CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-978

PROPRIETARY NAME REVIEW(S)

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: August 30, 2006

NDA #: 21-978

NAME OF DRUG: Verdeso (Desonide Foam) 0.05%

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 name, Verdeso, regarding potential name confusion with other proprietary or established drug names. DMETS reviewed the previously proposed proprietary names, Desilux™, in OSE Consult number 05-0103 and ———™, in OSE Consult number 05-0103-1. Both names were found unacceptable by DMETS on May 18, 2005 and on September 13, 2006, respectively. Verdeso draft carton labeling from IND 67,825 (submission dated November 9, 2005) and ———™ container labels and package insert labeling from the NDA (submission date August 24, 1006) were provided for review and comment.

PRODUCT INFORMATION

Verdeso Foam is a petrolatum-based emulsion aerosol foam containing the active ingredient desonide, a low potency corticosteroid. Verdeso Foam is indicated for the treatment of mild to moderate atopic dermatitis. The usual adult dosage is to dispense a small amount of the foam then massage the medication into the affected area(s) twice daily. Verdeso Foam will be available in 100 g 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 Verdeso 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 conducted[5]. The SAEGIS[6] 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 requisition studies and one verbal prescription study, involving[7] health care practitioners within the 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 (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Verdeso. 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 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 has no objections to the proposed proprietary name, Verdeso, from a promotional perspective.

2. The Expert Panel identified twenty-two proprietary names that were thought to have the potential for confusion with Verdeso. Similarly, through independent review, nine additional drug names were also determined to have potential for confusion with Verdeso. Of the thirty-one names identified, DMETS found that seven names warranted further evaluation based on their potential to look-alike, sound-alike and other product characteristics (see Table 1 on page 4). Upon further review, it was determined that the following names will not be investigated further in this review: Ceredase, Nardil, Urso, Vadazo, Vapo-Iso, Varidase, Varidasa, Variza, Verdazol, Verdex, Verdia, Veress, Vermox, Versed, Vertavis, Vertuss, Redisol, Restoril, Revatio, Nubain, Navane, Lantus, Uni dur, and Uvadex. These names lacked convincing look-alike/sound-alike similarities with Verdeso. Additionally, information on some of the drug names either could not be

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[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

found or the drug was taken off the market. The products also had differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration and/or dosage formulation. Thus, refer to Table 1 for the names that were evaluated in this review (see below).

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage Form(s) [illegible]	[illegible] adult dose*	Other**
Verdeso	Desonide Foam 0.05% 100 grams	[illegible] to affected area(s) twice daily. Do not use with occlusive dressing unless otherwise directed by a physician.	
Vantas	Histerlin implant 50 mg	50 mg implant surgically inserted every 12 months	LA
Verelan	Verapamil Hydrochloride Sustained Release Capsules 120 mg, 180 mg, 240 mg, 360 mg	Initial: 80-120 mg 3 times a day Range: 240-480 mg/day in 3-4 divided doses	LA
Vidaza	Azacitidine injection, powder for suspension 100 mg	75 mg/m^2 subcutaneously once daily for 7 days every 4 weeks	LA
Videx	Didanosine Delayed Release Capsules (Videx EC): 125 mg, 200 mg, 250 mg, 400 mg	<60 kg: 400 mg daily ≥ 60 kg: 250 mg daily	LA
Viread	Tenofovir Disoproxil Fumarate Tablets 300 mg	300 mg once daily	LA
Virilon	Methyltestosterone Capsule 10 mg	5 mg -200 mg per day depending on the indication	LA
[illegible]	[illegible]	[illegible]	LA

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (sound-alike)
***Name pending approval. Not FOI releasable.

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 Verdeso 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 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 Verdeso (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
Outpatient RX: Verdeso #2 Apply topically bid	Verdeso # 2 Apply topically twice daily
Inpatient RX: Verdeso apply topically bid	

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 for the complete listing of interpretations from the verbal and written studies.

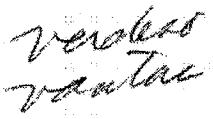
C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Verdeso, the primary concerns relating to look-alike and sound-alike confusion with Verdeso are Vantas, Verelan, Vidaza, Videx, Viread, Virilon and ——— ***.

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 predicative 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, Verdeso.

