

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-193

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO22, Mailstop 4447)**

DATE RECEIVED: October 9, 2007	DESIRED COMPLETION DATE: February 15, 2008 RUDFA DATE: July 24, 2008	OSE REVIEW #: 2007-2096
DATE OF DOCUMENT: September 15, 2007		

TO: Janice Soreth, MD
Director, Division of Anti-Infective and Ophthalmology Products
HFD-520

THROUGH: Linda Y. Kim-Jung, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Errors and Technical Support

FROM: Loretta Holmes, BSN, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME: Navstel
(Balanced salt intraocular irrigating solution enriched with bicarbonate, dextrose, glutathione and hypromellose)
250 mL and 500 mL

A #: 22-193

SPONSOR: Alcon Laboratories

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Navstel. 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 or established names from the signature date of this document.
2. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review in order to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name, Navstel, 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. Please copy DMETS on any correspondence to the sponsor pertaining to this issue. If you have further questions or need clarifications, please contact Anne Crandall, OSE Project Manager, at 301-796-2282.

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

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: January 2, 2008

NDA #: 22-193

NAME OF DRUG: Navstel
(Balanced salt intraocular irrigating solution enriched with bicarbonate, dextrose, glutathione and hypromellose)
250 mL and 500 mL

NDA HOLDER: Alcon Laboratories

I. INTRODUCTION:

This review was written in response to a request from the Division of Anti-Infective and Ophthalmology Products (HFD-520), for assessment of the proposed proprietary name, Navstel, regarding potential name confusion with other proprietary or established drug names. Container labels and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Navstel is a sterile intraocular irrigating solution indicated for use during surgical procedures involving perfusion of the eye. The solution should be used according to the standard technique employed by the operating surgeon. Navstel will be supplied in two sizes: 250 mL and 500 mL. Each size consists of two packages for reconstitution prior to use: the 250 mL size consists of a 250 mL glass bottle containing 240 mL (Part I) and a 10 mL glass vial (Part II); the 500 mL size consists of a 500 mL glass bottle containing 480 mL (Part I) and a 20 mL glass vial (Part II). Part I contains: hypromellose, sodium chloride, potassium chloride, dibasic sodium phosphate, sodium bicarbonate, hydrochloric acid and/or sodium hydroxide (to adjust pH) in water for injection USP. Part II contains: calcium chloride, magnesium chloride, dextrose, glutathione disulfide (oxidized glutathione), in water for injection USP. Navstel should be reconstituted just prior to use in surgery. This is done by transferring the contents of the Part I bottle to the Part II bottle via a "Vacuum Transfer Device" that is supplied with Navstel. The resulting solution in the Part II bottle is gently mixed until uniform and is then ready for use. Navstel is for single patient use and should be used within 6 hours of reconstitution.

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 "Navstel" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁵. The Saegis⁶ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name. Following completion of these initial steps, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates postmarketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the drug 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 proposed proprietary name, Navstel. 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, Navstel, acceptable from a promotional perspective.
2. The Expert Panel identified twenty-one proprietary names that were thought to have the potential for confusion with Navstel. They are: Navane, Navelbine, Nardil, Novafil, Navirel, Nasteril, Vantas, Vantin, Monistat, Novafed A, Havrix, Astelin, Nasarel, Novarel, Nastil, Novastan, Novacet, Novasal, Ponstel, Nortrel, and Levatol.

¹ MICROMEDEX Integrated Index, 2008, 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, 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

C. 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 Navstel with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employed a total of 123 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 Navstel (see below). 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. A total of 36 participants responded to these studies.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Inpatient RX:</u> <i>Navstel</i> <i>To be used before procedure</i></p>	<p>“Navstel, one bottle to be used before procedure”</p>
<p><u>Outpatient RX:</u> <i>Navstel</i> <i>41 bottle</i> <i>To be used before procedure</i></p>	

