

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-013

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; HFD-420)**

DATE RECEIVED: December 22, 2006	DESIRED COMPLETION DATE: January 12, 2007	OSE REVIEW #: 2006-1128
DATE OF DOCUMENT: December 18, 2006	PDUFA DATE: January 16, 2006	
TO: Susan J. Walker, M.D. Director, Division of Dermatology and Dental Products HFD-540		
THROUGH: Alina Mahmud, R.Ph., MS, Team Leader Denise Toyer, Pharm.D., Deputy Director Carol Holquist, R.Ph., Director Division of Medication Errors and Technical Support		
FROM: Kimberly Pedersen, RPh, Safety Evaluator Division of Medication Errors and Technical Support		
PRODUCT NAME: Olux-E (Clobetasol Propionate Foam) 0.05% Emollient NDA #: 22-013	NDA SPONSOR: Connetics Corporation	
RECOMMENDATIONS: Although DMETS does not have any look-alike or sound-alike concerns with Olux-E, DMETS generally does not recommend the use of a modifier that conveys no meaning. However, the modifier "E" has been used for similar topical products to convey an emollient formulation and thus, DMETS believes the use of the modifier "E" is appropriate for this emollient dosage form. 2. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review to minimize potential errors with the use of this product. 3. The Division and the CMC/Branch Chief recommended that the sponsor use CDER's manuscript entitled "Topical drug classification" authored by Lucinda Buhse and published in the <i>International Journal of Pharmaceutics</i> 295 (2005) pp. 101-112 for guidance. This contradicts the recommendation made by Dr. Guirag Poochikian that the established name should be "Drug Topical Aerosol". Therefore, DMETS recommends that the Division contact ONDQA for clarification of the established name as outlined in Section III of this review. DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion if needed. If you have further questions or need clarifications, please contact Angela Robinson, Project Manager, at 301-796-2284.		

**Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
HFD-420; WO 22; Mail Stop 4447
Center for Drug Evaluation and Research**

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: December 22, 2006

NDA #: 22-013

NAME OF DRUG: **Olux-E**
(Clobetasol Propionate Foam) 0.05%
Emollient

NDA SPONSOR: Connetics Corporation

*****NOTE:** This review contains proprietary and confidential information that should not be released to the public.***

I. INTRODUCTION:

This consult was written in response to a request from the Division of Dermatology and Dental Products (HFD-540) for assessment of the proprietary names of Olux-E with regard to the potential name confusion with other proprietary or established drug names. Carton labeling, container labels, and insert labeling were submitted for review and comment at this time.

This proposed product differs from the currently marketed Olux product by indication of use and formulation. The currently marketed Olux is indicated for short-term treatment of the inflammatory and pruritic manifestations of moderate to severe corticosteroid-responsive dermatoses of the scalp, and for short-term treatment of mild to moderate plaque-type psoriasis of non-scalp regions excluding face and intertriginous areas. Olux-E is proposed for the treatment of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses and is noted not to be used on the scalp, face and intertriginous areas. Olux-E is an emulsion; thus, heavier and not aesthetically appropriate for use in the scalp; whereas, Olux will not leave the residue typically associated with heavier creams and thus, cosmetically appealing. Both Olux and Olux-E share the warning of limiting use to less than 50 grams (1/2 can) within one week to prevent HPA suppression.

This is the fourth proprietary name proposal for this application. DMETS reviewed the previously proposed proprietary name, Primolux™, in OSE Consult number 05-0116 and 05-0116-1, which was found acceptable. DMETS also provided label and labeling recommendations. However, DDMAC did not recommend the use of the name Primolux. The proposed names of _____ (primary name) and _____ (secondary name) were submitted for review and comment. However, DDMAC did not recommend the use of the proposed name of _____ because the name could overstate the effectiveness of the drug product and misleadingly imply that it is superior to competitor products. This was accepted by the division; thus, _____ was not reviewed by DMETS from a safety perspective. Furthermore, the name _____ was not reviewed as per the 09 December 2006 internal meeting with the division, DDMAC, and DMETS where the proposal for the use of the same tradename of Olux with a modifier was suggested and agreed upon.

PRODUCT INFORMATION

Olux-E is a synthetic super-high potency corticosteroid in an emulsion aerosol foam for topical dermatologic use. Olux-E is indicated for the treatment of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. The recommended dose is a small amount of foam applied to the affected area(s) until foam is absorbed twice daily, once in the morning and night. Due to the drug potency, treatment should be limited to two consecutive weeks and amounts greater than 50 grams per week should not be used. Olux-E will be available in 100 gram aluminum cans to be stored at room temperature.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases^{3,4} for existing drug names which sound-alike or look-alike to Olux-E to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁵. The SAEGIS⁶ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Olux-E. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff with representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary names Olux-E acceptable from a promotional perspective.
2. The Expert Panel identified four (Olux, Choloxin, Alesse, and Aloxi) as having the potential for confusion with Olux-E. Independent investigation identified an additional thirty-three names (Olux, Luxiq, Lidex-E, Alrex, Orlex/Orlex HC, Aloxi, Celexa, Aleve, Belix, Urex, Alexa, Olexa, Alaxo, Alexia/Alexia D, Fluxid, Quixin, Ultiva, Videx EC, Slow-K, Proben-C,

¹ MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, Missouri.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-05, and the electronic online version of the FDA Orange Book.

