CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-122

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO 22, MAIL STOP 4447)

DATE RECEIVED: April 9, 2007	**DESIRED COMPLETION DATE:** June 9, 2007	**OSE REVIEW #:** 2007-790
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TO: Bob Rappaport, M.D.
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FROM: Walter Fava, R.Ph., Safety Evaluator
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PRODUCT NAME:	**NDA SPONSOR:** Novartis Consumer Health, Inc.
Voltaren Gel (Diclofenac Sodium, Topical Gel 1%) **NDA#:** 22-122	

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Voltaren Gel. DMETS considers this a final review. However, if approval of the application is delayed beyond 90 days from the signature date of this review then the name and its labels and labeling must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.

2. DMETS recommends the 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, Voltaren Gel, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy DMETS on any correspondence forwarded to the sponsor concerning this review. If you have further questions or need clarifications, please contact the medication errors Project Manager, Nancy Clark, at 301-796-1187.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
WO 22, Mail Stop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: April 25, 2007

NDA#: 22-122

NAME OF DRUG: **Voltaren Gel**
(Diclofenac Topical Gel 1%)

NDA HOLDER: Novartis Consumer Health Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Anesthesia and Rheumatology Products (HFD-170), for assessment of the proprietary name, Voltaren Gel, regarding potential name confusion with other proprietary or established drug names.

DMETS notes that "Voltaren Gel" is the secondary name proposed for this product. The primary name, [redacted], was not found to be acceptable by DDMAC and the Division concurred with DDMAC's objection. Therefore, DMETS did not review the name "[redacted]" OSE review #: 2007-473 dated April 16, 2007) from a safety perspective.

Voltaren Gel will be an extension to the Voltaren product line. Currently, Voltaren is available as an ophthalmic solution, delayed release tablets and extended-release tablets. Additionally, draft container labels and carton labeling, along with the package insert and proposed dosing card, were provided for review and comment.

PRODUCT INFORMATION

Voltaren Gel is a topical nonsteroidal anti-inflammatory drug indicated for [redacted] joints amenable to [redacted] treatment, such as the hands and knees. Voltaren Gel will be available in tubes of [redacted] and 100 grams. The usual adult dose is 4 grams applied to the affected areas four times a day (for lower extremities) and 2 grams applied to affected areas four times a day (for upper extremities). Voltaren Gel should be gently massaged into the skin ensuring application to the entire affected area. Total usage should not exceed 32 grams per day, over all affected joints. Each application is measured using disposable dosing cards supplied with the product. Patients should be cautioned to avoid using sunscreens or cosmetics on the treated skin area(s) because concominant use may result in skin reactions or change the absorption of Voltaren Gel.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of the internet, 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 Voltaren Gel, 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 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. Following completion of these initial components, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of a drug must be considered in the overall safety evaluator risk assessment.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Voltaren Gel. 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, Voltaren Gel, from a promotional perspective.

2. The Expert Panel identified two proprietary names which were thought to have the potential for confusion with Voltaren Gel. These products are listed in Table 1 (see page 6), along with the dosage form available and usual dosage.

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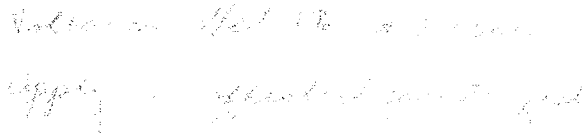
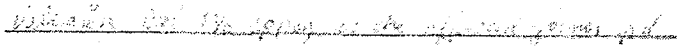
[1] MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-07, 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

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 Voltaren Gel with other 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 125 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 Voltaren Gel (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: 	Voltaren Gel 1% 2 tubes Apply to affected joints QID
Inpatient RX: 	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed US product. See Appendix A (page 5) for the complete listing of interpretations from the verbal and written studies.

C. ADVERSE EVENT REPORTING SYSTEM (AERS)

Since "Voltaren" is a currently marketed drug product in the U.S., (as an ophthalmic solution and as delayed release and extended-release tablets), we searched the FDA AERS database for post-marketing medication error reports related to Voltaren products. The high level group term (HLGT) "Medication Errors" was used as the search criteria. Seven pertinent cases were retrieved from AERS which identified name confusion between Voltaren and Ultram (between 1995 and 2004). Two of the cases were potential errors where the pharmacist reported that Ultram and Voltaren look similar when scripted. Three cases involved orders for Ultram 50 mg being misread as Voltaren 50 mg. Two of these errors were caught before they reached the patient, the third error reached the patient but no outcome was reported. The remaining two reports involved prescriptions for Ultram being incorrectly dispensed as Voltaren, however, no patient outcomes were reported.

DMETS acknowledges that orthographic similarities between Ultram and Voltaren, along with overlapping strengths (50 mg) and frequency of administration (QID), may have contributed to the actual errors described above. Considering that Voltaren Gel is a different dosage form compared to Ultram (gel vs tablets), and the directions for use are different for the two products (Apply two to four grams to affected area four times a day using dosing card vs take one tablet by mouth four times a day), the potential risk for confusion between the names is substantially minimized.

