# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 208219Orig1s000

# PROPRIETARY NAME REVIEW(S)

**PROPRIETARY NAME REVIEW**

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

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

| | |
|---|---|
| **Date of This Review:** | December 27, 2018 |
| **Application Type and Number:** | NDA 208219 |
| **Product Name and Strength:** | Lotemax SM (loteprednol etabonate) ophthalmic gel, 0.38% |
| **Product Type:** | Single Ingredient Product |
| **Rx or OTC:** | Prescription (Rx) |
| **Applicant/Sponsor Name:** | Bausch and Lomb, Inc. (Bausch and Lomb) |
| **Panorama #:** | 2018- 26774336 |
| **DMEPA Safety Evaluator:** | Millie Shah, PharmD, BCPS |
| **DMEPA Team Leader:** | Otto L. Townsend, PharmD |
| **DMEPA Deputy Director:** | Irene Chan, PharmD, BCPS |

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# 1 INTRODUCTION

This review evaluates the proposed proprietary name, Lotemax SM, 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. Bausch and Lomb submitted an external name study for this proposed proprietary name.[a]

## 1.1 REGULATORY HISTORY

Bausch and Lomb previously submitted the proposed proprietary name, (b) (4)***, under IND 102654, on March 3, 2014. However, we found the name, (b) (4)*** unacceptable due to phonetic similarities and shared product characteristics with the proprietary name, (b) (4) on July 23, 2014.[b]

Subsequently, under IND 102654, Bausch and Lomb submitted the proposed proprietary name, (b) (4)*** on October 24, 2014. However, on April 10, 2015, we found the name, (b) (4)*** vulnerable to medication errors due to name confusion with another proprietary name that was also under review.[c]

Thus, Bausch and Lomb submitted the proposed proprietary name, (b) (4)*** on May 21, 2015. We found the name, (b) (4)*** acceptable under IND 102654 on September 28, 2015.[d] Subsequently on October 30, 2015, Bausch and Lomb withdrew the proprietary name, (b) (4)*** because they made a business decision to cease further development of the drug product.

Bausch and Lomb submitted the name, (b) (4)***, for review on April 27, 2018 following their NDA submission on April 25, 2018, which we found acceptable on June 29, 2018.[e] Subsequently on October 19, 2018, Bausch and Lomb withdrew the proprietary name (b) (4)*** and submitted the name, Lotemax SM, for review on October 19, 2018.

## 1.2 PRODUCT INFORMATION

The following Lotemax SM product information is provided in the October 19, 2018 proprietary name submission. Lotemax SM is an extension of the Lotemax product line. For comparison, we included product information for the currently marketed Lotemax product.

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[a] The company that performed the external name study was not identified in the proprietary name submission.

[b] Kapoor, R. Proprietary Name Review for (b) (4)*** (IND 102654). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2014 JUL 23. Panorama No. 2014-17041.

[c] Kapoor, R. Proprietary Name Review for (b) (4)*** (IND 102654). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2015 APR 10. Panorama No. 2014-40634.

[d] Mistry, M. Proprietary Name Review for (b) (4)*** (IND 102654). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2015 SEP 28. Panorama No. 2015-477190.

[e] Myers, D. Proprietary Name Review for (b) (4)*** (NDA 208219). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JUN 29. Panorama No. 2018-22709721.

