

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761059Orig1s000

PROPRIETARY NAME REVIEW(S)

**MEMORANDUM
NONPROPRIETARY NAME SUFFIX**

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

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

Date of This Review:	April 11, 2019
Responsible OND Division:	Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
Application Type and Number:	BLA 761059
Product Name and Strength:	Hadlima (adalimumab-bwwd) Injection, 40 mg/0.8 mL
Product Type:	Combination Product (Drug-Biologic)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd. (Samsung)
FDA Received Date:	July 23, 2018
OSE RCM #:	2016-1977
DMEPA Primary Reviewer:	Carlos M Mena-Grillasca, BS Pharm
DMEPA Deputy Director:	Danielle Harris, PharmD, BCPS

1 PURPOSE OF MEMO

This memorandum summarizes our evaluation of the four-letter suffixes proposed by Samsung for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761059.

2 ASSESSMENT OF THE NONPROPRIETARY NAME

On July 23, 2018, Samsung submitted a list of three suffixes, in their order of preference, to be used in the nonproprietary name of their product^a. Table 1 presents a list of suffixes submitted by Samsung:

1.	(b) (4)
2.	bwwd
3.	(b) (4)

We reviewed Samsung's proposed suffixes in order of preference listed by Samsung, along with the supporting data they submitted, using the principles described in the applicable guidance.^b

2.1 (b) (4)

[Redacted content]

2.2 adalimumab-bwwd

Samsung's second proposed suffix, -bwwd, is composed of three distinct letters (b, w, d).

We determined that the proposed suffix -bwwd, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA'S ANALYSIS

These findings were shared with OPDP, TBBS, ORP, and OCC. In email correspondence dated April 11, 2019, the workgroup concurred with DMEPA's assessment and conclusion. DMEPA also communicated our findings to the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) via e-mail on April 11, 2019.

^a Suffix Name Request (BLA 761059). Incheon (Republic of Korea): Samsung Bioepis Co., Ltd.; 2018 Jul 23. Available from: <\\cdsesub1\evsprod\bla761059\0012\m1\us\suffix-name-request.pdf>

^b See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf>

4 CONCLUSION

We find Samsung's proposed suffix -bwwd acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to adalimumab-bwwd. DMEPA will communicate our findings to the Applicant via letter.

4.1 Recommendations for Samsung Bioepis Co., Ltd.

We find the nonproprietary name, adalimumab-bwwd, conditionally acceptable for your proposed product. Should your 351(k) BLA be approved during this review cycle, adalimumab-bwwd will be the proper name designated in the license. You should revise your proposed labels and labeling accordingly and submit the revised labels and labeling to your BLA for our review. However, please be advised that if your application receives a complete response, the acceptability of your proposed suffix will be re-evaluated when you respond to the deficiencies. If we find your suffix unacceptable upon our re-evaluation, we would inform you of our finding.

We also note that the first proposed suffix is unacceptable for the following reasons:

1. (b) (4)

[Redacted]

[Redacted]

[Redacted]

[Redacted]

^a See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf>

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CARLOS M MENA-GRILLASCA
04/11/2019 02:58:38 PM

DANIELLE M HARRIS
04/12/2019 08:04:21 AM

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:	November 1, 2018
Application Type and Number:	BLA 761059
Product Name and Strength:	Hadlima (adalimumab-xxxx) ^a Injection, 40 mg/0.8 mL Pre-filled Syringe Hadlima PushTouch (adalimumab-xxxx) ^a Injection, 40 mg/0.8 mL Autoinjector
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd. (Samsung)
Panorama #:	2018-25117362 2018-25169630
DMEPA Safety Evaluator:	Carlos M Mena-Grillasca, BS Pharm
DMEPA Team Leader:	Sarah K. Vee, PharmD
DMEPA Associate Director:	Mishale Mistry, PharmD, MPH

^a BLA 761059 has been developed as a proposed biosimilar to US-licensed Humira (adalimumab). Since the nonproprietary name for BLA 761059 has not been determined, the nonproprietary name placeholder (adalimumab-xxxx) is used throughout this review.

