CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

209844Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

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

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Date of This Review:	April 17, 2018
Application Type and Number:	NDA 209844
Product Name and Strength:	LymePak (doxycycline hyclate) 100 mg tablet
Product Type:	Single ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Chartwell Pharmaceuticals LLC
Panorama #:	2017- 19224001
DMEPA Safety Evaluator:	Sevan Kolejian, Pharm. D, MBA
DMEPA Team Leader:	Otto L. Townsend, Pharm D
Deputy Director	Irene Z. Chan, PharmD, BCPS

Contents

1 INTRODUCTION

This review responds to a March 14, 2018 request from Chartwell Pharmaceuticals LLC (Chartwell) to reconsider the previous determination that the proposed proprietary name, LymePak (NDA 209844) was unacceptable because it would misbrand the proposed product. This review also includes our evaluation of the proposed proprietary name, LymePak, from a safety perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. Chartwell submitted an external name study, conducted by (b) (4) for this product.

1.1 REGULATORY HISTORY

The Applicant previously submitted the proposed proprietary name, LymePak, under IND 125184 twice, but subsequently withdrew the name both times. For more details on the regulatory history related to the IND submissions, see DMEPA's previous review.[a] The Applicant submitted the proposed proprietary name, LymePak on November 20, 2017 to NDA 209844. However, we found the name, LymePak unacceptable as it would misbrand the proposed product on February 18, 2018.[a] As stated above, the Applicant has submitted a request for reconsideration of the proposed proprietary name LymePak.

1.2 PRODUCT INFORMATION

The following product information is provided in the November 20, 2017 proprietary name submission.

- Intended Pronunciation: lime' pak
- Active Ingredient: doxycycline hyclate
- Indication of Use: Treatment of early Lyme disease (as evidenced by erythema migrans) due to *Borellia burgdorferi*
- Route of Administration: oral
- Dosage Form: tablet
- Strength: 100 mg
- Dose and Frequency:
  - (b) (4)
  -

[a] Kolejian, S. Proprietary Name Review for LymePak NDA 209844. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); February 18, 2018. Panorama No. 2017- 19224001.

(b) (4)

- **How Supplied:**

  NDC # 62135-596-01: is supplied as a child-resistant blister card containing 14 tablets

(b) (4)

- **Storage:** Store at 20°C to 25°C (68°F to 77°F) excursions permitted to 15° to 30°C (59° to 86°F)
- **Reference Listed Drug:** (b) (4)

(b) (4)

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

In response to Chartwell's March 14, 2018 request for reconsideration, we requested that the Office of Prescription Drug Promotion (OPDP) reassess the proposed proprietary name, LymePak. On March 28, 2018, DMEPA, OPDP, and the Division of Anti-Infective Products (DAIP) met to discuss the Applicant's request for reconsideration considering the additional information provided by Chartwell. It was determined that the proposed proprietary name LymePak would not misbrand the proposed product.

In a subsequent email communication dated, March 29, 2018, OPDP stated:

"*In response to Chartwell Pharma NDA B2 Holdings, LLC's March 14, 2018 request for reconsideration, OPDP has re-evaluated the proposed tradename "LymePak." OPDP withdraws its objection to the trade name "LymePak" and has no additional comments".*

Both DMEPA and DAIP concurred with OPDP's determination.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

[b] USAN stem search conducted on March 28, 2018

2.2.2 Components of the Proposed Proprietary Name

Chartwell indicated in their submission that the derivation of the proposed name, LymePak, is Lyme disease pak and connotes the color lime green. This proprietary name is comprised of the word, "Lyme" that describes the indication for use and "pak" to describe the packaging configuration. The term "pak" has been commonly used as drug name suffix to convey a blister packaging configuration and is listed on the Institute for Safe Medication Practices' (ISMP) list of Products with Drug Name Suffixes[c]. According to ISMP, "'pak' indicates the medication is available in a dose card package". Thus, we found both components of the proposed proprietary name appropriate for the proposed product.

