

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-947

PROPRIETARY NAME REVIEW(S)



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

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Subject: Proprietary Name Review

Drug Name(s): Pennsaid
(Diclofenac Sodium) Topical Solution 1.5% w/w

Application Type/Number: NDA # 20-947

Applicant/Applicant: Nuvo Research Inc.

OSE RCM #: 2009-480

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EXECUTIVE SUMMARY

This re-assessment of the proprietary name is written in response to a notification that a regulatory action for NDA 20-947 will occur within 90 days. DMEPA found the proposed proprietary name, Pennsaid, acceptable in 3 previous reviews (OSE RCM# 02-0010 dated March 8, 2002; 02-0010-1 dated July 8, 2002; and 02-0010-2 dated October 12, 2006. Since the earlier reviews, Pennsaid's indication has been narrowed from _____

_____ However, we reviewed the names previously evaluated in these reviews and determined that this change in indication did not affect the analyses.

During this re-review we identified and evaluated 19 new names for their similarity to Pennsaid. DDMAC did not identify any promotional concerns with the name. The results of the Failure Mode and Effects Analysis found that the proposed name, Pennsaid, is not vulnerable to name confusion that could lead to medication errors with any of the 19 names. Thus, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Pennsaid, for this product.

DMEPA considers this a final review, however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Anesthesia, Analgesia, and Rheumatology Products should notify DMEPA because the proprietary name must be re-evaluated prior to the new anticipated approval date.

1 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a re-assessment of a proprietary name 90 days prior to approval of an application. Section 1.1 identifies the specific search criteria associated with the proposed proprietary name, Pennsaid.

1.1 PROPRIETARY NAME RISK ASSESSMENT

For this review, particular consideration was given to drug names beginning with the letter 'P' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.¹²

To identify drug names that may look similar to Pennsaid, the staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (eight letters), upstrokes (two, capital letter 'P' and lower case 'd'), downstrokes (one, if 'p' is lower case), cross-strokes (none), and dotted letters (one; lower case 'i'). Additionally, several letters in Pennsaid may be vulnerable to ambiguity when scripted, including the letter 'P' may appear as 'R', 'B', or 'D'; lower case 'e' may appear as lower case 'i' or 'o'; lower case 'n' may appear as lower case 'm', 'u', 'v', 'h', 's', or 'r'; lower case 's' may appear as lower case 'a' or 'n'; lower case 'a' may appear as lower case 'o' or 'u'; lower case 'i' may appear as lower case 'e'; and lower case 'd' may appear as lower case 't', 'ol', 'cl', or 'el'. As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Pennsaid.

When searching to identify potential names that may sound similar to Pennsaid, the medication error staff search for names with similar number of syllables (two or three), stresses (PENN-said or penn-SAID; pen-N-SAID or PEN-n-said), vowel sound pronunciation ("said" vs. "sed"), and placement of vowel

¹ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

² Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

b(4)

and consonant sounds. In addition, several letters in Pennsaid may be subject to misinterpretation when spoken, including the letter 'e' which may be misinterpreted as 'i'; the letter 's' may be misinterpreted as 'c' or 'z'; and the letter 'd' may be misinterpreted as 't'. As such, the staff also considers these alternate pronunciations when identifying drug names that may sound similar to Pennsaid. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

2 RESULTS

2.1 DATABASE AND INFORMATION SOURCES

The searches of the databases listed in Section 6 yielded a total of 12 names as having some similarity to the name Pennsaid.

Nine of the 12 names were thought to look like Pennsaid. These include Resaid, Penntuss, Pentasa, Pentids, Revlimid, Prevacid, Pencard _____ and Penecort. The remaining three names (Fensaid, Ansaid, and Pennsaid Plus) were thought to look and sound similar to Pennsaid. b(4)

Our searches also revealed that the proposed name, Pennsaid, is trademarked in many foreign countries. All of these trademarks are registered to Nuvo Research, Inc., which is the applicant of this NDA product. We note from the applicant's website (www.nuvoresearch.com) that Pennsaid, which contains diclofenac sodium, is currently available in foreign markets.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of July 6, 2009.

2.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by the DMEPA staff (see Section 2.1 above), and noted no additional names thought to have orthographic or phonetic similarity to Pennsaid.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

2.3 SAFETY EVALUATOR RISK ASSESSMENT

A total of 15 names were identified and evaluated in the previous Pennsaid proprietary name reviews. Since the earlier reviews, Pennsaid's indication has been narrowed from _____ b(4)

However, we reviewed the names previously evaluated in these reviews and determined that this change in indication did not affect the analyses. Therefore the original assessments are maintained.

Independent searches by the primary Safety Evaluator resulted in 15 additional names which were thought to look or sound similar to Pennsaid and represent a potential source of drug name confusion.

Five of the names were identified to have look-alike similarities (Pindac, Benemid, PemADD***, _____ and Renoquid). Four of the names were identified to have sound-alike similarities (Prinzide, Pimozide, Pepcid, and Femcet). The remaining 6 names (Fensaide, _____, Sensaid, Tensaid, _____ and Percocet), were identified to have look-alike and sound-alike similarities. b(4)

In this evaluation, a total of 27 names were identified by our searches. Eight of the 27 names identified by our searches were evaluated in previous OSE reviews of the proposed name (02-0010, 02-0010-1, and 02-0010-2). The 8 previously reviewed names were removed from further evaluation (See Appendix B). As such, a total of 19 newly identified names were analyzed to determine if the drug names could be confused with Pennsaid.

DDMAC had no concerns regarding the proposed name from a promotional perspective and did not offer any additional comments relating to the proposed name.

3 DISCUSSION

Nineteen names were evaluated for their potential similarity to the proposed name, Pennsaid.

Failure mode and effect analysis (FMEA) was applied to determine if the proposed name could potentially be confused with the 19 names and lead to medication errors. This analysis determined that the name similarity between Pennsaid was unlikely to result in medication errors with any of the 19 products for the reasons presented in Appendices C through H.

4 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Pennsaid, is not vulnerable to name confusion that could lead to medication errors. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Pennsaid, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Anesthesia, Analgesia, and Rheumatology Products should notify DMEPA because the proprietary name must be re-evaluated within 90 days of the anticipated approval date.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Chris Wheeler, OSE project manager, at 301-796-0151.