⁴ Phonetic and Orthographic Computer Analysis (POCA)

⁵ www location <http://www.uspto.gov/tmdb/index.html>.

⁶ Data provided by Thomson & Thomson's SAEGIS™ Online service, available at www.thomson-thomson.com

Afaxin, Ciloxan, Clobex, Floxin, ~~Luvox CR~~, Ovide, Eulexin, and Evex) as having the potential for confusion with Olux-E. Of the thirty-eight names identified, DMETS found that five names (Olux, Aloxi, Alesse, Aleve, and Ovide) warranted further evaluation based on look-alike, sound-alike, and product characteristics (See Table 1 below). The other thirty-three names are either foreign drugs, no longer marketed, or lacked convincing look-alike/sound-alike similarities with Olux-E, in addition to having differentiating product characteristics, such as product strength, indication for use, frequency of administration, route of administration, and/or dosage form. Thus, only Olux, Aloxi, Alesse, Aleve and Ovide will be discussed further in this review.

Table 1: Potential Look-Alike and Sound-Alike Names Identified for Olux-E

Product Name	Established name, Dosage form(s)	Usual adult dose*	Other**
Olux-E	Clobetasol Propionate Emulsion Foam 0.05%, 100 gram	Apply to affected area twice daily.	
Olux	Clobetasol Propionate Foam 0.05%, 50 gram and 100 gram	Apply to affected area twice daily.	LA/SA
Aloxi	Palonosetron Hydrochloride Injection, 0.25 mg/5 mL	0.25 mg as a single dose 30 minutes prior to chemotherapy	LA/SA
Alesse	Levonorgestrel/Ethinyl Estradiol Tablets, 0.1 mg/0.02 mg 28 tablets	One tablet daily.	SA
Aleve	Naproxen Sodium Tablets, Caplets, and Gelcaps- 220 mg	One every 8 to 12 hours.	LA
Ovide	Malathion Lotion, 0.5% 2 ounces bottle	Apply to hair and scalp, leave for 8 to 12 hours, then shampoo	

*Frequently used, not all-inclusive.
 **LA (look-alike)/SA (sound-alike).
 *** Proprietary and confidential information that should not be released to the public

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Olux-E 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. These studies employed a total of 123 health care professionals (pharmacists, physicians, and nurses). The exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and an outpatient prescription were written, each consisting of a combination of marketed and unapproved drug products with a prescription for Olux-E (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail and sent to a random sample of participating health professionals for their interpretation and review. After receiving either written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

*** Proprietary and confidential information that should not be released to the public.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p data-bbox="332 163 519 199"><u>Outpatient RX:</u></p> <p data-bbox="381 210 722 283">Olux-E 0.05%</p> <p data-bbox="511 283 592 336"># 1</p> <p data-bbox="438 346 844 472">Apply to the affected Area BID</p>	<p data-bbox="998 294 1169 325"><u>Olux-E 0.05%</u></p> <p data-bbox="998 325 1079 357"><u>1 tube</u></p> <p data-bbox="998 357 1323 388"><u>Apply to affected area BID</u></p>
<p data-bbox="332 514 495 546"><u>Inpatient RX:</u></p> <p data-bbox="332 567 1323 640">1 tube 0.05% apply to the affected area BID</p>	

2. Results:

None of the interpretations of the proposed name overlap, sounds similar, or looks similar to any currently marketed U.S. product. However, two participants of the inpatient study misinterpreted the “E” modifier as “SE” and “Ec.” See appendix A for the complete listing of interpretations from the verbal and written studies.

C. RESULTS OF THE FDA AERS and DQRS DATABASE SEARCHES

Olux-E is an addition to the Olux product line, which was approved in May 2000. Therefore, the Adverse Event Reporting System (AERS) and Drug Quality Reporting System (DQRS) were searched for all post-marketing safety reports concerning medication errors associated with Olux. For AERS, the following criteria were used: MedDRA High Level Group Term (HLGT) “Medication Errors” and Preferred Term (PT) Pharmaceutical Product Complaint with the tradename and verbatim letter string of “Olu%” and “Clobet.” The dates searched included May 2000 to December 2006. There were no reports found from the AERS search. In order to evaluate if there were problems with the use of the “foam” formulations, DMETS conducted a search of the AERS and DQRS databases for Olux, Verdeso, Luxiq, and Evoclin. This search revealed seven reports related to quality control issues (manufacturing) with the dispensing of the medication from the can; unrelated to adverse events or medication errors. Thus, DMETS has no comments at this time.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, five names (Olux, Aloxi, Aleve, Alesse, and Ovide) were identified as having the potential to be confused with the proposed name of Olux-E.

Prescription studies found no other names potentially leading to confusion with Olux-E; however, two participants from the inpatient study misinterpreted the “E” modifier as “SE” and “Ec.” The “SE” modifier identified by one participant is not in use at this time as a modifier, but does represent selenium on the periodic chart and selenomethionine has been identified as “SE-75.” However, this misinterpretation should not result in confusion with currently marketed products. The second modifier identified was “Ec”, which is associated with enteric-coated in the marketplace (e.g. Entocort EC and DuetDHA ec). DMETS does not believe this could lead to confusion with this

topical foam product as “enteric-coated” is associated with oral dosage forms.

1. Look-alike and Sound-alike Names with Olux-E

- a. Olux was identified as having look-alike and sound-alike similarities with the proposed name, Olux-E.