| Table 1. Relevant Product Information for Lotemax SM and Lotemax[f] | | |
|---|---|---|
| | **Lotemax SM** | **Lotemax** |
| **Intended Pronunciation** | LOW-tuh-macks ESS EM | LOW-tuh-macks |
| **Initial Approval Date** | Not Applicable (N/A) | March 9, 1998 (ophthalmic suspension/drops)<br>April 15, 2011 (ophthalmic ointment)<br>September 28, 2012 (ophthalmic gel) |
| **Active Ingredient** | loteprednol etabonate | |
| **Indication** | treatment of post-operative inflammation and pain following ocular surgery | Ophthalmic Suspension/Drops: treatment of steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, selected infective conjunctivitis, when the inherent hazard of steroid use is accepted to obtain an advisable diminution in edema and inflammation.<br><br>Ophthalmic Ointment: treatment of post-operative inflammation and pain following ocular surgery<br><br>Ophthalmic Gel[g]: treatment of post-operative inflammation and pain following ocular surgery |
| **Route of Administration** | ophthalmic | |
| **Dosage Form** | Ophthalmic gel | Ophthalmic suspension/drops; ophthalmic ointment; ophthalmic gel |
| **Strength(s)** | 0.38% | Ophthalmic suspension/drops, Ophthalmic ointment and Ophthalmic gel: 0.5% |

[f] Lotemax product information obtained online from DailyMed available at: https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=lotemax. Accessed on October 29, 2018.

[g] Same indication as the proposed gel product.

| Table 1. Relevant Product Information for Lotemax SM and Lotemax[f] | | |
|---|---|---|
| | **Lotemax SM** | **Lotemax** |
| **Dose and Frequency** | 1 drop in affected eye three times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period | Ophthalmic suspension/drops: Steroid Responsive Disease Treatment: Apply one to two drops of Lotemax into the conjunctival sac of the affected eye four times daily. During the initial treatment within the first week, the dosing may be increased, up to 1 drop every hour, if necessary.<br><br>Post-Operative Inflammation: Apply one to two drops of Lotemax into the conjunctival sac of the operated eye four times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period.<br><br>Ophthalmic ointment: Apply a small amount (approximately ½ inch ribbon) into the conjunctival sac(s) four times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period<br><br>Ophthalmic gel: Apply one to two drops of Lotemax into the conjunctival sac of the affected eye four times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period. |
| **How Supplied/ Container Closure** | 10 mL bottle | Ophthalmic suspension/drops: 5 mL, 10 mL and 15 mL bottles<br><br>Ophthalmic ointment: 3.5 gram tube<br><br>Ophthalmic gel: 10 mL bottle |
| **Storage** | 15º C to 25º C | Ophthalmic suspension/drops: Store upright between 15°–25°C (59°–77°F). Do not freeze.<br><br>Ophthalmic ointment: Store between 15°-25°C (59°-77°F).<br><br>Ophthalmic gel: Store upright at 15º-25º C (59º-77º F) |

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Lotemax SM would not misbrand the proposed product. The Division of Transplant and Ophthalmology Products (DTOP) did not concur with OPDP's assessment. The Division of Transplant and Ophthalmology Products (DTOP) expressed concern that the modifier "SM" is misleading. Specifically, DTOP expressed concerns that:

*SM" stands for a "submicron" formulation. Submicron formulation is not a recognized dosage form, and the established name is expected to remain loteprednol etabonate ophthalmic gel.*

*There is an approved Lotemax (loteprednol etabonate ophthalmic gel) 0.5% under NDA 202872. The currently proposed product, loteprednol etabonate ophthalmic gel 0.38%, has not been directly compared clinically to the approved Lotemax gel 0.5%. Thus, the relative efficacy of the two products is unknown.*

We shared DTOP's comments with OPDP. They re-evaluated the proposed proprietary name, Lotemax SM and maintained their non-objection to the proposed proprietary name.

We also discussed DTOP's comments with the Office of Pharmaceutical Quality (OPQ), and they do not have concerns with the modifier "SM" being used to describe the formulation as "submicron" because the particle size is less than 1 micron, which is smaller than the currently marketed Lotemax 0.5% gel drug product

Following OPDP's reassessment of the proposed proprietary name, we concurred with OPDP and DTOP did not express further concerns.