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1 INTRODUCTION

This review evaluates the proposed proprietary names, Hadlima and Hadlima PushTouch, 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. Samsung did not submit an external name study for this proposed proprietary name.

1.1 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 29, 2018.

- Intended Pronunciation: HAD lee mah
HAD lee mah Poosh tuch
- Active Ingredient: adalimumab-xxxx^b
- Indication of Use: Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Adult Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis.
- Route of Administration: Subcutaneous
- Dosage Form: Injection
- Strength: 40 mg/0.8 mL
- Dose and Frequency:
 - Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis:**
 - 40 mg every other week.
 - Some patients with RA not receiving methotrexate may benefit from increasing the frequency to 40 mg every week.
 - Juvenile Idiopathic Arthritis:**
 - *≥ 30 kg (66 lbs) and from 4 to 17 years of age:* 40 mg every other week
 - Adult Crohn's Disease and Ulcerative Colitis:**
 - Initial dose (Day 1): 160 mg
 - Second dose two weeks later (Day 15): 80 mg
 - Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week.
 - For patients with Ulcerative Colitis only:
Only continue Hadlima in patients who have shown evidence of clinical remission by eight weeks (Day 57) of therapy.
 - Plaque Psoriasis:**
 - 80 mg initial dose, followed by 40 mg every other week starting one week after initial dose.
- How Supplied: 40 mg/0.8 mL Pre-Filled Syringe pack of 2.
40 mg/0.8 mL PushTouch Autoinjector pack of 2.
- Storage: Refrigerated at 36°F to 46°F (2°C to 8°C)
- Reference Listed Drug/Reference Product: BLA 125057 US-licensed Humira

^b BLA 761059 has been developed as a proposed biosimilar to US-licensed Humira (adalimumab). Since the nonproprietary name for BLA 761059 has not been determined, the nonproprietary name placeholder (adalimumab-xxxx) is used throughout this review.

APPEARS THIS WAY ON ORIGINAL

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary names, Hadlima and Hadlima PushTouch.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Hadlima and Hadlima PushTouch would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) concurred with the findings of OPDP's assessment for Hadlima and Hadlima PushTouch.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Hadlima and Hadlima PushTouch.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary names Hadlima and Hadlima PushTouch^c.

2.2.2 Components of the Proposed Proprietary Name

Samsung did not provide a derivation or intended meaning for the proposed proprietary names, Hadlima and Hadlima PushTouch, in their submission. The proposed proprietary name, Hadlima, is comprised of a single word. We note that the proposed name Hadlima and root name of Hadlima PushTouch contain the letters 'ad' and 'im', which are the abbreviations for 'right ear' and the intramuscular route of administration, respectively. Additionally, we note that the modifier 'PushTouch' contains the letter string 'ou', which is an abbreviation for 'each/both eyes'. Although we typically discourage the inclusion of medical abbreviations in proprietary names, we determined that the location of the letter strings positioned in the middle of the name is unlikely to be separated from the surrounding letters in a manner that could lead to confusion in this case.

The proposed name Hadlima PushTouch is comprised of the root name, Hadlima, and modifier, PushTouch. The proposed modifier, PushTouch, refers to the name of the autoinjector device. We note that the naming convention of adding a modifier to represent a specific device has been used before to differentiate various presentations within a product line (in this case, to differentiate the autoinjector presentation from the prefilled syringe).

We note that omission and oversight of a modifier is cited in literature as a common cause of medication error^d. If the modifier 'PushTouch' is omitted (as seen in the FDA Name Simulation Study), the pharmacist may call the prescriber to seek clarification, or the patient may receive the prefilled syringe presentation. However, since the 40 mg/0.8 mL strength is available in both the prefilled

^c USAN stem search conducted on October 9, 2018.