5 REFERENCES

5.1 OSE REVIEWS

Jahng, J. Proprietary Name Review for Pennsaid. OSE Review# 02-0010-2, October 12, 2006.

Lee, M. Proprietary Name Memo for Pennsaid. OSE Review# 02-0010-1, July 8, 2002.

Roselle, N. Proprietary Name Review for Pennsaid. OSE Review# 02-0010, March 8, 2002.

5.2 DATABASES

1. *Micromedex Integrated Index (<http://csi.micromedex.com>)*

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

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

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. 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. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. *Drug Facts and Comparisons, online version, St. Louis, MO (<http://factsandcomparisons.com>)*

Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. *AMF Decision Support System [DSS]*

DSS is a government database used to track individual submissions and assignments in review divisions.

5. *Division of Medication Errors Prevention and Analysis proprietary name consultation requests*

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

6. *Drugs@FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)*

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

7. *Electronic online version of the FDA Orange Book (<http://www.fda.gov/cder/ob/default.htm>)*

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. *U.S. Patent and Trademark Office (<http://www.uspto.gov>)*

USPTO provides information regarding patent and trademarks.

9. *Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)*

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

10. *Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at (www.thomson-thomson.com)*

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. *Natural Medicines Comprehensive Databases (www.naturaldatabase.com)*

Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. *Stat!Ref (www.statref.com)*

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

13. *USAN Stems (<http://www.ama-assn.org/ama/pub/category/4782.html>)*

USAN Stems List contains all the recognized USAN stems.

14. *Red Book Pharmacy's Fundamental Reference*

Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. *Lexi-Comp (www.lexi.com)*

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. *Medical Abbreviations Book*

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.³

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.⁴ DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.⁵ DMEPA provides the product characteristics considered for this review in section one.

³ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

⁴ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

⁵ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

⁶ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

Appendix B: Names previously reviewed and determined not to pose a safety risk.

Name	Name
Revlimid	Ansaid
Prevacid	Pimozide
Penecort	Pepcid
Benemid	Percocet

Appendix C: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Pennsaid	Country	Description
_____	Look	Greece	Isosorbide dinitrate
Fensaid	Look/Sound	Australia (no longer marketed)	Piroxicam
Fensaide	Look/Sound	India (no longer marketed)	Diclofenac sodium
_____	Look/Sound	India (no longer marketed)	Diclofenac sodium/paracetamol

b(4)

Appendix D: Proposed proprietary name that has never been marketed in the U.S.

Proprietary Name	Similarity to Pennsaid	Description	Disposition of Name
PemADD***	Look	(pemoline) tablets: 18.75 mg, 37.5 mg, 75 mg ANDA #: 75-726	Proposed name found acceptable by DMEPA; DDMAC objected to the name ; product was approved 3/30/01 without a proprietary name; product has been discontinued

Appendix E: Discontinued products (no generics available)

Proprietary Name	Similarity to Pennsaid	Description	Date discontinued
Resaid	Look	(phenylpropanolamine hydrochloride 75 mg/ chlorpheniramine maleate 12 mg) extended release capsule OR (phenylpropanolamine hydrochloride 50 mg/ chlorpheniramine maleate 8 mg/isopropamide 2.5 mg) timed release capsule	Discontinued in 2000; no information in DSS
Penntuss	Look	(chlorpheniramine polistirex 4 mg /codeine polistirex 10 mg) per 5 mL extended release oral suspension	Withdrawn by Commissioner 8/5/96 (per DSS)
Pentids	Look	(penicillin G potassium) Pentids '200': oral tablet 200,000 units; oral solution 200,000 units/5 mL Pentids '250': oral tablet 250,000 units Pentids '400': oral tablet 400,000 units; oral solution 400,000 units/5 mL Pentids '800': oral tablet 800,000 units	No information in DSS
Pencard Tab	Look	No information	Withdrawn by Commissioner 6/29/82 (per DSS)
—— Inj	Look	No information	Withdrawn by Commissioner 7/24/70 (per DSS)

b(4)

Pindac	Look	(pinacidil) extended release capsules; 12.5 mg, 25 mg	Withdrawn by Commissioner 8/5/96 (per DSS)
Renoquid	Look	(sulfacytine) tablet; 250 mg	Withdrawn by Commissioner 6/16/06 (per DSS)

Appendix F: Proprietary name identified on the USPTO website; no further information found in standard references listed in Section 5

Proprietary Name	Similarity to Pennsaid	Description
Pennsaid Plus	Look/Sound	Categorized as pharmaceuticals, namely, a topical prescription non-steroidal anti-inflammatory drug; according to the applicant's website Pennsaid Plus is an improved version of Pennsaid and is in preliminary testing; Pennsaid Plus contains the same active ingredient as Pennsaid (diclofenac)
Sensaid	Look/Sound	Live trademark; medical devices, namely, pulse oximeter sensors, probes and clips; owned by Sensidyne Acquisition, LP
Tensaid	Look/Sound	Dead trademark; medical apparatus, namely, a transcutaneous electrical nerve stimulator; cancelled 5/16/09; held by Electro-Therapeutic Devices, Inc.

	Look/Sound	Dead trademark; phospholipid associated pharmaceutical preparations for the treatment of pain, inflammation, fever and arthritis; abandoned 9/9/04; held by PLx Pharma, Inc.
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Appendix G: Products with no overlap in strength or dose

Proprietary Name	Similarity to Pennsaid	Strength	Usual Dose
Pentasa (mesalamine) controlled release capsules	Look	250 mg; 500 mg	1 gram orally 4 times a day
Prinzide (lisinopril/hydrochlorothiazide) tablets	Sound	10 mg/12.5 mg; 20 mg/12.5 mg; 20mg/25 mg (discontinued)	Initial: Lisinopril 10 mg/hydrochlorothiazide 12.5 mg or lisinopril 20 mg/hydrochlorothiazide 12.5 mg with further increases of either or both components could depend on clinical response.