### 2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Lotemax SM.

#### *2.2.1 United States Adopted Names (USAN) Search*

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

#### *2.2.2 Components of the Proposed Proprietary Name*

The proposed proprietary name, Lotemax SM, is comprised of a root name "Lotemax" and modifier "SM." Bausch and Lomb did not provide a derivation or intended meaning for the root name, Lotemax, in their submission. Bausch and Lomb indicated that the modifier "SM" refers to the new "submicron" formulation of loteprednol etabonate. We further discuss our safety assessment of the root name and the modifier in Section *2.2.7 Safety Assessment of the Proposed Name Lotemax SM*.

[h] USAN stem search conducted on October 26, 2018.

### *2.2.3 Comments from Other Review Disciplines at Initial Review*

In response to the OSE email dated November 5, 2018, the Division of Transplant and Ophthalmology Products (DTOP) forwarded misbranding concerns relating to Lotemax SM at the initial phase of the review (See *Section 2.1 Misbranding Assessment* above).

### *2.2.4 FDA Name Simulation Studies*

Forty-five practitioners participated in DMEPA's prescription studies for Lotemax SM. The responses did not overlap with any currently marketed products nor did the responses sound or look like 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*

The root name, Lotemax, is already marketed for the ophthalmic suspension/drops (NDA 020583), ointment (NDA 200738), and gel (NDA 202872) formulations in the 0.5% strength. We are not aware of any postmarketing cases of name confusion involving Lotemax (see *Section 2.2.6 Medication Error Data Selection of Cases*). Therefore, we did not conduct a POCA search for the root name, Lotemax.

The Applicant submitted an external study that included a POCA search which identified names of possible concern based on orthographic and/or phonetic similarities.

### *2.2.6 Medication Error Data Selection of Cases*

We searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving the currently marketed Lotemax products that would be relevant for this review.

| **Table 2. FAERS Search Strategy** | |
|---|---|
| **Search Date** | October 29, 2018 |
| **Product Name** | Lotemax |
| **Product Verbatim** | Lotemax (Loteprednol Etabonate Ophthalmic Gel 0.5%);Lotemax 0.5% Susp (Loteprednol Etabonate);Lotemax 5;Lotemax (Eye Ointment);Lotemax (Loteprednol Etabonate);Lotemax 0.5% Ophthalmic Gel-Loteprednol Etabonate;Lotemax 0.5%/Bausch & Lomb;Lotemax Suspension;Lotemax ;Lotemax;Lotemax (Loteprednol Etabonate Ophthalmic Suspension, 0.5%);Lotemax .05% Eye Drop;Lotemax Augentropfen;Lotemax Oph Sol 0.5% 5ml;Lotemax (Loteprednol Etaabonate);Lotemax (Non-Abbott);Lotemax 0.5% Eye Drops;Lotemax 0.5% Gel Drops Bausch And Lomb;Lotemax 5 Mg;Lotemax Sus;Loteprednol (Lotemax);Bausch & |