D. SAFETY EVALUATOR RISK ASSESSMENT

1. Look and Sound-alike Name Confusion

In reviewing the proprietary name, Voltaren Gel, nine names were identified as names with potential look-alike and sound-alike similarities to Voltaren Gel. These names are Volmax, Voltaren Emulgel, Verelan, Adrenalin, Ventolin, Demulen, Voltaren, Voltaren XR, and Viractin Gel. An independent name search identified the names Solaraze (diclofenac sodium) 3% gel, and Cataflam (diclofenac potassium) as having the potential for confusion with Voltaren Gel due to the overlapping established names between the products.

DMETS also 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. Additionally, postmarket reporting has not demonstrated any confusion with the aforementioned names. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Voltaren Gel.

Upon initial analysis of the eleven aforementioned names, Volmax, Voltaren Emulgel, Verelan, Adrenalin, Ventolin, Demulen, Cataflam, Solaraze, and Viractin Gel, will not be reviewed further due to lack of convincing look-alike and sound-alike similarites with Voltaren Gel, in addition to having a lack of overlapping product characteristics with

Voltaren Gel. Although Voltaren Emulgel is diclofenac topical gel 1%, it was not reviewed further because it is only available outside of the United States. Additionally, Cataflam and Solaraze were not reviewed further due to lack of overlapping product characteristics as well as distinctively different tradenames between the products. The remaining two names, Voltaren and Voltaren XR, warranted further evaluation based on look-alike, sound-alike and product characteristics (see Table 1 below).

Table 1: Potential Look-Alike Names Identified for Voltaren Gel.

Product Name	**Dosage form(s), Established name**	**Usual adult dose***	**Other****
Voltaren Gel	Diclofenac Topical Gel 1%	Upper extremities: Apply 2 grams to affected joints four times a day. Lower extremities: Apply 4 grams to affected joints four times a day.	N/A
Voltaren Ophthalmic	Ophthalmic solution 0.1%	*Cataract surgery*: Instill one drop to the affected eye 4 times a day beginning 24 hours after surgery for 2 weeks post surgery. *Corneal Refractive Surgery*: Instill 1 or 2 drops within 1 hour prior to surgery and within 15 minutes after surgery to affected eye(s). Continue to instill 1 or 2 drops in affected eye(s) 4 times a day for up to 3 days.	LA/SA
Voltaren	Delayed Release Tablets 25 mg, 50 mg, and 75 mg	*Osteoarthritis*: 50 mg two or three times daily or 75 mg twice a day. *Rheumatoid arthritis*: 50 mg three to four times a day or 75 mg twice a day. *Ankylosing spondylitis*: 25 mg four times daily and 25 mg at bedtime *Analgesia and primary dysmenorrhea*: 50 mg three times a day.	LA/SA
Voltaren XR	Extended Release Tablets 100 mg	*Chronic therapy*: 100 mg once a day	LA

*Frequently used, not all-inclusive.
**LA (look-alike), SA (sound-alike), NA (not applicable)

Based on postmarketing experience, DMETS acknowledges the potential for confusion of Voltaren Gel with other currently marketed dosage forms of Voltaren, due to a knowledge deficit on the part of healthcare providers upon initial release of the new product, Voltaren Gel. Currently, Voltaren is available in the marketplace as an ophthalmic solution (Voltaren Ophthalmic), and in delayed-release (Voltaren) and extended-release (Voltaren XR) tablets.

Currently marketed Voltaren products, (Voltaren Ophthalmic (diclofenac 0.1%) solution, Voltaren, and Voltaren XR) and the proposed proprietary name Voltaren Gel, share the same root name "Voltaren", which is the main contributing factor to the look-alike and

Voltaren 0.1% drops Voltaren Voltaren XR
Voltaren 1% gel Voltaren 1% Voltaren Gel

sound-alike similarities with Voltaren Gel. However, there are also differences between these products which may help to minimize the potential for confusion between the names as discussed below.

a. Voltaren Ophthalmic 0.1% solution is indicated for the treatment of postoperative inflammation following cataract extraction and for the temporary relief of pain and photophobia following corneal refractive surgery.

   Although the dosage forms are different (Ophthalmic vs Gel), it is possible for the dosage form to be omitted by prescribers when writing orders for Voltaren, which may cause confusion. The potential for confusion may be compounded by the fact that the two products have similar numerical strengths (0.1% vs 1%), and the same frequency of administration (four times a day). However, the detailed directions needed for proper administration of ophthalmic drops following eye surgery may minimize the potential for confusion between the two names because prescribers would need to include the route of administration and indicate into which eye(s) to instill drops.