2.2.3 FDA Name Simulation Studies

Ninety four (94) practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline.

2.2.4 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[d] identified thirty three (33) names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70**.** These names are included in Table 1 below.

2.2.5 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search, and the (b) (4) external study. 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 ≥70%	None
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	34
Low similarity name pair: combined match percentage score ≤54%	4

[c] ISMP's list of Products with Drug Name Suffixes. Available online at https://www.ismp.org/tools/drugnamesuffixes.pdf

[d] POCA search conducted on March 28, 2018 in version 4.2.

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

Our analysis of the thirty eight (38) names contained in Table 1 determined none of the names will pose a risk for confusion as described in Appendices C through H.

2.2.1 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings, OPDP's assessment and DMEPA's safety assessment, to the Division of Division of Anti-Infective Products (DAIP) via e-mail on April 10, 2018. At that time we also requested additional information or concerns that could inform our review. DAIP did not provide any new concerns with the proposed proprietary name, LymePak.

3 CONCLUSION

The proposed proprietary name is acceptable from both a safety and misbranding perspective. See section 3.1 for comments to be conveyed to the Applicant.

If you have any questions or need clarifications, please contact Ameet Joshi, OSE Project Manager, at 301-796-6345.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, LymePak, and your request for reconsideration. Based on the information you submitted, we have concluded that the proposed proprietary name, LymePak is acceptable for your product.

If any of the proposed product characteristics as stated in your November 20, 2017 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

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

   USAN Stems List contains all the recognized USAN stems.

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

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

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

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

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

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

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

3. ***Electronic Drug Registration and Listing System (eDRLS) database***

The electronic Drug Registration and Listing System (eDRLS) was established to supports the FDA's Center for Drug Evaluation and Research (CDER) goal to establish a common Structured Product Labeling (SPL) repository for all facilities that manufacture regulated drugs. The system is a reliable, up-to-date inventory of FDA-regulated, drugs and establishments that produce drugs and their associated information.

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. [e]

[e] 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[f]. 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.

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[f] 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.			
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.

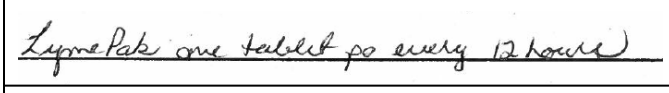
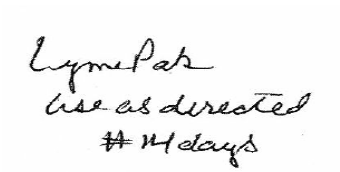
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length 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 B: Prescription Simulation Samples and Results

Figure 1. :LymePak Study (Conducted on December 8, 2017)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	LymePak Use as directed
Outpatient Prescription:  	Dispense 14 day supply.

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: LymePak

294 People Received Study/94 People Responded

Total	**29**	**26**	**39**	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
LIME PACK	0	2	0	2
LIME PAK	0	2	0	2
LIMEPACK	0	1	0	1
LIMEPAK	0	2	1	3
LIMETAC	0	1	0	1
LINEPAC	0	2	0	2
LINEPACK	0	2	0	2
LINEPAK	0	1	0	1
LYME PAC	0	1	0	1
LYME PACK	0	5	0	5
LYME PAK	3	0	9	12
LYMEPACK	0	1	0	1
LYMEPAK	23	4	25	52
LYME-PAK	0	1	0	1
LYMEPAS	1	0	0	1
LYMPAS	1	0	0	1
LYNE PAK	0	0	1	1
LYNEPAK	0	0	1	1
LYNNEPAK	0	0	1	1
LYONE PAK	0	0	1	1
WYNPACK	0	1	0	1
ZYMEPAR	1	0	0	1

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

No.	**Proposed name:** LymePak **Established name:** doxycycline **Dosage form:** Tablet **Strength(s):** 100 mg **Usual Dose:** 100 mg twice daily (b) (4) (for (b) (4) 21 days)	**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.	LymePak	100	*Subject of this review*
2.	Zema-Pak	74	The prefixes of this name pair have sufficient orthographic differences. The first and second syllables of this name pair sound different. Zema-Pak has extra syllables. Name identified in external study (b) (4) Zema-Pak brand of dexamethasone tablets is no longer marketed under the ANDA. Currently marketed dexamethasone tablets are not available in a "Pak" configuration, but are available in institutional unit-dose and bottle configurations.