Olux is phonetically and orthographically identical to Olux-E, if the modifier of “E” is inadvertently omitted.

DMETS observes that the active ingredient, strength, dosage form (foam), and directions for use are identical for the proposed drug product and the currently marketed “Olux” drug product. Their indications differ with Olux being used for the scalp and mild to moderate plaques in comparison to the proposed product’s indication for use in inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses of the skin without specific indication to area of use. The proposed product is not recommended for the use on the scalp due to the cosmetic ramifications of using an emollient on the scalp and Olux if not to be used on severe plaques as the product contains an alcohol that may result in discomfort. Upon initial approval, practitioners will need to further clarify which dosage form will be appropriate for the individual patient prior to dispensing the drug. DMETS anticipates confusion when Olux-E is added to the existing product line of Olux. However, there will need to be an education campaign to alert health care practitioners to the new dosage form including product differences. The product packaging appears to be distinct (different color schemes and “emollient” banner) and in conjunction with an education campaign to alert practitioners to the availability of this product, DMETS believes the long-term possibility for confusion to be minimal.

- b. Aloxi was identified as having look-alike and sound-alike similarities with the proposed name, Olux-E.

Aloxi contains palonosetron hydrochloride as an injectable formulation for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately to highly emetogenic cancer chemotherapy. The recommended dosing is 0.25 mg as a single dose thirty-minutes before the start of chemotherapy. The dose should not be repeated within seven days of the initial dose. Aloxi is to be infused over thirty seconds and should not be mixed with other drugs. Aloxi is supplied as 0.25 mg in 5 mL.

The phonetic similarities stem from the shared central “lux” and “lox”, which may sound identical in speech. In addition, the leading “A” and “O” may sound similar if the “A” is pronounced as a short “ă.” Furthermore, the concluding modifier of “E” (ē) for Olux may sound identical to the concluding “I” of Aloxi. The orthographic similarities stem from the potential for Olux to resemble “Alox”, with the shared “l” and “x.” However, the concluding modifier “E” will likely be written as a capital letter, which will distinguish the names upon scripting.

Olux-E
Alesse

Although the names sound similar when spoken, they do not overlap in any product characteristics. They differ in strength (0.25 mg compared to 0.05%), dosage form (injection compared to foam), route of administration (intravenous compared to topical), dosing frequency (once prior to chemotherapy compared to twice daily), context of use (with chemotherapy, likely in a hospital or clinic setting compared to at home use), and dispensing amount (5 mL/one vial compared to 100 gram can). As Aloxi is likely to be used in hospital or clinic settings and in light of JCAHO requirements, the practitioner will indicate route of administration and dosing frequency to further help differentiate the products. Since the products differ in all product characteristics, DMETS believes the possibility for confusion to be minimal.

- c. Alesse was identified as having sound-alike similarities with the proposed name, Olux-E.

Alesse is an oral contraceptive containing levonorgestrel (0.1 mg) and ethinyl estradiol (0.02 mg) in a tablet form. This formulation contains twenty-one active tablets and seven days of inactive tablets. Recommended dosage is one tablet daily.

The phonetic similarities stem from the potential for a shared leading “ä” sound followed by the shared “l.” In addition, there is the potential for Alesse to be pronounced as two syllables with the concluding “e” to be spoken as a long “ē”, which overlaps with the “E” modifier of Olux. However, it is more likely the product name will be pronounced as a single syllable as “äless” or “älëss,” which would differentiate the two names on a verbal order.

On initial observation, the products share no similar characteristics: strengths (0.1 mg/0.02 mg compared to 0.5%), package size (28 tablet dial pack compared to 100 gram can), frequency of dosing (daily compared to twice daily), route of administration (oral compared to topical), context of use/indication (oral contraceptive compared to dermatoses), and dosage form (tablet compared to foam). However, both products can be ordered as #1 and “use as directed.” Although there is potential for sound-alike characteristics and similar nondescript ordering, DMETS believes the possibility for confusion to be limited.

- d. Ovide was identified as having look-alike similarities with the proposed name, Olux-E.

Ovide contains 0.5% malathion as a lotion dosage form for the treatment of head lice. The product should be applied to dry hair to thoroughly wet the hair and scalp, and then allow to dry. After 8 to 12 hours, the hair should be shampooed and combed (with fine-toothed comb). A second application may be used if lice are still present after 7 to 9 days.

The orthographic similarities stem from the shared leading “O” with the potential for the following “vi” of Ovide to look like the “li” of Olux. However, the concluding modifier for Olux will likely be written as a capital letter; which would serve to differentiate the names. In addition, the “v” and the upstroke of the “d” of Ovide and the upstroke of the “l” and “x” of Olux should help differentiate the names upon scripting.



The drug products share numerically similar strengths (0.5% compared to 0.05%), but differ in package size (59 mL bottle compared to 100 gram can), frequency of dosing (one time use compared to twice daily use), context of use/indication (treatment of head lice compared to dermatoses), and dosage form (lotion compared to foam). Although both drug products can be written as “#1” and “UD” (use as directed), the scripting differences should help distinguish the two names when written. Therefore, DMETS believes the possibility for confusion to be minimal due to weak orthographic similarities and differing indications.

- e. Aleve was identified as having look-alike and sound-alike similarities with the proposed name, Olux-E.