1. Vantas was identified as a name with look-alike similarities to Verdeso. Vantas, histrelin acetate, is a potent inhibitor of gonadotropin secretion, which is used for the palliative treatment of advanced prostate cancer. The Vantas implant is a sterile, non-biodegradable, diffusion-controlled reservoir drug delivery system designed to deliver histrelin hormonal therapy continuously for a duration of 12 months upon subcutaneous implantation. One implant contains 50 mg of histrelin acetate. The implant is inserted subcutaneously in the inner aspect of the upper arm. Verdeso must be removed after 12 months of therapy.

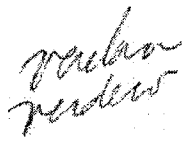
   The look-alike similarities of this name pair stem from the resemblance between the beginning letters of each name, "Vantas" and "Verdes", when scripted. In addition, the endings of both names ("tas" vs. "deso") can look-alike if the "deso" in Verdeso is not prominently scripted (see page 6).



Vantas and Verdeso do not share any product characteristics. They differ in route of administration (subcutaneous implantation vs. topical), strength (50 mg vs. 0.05%), dosage form (diffusion-controlled reservoir drug delivery system vs. foam) and patient population (oncology vs. dermatology). In addition, Vantas is not for self-administration. It must be given in a hospital or clinical setting. DMETS believes that these product differences will minimize the risk for confusion and error between Vantas and Verdeso.

2. Verelan was identified as a name with similar appearance to Verdeso when scripted. Verelan, verapamil hydrochloride, is an oral calcium channel blocker, useful for the treatment of angina, hypertension, and supraventricular tachyarrhythmias. Verelan is available as 120 mg, 180 mg, 240 mg, and 360 mg extended release capsules. The usual dose for Verelan ranges from 240 mg to 480 mg per day in three to four divided doses.

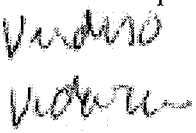
   Orthographically, the names share the same beginning ("Ver-"). In addition, similarities can be seen in the resemblance between the letters "ela" of Verelan and "de" of Verdeso when scripted.



   The two products differ in strength (120 mg, 180 mg, 240 mg, 360 mg vs. 0.05%), dosage form (extended release capsules vs. foam), route of administration (oral vs. topical) and dosage frequency (three to four times a day vs. twice daily). Furthermore, since Verelan is available in multiple strengths, the strength would likely be indicated on an order. Despite some orthographic similarities, the product characteristics listed above decrease the likelihood for potential confusion between the two drugs.

3. Vidaza and Verdeso were identified as names that may look similar when scripted. Vidaza, azacitidine, is a pyrimidine nucleoside analog that has activity as a cancer chemotherapy agent. Vidaza is used for the for the treatment of myelodysplastic syndrome (MDS) and chronic myelomonocytic leukemia. The usual dose is 75 mg/m^2 subcutaneously once daily for 7 days every 4 weeks. Vidaza is available as a powder for suspension in 100 mg vials. Each vial is reconstituted aseptically with 4 ml sterile water for injection to yield a resulting suspension of azacitidine 25 mg/mL.

   The two names share similar beginnings ("Vi-' vs. "Ve-") and the endings of each name ("-daza" vs. "-deso") can look alike when scripted.



   However, Vidaza and Verdeso differ in route of administration (subcutaneous vs. topical), strength (25 mg/mL vs. 0.05%), dosage form (powder for suspension vs. foam), dosage frequency (once daily for 7 days every 4 weeks vs. twice daily), patient population (oncology/hematology vs. dermatology) and dose (individualized vs. small amount).

Based on the product characteristic differences such as route of administration, strength, dosage form, dosage frequency and patient population, DMETS believes that the likelihood for confusion is minimal between the names Vidaza and Verdeso.

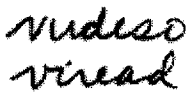
4. Videx was identified as a name with similar appearance to Verdeso when scripted. Videx, didanosine, is indicated for the treatment of human immunodeficiency virus (HIV) infection in combination with other antiretroviral agents. The usual dose for adults less than 60 kg is 400 mg once daily by mouth. The dose for adults greater than 60 kg is 250 mg once daily by mouth. Videx is available as 125 mg, 200 mg, 250 mg, and 400 mg extended release capsules (Videx EC).

   Both names share similar prefixes ("Vi" vs. "Ve"). However the length (five letters vs. seven letters) and the endings ("-ex" vs. "-eso") should help distinguish between the two names when scripted.

   Videx and Verdeso do not share overlapping product characteristics. The two products differ in strength (125 mg, 200 mg, 250 mg, and 400 mg vs. 0.05%), dosage form (capsules vs. foam), route of administration (oral vs. topical) and dosing frequency (once daily vs. twice daily). Moreover, a prescription for Videx will most likely indicate the strength. Based on the product characteristics listed above, DMETS believes the likelihood for confusion is minimal between the names Videx and Verdeso.