^d Lesar TS. Prescribing Errors Involving Medication Dosage Forms. J Gen Intern Med. 2002; 17(8): 579-587.

syringe and autoinjector presentations, the patient would still receive the correct product and dose. Furthermore, as with any product that is available in multiple packaging presentations, the prescriber would need to indicate the intended product on the prescription. We note that the 'PushTouch' device is not available on its own and we do not anticipate that the modifier 'PushTouch' will be written on their own without the root name.

In summary, we acknowledge that the use of the proposed modifier, 'PushTouch', is consistent with the naming strategy used for other products and provides a safe means to differentiate the autoinjector from the prefilled syringe presentation. Therefore, we find the use of the modifier 'PushTouch' acceptable.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, August 30, 2018 e-mail, the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) did not forward any comments or concerns relating to Hadlima and Hadlima PushTouch at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Hadlima

Sixty-seven (n=67) practitioners participated in DMEPA's prescription studies for Hadlima. 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.

Hadlima PushTouch

Sixty-five (n=65) practitioners participated in DMEPA's prescription studies for Hadlima PushTouch. 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 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search^e identified 66 names with a combined phonetic and orthographic score of $\geq 55\%$ or an individual phonetic or orthographic score $\geq 70\%$. These names are included in Table 1 below.

^e POCA search conducted on October 9, 2018 in version 4.3.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Similarity Category	Number of Names
Highly similar name pair: combined match percentage score $\geq 70\%$	2
Moderately similar name pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$	64
Low similarity name pair: combined match percentage score $\leq 54\%$	0

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

Our analysis of the 66 names contained in Table 1 determined none of the names will pose a risk for confusion with Hadlima 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 Pulmonary, Allergy, and Rheumatology Products (DPARP) via e-mail on October 30, 2018. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) on November 1, 2018, they stated no additional concerns with the proposed proprietary names, Hadlima and Hadlima PushTouch.

3 CONCLUSION

The proposed proprietary names, Hadlima and Hadlima PushTouch, are acceptable.

If you have any questions or need clarifications, please contact Saharat Patanavanich, OSE project manager, at 240-402-0139.

3.1 COMMENTS TO SAMSUNG BIOEPIS CO., LTD.

We have completed our review of the proposed proprietary names, Hadlima and Hadlima PushTouch, and have concluded that these name are acceptable.

If any of the proposed product characteristics as stated in your submission, received on August 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. 6F^f

*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.

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

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 $\geq 70\%$.
 - Moderately similar pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$.
 - Low similarity: combined match percentage score $\leq 54\%$.

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 names⁹. 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 a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

⁹ Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

- 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.			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
Y/N	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? <i>* FDA considers the length of names different if the names differ by two or more letters.</i>	Y/N	Do the names have different syllabic stresses?

Y/N	Considering variations in scripting of some letters (such as z and ž), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

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

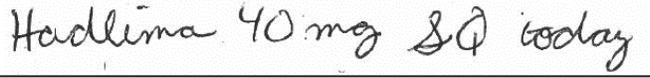
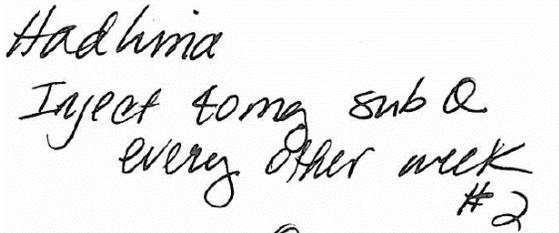
	<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* 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 <i>z</i> and <i>x</i>), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted? 	<p>Phonetic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?
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Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤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 B: Prescription Simulation Samples and Results

Figure 1. Hadlima Study (Conducted on September 9, 2018September 9, 2018)

Handwritten Medication Order/Prescription	Verbal Prescription
<p>Medication Order:</p> 	<p>Hadlima</p> <p>Inject 40 mg subcutaneously every other week.</p> <p>Dispense #2</p>
<p>Outpatient Prescription:</p> 	