Appendix H: Single Strength Product with Differentiating Product Characteristics

Product name with potential for confusion	Similarity to Pennsaid	Strength	Usual Dose	Other Differentiating Product Characteristics
Femcet * Product discontinued (no information in DSS); generics available	Sound	Capsules: (acetaminophen 325 mg /butalbital 50 mg/ caffeine 40 mg)	1 to 2 capsules orally every 4 hours as needed. Maximum of 6 capsules per day	Dosage form: Oral capsule vs. topical solution Route of administration: Oral vs. topical Dose: 1 to 2 capsules vs. 40 drops per knee Frequency: Every 4 hours as needed vs. 4 times a day

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

/s/

KELLIE A TAYLOR
07/29/2009

DENISE P TOYER
07/30/2009

CAROL A HOLQUIST
07/30/2009

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; White Oak 22, Mail Stop 4447)

DATE RECEIVED: 08/11/2006	DESIRED COMPLETION DATE: 10/27/2006	OSE REVIEW #: 02-0010-2
DATE OF DOCUMENT: 06/28/2006	PDUFA DATE: 12/28/2006	

TO: Bob Rappaport, M.D.
Director, Division of Anesthesia, Analgesia, and Rheumatology Products
HFD-170

THROUGH: Alina R. Mahmud, R.Ph., MS, Team Leader
Denise P. Toyer, Pharm.D., Deputy Director
Carol A. Holquist, R.Ph., Director
Division of Medication Errors and Technical Support, HFD-420

FROM: Jinhee L. Jahng, Pharm.D., Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME:
Pennsaid
(Diclofenac Sodium) Topical Solution
1.5%

SPONSOR: Dimethaid International, Inc.
(c/o Nuvo Research, Inc.)

NDA #: 20-947

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Pennsaid. We consider this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name with its associated labels and labeling must be re-evaluated. A re-review of the name before the NDA approval will rule out any objections based upon approvals of other proprietary/established names from this date forward.
2. DMETS recommends implementation of the label and labeling recommendations 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 Pennsaid acceptable from a promotional perspective.

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 Diane Smith, Project Manager, at 301-796-0538.

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

PROPRIETARY NAME, LABEL, AND PACKAGING REVIEW

DATE OF REVIEW: October 12, 2006

NDA #: 20-947

NAME OF DRUG: Pennsaid
(Diclofenac Sodium) Topical Solution
1.5%

NDA HOLDER: Dimethaid International, Inc. (c/o Nuvo Research, Inc.)

*****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 Anesthesia, Analgesia, and Rheumatology Products (HFD-170), for re-assessment of the proprietary name, "Pennsaid", regarding potential name confusion with other proprietary or established drug names. DMETS found the name, Pennsaid, acceptable in two previous reviews dated March 8, 2002 and July 8, 2002 (ODS Consult 02-0010 and ODS Consult 02-0010-1, respectively). Container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Pennsaid is the proposed proprietary name for diclofenac sodium topical solution. Pennsaid is indicated for use as a topical treatment for relief of the signs and symptoms of osteoarthritis of the knee(s). Pennsaid will be available as a 1.5% clear, colorless to faintly pink solution in 15 mL (Physician Sample), _____ and 60 mL bottles with dropper caps. The recommended dosage is the application of 40 drops per knee, four times a day. To avoid spillage, dispense Pennsaid 10 drops at time either directly onto the knee or first into the hand and then onto the knee. Spread Pennsaid evenly around the front, back and sides of the knee. Repeat this procedure until 40 drops have been applied and the knee is completely covered with solution. To treat the other knee, repeat the procedure. Allow several minutes for Pennsaid to dry. Avoid contact with the eyes or mucous membranes. After application, wash the hands. The Pennsaid is contraindicated in patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDS. It is also contraindicated for the treatment of peri-operative pain in the setting of the coronary artery bypass (CABG) surgery and in those patients with known hypersensitivity to diclofenac sodium or any other component of Pennsaid.

b(4)

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 Pennsaid 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. Since this was a re-review, DMETS did not conduct another prescription study on 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, Pennsaid. 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 finds the proprietary name Pennsaid acceptable from a promotional perspective.
2. The Expert Panel identified eleven proprietary/established names that were thought to have the potential for confusion with Pennsaid. Similarly, through independent search, two additional names, Revlimid and _____^{***} were also determined to have potential for confusion with Pennsaid. These products are listed in Table 1 (see pages 4 and 5), along with the dosage forms available and usual dosage.

b(4)

¹ MICROMEDEX Integrated Index, 2006, 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 98-06, 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

*** Name pending approval. Not FOI releasable.

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

Benemid (discontinued)	Probenecid Tablets 500 mg	For gout: ½ tablet (250 mg) twice a day for 1 week, followed by 500 mg twice a day thereafter.	LA
PanMist-DM	Dextromethorphan, Guaifenesin, & Pseudoephedrine HCl Syrup 15 mg/100 mg/40 mg	Up to 10 mL three to four times daily.	LA
PanMist-S	Pseudoephedrine HCl & Guaifenesin Syrup 40 mg/200 mg	≤ 10 mL four times daily.	
PanMist JR	Pseudoephedrine HCl & Guaifenesin Tablets 48 mg/595 mg	1 or 2 tablets every 12 hours up to 4 tablets/day.	
Paragard T 380A	Intrauterine Copper Contraceptive	As directed.	LA
Pimozide (established name)	Orap Tablets (proprietary name) 1 mg, 2 mg	Initial dose: 1 to 2 mg/day in divided doses. Thereafter increase dose every other day. Maintenance dose: Less than 0.2 mg/kg/day or 10 mg/day, whichever is less.	LA
Penecort	Hydrocortisone Solution, 1%	Apply to affected area 2 to 4 times daily depending on the severity of the condition.	LA
Percocet	Oxycodone HCl and Acetaminophen Tablets 2.5 mg/325 mg, 5 mg/325 mg, 7.5 mg/325 mg, 10 mg/325 mg, 7.5 mg/500 mg, 10 mg/650 mg	1 tablet every 6 hours. (Total daily dosage should not exceed 4000 mg APAP/60 mg oxycodone.)	LA
Periogard	Chlorhexidine Gluconate Oral Rinse, 0.12%	½ fluid ounce twice daily oral rinsing for 30 seconds, morning and evening after toothbrushing.	LA
Prevacid	Lansoprazole Delayed-release Capsules 15 mg, 30 mg	15 mg to 30 mg once or twice daily depending on indication. Duration of therapy depends on indication.	LA
	Lansoprazole Delayed-release Granules for Oral Suspension 15 mg		
Prevacid SoluTab	Lansoprazole Delayed-release Tablets, orally disintegrating 15 mg, 30 mg		
Prevacid IV	Lansoprazole Powder for Injection, lyophilized 30 mg/vial	30 mg IV per day for up to 7 days.	
Prinivil	Lisinopril Tablets 2.5 mg, 5 mg, 10 mg, 20 mg, 30 mg, 40 mg	2.5 mg to 40 mg daily, depending on indication and concomitant disease states.	LA
Provigil	Modafinil Tablets 100 mg, 200 mg	200 mg daily.	LA
Remicade	Infliximab Powder for Injection, lyophilized 100 mg	5 mg/kg IV at 0, 2, and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 to 8 weeks, depending on indication.	LA
Revlimid	Lenalidomide Capsules 5 mg, 10 mg, 15 mg, 25 mg	10 mg daily. Restricted distribution program.	LA