Aleve is an over-the-counter medication containing naproxen sodium (220 mg) in caplets, tablets, and gels. Aleve is indicated for pain relief or fever reduction, with a recommended dosing of one tablet every 8 to 12 hours.



The orthographic similarities stem from the leading “Ale” and “Olu” that appear similar when scripted. In addition, the following “v” and “x” may appear similar depending on scripting style. However, the modifier of “E” for Olux will likely be written in upper case, which would likely differentiate the names.

Although the names may appear similar when scripted, the products only share the product characteristic of dosing frequency (every 12 hours). In contrast, they differ in strength (220 mg compared to 0.05%), dosage form (tablet compared to foam), route of administration (oral compared to topical), and prescription status. Since the products differ in most product characteristics, DMETS believes the possibility for confusion to be minimal.

2. Addition of the modifier “E”

The division is considering the addition of a modifier, specifically “E”, to help differentiate the two drug products.

DMETS typically does not recommend the use of modifiers that convey no meaning. In light of the July 20, 2006, IOM Report “Preventing Medication Errors” (www.iom.edu/CMS/3809/22526/35939.aspx) recommendation number 4, which urges the FDA to standardize abbreviations, acronyms, and terms to the extent possible, we would normally recommend that the sponsor utilize the existing tradename “Olux” for the proposed product in conjunction with the labeling statement of “emulsion” rather than using a misleading and/or ambiguous modifier.

However, we also consider prescribing habits/practices and pharmacy practice. DMETS is unsure if practitioners would indicate "Olux emollient" on the prescription/order; we are also concerned that pharmacy personnel would not properly differentiate the two Olux products on the shelf without the modifier. This is especially true as both products are labeled as "foams." The inclusion of the "E" modifier may lead to an increased awareness that the products are different and thus, not lead to an assumption that the products would be clinically interchangeable

In addition, the extension of the name would provide the pharmacist a means to innately understand the content of the proposed drug product. Practitioners would be aware of the active ingredient and the label statement of "emollient" would help to provide an explanation to the products actions or use. Furthermore, incorrect selection is a common cause for medication errors in the pharmacy. These selection errors may occur in the computer or on the pharmacy shelf. The inclusion of the "E" modifier may help to differentiate the products in both places; of course, this would be especially true of the computer where there is no label or color differentiation to help with selection.

There is also precedence for the addition of the "E" modifier from a historical dermatological perspective, since such products as Psorcon-E, Florone E, Lidex-E, Temovate-E, Embeline-E, and Halog-E have been marketed. The "E" in these cases refers to "emollient." At this time, Temovate-E, Lidex-E, Psorcon-E, and Embeline-E (generic) are marketed. A review of the AERS database found no reports of medication error with any dermatologic product including an "E" modifier. However, as most of these products were approved before 1988, one can not conclude definitely that there have been no errors with these products. Although, there could have been prescription misfills within the product lines (e.g. Lidex filled when Lidex-E ordered), these cases may not be reported to the Agency. We also suspect that confusion may occur within the product line (Olux and Olux-E); thus, the sponsor should consider an education program for patients and practitioners.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the carton labeling, container label and package insert labeling for Olux-E, DMETS focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. We note that Patient Information materials have been provided with other similar products marketed by Connetics Corporation, e.g., Luxiq® and Olux®. DMETS believes that Patient Information should also be provided with this product.
2. To attempt to limit confusion for the two "Olux" drug products, consider the addition of the statements "Not for use on the scalp" to the proposed drug product carton labeling and container label and "Not for severe plaque-type psoriasis" to the currently marketed Olux carton labeling and container label.
3. In a memorandum of telecon dated August 7, 2006, for NDA 22-013 (Primolux), the Division noted that the sponsor expressed that they were "trying to differentiate between two different types of foam and want to add emulsion foam as a new category." The Division suggested that the sponsor use CDER's manuscript entitled "Topical drug classification" authored by Lucinda Buhse and published in the *International Journal of Pharmaceutics* 295 (2005) pp. 101-112 for guidance. Prior to DMETS knowledge of the memorandum of telecon, we contacted Dr.

Guiragos Poochikian, Acting Chair of the CDER Labeling and Nomenclature Committee, in regards to the proper designation of the established name for the Primolux™. Dr. Poochikian indicated that the established name should be "Desonide Topical Aerosol". His comment on the proper designation of the established name differs from the recommendation given to the sponsor by the Division (see below).

"Based on current convention and what I know about this product the established name should be "Drug Topical Aerosol" or "Drug Metered Topical Aerosol", depending whether it is metered or not. Moreover, there could be reservation with the use of the phrase "Emulsion Formulation" on the label."

Thus, DMETS defers this issue to the Division and recommends that the Division contact ONDQA for clarification of the established name for this drug product.