FDA Prescription Simulation Responses (Aggregate Report)

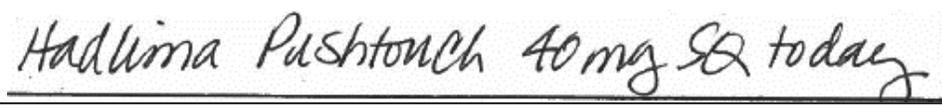
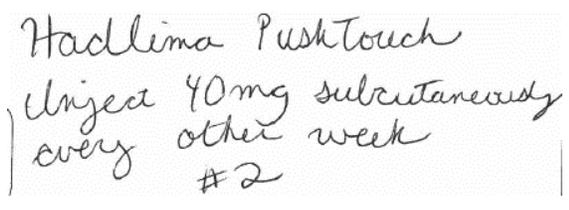
As of Date 10/9/2018

307 People Received Study
67 People Responded

Study Name: Hadlima

Total	19	13	15	20	
INTERPRETATION	OUTPATIENT	CPOE	VOICE	INPATIENT	TOTAL
ADLEEMA	0	0	1	0	1
ADLEMA	0	0	1	0	1
ADLIMA	0	0	9	0	9
HADHIMA	6	0	0	0	6
HADHINA	4	0	0	0	4
HADHMA	1	0	0	0	1
HADHMIA	2	0	0	0	2
HADHVIA	1	0	0	0	1
HADLEEMA	0	0	1	0	1
HADLEMA	0	0	1	0	1
HADLIMA	4	13	1	20	38
HADLUNIA	1	0	0	0	1
HEDLIMA	0	0	1	0	1

Figure 2. Hadlima PushTouch Study (Conducted on September 4, 2018)

Handwritten Medication Order/Prescription	Verbal Prescription
<p>Medication Order: `</p> 	<p>Hadlima PushTouch</p> <p>Inject 40 mg subcutaneously every other week.</p> <p>Dispense #2</p>
<p>Outpatient Prescription:</p> 	

FDA Prescription Simulation Responses (Aggregate Report)

As of Date 10/9/2018

306 People Received Study
65 People Responded

Study Name: Hadlima PushTouch

Total	19	17	11	18	
INTERPRETATION	OUTPATIENT	CPOE	VOICE	INPATIENT	TOTAL
HADHMA PUSHTOUCH	0	0	0	1	1
HADLEMA PUSH TOUCH	0	0	2	0	2
HADLIM	0	1	0	0	1
HADLIMA	2	0	1	0	3
HADLIMA PUSH TOUCH	4	0	3	0	7
HADLIMA PUSHTOUCH	13	16	1	16	46
HADLIMA PUSHTOUCH SQ	0	0	0	1	1
HADLIMI PUSH TOUCH	0	0	1	0	1
HATLIMA PUSH-TOUCH	0	0	1	0	1
HEADLIMA PUSH TOUCH	0	0	2	0	2

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

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	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.	Hadlima	100	Root name is the subject of this review.
2.	Hadlima PushTouch	100	Name is the subject of this review.

Appendix D: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with no overlap or numerical similarity in Strength and/or Dose

N/A

Appendix E: Moderately Similar Names (e.g., combined POCA score is $\geq 55\%$ to $\leq 69\%$) with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	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
3.	Hemlibra	66	<p>The prefixes ('Had' vs. 'Hem') and suffixes ('ma' vs. 'bra') of this name pair have sufficient orthographic differences.</p> <p>The first syllables ('Had' vs. 'Hem') and last syllables ('ma' vs. 'bra') provide some phonetic differences.</p> <p>In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors:</p> <p>Strength: Hadlima/Hadlima PushTouch is available in a strength of 40 mg/0.8 mL vs. Hemlibra which is available in strengths of 30 mg/mL, 60 mg/0.4 mL, 105 mg/0.7 mL and 150 mg/mL. There is no overlap in strength.</p>

^h BLA 761059 has been developed as a proposed biosimilar to US-licensed Humira (adalimumab). Since the nonproprietary name for BLA 761059 has not been determined, the nonproprietary name placeholder (adalimumab-xxxx) is used throughout this review.