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

b(4)

B. SAFETY EVALUATOR RISK ASSESSMENT

1. Look-alike/Sound-alike Names

In reviewing the proprietary name, Pennsaid, the primary concerns relating to look-alike and sound-alike confusion with Pennsaid are Benemid, PanMist product line, Paragard, Pimozide, Penecort, Percocet, Periogard, Prevacid, Prinivil, Provigil, Remicade, ———, and Revlimid.

b(4)

Upon further analysis of the names, Paragard, Pimozide, Provigil, and Revlimid were not reviewed further due to a lack of convincing look-alike similarities with Pennsaid in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration and dosage formulation.

In review of the remaining names, we have the following comments:

- a. Benemid was found to have look-alike potential with Pennsaid. Benemid is a product containing probenecid and has been discontinued, however, it is still available in its generic form. Benemid was available as a 500 mg tablet. The usual dose for gout is ½ tablet (250 mg) twice a day for 1 week, followed by 500 mg twice a day thereafter.

Pennsaid
Benemid

Benemid and Pennsaid owe their look-alike characteristics to their similar looking beginnings and endings. The "B" and "P" may resemble each other, especially if the loop in "B" is not closed completely (see writing sample above). The middle letters, "-en-" and the last two letters "-id" are identical and placed in similar positions, but the "-sa-" in Pennsaid is distinct from the "m" in Benemid, and helps to differentiate the two names from one another.

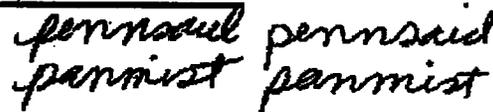
Benemid and Pennsaid vary with respect to dosage form (tablet vs. solution), route of administration (oral vs. topical), frequency of

*** Name pending approval. Not FOI releasable.

administration (twice daily vs. four times daily), and strength (500 mg vs. 1.5%). Both products are available in only one strength, which allows the prescriber to order either product without specifying the strength. A prescription written as "Pennsaid – As directed #60 mL" may be misinterpreted for "Benemid – As directed #60 tabs". However, according to data provided by Thomson & Thomson's SAEGIS™ Online Service, the last recorded sales of Benemid was in 1999. Thus, DMETS believes the potential for confusion is low given the aforementioned information in conjunction with the differences in appearance.

- b. PanMist and Pennsaid were found to have look-alike characteristics. The root name "PanMist" is part of a product line that is available by prescription only. PanMist is available as "PanMist-DM", "PanMist-S", and "PanMist JR". Each of the PanMist products contains guaifenesin and pseudoephedrine in varying amounts. PanMist-DM also contains dextromethorphan. The guaifenesin and pseudoephedrine act as a decongestant and expectorant combination used to relieve congestion and to treat cough due to colds, flu, or hay fever. The dextromethorphan component of PanMist-DM acts as a cough suppressant. PanMist-DM and Panmist-S are syrups and PanMist JR is in tablet form. The usual dose for the syrup products is up to 10 mL three to four times daily. For the tablet version, the usual dose is 1 or 2 tablets every 12 hours up to 4 tablets daily.

PanMist and Pennsaid's look-alike similarities may be attributed to their similar-looking beginnings ("Pan-" vs. "Pen-") and the presence of an upstroke character at the end of each name ("-d" and "-t"). The remaining letters help to differentiate the two names from each other (see writing samples below).



The PanMist syrups have an overlapping frequency of administration with Pennsaid (four times daily), but PanMist and Pennsaid vary with respect to dosage form (syrup or tablet vs. solution), route of administration (oral vs. topical), and strength (15 mg/100 mg/40 mg, 40 mg/200 mg, 48 mg/595 mg vs. 1.5 %). Also, since each "PanMist" product comes in different formulations, it is likely that the prescriber will have to specify which product they are ordering by including a modifier in their prescription. Thus, DMETS believes the potential for confusion to be minimal due to the differences in their appearance and dosage form.

- c. Penecort looks like Pennsaid when scripted. Penecort (hydrocortisone) is a corticosteroid used to reduce itching, redness, and swelling associated with various skin conditions. Penecort is available as a 1% topical solution by prescription only. The usual dose is to apply to the affected area two to four times daily, depending on the severity of the condition.

Penecort and Pennsaid have identical prefixes ("Pen-") and both have an upstroke character at the end ("t" vs. "d"). However, the letters "-ec-" vs. "

ns-" are distinct and may be differentiated when scripted (see writing sample below).

Pennsaid
Penecort

Penecort and Pennsaid share the same route of administration (topical), dosage form (solution), and frequency of administration (four times daily). Additionally, both products are available in only one strength, which allows the prescriber to order either product without specifying the strength. However, according to data provided by Thomson & Thomson's SAEGIS™ Online Service, the last recorded sales of Penecort was in 2003 and the sales value indicator was "low", which was also confirmed by Verispan. Thus, DMETS believes the potential for confusion is low given the aforementioned information in conjunction with the differences in appearance.

- d. Percocet was found to have look-alike similarities to Pennsaid when handwritten. Percocet is a narcotic analgesic containing oxycodone, an opioid, and acetaminophen. Percocet is indicated for moderate to severe pain and the usual dose is 1 tablet every 6 hours. Percocet comes available in multiple tablet strengths (2.5 mg/325 mg, 5 mg/325 mg, 7.5 mg/325 mg, 10 mg/325 mg, 7.5 mg/500 mg, 10 mg/650 mg).