B. CONTAINER LABELS

1. See GENERAL COMMENT A-2.
2. Duplicate the "For Topical Use Only....." statement from the side panel to the principal display to help alleviate improper use of this potent corticosteroid. In addition, the color scheme (light green font on white background) used to highlight the route of administration does not provide adequate contrast and makes the information difficult to read. Change the color scheme to provide more contrast, improve readability and increase the visibility to the user.
3. The color scheme (light green font on white background) used to highlight the "EMOLLIENT" label statement, "Rx Only" statement, and warnings "Not for Ophthalmic, Oral or Intravaginal Use" does not provide adequate contrast and makes the information difficult to read. Change the color scheme to provide more contrast, improve readability and increase the visibility to the user. However, this color should be distinct from the current blue used on the Olux label to assure patients and practitioners are aware of the different formulation.
4. We refer you to the labeling requirements for medicinal aerosols set forth in the Aerosols Chapter (General Chapters <1151>), of the United States Pharmacopeia. To meet these labeling requirements, please amend or supplement your labeling as follows:

"Warning: Contents under pressure....", instead of ""

5. Add the statement "Refer to full directions before using" underneath the directions for use pictorial and text appearing on the side panel. The sponsor may also choose to delete the pictorial.
6. The "V" vignette appearing on the principal display panel(s) is too large and distracts from important labeling statements. Please delete or decrease the prominence of this symbol.
7. Revise "" to read "Chlorofluorocarbons (CFC) Free".

C. CARTON LABELING

1. See Comments B-2, B-3, B-6, and B-7.

2. We refer you to the labeling requirements for medicinal aerosols set forth in the Aerosols Chapter (General Chapters <1151>), of the United States Pharmacopeia. To meet these labeling requirements, please amend or supplement your labeling as follows:

“Warning: Contents under pressure....”, instead of “_____”

3. Add the statement “Refer to full directions before using” underneath the directions for use pictorial and text appearing on the side panel. The sponsor may also choose to delete the pictorial.

D. INSERT LABELING

1. See GENERAL COMMENTS A-1 and A-2.
2. Delete the use of trailing zeros (i.e. 1.0% in the adverse event section) and abbreviations (“g” in “50g” in the Dosage and Administration section). FDA launched a campaign on June 14, 2006, warning health care providers and consumers not to use error-prone abbreviations, acronyms, or symbols (e.g., trailing zeros). Thus, we request that the Divisions not approve or use trailing zeros in their labels and labeling as the potential for a ten-fold dosing error exists if the decimal point is not readily apparent. Additionally, the use of terminal zeroes in the expression of strength or volume is not in accordance with the General Notices (page 10) of 2004 USP, which states, “... to help minimize the possibility of error in the dispensing and administration of the drugs...the quantity of active ingredient when expressed in whole numbers shall be shown without a decimal point that is followed by a terminal zero.” We further note that the use of trailing zeros are specifically listed as dangerous abbreviations, acronyms, or symbols in the 2006 National Patient Safety Goals of The Joint Commission for Accreditation of Hospitals (JCAHO). Lastly, safety groups, such as the Institute for Safe Medication Practices (ISMP), also list trailing zeros on their dangerous abbreviations and dose designations list.

4. PRECAUTIONS (Information for Patients)

If patient information becomes available for this product, add reference to the patient information available for this product in this section.

5. DOSAGE AND ADMINISTRATION

Define “small amount” in the statement “Dispense a small amount...” (e.g., “This amount should be no more than 1 and ½ capful.” Or “Approximately the size of a- chose the appropriate descriptor.

6. HOW SUPPLIED

Include the established name of this drug product with the first occurrence of the proprietary name in this section.

Appendix A: Prescription Study Results

Inpatient	Outpatient	Voice
olux E	Olnx E	Olux E
Olux E	Olux-E	Olux E
Olux-E	Olnx-E	Olux E
Olux E	Olux-E	Ola E
Olux.E	Olnx-E	Bolux E
Obux-E	Olnx-E	Olux E
Olux -E	Olux-E	Olux E
Olux E	Olux-E	
Oluxel	Olux-E	
Olux-E	Olux-E	
Olux E	Olux-E	
Olux Ec	Olux-E	
Obex E	Olux-E	
Olux SE	Olux-E	
Olux-E		
Olux-E		

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CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED:

May 12, 2005

DESIRED COMPLETION

DATE: August 5, 2005

ODS CONSULT #: 05-0116

DOCUMENT DATE:

April 2, 2005

TO:

Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
HFD-540

THROUGH:

Melinda Harris-Bauerlien
Project Manager
HFD-540

PRODUCT NAME:

Primolux™
(Clobetasol Propionate Foam) 0.05%

SPONSOR: Connetics Corporation

IND#: 67,818

SAFETY EVALUATOR: Todd Bridges, R.Ph.

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Primolux™. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be reviewed upon submission of the NDA and approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.
2. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review in order to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name, Primolux™, acceptable from a promotional perspective.
4. The CDER Labeling and Nomenclature Committee has been contacted regarding the proper designation of the established name.

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**Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: June 1, 2005

IND#: 67,818

NAME OF DRUG: **Primolux™**
(Clobetasol Propionate Foam) 0.05%

IND SPONSOR: Connetics Corporation

*****NOTE:** This review contains proprietary and confidential information that should not be released to the public.***

I. INTRODUCTION

This consult was written in response to a request from the Division of Dermatologic and Dental Drug Products (HFD-540), for an assessment of the proprietary name, Primolux™ regarding potential name confusion with other proprietary or established drug names. Draft container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Primolux™, is a synthetic corticosteroid for topical dermatologic use. It is an analog of prednisolone and has a high degree of glucocorticoid activity and a slight degree of mineralocorticoid activity. Primolux™ is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. The recommended dose is a small amount of foam applied to the affected area(s) twice daily. Primolux™ will be available in _____ 100 gram aluminum cans to be stored at room temperature.