| Table 2. FAERS Search Strategy | |
|---|---|
| | Lomb "Lotemax" 0.5% Sus Bsc Lot.Etab.Optha-Snsp.;Lotemax (Loteprednol Etobonate), Refrest Tears;Lotemax 0.5 Mg Bausch & Lomb;Lotemax 0.5 Susp (L0teprednol Etabonate);Lotemax Eye Drops(Loteprednol Etabonate);Lotemax Loteprednol Etabonate .5% Opthalmic Suspension;Lotemax Ophthalmic Solution(Loteprodenol Etabonate);Lotemax Opthalmic Gel;Lotemax Susp 0.5%;Lotemax 5% Bausch & Lomb;Lotemax Eye Drops 1 Ml) 0.5% Sample Prescription Lotemax 5 Ml;Lotemax Loteprednol Etabonate Bausch + Lomb;Lotemax (Loteprednol Etabonate Ophthalmic Suspension 0.5%);Lotemax Gel;Lotemax (Loteprednol Etabonate Ophthalmic Suspension; 0.5 %);Lotemax 0.5% Gel Bausch-Lomb;Lotemax Ophthalmic Suspension;Lotemax 0.5% Bausch & Lomb;Loteprednol Etabonae (Lotemax);Loteprednol Etabonate (Lotemax);Lotemax 0.5% Eye Drops, Suspension;Lotemax 5ml Bausch & Lomb;Lotemax Bausch & Lomb;Lotemax Ointment;Lotemax Ophthalmic;Lotemax (Loteprednol Etabonate Ophathalmic Suspension, 0.5%);Lotemax Bausch & Lomb Lotepredrol Etabonate Ophthalmic Gel .5%;Lotemax Eye Drop;Lotemax Eye Gel;Lotemax Loteprednol Etabonate Opathalnine Get 0.5% Bausch & Lomb;Lotemax Ohthalmic Suspension;Lotemax (Loteprednol Etabonate Ophthalmic Suspension 0.5%) (Loteprednol Etabonate);Lotemax (Loteprednol Etabonate Opthalmic Suspension, 0.5%);Lotemax .5% Bausch & Lomb;Lotemax Drops;Lotemax (Loteprednol Etabonate Ophthalmic Suspensioin); 0.5 %;Lotemax 0.5% Bausch + Lomb;Lotemax 0.5% Baush & Lomb;Lotemax 0.5% Ophthalmic Gel;Lotemax Gel 0.5% Bausch +Lomb;Lotemax Loteprednol Etabonate;Pherma Generic For The Lotemax;Lotemax (Loteprednol Etabonate) (Loteprednol Etabonate);Lotemax (Loteprednol Etabonate) 0.5%);Lotemax Opth Susp;Lotemax Opth Susp Bausch An Lomb;Lotemax (Loteprednol Etabonate Ophthalmic Suspension); 0.5%;Lotemax (Loteprednol Etabonate Ophthalmic Suspension; 0.5%);Lotemax (Loteprednol Etabonate Ophthalmic Solution) 0.5%;Lotemax 0.5%, 5 Mg/Ml, Krople Do Oczu, Zawiesina;Lotemax 5% Baush & Lomb;Lotemax (Loteprednol Etabonate Ophthalmic |

| Table 2. FAERS Search Strategy | |
|---|---|
| | Suspension) 0.5%;Lotemax (Loteprednol Etabonate Ophthalmic Ointment 0.5%);Lotemax (Unspecified);Lotemax .5% Opthalmic Gel Drops Bausch & Lomb;Lotemax 0.5;Lotemax 0.5% Bausch&Lomb;Lotemax Eye Drops;Lotemax Opht Soln;Lotemax (1ml) (Bausch And Lomb);Lotemax (Lotemax) (Bausch & Lomb Pharmaceuticals) |
| **Event (MedDRA Terms)** | **DMEPA Official PNR Name Confusion Search Terms Event List:**<br>Preferred Terms:<br>CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR<br>DRUG ADMINISTRATION ERROR<br>DRUG DISPENSING ERROR<br>DRUG PRESCRIBING ERROR<br>INTERCEPTED DRUG DISPENSING ERROR<br>INTERCEPTED DRUG PRESCRIBING ERROR<br>INTERCEPTED MEDICATION ERROR<br>MEDICATION ERROR<br>PRODUCT NAME CONFUSION<br>TRANSCRIPTION MEDICATION ERROR<br><br>Lower Level Terms:<br>INTERCEPTED PRODUCT SELECTION ERROR<br>INTERCEPTED WRONG DRUG PRODUCT SELECTED<br>INTERCEPTED WRONG DRUG SELECTED<br>PRODUCT SELECTION ERROR<br>WRONG DEVICE DISPENSED<br>WRONG DRUG ADMINISTERED<br>WRONG DRUG DISPENSED<br>WRONG DRUG PRESCRIBED<br>WRONG DRUG PRODUCT SELECTED<br>WRONG DRUG SELECTED<br>WRONG PRODUCT SELECTED |
| **Event PT** | Medication Error |
| **Date Limits** | All cases through October 29, 2018 |

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

After individual review, all 11 reports were excluded from the final analysis because they did not describe name confusion errors.