Percocet and Pennsaid share similar beginnings ("Per-" vs. "Pen-") and they each have an upstroke character ("d" vs. "t") placed at the end. However, the middle letters ("-co-" vs. "-ns-") help to distinguish the two names from each other when scripted (see below).

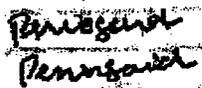
Pennsaid
Percocet

Percocet and Pennsaid vary with respect to dosage form (tablet vs. solution), route of administration (oral vs. topical), strength (2.5 mg/325 mg, 5 mg/325 mg, 7.5 mg/325 mg, 10 mg/325 mg, 7.5 mg/500 mg, 10 mg/650 mg vs. 1.5%), and controlled status (Schedule II vs. Schedule VI). And although they have a common frequency of administration (every 6 hours or four times daily), Percocet is available in multiple strengths and must be specified on the prescription. If a prescription for Pennsaid is misinterpreted as Percocet, omission of the strength would prompt the pharmacist to contact the prescriber for further clarification. Thus, DMETS believes the likelihood for confusion to be minimal given the differences in product characteristics and appearance.

- e. Periogard and Pennsaid were found to have look-alike characteristics. Periogard, an oral antibacterial cleansing agent containing chlorhexadine gluconate, is used for gingivitis. The usual dose is ½ fluid ounce for oral rinsing (30 seconds) twice daily after toothbrushing.

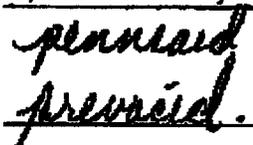
Both Periogard and Pennsaid have similar looking beginnings ("Per-" vs. "Pen-") and the endings ("-gard" vs. "-said") look-alike if the downstroke letter, "g" is not prominently scripted as demonstrated on page 8.

However, the "-io-" in Periogard helps to differentiate the two names from each other since it is distinct from the second "n" present in Pennsaid.

Handwritten cursive text showing "Periogard" on the top line and "Pennsaid" on the bottom line, illustrating the difference in the "io" and "n" characters.

Periogard and Pennsaid vary with respect to dosage form (oral rinse vs. solution), route of administration (oral vs. topical), frequency of administration (twice daily vs. four times daily), and strength (0.12% vs. 1.5%). Both are available in only one strength, which allows the prescriber to order either product without specifying the strength, however, the differences in appearance and product characteristics help lessen the potential for confusion. Thus, DMETS believes the likelihood for confusion is minimal.

- f. Prevacid and Pennsaid were found to look-alike when scripted. Prevacid (lansoprazole) is a proton pump inhibitor indicated for duodenal ulcer disease, erosive esophagitis, gastric hypersecretion, gastric ulcer, and gastroesophageal reflux disease. The usual dose is 15 mg to 30 mg once or twice daily, depending on the indication. If the patient is unable to tolerate the oral forms, there is an injectable product available.

Handwritten cursive text showing "Pennsaid" on the top line and "Prevacid" on the bottom line, illustrating the similarity in the "P" and "-acid/-said" endings.

Prevacid and Pennsaid both start with the letter "P" and have similar looking endings ("-acid" vs. "-said"). However, the remaining letters in each name are distinct and help to differentiate the two names from each other (see sample above).

Prevacid and Pennsaid vary with respect to dosage form (tablets/capsules/granules/injection vs. solution), route of administration (oral or intravenous vs. topical), and frequency of administration (once or twice daily vs. four times daily). They share a numerical similarity in strength (15 mg vs. 1.5%), however, the differences in orthographic and product characteristics help minimize the potential for confusion.

- g. Prinivil was found to have look-alike similarities with Pennsaid. Prinivil (lisinopril) is an angiotensin-converting enzyme inhibitor that is indicated for the treatment of hypertension, heart failure, and hemodynamically stable patients within 24 hours of acute myocardial infarction. The usual dose is 2.5 mg to 40 mg daily, depending on the indication and concomitant disease states. Prinivil is available as 2.5 mg, 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg tablets.

Prinivil and Pennsaid lend themselves to looking similar because they both begin with the letter "P" and end with upstroke letters ("l" vs. "d"). Additionally, they have an "n" and "i" in identical positions (fourth and seventh, respectively). Nonetheless, the letters present in the middle of each name ("-niv-" vs. "-nnsa-") help to differentiate the two from each other when scripted (see sample on page 9).

Pennsaid
Prinivil

Prinivil and Pennsaid also vary with respect to dosage form (tablets vs. solution), route of administration (oral vs. topical), frequency of administration (once daily vs. four times daily), and strength (2.5 mg, 5 mg, 10 mg, 20 mg, 30 mg, and 40 mg vs. 1.5%). Since multiple tablet strengths exist for Prinivil, the possibility that Prinivil and Pennsaid would be confused is minimized since the Prinivil strength must be specified. DMETS therefore believes the potential for confusion to be minimal given the differences in appearance and product characteristics.

- h. Remicade was found to look similar to Pennsaid when scripted. Remicade (infliximab) is an immunomodulator indicated for ankylosing spondylitis, crohn disease, psoriatic arthritis, rheumatoid arthritis, and ulcerative colitis. The usual dose is 5 mg/kg at 0, 2, and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 to 8 weeks, depending on the indication. Remicade is available as a 100 mg lyophilized powder for injection.

Remicade
Pennsaid

Remicade and Pennsaid share similar looking beginnings ("Remi-" vs. "Penn-") and the presence of a "d" at the end of each name. The "e" which trails the "d" in Remicade is easy to overlook if it is not precisely scripted (see writing sample above). Additionally, Remicade will most likely be used in an inpatient or clinic setting, whereas Pennsaid may be used on an outpatient basis. Remicade and Pennsaid vary with respect to dosage form (injection vs. solution), route of administration (intravenous vs. topical), frequency of administration (once every 0, 2, and 6 weeks vs. four times daily), and dosage strength (100 mg vs. 1.5%). For the aforementioned differences in product characteristics, DMETS believes the potential for error is minimal.