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

No.	Name	POCA Score (%)
3.	Lymerix	66
4.	Sele-Pak	65
5.	Multe-Pak-4	64
6.	Multe-Pak-5	64
7.	(b) (4)	62
8.	Ribapak	62
9.	Levacet	55
10.	Pedte-Pak-4	55

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

No.	**Proposed name:** LymePak **Established name:** doxycycline **Dosage form:** Tablet **Strength(s):** 100 mg **Usual Dose:** 100 mg twice daily (b) (4) (for (b) (4) or 21 days)	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.	Clenpiq***	56	This name pair has sufficient orthographic and phonetic differences.
12.	Lysimax	56	This name pair has sufficient orthographic and phonetic differences.
13.	Zenapax	55	This name pair has sufficient orthographic and phonetic differences.

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

No.	Name	POCA Score (%)
14.	Zpak	46
15.	Lovenox	39
16.	Alvimopan	50
17.	Trymex	50

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
18.	Amipak	66	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
19.	Lok-Pak	61	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
20.	Sensipak	57	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
21.	Lok-Pak-N	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
22.	(b) (4)	56	This is a secondary proposed proprietary name for NDA 203696 and NDA 203696 was approved under proprietary name Lupaneta Pak.
23.	Zymecot	56	International product marketed in Philippines.
24.	Lumen C	55	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases
25.	Dynabac	52	Brand discontinued with no generic equivalents available. NDA 050678 withdrawn FR effective 12/07/2007.
26.	Renitec	46	This an international product marketed in Argentina, Australia, Austra, Brazil, Belgium, China, Greece, Ukraine, Spain, Sweden, Singapoor, Russia, South Africa, Hungary, Malaysia, Mexico, Finland, France, Phillippines, Portugal, Norway, Nethelands, Venezuela and Malaysia.
27.	Rinatec	48	This an international product marketed in Ireland and the UK.
28.	Zinotic	35	Chloroxylenol containing product withdrawn from the market for safety reasons, FR Notice 7/2/2015.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[g].

No.	Name	POCA Score (%)
29.	Dimetapp	60
30.	Plemex	58
31.	Phenytek	57
32.	Phenapap	56
33.	Phlemex	56
34.	Rimapam	56
35.	Symdeko	56
36.	Vimpat	56
37.	Ela-Max	55
38.	Ela-Max 5	55

[g] 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

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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
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***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	February 16, 2018
Application Type and Number:	NDA 209844
Product Name and Strength:	LymePak (doxycycline hyclate) 100 mg tablet
Product Type:	Single ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Chartwell Pharmaceuticals LLC
Panorama #:	2017- 19224001
DMEPA Safety Evaluator:	Sevan Kolejian, Pharm. D, MBA
DMEPA Team Leader:	Otto L. Townsend, Pharm D
DMEPA Director:	Todd Bridges, RPh

1 INTRODUCTION

This review evaluates the proposed proprietary name LymePak for NDA 209844, from a safety and misbranding perspective. The Applicant submitted an external name study, conducted by (b) (4) for this proposed proprietary name.

