosage forms are available in a 20 mg strength

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[b] https://www.medilexicon.com/abbreviations?search=LD&target=abbreviations, viewed December 18, 2018.

[c] https://www fda.gov/Drugs/ucm245106 htm, viewed December 19, 2018

[d] ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2017 [cited 2018 DEC 19]. Available from: https://www.ismp.org/sites/default/files/attachments/2017-11/Error%20Prone%20Abbreviations%202015.pdf.

[e] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

and we note there is a possibility of wrong dose errors if the modifier is omitted. If the intended dose was Absorica LD 20 mg, but the modifier was omitted, the patient might receive Absorica 20 mg instead, which is comparable to Absorica LD 16 mg. This would result in an underdose. While inadequate acne control is not a desirable clinical outcome, if this occurred the patient would most likely speak with their health care provider due to a lack of efficacy.

An alternative to using a modifier to distinguish this product from the currently marketed products is to use a totally different root name. However, marketing the new product under a unique proprietary name also carries a risk of medication errors, such as therapeutic duplication and overdoses. These errors may have greater associated safety risks than the omission or oversight of the modifier as discussed above. Therefore, for the aforementioned reasons, DMEPA finds that the proprietary name 'Absorica LD', although not free from the risk of error, is acceptable at this time.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Dermatology and Dental Products (DDDP) via e-mail on January 3, 2019. At that time we also requested additional information or concerns that could inform our review. DDDP did not state additional concerns with the proposed proprietary name, Absorica LD.

3 CONCLUSION

The proposed proprietary name, Absorica LD, is acceptable.

If you have any questions or need clarifications, please contact Tri Bui-Nguyen, OSE project manager, at 240-402-3726.

3.1 COMMENTS TO SUN PHARMACEUTICAL INDUSTRIES LIMITED

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

If any of the proposed product characteristics as stated in your submission, received on October 29, 2018, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

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 DNDP. OPDP or DNDP 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 DNDP 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. [f]

[f] 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 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 55% 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 ≥55% to ≤ 69%.

- Low similarity: combined match percentage score ≤54%.

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 are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[g]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information 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) may be limited when the strength or dose overlaps. DMEPA reviews 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

[g] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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 does 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 ≥55% 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: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
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 ≤54%).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix A1: Description of FAERS

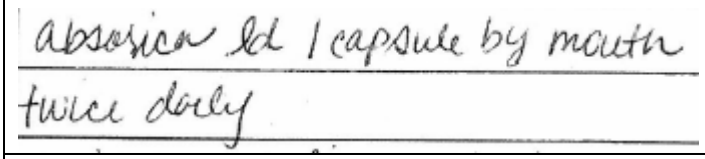
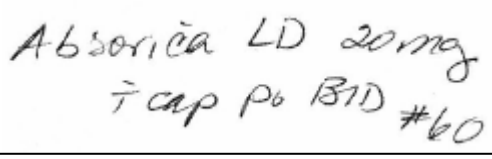
The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at:

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

APPEARS THIS WAY ON ORIGINAL

Appendix B: Prescription Simulation Samples and Results

Figure 1. Absorica LD Study (Conducted on November 21, 2018)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Absorica LD 20 mg Take 1 capsule by mouth twice daily. Dispense # 60
Outpatient Prescription:  	

FDA Prescription Simulation Responses (Aggregate Report)

252 People Received Study
67 People Responded

Study Name: Absorica LD

Total	27	16	24	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
ABSARICA LD	0	0	1	1
ABSOBICA LD	0	0	1	1
ABSORBAQI LD	0	1	0	1
ABSORIA LD	1	0	0	1
ABSORICA	1	0	3	4
ABSORICA ED	0	0	1	1
ABSORICA ID	0	0	2	2
ABSORICA LD	24	9	13	46
ABSORICA LD 20MG	1	0	0	1
ABSORICQA LD	0	1	0	1
ABSORICU LD	0	0	1	1

ABSORIKA LD	0	2	0	2
ABSORKA LD	0	3	0	3
ABSOSICA LD	0	0	2	2

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/s/

MADHURI R PATEL
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