- i. _____ was identified as a name with similar appearance to Pennsaid. _____ is a proposed proprietary name for _____ and is currently under review by the Agency.

b(4)

b(4)

The names are orthographically similar because _____

b(4)

b(4)

2. Safety concerns with packaging configuration of _____ bottle

We note that the Pennsaid bottles will be packaged in _____ bottles with a dropper cap. However, we are concerned that the _____ bottle will resemble an ophthalmic, nasal, or otic dropper and that the dispenser (dropper) tip could promote the inadvertent use of Pennsaid topical solution to routes that would normally not be accessible if the tip was obtrusive. We question whether the packaging will be similar to the packaging of an ophthalmic, otic, inhalation, and/or nasal drug products. If so, then the dropper bottle with lid may be confusing for patients, leading the user to believe that Pennsaid is an ophthalmic, otic, nasal, or inhalation product. Post-marketing evidence demonstrates confusion exists with dermatologic products packaged in non-dermatologic container systems. DMETS has had several cases in which a topical product (i.e. Lotrisone), resembling an ophthalmic/otic product, was administered in the eyes or ears. We therefore recommend that if Pennsaid resembles any of the aforementioned packaging configurations, that it be repackaged into a container system that resembles those commonly used for dermatologic use, such as a roll-on applicator or a fabric-tipped applicator.

b(4)

III. COMMENTS TO THE SPONSOR:

Labeling, Packaging, and Safety Related Issues

In the review of the container labels, carton and insert labeling of Pennsaid, 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. SAFETY CONCERNS WITH THE PACKAGING CONFIGURATION OF THE _____ BOTTLE

b(4)

We note that the Pennsaid bottles will be packaged in _____ bottles with a dropper cap. However, we are concerned that the _____ bottle will resemble an ophthalmic, nasal, or otic dropper and that the dispenser (dropper) tip could promote the inadvertent use of Pennsaid topical solution to routes that would normally not be accessible if the tip was obtrusive. We question whether the packaging will be similar to the packaging of an ophthalmic, otic, inhalation, and/or nasal drug products. If so, then the dropper bottle with lid may be confusing for patients, leading the user to believe that Pennsaid is an ophthalmic, otic, nasal, or inhalation product. Post-marketing evidence demonstrates confusion and error exists with dermatologic products packaged in non-dermatologic container systems. DMETS has had several cases in which a topical product (i.e. Lotrisone), resembling an ophthalmic/otic product, was administered in the eyes or ears. We therefore recommend that if Pennsaid resembles any of the aforementioned packaging configurations, that it be repackaged into a container system that resembles those commonly used for dermatologic use, such as a roll-on applicator or a fabric-tipped applicator.

B. CONTAINER LABEL

1. Although we prefer that the sponsor repackage their product so that it does not resemble an ophthalmic/otic agent, if the Division allows them to market the proposed configuration, increase the prominence of the statement, _____ . We also recommend relocating this statement to the main principal display panel and revise it to read "For Topical Use Only". We would not recommend the _____ warning because we have learned from post-marketing medication error reports that this confuses health providers and patients alike. They see the word, _____ and think it can be used in the eye because they overlook the _____ statement.
2. The light grey and light blue font colors used for the proprietary and established names, as well as for the strength and dosage form are difficult to read against the white background color. To improve readability, use a darker font color. Also, having the proprietary name presented in two different font colors makes it appear that they are two separate names. Since this is not the case, revise the labels and labeling so that the proprietary name is in one uniform color.
3. Re-position the net quantity statements stated in "mL" and "fl oz" so that they are immediately adjacent to each other. In their current positions, it appears these volumes are independent of each other, rather than being varying expressions of same volume.

b(4)

4. Per 21 CFR 207.35(b)(i), the NDC number shall appear prominently in the top third of the principal display panel or it may appear as part of and contiguous to any bar-code symbol. Seeing as neither of these two conditions are met, relocate the NDC number so that it either appears in the top third of the principal display panel or so that it appears contiguous to the bar-code symbol.
5. A graphic design in the shape of a teardrop appears by the proprietary name and also as a graphic shadow. Per 21 CFR 202.1(a)(1), eliminate this graphic design or decrease the size so that it does not compete with the proprietary and established names and the strength. Similarly, the teardrop looks like an eye drop rather than a topical product. We are concerned that having this teardrop on the labels and labeling might encourage users to think that it may be used via the ophthalmic route.
6. Delete the blue line separating the proprietary name from the established name. There should be no intervening matter. Also, "Topical Solution" should immediately follow the established name and the strength should be its own statement. For example:

Pennsaid
(diclofenac sodium) Topical Solution
1.5 %

C. CARTON LABELING

1. See comments B1, B2, B4, B5, and B6.
2. Bar codes are not present on the labeling. Revise the labeling so that a bar code appears per 21 CFR 201.25.
3. The established name appears to be less than ½ the size of the proprietary name. Per 21 CFR 201.10(g)(2), revise the labeling so that it is at least ½ the size of the proprietary name.

D. INSERT LABELING

No comments

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

/s/

Jinhee Jahng
11/29/2006 04:45:52 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
11/29/2006 04:53:49 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
11/30/2006 08:52:56 AM
DRUG SAFETY OFFICE REVIEWER

Memo

To: Lee Simon, MD
Director, Division of Anti-Inflammatory, Analgesic, and Ophthalmologic Drug Products
HFD-550

From: Marci Lee, PharmD
Safety Evaluator, Division of Medication Errors and Technical Support, Office of Drug Safety
HFD-420

Through: Carol Holquist, RPh
Deputy Director, Division of Medication Errors and Technical Support, Office of Drug Safety
HFD-420

CC: Nancy Halonen
Project Manager
HFD-550

Date: July 8, 2002

Re: ODS Consult 02-0010-1; Pennsaid (Diclofenac Sodium Topical Solution) 1.5%; NDA 20-947

This memorandum is in response to a May 2, 2002 request from your Division for a re-review of the proprietary name, Pennsaid.

The Division of Medication Errors and Technical Support has not identified any additional proprietary or established names that have the potential for confusion with Pennsaid since we conducted our initial review on March 8, 2002 (ODS Consult 02-0010). Therefore, we have no objections to the use of this proprietary name. However, in addition to the labeling and packaging recommendations included in our initial review of Pennsaid, the sponsor should provide contact information for a US agent that will respond to any medical inquiries on the labels and labeling.

ODS considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary and/or established names from this date forward.

If you have any questions or need clarification, please contact Sammie Beam, Project Manager, at 301-827-3242.