1.1 REGULATORY HISTORY

Chartwell Pharmaceuticals LLC previously submitted the proposed proprietary name, LymePak, on May 20, 2016 under IND 125184. In that submission, Chartwell Pharmaceuticals LLC intended to seek approval for all currently approved infectious disease indications for doxycycline in addition to the proposed indication of Lyme disease. In response to the OSE June 9, 2016 e-mail to the Division of Anti-Infective Products (DAIP) seeking input on the proposed name, DAIP expressed concerns with the proposed proprietary name, LymePak. DAIP stated "*having the disease name (Lyme disease) incorporated in the product name (LymePak) does seem promotional in nature and may imply particular effectiveness. Furthermore, this is a literature based NDA, and the dataset will incorporate information from a number of doxycycline products*".

DMEPA communicated DAIP's misbranding concerns to OPDP. OPDP stated "*As long as a proposed tradename's suggestion of the indication is accurate and not misleading, OPDP's current stance is that this is acceptable. Thus, for the "lyme" portion of the proposed tradename to imply that it is for Lyme disease is accurate because the proposed indication is for "the treatment of Lyme disease." We do not see any potential misleading efficacy suggestions or implications from "LymePak.*"

In response to OPDP's response, DAIP stated their key concerns were:

- *"The efficacy of the proposed product for early Lyme disease relies upon information from the literature from a variety of other doxycycline products, and therefore is not specific to this particular doxycycline product. Any bioequivalent doxycycline product could treat early Lyme."*

- "*The Sponsor intends* (b) (4) *for doxycycline hyclate. The proposed product is a fixed dose blister pack for* (b) (4) *days of treatment, but some doxycycline indications are treated for less than* (b) (4) *days."*

On June 27, 2016, DMEPA, OPDP, and DAIP met to discuss DAIP's promotional concerns with the proposed proprietary name. It was determined that the proposed proprietary name LymePak would not misbrand the proposed product (*see Pre-NDA meeting Request, May 6, 2016*[a] *which includes a list of all proposed indications*), but the proposed indications and packaging are subject to review and will be further evaluated when the NDA is submitted. Additionally, during the meeting DAIP expressed concern with the way the product will be packaged (blister package) targeting a (b) (4)-day course proposed for the treatment of early Lyme borreliosis

[a] Pre- NDA Meeting Request with References: LymePak (doxcyline hyclate, USP) Tablets and Capsules, May 6, 2016. Available at: \\cdsesub1\evsprod\ind125184\0000\m1\us\1-6-meetings\1-6-1-meeting-request\meeting-request.pdf

(erythema migrans), although the courses for other approved indications vary in duration from 7-10 days (majority of indications) to 60 days (anthrax prophylaxis). DMEPA was also concerned with the inconsistencies between the proposed packaging configurations and proposed dosing recommendations. We conveyed our concerns to the medical officer via email communication on August 17, 2016. The medical officer stated that because the Sponsor has an indication for early Lyme disease (erythema migrans) which is treated from (b) (4) 21 days in various published reports. (b) (4)

DMEPA and DAIP communicated these concerns (*inconsistency between dosage and administration for the indications being proposed and the proposed packaging configurations)* to the Sponsor via Teleconference on November 1, 2016. Subsequently, Chartwell Pharmaceuticals LLC withdrew the proprietary name review request for LymePak.

On April 27, 2017, the Sponsor resubmitted the proposed proprietary name for Agency review with only Lyme disease as the indication. Again, we noted an inconsistency between the proposed duration of therapy of (b) (4) 21 days and the proposed packaging configuration of 14-count blister pack cards (7 days therapy). To clarify these inconsistencies, we sent information requests to Charwell Pharmaceuticals. In response to DMEPA's information requests dated May 16, 2017 and June 1, 2017, Chartwell provided additional information stating that this product will be available as a 14-count blister pack card and the physician is to prescribe the appropriate number of packs to correspond with the individual patient's duration of therapy of 14, 21 (b) (4) days.

In response to the OSE May 11, 2017 e-mail, DAIP concurred with OPDP's assessment of the proprietary name, LymePak but continued to express concern regarding the number of tablets proposed in packaging.

DMEPA shared DAIP's concern with the packaging configuration and inconsistency with the proposed duration of treatment.