### *2.2.7 Safety Assessment of the Proposed Name Lotemax SM*

In this section we provide a safety analysis of the proposed name Lotemax SM. The Applicant currently markets Lotemax (loteprednol etabonate) as suspension/drops, ointment, and gel ophthalmic formulations. The Applicant proposes to differentiate the proposed ophthalmic gel from the currently marketed formulations with the modifier SM.

**Safety Assessment of the root name "Lotemax"**

The first Lotemax (loteprednol etabonate) ophthalmic formulation was approved on March 9, 1998. Our search of the FDA Adverse Event Reporting System (FAERS) database did not identify any cases of name confusion related to the root name Lotemax (see *Section 2.2.6 Medication Error Data Selection of Cases*). Moreover, Lotemax and Lotemax SM have the same active ingredient, indication, and route of administration. We have determined that in this case the use of the root name is acceptable for this product at this time.

**Safety Assessment of the modifier, "SM"**

Individually, the modifier SM may be new to the marketplace. We searched the Institute of Safe Medication Practices' (ISMP) List of Products with Drug Name Suffixes[i] and did not identify any marketed names that have this modifier (we acknowledge that this is not an exhaustive list of such names). Additionally, we searched our internal databases and did not identify any completed reviews for names that contain this modifier. The Applicant indicated that the intended meaning of the modifier SM is "submicron." The Office of Pharmaceutical Quality (OPQ) did not express concerns with the modifier "SM" to describe the product's formulation as submicron because the particle size is less than 1 micron, which is smaller than the currently marketed Lotemax 0.5% gel drug product. The modifier may serve as a signal to health care practitioners that this product differs from the currently marketed Lotemax ophthalmic formulations.

Although we acknowledge that modifiers may be omitted or overlooked, in this case, inclusion of a modifier signaling the submicron formulation of this drug may provide an incremental increased level of safety. Therefore, we find the inclusion of the proposed modifier SM acceptable at this time.

## 3 CONCLUSION

The proposed proprietary name, Lotemax SM, is acceptable.

If you have any questions or need clarifications, please contact Danyal Chaudhry, OSE project manager, at 301-796-3813.

### 3.1 COMMENTS TO BAUSCH AND LOMB, INC.

[i] ISMP's List of Products with Drug Name Suffixes [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2010 [cited 2018 Nov 6]. Available at: https://www.ismp.org/sites/default/files/attachments/2018-04/drugnamesuffixes.pdf.

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

If any of the proposed product characteristics as stated in your submission, received on October 19, 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. [j]

[j] 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[k]. 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

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

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

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

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned, and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

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

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

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

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

| Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose. | | | |
|---|---|---|---|
| Orthographic Checklist | | Phonetic Checklist | |
| **Y/N** | Do the names begin with different first letters?<br>*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?<br>**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.<br><br>For single strength products, also consider circumstances where the strength may not be expressed.<br><br>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.<br><br>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:<br><br>• 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.<br><br>• Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity.<br><br>• 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)<br>• Do the names begin with different first letters?<br>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.<br>• Are the lengths of the names dissimilar* when scripted?<br>*FDA considers the length of names different if the names differ by two or more letters.<br>• 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?<br>• Is there different number or placement of cross-stroke or dotted letters present in the names?<br>• Do the infixes of the name appear dissimilar when scripted?<br>• Do the suffixes of the names appear dissimilar when scripted? | Phonetic Checklist (Y/N to each question)<br>• Do the names have different number of syllables?<br>• Do the names have different syllabic stresses?<br>• Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?<br>• Across a range of dialects, are the names consistently pronounced differently? |

**Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).**

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

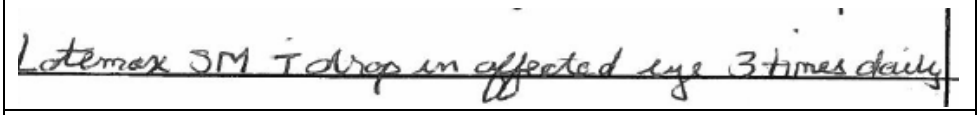
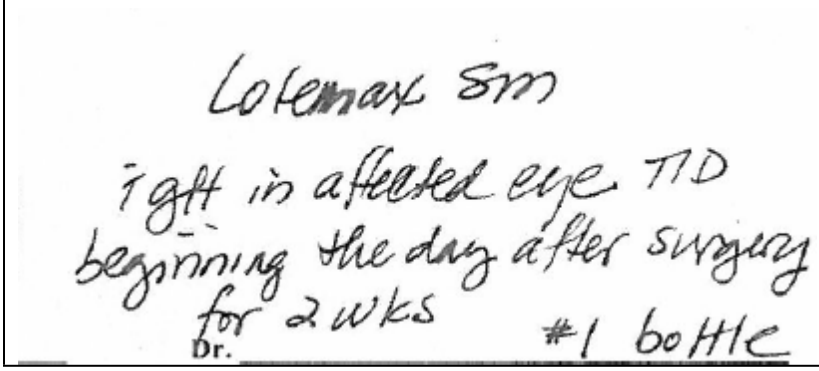
## Appendix A1: Description of FAERS

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

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

**Appendix B: Prescription Simulation Samples and Results**

**Figure 1. Lotemax SM Study (Conducted on October 25, 2018)**

| Handwritten Medication Order/Prescription | Verbal Prescription |
|---|---|
| Medication Order:<br>  <br><br>Outpatient Prescription:<br>  <br> | Lotemax SM<br>Instill 1 drop in affected eye three times a day beginning the day after surgery for 2 weeks |

**FDA Prescription Simulation Responses (Aggregate Report)**

45 People Responded

Study Name: Lotemax SM

| Total | 18 | 10 | 17 | |
|---|---|---|---|---|
| INTERPRETATION | OUTPATIENT | VOICE | INPATIENT | TOTAL |
| LOFENAX SM | 1 | 0 | 0 | 1 |
| LOLENAX GM | 1 | 0 | 0 | 1 |
| LOTAMAX SM | 0 | 1 | 0 | 1 |
| LOTAMAX SM | 0 | 4 | 0 | 4 |
| LOTEMAX | 2 | 0 | 0 | 2 |
| LOTEMAX OM | 0 | 0 | 1 | 1 |
| LOTEMAX SM | 9 | 3 | 15 | 27 |
| LOTEMAXSM | 1 | 0 | 1 | 2 |
| LOTENAX SM | 2 | 0 | 0 | 2 |
| LOTENMAX | 1 | 0 | 0 | 1 |
| LOTENOX | 1 | 0 | 0 | 1 |
| LOTOMAX SM | 0 | 2 | 0 | 2 |

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/s/

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OTTO L TOWNSEND on behalf of MILLIE B SHAH
12/27/2018 04:11:22 PM

OTTO L TOWNSEND
12/27/2018 04:12:35 PM

IRENE Z CHAN
12/27/2018 05:04:21 PM

**PROPRIETARY NAME REVIEW**

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

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

| | |
|---|---|
| **Date of This Review:** | June 29, 2018 |
| **Application Type and Number:** | NDA 208219 |
| **Product Name and Strength:** | (b) (4) (lotepredol etabonate) ophthalmic gel, 0.38% |
| **Product Type:** | Single-Ingredient Product |
| **Rx or OTC:** | Rx |
| **Applicant/Sponsor Name:** | Bausch and Lomb, Inc. |
| **Panorama #:** | 2018-22709721 |
| **DMEPA Safety Evaluator:** | Deborah Myers, RPh, MBA |
| **DMEPA Team Leader:** | Otto L. Townsend, PharmD |

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/s/

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DEBORAH E MYERS
06/29/2018

OTTO L TOWNSEND
07/02/2018