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

/s/

Marci Ann Lee
7/8/02 02:28:28 PM
PHARMACIST

Carol Holquist
7/8/02 04:16:15 PM
PHARMACIST

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(ODS; HFD-400)

DATE RECEIVED: 1/29/02

DUE DATE: 3/31/02

ODS CONSULT: 02-0010

TO:

Lee Simon, M.D.
Director, Division of Anti-Inflammatory, Analgesic, and Ophthalmologic Drug Products
HFD-550

THROUGH:

Nancy Halonen
Project Manager
HFD-550

PRODUCT NAME:

Pennsaid
(Diclofenac Sodium Topical Solution) 1.5%

NDA SPONSOR:

Dimethaid Research, Inc. (Canada)

NDA #: 20-947

SAFETY EVALUATOR: Nora Roselle, PharmD

SUMMARY: In response to a consult from the Division of Anti-Inflammatory, Analgesic, and Ophthalmologic Drug Products (HFD-550), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name "Pennsaid" to determine the potential for confusion with approved proprietary and established names as well as pending names.

DMETS RECOMMENDATION:

DMETS has no objection to the use of the proprietary name, Pennsaid. This name must be re-evaluated 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 names from the signature date of this document. In addition, DMETS recommends implementation of the labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.

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**Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-400; Rm. 15B32
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: March 8, 2002
NDA NUMBER: 20-947
NAME OF DRUG: Pennsaid (Diclofenac Sodium Topical Solution) 1.5%
NDA HOLDER: Dimethaid Research, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Anti-Inflammatory, Analgesic, and Ophthalmologic Drug Products (HFD-550), for assessment of the tradename "Pennsaid", regarding potential name confusion with other proprietary/generic drug names. The proprietary name was also reviewed by the CDER Labeling and Nomenclature Committee on April 4, 1998 and found acceptable.

PRODUCT INFORMATION

Pennsaid is the proposed proprietary name for diclofenac sodium topical solution. Pennsaid is indicated for use as a topical treatment to relieve _____ Pennsaid will be supplied as a clear, colorless to faintly pink solution in 15 mL (Physician Sample), _____ and 60 mL bottles with dropper caps. The recommended dosage is the application of _____ four times a day. To avoid dripping, the solution should be applied a few drops at a time and spread over the entire joint area and allowed to dry. The use of Pennsaid is contraindicated in patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other oral NSAIDs or those with a known hypersensitivity to diclofenac sodium or any other component of Pennsaid.

b(4)

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 databases³ for existing drug names that sound alike or look alike to "Pennsaid" 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 trademark electronic search system⁴ (TESS) was conducted.

¹ MICROMEDEX Healthcare Intranet Series, 2002, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2002).

² Facts and Comparisons, 2002, Facts and Comparisons, St. Louis, MO.

³ The Established Evaluation System [EES], the Division of Medication Errors and Technical Support [DMETS] database of proprietary name consultation requests, New Drug Approvals 98-02, and the electronic online version of the FDA Orange Book.

⁴ WWW location <http://www.uspto.gov/web/menu/tm.html>

⁵ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

The Saegis⁵ 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 "Pennsaid". 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.

Several product names were identified in the Expert Panel Discussion (EPD) that were thought to have potential for confusion with Pennsaid. These products are listed in Table 1 (see page 4), along with the dosage forms available and usual FDA-approved dosage.

DDMAC did not have concerns about the name with regard to promotional claims.

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

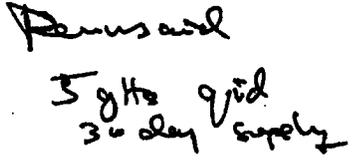
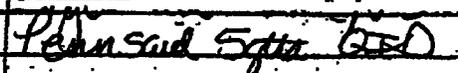
Product Name	Generic name, Dosage form(s)	Usual adult dose	Other**
Pennsaid	Diclofenac Sodium Topical Solution, 1.5%	Small joint (e.g. finger): 5 drops to affected area four times a day Medium joint (e.g. wrist): 20 drops to affected area four times a day Large joint (e.g. knee): 40 drops to affected area four times a day	
Ansaid	Flurbiprofen, 50 mg, 100 mg tablets	200-300 mg/day in 2, 3, or 4 divided doses	S/A
Pepcid	Famotidine, Tablet: 20 mg, 40 mg Powder-oral suspension: 40 mg/5 mL (50 mL) Injection: 10 mg/mL (2 mL, 4 mL), 0.4 mg/mL (50 mL)	Oral: Duodenal or gastric ulcer: 40 mg/day at bedtime for 4-8 weeks GERD: 20 mg twice daily for 6 weeks Hypersecretory conditions: 20 mg every 6 hours, up to 160 mg every 6 hours IV: 20 mg every 12 hours	S/A
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three studies were conducted by DMETS and involved 114 health professionals comprised of pharmacists, physicians, and nurses within FDA to determine the degree of confusion of Pennsaid with other drug names due to similarity in handwriting and verbal pronunciation of the name. An inpatient order and outpatient prescriptions were written, each consisting of marketed and unapproved drug products and a prescription for Pennsaid (see below). These prescriptions were scanned into a computer and were then 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 interpretation 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.

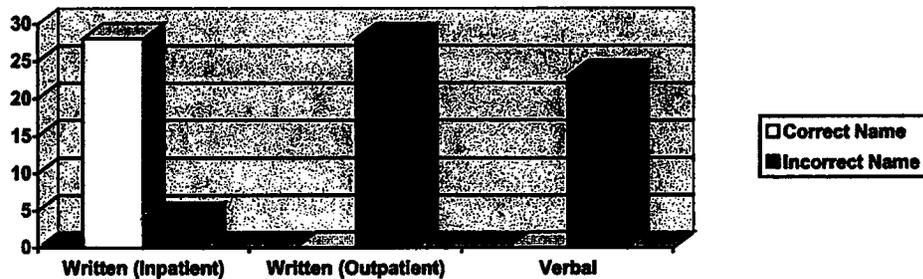
HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u></p> 	<p>Pennsaid Use 5 drops four times a day. Dispense a 30 day supply.</p>
<p><u>Inpatient RX:</u></p> 	

2. Results:

The results are summarized in Table I.