Per e-mail correspondence from the DAIP on August 16, 2017, DAIP stated:

"Our team does not have any new comments, as DAIP and DMEPA have already discussed this issue last year over several email threads and meetings. I am quoting a comment from one of our reviewers below which I think summarizes our team's point of view. 'Previously many of us thought the name LymePak seemed promotional. However, my understanding is that DMEPA did not agree with this assessment. I have no other reasons to find the name objectionable. Based on the above, my position is that I do not have any basis for objecting to this proposed proprietary name at this time.'"

On August 18, 2017 Chartwell submitted a New Drug Application (NDA 209844) for LymePak (doxycycline hyclate, USP) tablets, for the treatment of early Lyme disease.

On September 26, 2107, DMEPA notified Chartwell via Teleconference[b] of our preliminary concerns with the proposed packaging configuration submitted under (b) (4) and NDA

[b] Memorandum of Teleconference, LymePak (doxycycline hyclate) tablets, 100 mg tablet, NDA 209844, Tuesday, September 26, 2017.

209844. [redacted] of one 100 mg tablet taken twice daily. This packaging configuration did not support any treatment durations that were proposed to treat Lyme disease.

On October 6, 2017, in an email communication from Chartwell, they requested FDA's recommendation on the next steps regarding their request for review of their proposed proprietary name, LymePak. On October 17, 2017, via teleconference, DMEPA[c] suggested that Chartwell could withdraw the proprietary name review request submitted to IND 125184 and submit a request for proprietary name review under the NDA, and include in their request any information regarding the revised dosing and proposed packaging configurations. Subsequently, Chartwell withdrew the proprietary name request for LymePak on October 23, 2017 under IND 125184.

On November 20, 2017, Chartwell submitted proprietary name LymePak to the NDA with an additional packaging configuration, blister cards [redacted], to support the proposed dosing in the labeling.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on November 20, 2017.

- Intended Pronunciation: lime' pak
- Active Ingredient: doxycycline hyclate
- Indication of Use: Treatment of early Lyme disease (as evidenced by erythema migrans) due to *Borellia burgdorferi*
- Route of Administration: oral
- Dosage Form: tablet
- Strength: 100 mg
- Dose and Frequency: [redacted]

[c] Memorandum of Teleconference, LymePak (doxycycline hyclate) tablets, 100 mg tablet, NDA 209844, Tuesday, October 17, 2017.

(b) (4)

- **How Supplied:**

  NDC # 62135-596-01: is supplied as a child-resistant blister card containing 14 tablets