II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference textsⁱ as well as several FDA databasesⁱⁱⁱ for existing drug names which sound-alike or look-alike to Primolux™ to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database^{iv} and the data provided by Thomson &

ⁱ MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

ⁱⁱ Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

ⁱⁱⁱ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support proprietary name consultation requests, New Drug Approvals 1998-2005, and the electronic online version of the FDA Orange Book.

^{iv} WWW location <http://www.uspto.gov>.

Thomson's SAEGIS™ Online Service^v were also conducted. An Expert Panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Primolux™. Potential concerns regarding drug marketing and promotion related to the proposed name was also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the name, Primolux™, acceptable from a promotional standpoint.
2. The Expert Panel identified eight proprietary or established names which were thought to have the potential for confusion with Primolux™. These products are listed in Table 1 (see below and page 4), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified for Primolux™

Product Name	Dosage form(s), Established name	Usual adult dose*	Other
Primolux	Clobetasol propionate 0.05% foam	Apply twice daily	
Premarin	Conjugated estrogens 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg tablets; 25 mg injection; 0.625 mg/g cream	0.3 mg to 1.25 mg once daily; 25 mg IV or IM then repeat in 6 to 12 hours if necessary; 0.5 to 2 g/day intravaginally	LA
Precedex	Dexmedetomidine HCl 100 mcg/mL IV injection	1 mcg/kg over 10 minutes then 0.2 to 0.7 mcg/kg/hr	LA
Primaxin	Imipenem-cilastatin 250 mg/250 mg, 500 mg/500 mg IV injection; 500 mg/500 mg, 750 mg/ 750 mg IM injection	125 mg to 1 g over 20 to 60 minutes then 1 to 4 g daily in three or four divided doses; 500 to 750 mg every 12 hours	LA/SA
Primsol	Trimethoprim 50 mg/5 mL oral solution	5 mg/kg every 12 hours	LA
Trimox	Amoxicillin 250 mg, 500 mg capsules; 125 mg, 250 mg chewable	250 mg to 1,750 mg daily in 2 to 3 divided doses; >3 months and <40 kg: 20 to 45	LA

^v Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

Product Name	Dosage form(s), Established name	Usual adult dose*	Other **
Primolux	Clbetasol propionate 0.05% foam	Apply twice daily	
	tablets; 125 mg/5 mL, 250 mg/5 mL powder for oral suspension	mg/kg/day in 2 to 3 divided doses	
Primacor	Milrinone lactate 1 mg/mL injection; 200 mcg/mL in 5% dextrose injection	Initial loading dose: 50 mcg/kg, by continuous IV infusion. Usual maintenance IV infusion rate: 0.5 mcg/kg/min (0.77 mg/kg/day)	LA
Primidone	50 mg, 250 mg tablets	250 mg 3 to 4 times a day	LA
Previfem	Ethinyl estradiol 0.035 mg, norgestimate 0.25 mg	1 tablet once daily	LA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

B. PHONETIC ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search modules return a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered having significant phonetic or orthographic similarities to Primolux™ were discussed by the Expert Panel (EPD).

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Primolux™ with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. Each study employed a total of 119 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Primolux™ (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were 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 sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u></p> <p>Primolux 0.05% AAA BID #1 50g can</p>	<p>Primolux 0.05% Dispense one 50 g can Apply to affected area twice daily</p>
<p><u>Inpatient RX:</u></p> <p><i>Primolux 0.05% #1 50g can apply to affected area twice a day</i></p>	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A (page 12) for the complete listing of interpretations from the verbal and written studies.

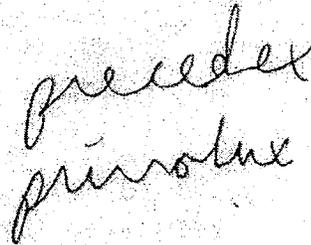
D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Primolux™, the primary concerns raised were related to look-alike and/or sound-alike confusion with Premarin®, Precedex®, Primaxin®, Primsol™, Trimox®, Primacor®, Primidone, and Previfem™. Upon further review of the names gathered from EPD, the names Premarin®, Primaxin®, Primsol™, Trimox®, and Primacor® were not reviewed further due to either a lack of convincing look-alike and/or sound-alike similarities with Primolux™ in addition to differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage form. Moreover, the potential for confusion and error between Trimox® and Primolux™ is further minimized because a prescription for Trimox®, unlike Primolux™ which is only supplied in one strength, necessitates an expression of strength prior to dispensing.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predictive as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Primolux™.

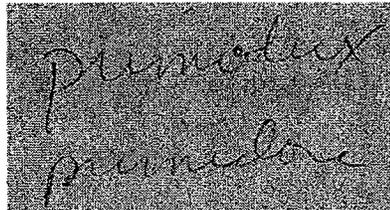
1. Precedex® was identified to have look-alike similarities to the proposed name, Primolux™. Precedex® is indicated for sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting. The usual dose is a loading infusion of 1 mcg/kg over 10 minutes, followed by a maintenance infusion of 0.2 mcg to 0.7 mcg/kg/hr. Both names