Table I

Study	# of Participants	# of Responses (%)	Correctly Interpreted Pennsaid	Incorrectly Interpreted
Written: Inpatient	40	32 (80%)	28 (88%)	4 (12%)
Outpatient	39	28 (72%)	0 (0%)	28 (100%)
Verbal: Outpatient	35	23 (66%)	0 (0%)	23 (100%)
Total	114	83 (73%)	28 (34%)	55 (66%)



Among the verbal outpatient Pennsaid prescriptions, none of the respondents interpreted the name correctly. Many of the incorrect name interpretations were misspelled/phonetic variations of "Pennsaid". Some of the incorrect interpretations included Pencid, Pensaid, Kensed, Pensed, Tensed, Kensaid, Pensid, Pensad, and Kenced.

When examining the interpretations from the written inpatient prescriptions, 28 of 32 (88%) respondents interpreted the name correctly. None of the respondents from the written outpatient prescriptions interpreted the name correctly. Some of the incorrect interpretations included Penn said, Pensaid, Perusaid, Renusaid, Penusaid, Pernusiel, Perusal, and Remersal.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name "Pennsaid", the primary concerns raised were related to sound-alike, look-alike names that already exist in the U.S. marketplace. The products considered having the greatest potential for name confusion with Pennsaid were Ansaid and Pepcid.

Ansaid (flurbiprofen) is a non-steroidal anti-inflammatory drug used in the acute or long-term treatment of the signs and symptoms of rheumatoid and osteoarthritis. Ansaid is available as a 50 mg or 100 mg oral tablet and is available only by prescription. Although Ansaid can sound-alike to Pennsaid (both contain the stem "nsaid") and both are used in the treatment of osteoarthritis, there are differences between the two that help to limit the risk for confusion. Ansaid is available as oral tablets, and Pennsaid is available as a topical solution. Ansaid is available in two different strengths (50 mg and 100 mg) and therefore would likely be prescribed with an accompanying strength. However, Pennsaid is only available in one strength (1.5%) and does not require a designating strength to be prescribed. In addition, a prescription for Pennsaid would most likely include the use of the word "drops/gtts" or "mL/cc" in order to provide dosing instructions or total amount dispensed, thus adding another checkpoint for errors. Due to the differences in dosage form, strength, route of administration, and dosing instructions the risk of a product mix-up between Ansaid and Pennsaid is minimal.

Pepcid (famotidine) is an antihistamine/H₂-blocker used in the treatment of duodenal ulcer, gastric ulcer, gastroesophageal reflux disease, and pathological hypersecretory conditions. The usual adult dose in the treatment of duodenal or gastric ulcer is 40 mg/day at bedtime for 4-8 weeks. Pepcid is available as 20 mg and 40 mg oral tablets, a 40 mg/5 mL (50 mL) powder for oral suspension, a 10 mg/mL injection (2 mL and 4 mL), and a 0.4 mg/mL injection (50 mL). Pepcid and Pennsaid can sound-alike because each name begins with the letter "Pe" and ends in the sound-alike stem "said" or "cid". Although Pepcid and Pennsaid sound slightly similar, the two drugs have many factors that help to distinguish one from the other. Both drugs have different indications for use and are available in different dosage forms (tablet/suspension/injection vs. topical solution). Similarly, Pepcid and Pennsaid have different dosage strengths and routes of administration. Thus, due to the differences in indication, dosage form, strength, and route of administration the risk of confusion between these two products is low.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In review of the container labels and insert labeling of Pennsaid, DMETS has attempted to focus on the safety issues relating to possible medication errors. DMETS has reviewed the current container labels and carton and insert labeling and has identified several areas of possible improvement, which might minimize potential user error. Container labels and carton labeling for the 15 mL (Physician Sample) and _____ bottles were not provided for review and comment.

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A. CONTAINER LABEL (60 mL)

1. Relocate the established name to appear beneath the proprietary name. Additionally, revise the established name to read "Diclofenac Sodium Topical Solution". The strength should appear outside of the established name. For example:

PENNSAID
(Diclofenac Sodium Topical Solution) 1.5%

2. We recommend the inclusion of the statement "FOR EXTERNAL USE ONLY" on the principal display panel.
3. Revise _____ to read "USUAL DOSAGE".

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B. CARTON LABELING

1. See comments above.
2. We recommend relocating the net quantity statement lower on the principal display panel of the carton labeling so that it appears away from the product strength and has less prominence. Additionally, a space should be inserted between "60" and "mL".
3. We recommend adding the "Rx only" statement to appear on the principal display panel.
4. We recommend relocating the "Marketed by" statement to the side display panel in conjunction with the associated manufacturer statements.

C. INSERT LABELING

1. See comment A1.
2. Revise the insert labeling so that the proprietary and established names are written the same way throughout the text.

IV. RECOMMENDATIONS:

DMETS has no objections to the use of the proprietary name, Pennsaid.

This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated 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 names from this date forward.

DMETS recommends the above labeling revisions 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.

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 Sammie Beam, project manager, at 301-827-3242.

Nora Roselle, PharmD
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

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

/s/

Nora L. Roselle
3/11/02 07:48:02 AM
CSO

Carol Holquist
3/11/02 07:49:51 AM
PHARMACIST

Jerry Phillips
3/12/02 06:40:32 AM
DIRECTOR

REQUEST FOR TRADEMARK REVIEW

438
3-11-98

TO: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair, (HFD-530) CRP2

FROM: Division of Anti-inflammatory, Analgesic and Ophthalmic Products, HFD-550
Attention: Charlotte Yaciw Phone: 827-2511

DATE: 3/12/98

SUBJECT: Request for Assessment of a Trademark for a Proposed Drug Product

Application: NDA 20-947

Proposed Trademark: Pennsaid™

Company Name: Dimethaid Research, Inc (Canada)

Established name, including dosage form: diclofenac sodium topical lotion

Other trademarks by the same firm for companion products: None

Indications for Use (may be a summary if proposed statement is lengthy): _____
_____ Studies were done on osteoarthritic knee pain.

b(4)

Initial comments from the submitter (concerns, observations, etc.): This product is a solution of diclofenac sodium (1.5%) in a vehicle which contains DMSO, glycerin, propylene glycol ethanol and water. It is rubbed on the skin over the affected joint.