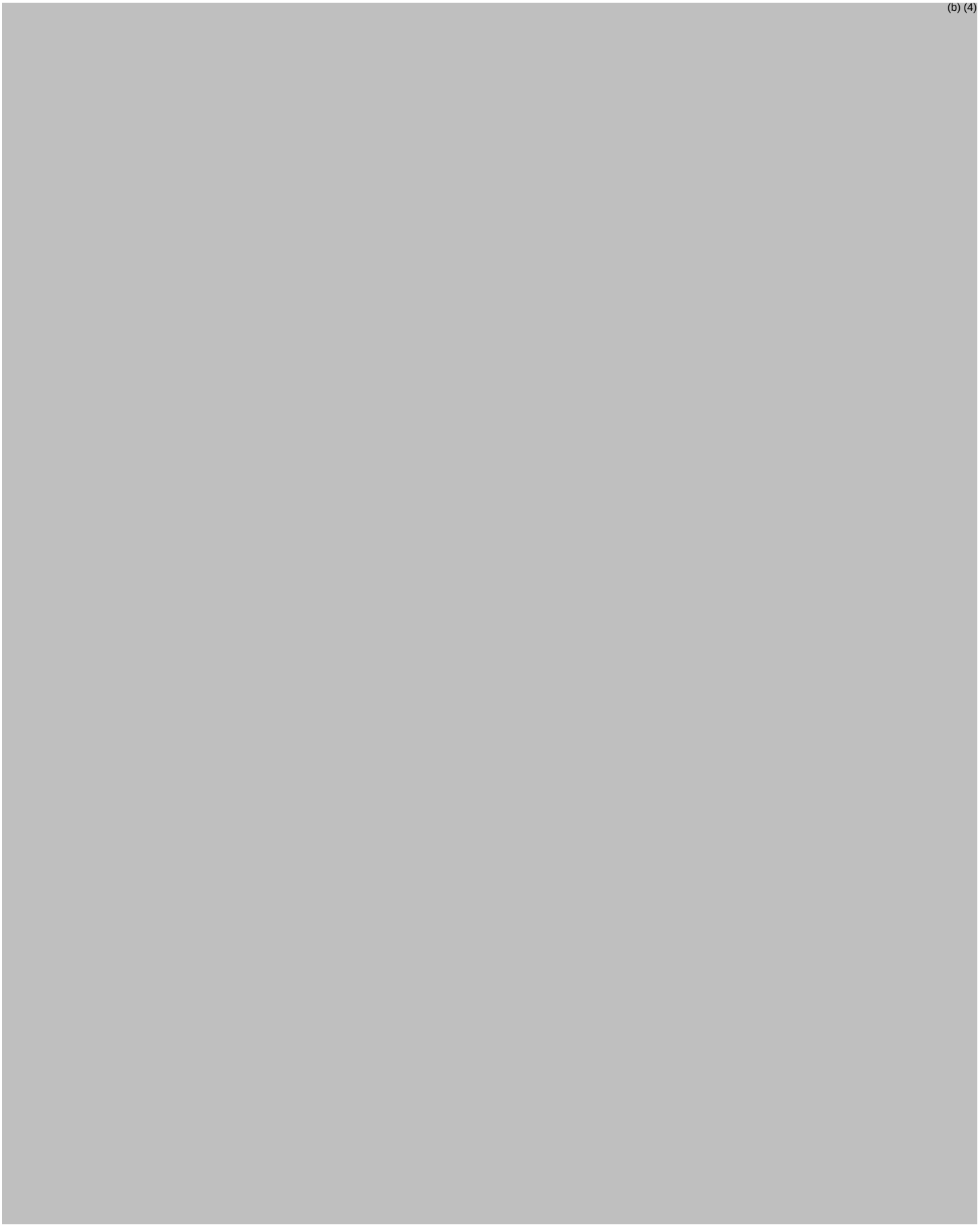
(b) (4)

- **Storage:** Store at 20°C to 25°C (68°F to 77°F) excursions permitted to 15° to 30°C (59° to 86°F)
- **Reference Listed Drug:** (b) (4)

2 DISCUSSION

During the initial steps of the proprietary name review process under the NDA, the Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA communicated our findings to DAIP via e-mail on January 29, 2018. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence on February 7, 2018, DAIP provided the following comments:

(b) (4)


(b) (4)

3 CONCLUSION AND RECOMMENDATIONS

The proposed proprietary name, LymePak, is unacceptable as it would misbrand the proposed product. Chartwell Pharmaceuticals LLC will be notified of FDA's decision via letter.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, LymePak, and have concluded that this name is unacceptable for the following reason:

(b) (4)

[redacted]

Please note that the Federal Food, Drug, and Cosmetic Act (FD&C Act) provides that labeling or advertising can misbrand a product if misleading representations are made (See 21 U.S.C. 321(n)). The FD&C Act also provides that a drug is misbranded if its labeling is false or misleading in any particular (21 U.S.C. 352(a)). A proprietary name, which appears in labeling, could result in such misbranding if it is false or misleading, such as by making misrepresentations with respect to safety or efficacy.

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

/s/

SEVAN H KOLEJIAN
02/16/2018

OTTO L TOWNSEND
02/16/2018

TODD D BRIDGES
02/16/2018