start with the letters “Pr” and end with the letter “x”, which contributes to the look-alike similarity between the two names. Additionally, the letter “d” in Precedex® and the letter “l” in Primolux™ are both upstroke letters and are located in the same position within each name (see below). However, Precedex® has a unique context of use compared to Primolux™ in that Precedex® is not dispensed directly to patients and is only administered in a controlled intensive care unit setting by appropriately trained personnel who are familiar with the product and its use. Additionally, a prescriber may order Primolux™ with “as directed” for the directions of use while an order for Precedex®, which is dosed based upon patient weight, will likely include the route of administration (IV infusion) and a patient specific dose based on the patient’s weight. This indication of an individualized dosing and route of administration on an order will help to differentiate these names from one another. Moreover, Precedex®, unlike Primolux™, is not to be administered for greater than twenty-four hours. Thus, Precedex® will be written as a twenty-four hour order or may be covered under the Automatic Stop-Order Policy of most hospitals. Such a policy requires the automatic discontinuation of toxic drugs based upon preset durations (e.g., twenty-four hours with Precedex®) to prevent or reduce the chance of harm occurring to patients. The short duration of administration of Precedex® may be indicated on the medication order and Precedex® may also be “flagged” as being a drug with an automatic stop-order, both of which will help to decrease the risk of confusion between this name pair. DMETS believes that the aforementioned product differences in combination with the patient specific dosing will minimize the risk of confusion and error due to look-alike similarities between Precedex® and Primolux™.



A handwritten cursive comparison of the words "precedex" and "primolux". The word "precedex" is written above "primolux". Both words are written in a similar cursive style, highlighting the orthographic similarities between them.

2. Primidone could potentially have look-alike similarity with Primolux™ when scripted. Primidone is an anticonvulsant indicated for the control of grand mal, psychomotor, or focal epileptic seizures, either alone or with other anticonvulsants. Primidone is available as 50 mg and 250 mg tablets. The usual dose is 250 mg three or four times each day. Primidone and Primolux™ have orthographic similarities such as the first four letters “Prim” and similar word lengths. Additionally, both names have an upstroke letter (“d” vs. “l”) in the sixth position (see below).

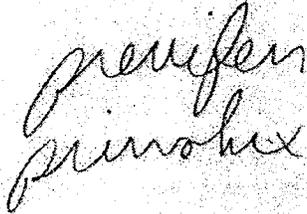


A handwritten cursive comparison of the words "primolux" and "primidone". The word "primolux" is written above "primidone". Both words are written in a similar cursive style, highlighting the orthographic similarities between them.

However, the two products have no overlapping product characteristics. They differ in strength (50 mg or 250 mg vs. 0.05%), indication for use (seizures vs. inflamed and itchy skin), frequency of administration (three to four times daily vs. twice daily), route of administration (oral vs. topical), and dosage form (tablet vs. foam). Moreover, the dose of Primidone will contain numeral(s) whereas the dose for Primolux will not (e.g., 1 tablet or 250 mg vs. apply to affected area). Additionally, since Primidone is available in two different strengths, the strength of

primidone will be indicated on a prescription and this will help to distinguish these two names. Furthermore, the frequency of administration (three to four times daily vs. twice daily), which will likely be present on a Primidone order, will aid in minimizing the potential for confusion between these products. Although there are some orthographic similarities between the name pair, the different product characteristics between Primidone and Primolux™ will help to differentiate the two names and minimize the potential for medication errors.

3. Prevfem™ may look similar to Primolux™. Prevfem™ is a monophasic oral contraceptive indicated for the prevention of pregnancy. Prevfem™ is a combination drug product, containing ethinyl estradiol and norgestimate, in strengths of 0.035 mg and 0.25 mg, respectively. The usual oral dose is one tablet once daily. Both names contain eight letters, and the first four letters of the names (“Prev” vs. “Prim”) can look similar (see below). However, the downstroke of the letter “f” in Prevfem™ and the fact that the names have differing letters (“i” vs. “o”) in the fifth position, may help to prevent name confusion between the two product names. Additionally, the two ending letters (“-em” vs. “-ux”) help to distinguish Prevfem™ from Primolux™. Furthermore, there are product characteristics that may help to differentiate the two names. These include product strength (0.035 mg/0.25 mg vs. 0.05%), therapeutic class (oral contraceptive vs. topical corticosteroid), frequency of administration (once daily vs. twice daily), route of administration (orally vs. topically), and dosage form (tablet vs. foam). These differentiating product characteristics coupled with a lack of convincing orthographic similarities will help to minimize the potential for error involving these two products.



III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Primolux™, DMETS has attempted to focus on safety issues relating to possible medication errors. However, copies of the labels and labeling were provided in black and white, and may not represent the true color of the labels and labeling. Therefore, DMETS cannot assess if there are any safety concerns due to the colors utilized on the labels and labeling. Upon review of the draft labels and labeling DMETS has identified the following areas of improvement, in the interest of minimizing user error and maximizing patient safety. Please forward copies of the revised labels and labeling, in color and reflective of the presentation that will actually be used on the marketplace, when they are available. Additionally, professional sample labeling was not submitted for review and comment. Please forward the professional sample labeling for review and comment when it becomes available.

A. GENERAL COMMENTS

1. We note that Patient Information materials have been provided with other similar products marketed by Connetics Corporation, e.g., Luxiq® and Olux®. DMETS believes that Patient Information should be provided with this product also, especially because of the special application instructions for Primolux™.