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	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
4.	Alimta	62	<p>The additional letter 'H' at the beginning of the name Hadlima and the additional upstroke letter 't' at the end of the name Alimta provide sufficient orthographic differences.</p> <p>The ending of the first syllable ('d') in Hadlima and the beginning of the last syllables ('ma' vs. 'ta') provide some phonetic differences.</p> <p>In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors:</p> <ul style="list-style-type: none"> • The dose of Alimta is based on patients' body surface area (500 mg/m²), requiring assessment of creatinine clearance and blood count, and the frequency is Day 1 of each 21-day cycle whereas the usual dose/frequency of Hadlima/Hadlima PushTouch is 40 mg weekly or 40 mg every other week. Furthermore, Hadlima/Hadlima PushTouch would be prescribed "Inject xx mg or as directed" whereas Alimta would require a rate for intravenous infusion; these instructions help mitigate the probability of error. • Hadlima/Hadlima PushTouch is an injection available in pre-filled syringe and autoinjector presentations whereas Alimta is available as a lyophilized powder for reconstitution. Therefore, the former is ready to be administered at the prescriber's office or self-administered by a patient or caregiver versus Alimta which requires additional reconstitution and dilution instructions. These instructions help mitigate the risk the probability of error. •

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	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
5.	Halenol Note: Discontinued acetaminophen liquid 160 mg/mL with branded and generic equivalents available.	60	Hadlima contains an additional up stroke letter 'd' in its prefix and Halenol contains an additional up stroke letter 'l' at the end of the name, which provides some orthographic differences between the names. The last syllables ('ma' vs. 'nol') provide some phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: <ul style="list-style-type: none"> • Frequency: Hadlima is administered once weekly or every other week whereas Halenol is administered every 4, 6, 8 or 12 hours as needed. There is no overlap in frequency of administration.
6.	Histamine Phosphate	59	This name pair have sufficient orthographic and phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: <ul style="list-style-type: none"> • Dose: Hadlima (PushTouch) is dosed at 40 mg, 80 mg, or 160 mg whereas Histamine Phosphate is dosed at 0.01 mL or 0.02 mL or 1 drop. Therefore, there is no overlap in dose. • Frequency: Hadlima (PushTouch) is administered once weekly or every other week whereas Histamine Phosphate is used once during the allergy skin testing evaluation. There is no overlap in frequency of administration.
7.	Hexadrol Phosphate Note: Discontinued dexamethasone sodium phosphate product with generic equivalents available.	58	This name pair have sufficient orthographic and phonetic differences.
8.	Adalimumab	57	This name pair have sufficient orthographic and phonetic differences.

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	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
9.	Haldol	56	<p>The suffixes ('ima' vs. 'ol') provides some orthographic differences between this name pair. Hadlima contains an extra syllable, which provides phonetic differentiation between this name pair. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors:</p> <ul style="list-style-type: none"> • Dose: Hadlima (PushTouch) is dosed at 40 mg, 80 mg, or 160 mg whereas Haldol is dosed between 2 mg to 5 mg. Therefore, there is no overlap in dose. • Frequency: Hadlima (PushTouch) is administered once weekly or every other week whereas Haldol is administered every hour or every 4 to 8 hours. There is no overlap in frequency of administration.
10.	Fiasp FlexTouch	56	<p>The root names Hadlima and Fiasp have sufficient orthographic and phonetic differences. The modifier prefixes 'Push' versus 'Flex' within the modifiers PushTouch and FlexTouch have sufficient orthographic differences. Furthermore, the modifiers PushTouch and FlexTouch are unlikely to be written on a prescription without the root name. The modifier FlexTouch is used with multiple products (i.e. Levemir FlexTouch, Tresiba FlexTouch, Fiasp FlexTouch, and NovoLog FlexTouch). Therefore, a root name must always accompany the modifier FlexTouch to dispense a prescription. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors:</p> <ul style="list-style-type: none"> • Frequency: Hadlima (PushTouch) is administered once weekly or every other week whereas Fiasp FlexTouch is administered at the start of a meal or within 20 minutes after starting a meal. There is no overlap in frequency of administration.