5. Viread was identified as a name with similar appearance to Verdeso when scripted. Videx, tenofivir disoproxil fumurate, is indicated for the treatment of human immunodeficiency virus (HIV). The recommended dose is 300 mg once daily with or ——————: Viread is available as 300 mg tablets.

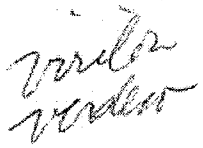
   Orthographically, Viread and Verdeso share similar beginnings "Vir" vs. "Ver", respectively. However, the upstroke of the letter "d" in the fourth position of the name Verdeso may help to differentiate between the two names when scripted.



   Both products can be ordered without an indication of strength as each is available in only one strength. Moreover, Viread and Verdeso differ in dosage form (tablets vs. foam), route of administration (oral vs. topical) and dosing frequency (once daily vs. twice daily). The distinguishing orthographic characteristics, in addition to the product characteristics, make it unlikely that the two products will be confused with one another.

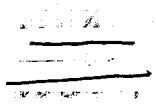
6. Virilon can look similar to the proposed name, Verdeso when scripted. Virilon, methyltestosterone, is indicated in males for the treatment hypogonadism, delayed puberty, impotence and climacteric issue. In females, Virilon is used as palliative treatment for metastatic breast cancer. The normal adult dose ranges from 10 mg to 200 mg per day depending on the indication. Virilon is available as 10 mg capsules.

The prefixes "Vir" of Virilon and "Ver" of Verdeso can look similar when scripted. Additionally, both names share an upstroke letter in similar positions ("l" vs. "d"). Furthermore, the endings of both names ("lon" vs. "deso") can look-alike if the "deso" in Verdeso is not prominently scripted (see below).



Virilon and Verdeso can share an overlapping dosing frequency of twice daily; however, the two products differ in strength (10 mg vs. 0.05%), route of administration (oral vs. topical) and dosage form (tablet vs. foam). DMETS believes that the product characteristics listed above decrease the likelihood for potential for confusion between the two drugs.

7. [redacted]



[redacted]

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

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the carton labeling of Verdeso and container label and package insert labeling for [redacted] 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 be provided with this product also, especially because of the special application instructions for Verdeso™.

2. 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, in conjunction with the CMC/Branch chief, 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. Guirag Poochikian, Acting Chair of the CDER Labeling and Nomenclature Committee, in regards to the proper designation of the established name for [redacted] (Verdeso). 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 Dr. Poochikian for clarification of the established name for this drug product. Since the sponsor has several products with this dosage form, it is imperative that the center is consistent with the established name.

3. Relocate the statement "For Topical Use Only" to appear with prominence on each principal display panel rather than on the side panels.

4. [redacted]

5. To help ensure that the product strength is more prominent than the net weight, debold the net weight statement.

6. Delete the term "Emulsion Formulation", 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.

7. 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:

   i. Revise to read, "Warning: Contents under pressure...." instead of "contents under pressure".

   ii. Add the following statement, "Warning: Avoid spraying into eyes or onto other mucous membranes."

8. Regarding the pictorial and text, "Invert can and..." appearing on the side panel, [redacted]

9. [redacted]

10. [redacted]

B. CONTAINER LABEL

See GENERAL COMMENTS A2 through A10.

C. CARTON LABELING

See GENERAL COMMENTS A2 through A10.

D. PACKAGE INSERT LABELING

Delete the use of trailing zeros (2.0 g). FDA launched a campaign on June 14, 2006, warning health care providers not to use error-prone abbreviations, acronyms, or symbols (e.g., trailing zeros) in their prescribing and warned consumers about the errors that can arise from these abbreviations and dose designations. 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.

Appendix A. Prescription Study Results for Verdeso

Inpatient	Outpatient	Voice
Verdeso	Verdeso	Ferdeso
Verdeso	Verdeso	Prediso
Verdezo	VERDESO	Burdeso
Verdeso	Verdeso	Furdesso
Verdeso	Verdeso	Fordeso
Verdero	Verdeso	Verdiso or Ferdiso
Verdeso	Verdeso	Verdeso
Verdeso	Verdesa	Verdeso
Verdeso	Verdeso	Purdeso
Verdeso	Verdeso	Valdeso
Verdeso	Verdeso	
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Verdeso	Verdeso	

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