2. The CDER Labeling and Nomenclature Committee has been contacted regarding the proper designation of the established name for this drug product. Their comments will be communicated to the Division when they become available.
3. The sponsor has used the phrase "For Dermatologic Use Only" on the container labels and carton labeling for this product to indicate the route of administration. However, the term "Dermatologic" does not appear in the CDER Data Standards Manual under the listing for Data Element Name: Route of Administration. Other terminology listed in the CDER Data Standards Manual for the Route of Administration that may be appropriate includes "Topical" and "Cutaneous". To be consistent with CDER terminology and the route of administration appearing in the Title of the package insert labeling, we recommend revising the route of administration to read "For Topical Use Only", and relocating the statement to appear with prominence on each principal display panel rather than on the side panels.
4. DMETS notes the sponsor is proposing a similar layout or corporate dress for this product as used for the marketed product, Evoclin (NDA 50-801) and pending products, Extina^{***} (NDA 21-738) and ~~_____~~ and ~~_____~~. Images of this layout appear below in Figures 1 (below) & 2 (see page 9).

***** NOTE: This review contains proprietary and confidential information that should not be released to the public.*****

labeling for ~~_____~~ alongside the proposed carton labeling for Primolux.

Figure 2. Carton

- Postmarketing surveillance has shown that similar labeling across manufacturers' product lines may result in medication errors. DMETS recommends that the sponsor differentiate each product label and labeling so that it is readily distinguishable from other topical products.
5. Delete the term "~~_____~~", as it detracts from other important statements. This information may appear in the DESCRIPTION section of professional package insert labeling as long as it is clearly defined.
 6. We refer you to the labeling requirements for medicinal aerosols set forth in the Aerosols Chapter (General Chapters <1151>), of the United States Pharmacopeia. To meet these labeling requirements, please amend or supplement your labeling as follows:
 - a. Revise to read, "Warning: Contents under pressure....", instead of "~~_____~~".
 - b. Add the following statement, "Warning: Avoid spraying into eyes or onto other mucous membranes."
 7. Delete the use of "µg" throughout the label and labeling. DMETS is aware from postmarketing reports of confusion resulting from the confusion of the abbreviation "µg" for microgram. We further note that the Joint Commission for Accreditation of Hospitals, 2006 Hospitals National Patient Safety Goals includes the goal: Improve the effectiveness of communication among caregivers. A requirement to meet this goal is that each hospital must 'Standardize a list of abbreviations, acronyms and symbols that are not to be used throughout the organization. The use of "µ" is specifically listed as a dangerous symbol. Other healthcare organizations, such as ISMP have also published similar lists containing symbols that can lead to medication errors. Thus, where "µg" appears in the label and labeling, revise to read "mcg".

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8. Regarding the pictorial and text, "~~_____~~", appearing on the side panel, please refer to full directions for use or delete. An appropriate statement would be, "Refer to full directions before using".
9. The "V" vignette appearing on the principal display panel(s) is too large and distracts from important labeling statements. Please delete or decrease the prominence of this symbol.

B. CONTAINER LABEL

See GENERAL COMMENTS A-2 through A-9.

C. CARTON LABELING

See GENERAL COMMENTS A-2 through A-9.

D. INSERT LABELING

1. See GENERAL COMMENTS A-1, A-2, and A-6.
2. Please include patient's instructions for use of this product as you have for other "foam" products in the Connetics product line (e.g., Olux®).
3. In accordance with 21 CFR 201.10(g)(1), the established name shall be used at least once in association with the proprietary name on each page or column with running text.

4. PRECAUTIONS (Information for Patients)

If patient information becomes available for this product, add reference to the patient information available for this product in this section. Reprint the full text of the patient information at the end of the labeling. We refer you to 21 CFR 201.57(f)(2) for guidance.

5. DOSAGE AND ADMINISTRATION

Define "small amount" in the statement "Dispense a small amount..." (e.g., "This amount should be no more than 1 and ½ capful.").

6. HOW SUPPLIED

Include the established name of this drug product with the first occurrence of the proprietary name in this section.

IV. RECOMMENDATIONS:

- A. DMETS has no objections to the use of the proprietary name, Primolux™. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be reviewed upon submission of the NDA and approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.
- B. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.
- C. DDMAC finds the proprietary name, Primolux™, acceptable from a promotional perspective.
- D. The CDER Labeling and Nomenclature Committee has been contacted regarding the proper designation of the established name.

DMETS would appreciate feedback of the final outcome of this consult. We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Diane Smith, Project Manager, at 301-827-1998.

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Concur:

Linda Kim-Jung, Pharm.D.
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Appendix A. DMETS prescription study results for Primolux™

Outpatient	Voice	Inpatient
Primolux	Pemalax	Primalne
Primolax	Permalot	Primalue
Primolax	Permalox	Primelux
Primolax	Premalat	Primolin
Primolax	Premalock	Primoline
Primolax	Premalot	Primoline
Primolax	Premalot	Primoline
Primolux	Premalox	Primoline
Primolux	Premalox	Primoline
Primolux	Premalox	Primoline
Primolux	Premolot	primoline
Primolux	Primalone	Primolire
Primolux	primalot	Primolix
Primolux	Primalot	Primolue
Primolux	Primalox	Primolux
Primolux	Primalox	Primolux
Primolux	Primelac	Pulmolinx
Primolux	Primelox	
Primolux	Primilot	
Primolux	Primilux	
Primolux	Primoline	
Primolux	Primolot	
Primolux	Primolot	
Primolux	Primolox	
Primolux	promolot	

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