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	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
11.	Halotussin DAC Note: Discontinued codeine/guaifenesin/pseudoephedrine product with branded and generic equivalents available.	56	This name pair have sufficient orthographic and phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: <ul style="list-style-type: none"> • Frequency: Hadlima is administered once weekly or every other week whereas Halotussin DAC is administered every 4-6 hours. There is no overlap in frequency of administration.
12.	Hydramine Compound Note: Discontinued diphenhydramine product with branded and generic equivalents available.	56	This name pair have sufficient orthographic and phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: <ul style="list-style-type: none"> • Frequency: Hadlima is administered once weekly or every other week whereas diphenhydramine is administered every 6 hours. There is no overlap in frequency of administration.
13.	Haltran Note: Discontinued ibuprofen product with branded and generic equivalents available.	56	This name pair have sufficient orthographic and phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: <ul style="list-style-type: none"> • Frequency: Hadlima is administered once weekly or every other week whereas Haltran is administered every 4-6 hours. There is no overlap in frequency of administration.

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	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
14.	Humulin	56	<p>This name pair have sufficient orthographic and phonetic differences.</p> <p>In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors:</p> <ul style="list-style-type: none"> • Strength: Hadlima is a single strength product available as 40 mg/0.8 mL whereas Humulin is available as Humulin R U-100, Humulin N, Humulin 70/30, Humulin R U-500. There is no overlap between product strengths available. • Frequency: Hadlima is administered once weekly or every other week whereas Humulin is administered 30-45 minutes before meals. There is no overlap in frequency of administration.
15.	Falmina	56	<p>Hadlima and Falmina begin with different letters and Hadlima contains an additional up stroke letter 'd' in its prefix, which provides some orthographic differentiation from Falmina.</p> <p>The first syllables ('Had' vs. 'Fal') provide some phonetic differences.</p> <p>In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors:</p> <ul style="list-style-type: none"> • • Frequency: Hadlima is administered once weekly or every other week whereas Falmina is administered once daily. There is no overlap in frequency of administration.

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
16.	Calcimar Note: Discontinued calcitonin salmon product with a branded equivalent available.	55	Hadlima and Calcimar begin with different letters and Hadlima contains an additional up stroke letter 'd' in its prefix, which provides some orthographic differentiation from Calcimar. The first syllables ('Had' vs. 'Cal') provide some phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: <ul style="list-style-type: none"> • Frequency: Hadlima is administered once weekly or every other week whereas Calcimar is administered every 6 hours, every 12, or once daily. There is no overlap in frequency of administration.
17.	Halotussin AC Note: Discontinued codeine/guaifenesin product with branded and generic equivalents available.	55	This name pair have sufficient orthographic and phonetic differences. In addition to the above orthographic and phonetic differences, the following differences in product characteristics may also help to mitigate the risk of errors: <ul style="list-style-type: none"> • Frequency: Hadlima is administered once weekly or every other week whereas Halotussin AC is administered every 4-6 hours. There is no overlap in frequency of administration.
18.	Lenvima	55	Hadlima contains two up strokes letter 'dl' in its prefix, which provides some orthographic differentiation from Falmina. The first syllables ('Had' vs. 'Len') provide some phonetic differences. In addition to the above orthographic differences, the following differences in product characteristics may also help to mitigate the risk of errors: <ul style="list-style-type: none"> • Dose: Hadlima is dosed at 40 mg, 80 mg, or 160 mg whereas Lenvima is dosed at 14 mg or 24 mg. There is no overlap in frequency of administration. • Frequency: Hadlima is administered once weekly or every other week whereas Lenvima is administered once daily. There is no overlap in frequency of administration.
19.	Herzuma ^{***}	55	This name pair has sufficient orthographic and phonetic differences.