   Likewise, prescribers would need to include specific directions when ordering Voltaren Gel because the dose (2 grams vs 4 grams), varies depending on the affected area being treated. Voltaren Gel will also be provided with dosing cards for measuring out the prescribed dosage which should also minimize the potential for confusion.

b. Voltaren (delayed release) and Voltaren XR (extended-release) are nonsteroidal anti-inlfammatory drug products indicated for the treatment of pain as well as fever. There are also numerous generic, delayed-release and extended-release, diclofenac sodium products available in the market.

   The modifier "gel", in the proposed proprietary name "Voltaren Gel", may however help to distinguish it from other Voltaren products. Although prescribers may omit the modifier when ordering Voltaren Gel, the different product characteristics of the gel dosage form may help to distinguish it from the oral tablet formulations. For example, Voltaren Gel will be available in a 1% strength and is dosed in either 2 gram or 4 gram applications which is very different from the multiple strengths of Voltaren delayed release tablets (25 mg, 50 mg, and 75 mg), and the strength of Voltaren extended-release tablets (100 mg). Despite the overlap in the frequency of administration (four times a day) for some of the indications of both products, their

different product characteristics may minimize confusion and decrease the potential for errors to occur. Additionally, if Voltaren Gel is approved, there will be three different dosage forms of diclofenac sodium products in the market, which will require prescribers to include the dosage form on prescriptions to ensure that the correct drug is dispensed. Furthermore, the sponsor should implement an educational campaign for all healthcare providers to inform them of the new dosage form of diclofenac sodium.

Considering the different dosage forms and product characteristics for currently marketed Voltaren products discussed above, DMETS believes that the potential risk for confusion between the currently marketed Voltaren products discussed above, and Voltaren Gel, is sufficiently minimized.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels and carton labeling of Voltaren Gel, DMETS has focused on safety issues relating to possible medication errors. We have identified the following areas of improvement, in the interest of minimizing potential user error and maximizing patient safety.

1. GENERAL COMMENTS

   a. Ensure that the established name is at least ½ the size of the proprietary name and that it appears prominently in accordance with 21 CFR 201.10(g)(2).

   b. Remove or decrease the prominence of the graphic located to the right of the tradename. As currently presented, it is distracting and draws attention away from important information such as the tradename, established name, and product strength.

   c. Delete the word "topical", that is currently in the established name. "Topical gel" is not a part of the recognized dosage form.

   d. Include a route of administration statement under the established name. For example, the label may read:

      "(diclofenac sodium) gel 1%
      For Topical Use Only"

2. CONTAINER LABEL

   a. See GENERAL COMMENTS 1a through 1d.

3. PHYSICIAN SAMPLE CONTAINER LABEL

   a. See GENERAL COMMENTS 1a through 1d.

   b. Revise ' ——› ' to read "Physician's Sample". Additionally, increase the prominence of this statement.

4. CARTON LABELING

a. The statement ' _____ ' should be changed to read "For topical use only".

5. DOSING CARDS

DMETS recommends that each dosing card provide only one designated area on which to apply Voltaren Gel to avoid dosing errors. Using a single application area which is clearly demarcated to show measured dosing amounts of 2 grams vs

4 grams, similar to a measuring tape, may be more effective for patients to use correctly.

ii. Include more specific instructions for patients to consistently dispense the correct dose using the dosing card.

iii. Provide instructions for how patients are to apply the gel to the affected area.

iv. The dosing card instructions state, '

The sponsor should consider ways to make it more apparent to all patients, which side of each dosing sheet is the printed side.

v. DMETS questions whether enough dosing sheets will be enclosed in each package for a patient to apply Voltaren Gel four times a day for the prescribed treatment period. Patients may have more than one affected area on which to apply Voltaren Gel and may need more than one dosing card for each prescribed treatment area.

vi. Include i

vii. Include instructions for discarding used dosing cards in a safe place out of the reach of children and pets.

5. PACKAGE INSERT LABELING

DMETS recommends including a Patient Package Insert which gives clear and detailed instructions for how to use the dosing card to optimize treatment. Instructions with diagrams would be very useful for patients to maximize effective administration and minimize medication errors.

Appendix A. DMETS prescription study results for Voltaren Gel

Inpatient	Outpatient	Voice
Voltaren Gel 1%	Voltaren Gel 1%	Voltaren Gel 1%
Voltaren Gel 1%	Voltaren Gel 1%	Voltaren Gel 1%
Voltaren Gel 1%	Voltaren Gel 1%	Volperingel 1%
Voltaren Gel 1%	Voltaren gel 1%	Paringel 1%
Voltaren Gel 1%	Voltaren Gel 1%	Volperengel
Voltaren Gel 1%	Voltaren Gel 1%	Voltaren gel 1%
Voltaren Gel 1%	Voltaren Gel 1%	Parengel 1%
Voltaren Gel 1%	Voltaren Gel 1%	Voltaren gel 1%
Voltaren Gel 1%	Voltaren Gel 1%	Volparen Gel
Voltaren Gel 1%	Voltaren Gel	Voltaren Gel
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