No.	Proposed name: Hadlima and Hadlima PushTouch Established name: adalimumab-xxxx ^h Dosage form: Injection Strength(s): 40 mg/0.8 mL Usual Dose: 40 mg, 80 mg or 160 mg, followed by either 40 mg weekly or 40 mg every other week.	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
20.	PushTouch ^{***}	52	Modifier subject of this review.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%)

N/A

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
21.	Hedulin	66	Discontinued phenindione product with no generic equivalents available.
22.	Calimal	64	International chlorpheniramine maleate product distributed in the UK.
23.	(b) (4) ^{***}	64	Proposed name for IND (b) (4) found unacceptable by DMEPA (b) (4).
24.	Helidac	64	Discontinued bismuth salicylate/metronidazole/tetracycline hydrochloride product with no generic equivalents available.
25.	Hexametaphosphate	61	Not a drug. Sodium Hexametaphosphate is an emulsifier used as a food additive.
26.	Hamarin	60	Discontinued international allopurinol product formerly marketed in the UK.
27.	(b) (4) ^{***}	58	Proposed name for IND (b) (4) found unacceptable by DMEPA (b) (4)
28.	Helium	58	Not a drug, but a medical gas.
29.	Hand-Kleen	58	Not a drug, but an over-the-counter antiseptic hand wash.
30.	(b) (4) ^{***}	57	Proposed name for IND (b) (4) found unacceptable by DMEPA on June 1, 2016 (Panorama # 2015-2318722). The proposed name Hyrimoz ^{***} for BLA 761071 was found conditionally acceptable by DMEPA on January 4, 2018 (Panorama # 2017-18755325).
31.	Highland DM	56	Discontinued brompheniramine/dextromethorphan/phenylpropanolamine product with no generic equivalents available.

No.	Name	POCA Score (%)	Failure preventions
32.	Avima	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
33.	Monarch Soft touch	56	Not a drug. This is a veterinary iodine product use as a sanitizing teat spray.
34.	Haelan	56	Not a drug. This is an over-the-counter fermented soy beverage.
35.	Halfan	56	Discontinued halofantrine hydrochloride product with no generic equivalents available.
36.	Halometasone	56	International product marketed in China, Germany, Switzerland, and Turkey.
37.	Dlin-Mc3-Dma	52	Not a drug. This is a cationic lipid that has been synthesized for lipid nanoparticles.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion^{8F}.

No.	Name	POCA Score (%)
38.	Calcium Phosphate	62
39.	Dicalcium Phosphate	60
40.	Sodium Phosphate	60
41.	Cadalira***	58
42.	Tricalcium Phosphate	58
43.	Aluminum Phosphate	58
44.	Sodium Phosphate P 32	58
45.	Sodium Phosphate P32	58
46.	(b) (4)***	58
47.	Calcium Hypophosphite	57
48.	Calcium Aspartate	57
49.	Cablivi***	57
50.	Thallium	56
51.	Salonsip Aqua-Patch	56
52.	Potassium Phosphate	56
53.	(b) (4)***	56
54.	Gadolinium Cation (3+)	56
55.	Theraflu Vapor Stick	56
56.	Sodium Hypophosphite	56
57.	Polymetaphosphate	56
58.	Gadolinium Oxide	56
59.	Calcium Pyrophosphate	55

ⁱ Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

No.	Name	POCA Score (%)
60.	(b) (4) ***	55
61.	(b) (4) ***	55
62.	Thalomid	54
63.	Calm-Aid	53
64.	Dicalphos Plus D	52
65.	Calcium Phosphate Dibasic	50
66.	Amibid La	48

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/s/

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11/01/2018

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