2. Results:

Three respondents from the verbal prescription study misinterpreted the proposed name as Nafcil, a previously marketed U.S. drug product and one respondent in the same study misinterpreted the name as Nafsil which sounds and looks similar to Nafcil. Additionally, two respondents from the verbal prescription study misinterpreted the name as Nastil, a drug product marketed in Mexico. See Appendix A for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Navstel, the following names were identified as having a similar appearance or sound to Navstel: Navane, Navelbine, Nardil, Novafil, Navirel, Nasteril, Vantas, Vantin, Monistat, Novafed A, Havrix, Astelin, Nasarel, Novarel, Nastil, Novastan, Novacet, Novasal, Ponstel, Nortrel, and Levatol.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was confirmation that Navstel could be confused with Nafcil and Nastil. Three respondents from the verbal prescription study misinterpreted the name as Nafcil

and one respondent in the same study misinterpreted the name as Nafsil which looks and sounds similar to Nafcil. Nafcil was not identified by the EPD panel as having look-alike/sound-alike similarities to Navstel. Nafcil was a previously marketed drug product in the U.S., however, it has been discontinued. Additionally, two respondents from the verbal prescription study misinterpreted the name as Nastil, a foreign drug product marketed in Mexico. The remaining misinterpretations were misspelled/phonetic variations of the proposed name, Navstel.

Upon initial review of the twenty-two names identified as having similar appearance and/or sound to Navstel, it was determined that the following nineteen (19) names (Navane, Navelbine, Nardil, Novafil, Navirel, Nasteril, Vantas, Vantin, Monistat, Novafed A, Havrix, Astelin, Nastil, Novastan, Novacet, Novasal, Ponstel, Nortrel, and LevatoI) lacked convincing look-alike/sound-alike similarities with Navstel and/or have numerous differentiating product characteristics such as the product strength, indication of use, frequency of administration, route of administration and dosage formulation (see below):

- The following products differ from Navstel in strength, dose, route of administration, indication of use, and context of use: Navane (thiothixene), Navelbine (vinorelbine tartrate), Nardil (phenelzine sulfate), Vantas (histrelin acetate), Vantin (cefepodoxime proxetil), Monistat (miconazole nitrate), Novafed A (chlorpheniramine maleate and pseudoephedrine hydrochloride), Havrix (hepatitis A vaccine, inactivated), Astelin (azelastine hydrochloride), Novasal (magnesium salicylate tetrahydrate), Ponstel (mefenamic acid), Nortrel (norethindrone and ethinyl estradiol), and LevatoI (penbutolol).
- Novafil: Novafil is not a drug product. It is a brand of surgical sutures and, therefore, the context of use for this product differs from that of Navstel.
- Navirel, Nasteril, Nastil, and Novastan: These are foreign drug products in Denmark and Poland (Navirel), Argentina (Nasteril), Mexico (Nastil), and Sweden and Japan (Novastan). Product specific information such as strength, indication of use, dosage and administration was not available for these products.
- Novacet (sodium sulfacetamide and sulfur): Product specific information for this product was not available. It appears that this product has been discontinued. The year of last recorded sales for this product was 2002⁷.

The remaining three names (Novarel, Nasarel, and Nafcil) warranted further evaluation based on orthographic and/or phonetic similarities. However, upon further analysis, Novarel, Nasarel, and Nafcil were assessed as having minimal risk of confusion because of differentiating product characteristics listed in the “Differing Product Characteristics” column in Table 1 (page 6).

⁷ Data provided by Thomson & Thomson’s SAEGIS™ Online Service, available at www.thomson-thomson.com

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

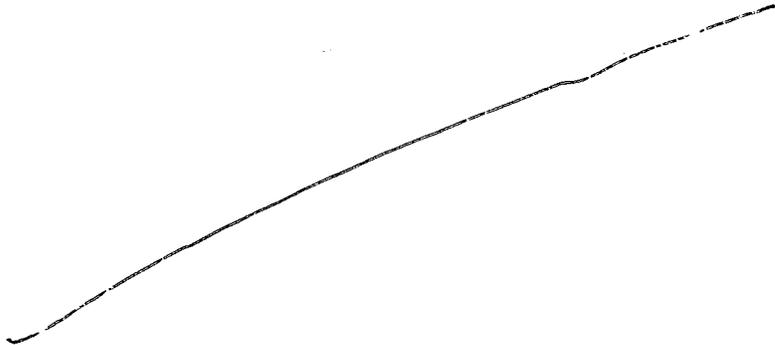
Product Name	Similar Product Name	Other	Differentiating Characteristics
Novarel	Human chorionic gonadotropin Powder for injection 10,000 units/vial	Administered by intramuscular (IM) route of administration: <u>Prepubertal cryptorchidism</u> : 4,000 units three times per week for 3 weeks; 5,000 units every second day for 4 injections; 15 injections of 500 units to 1,000 units over a period of 6 weeks, or 500 units three times per week for 4-6 weeks. <u>Hypogonadism</u> : 500 units to 1,000 units three times per week for 3 weeks, followed by the same dose twice a week for 3 weeks; 4,000 units three times per week for 6-9 months following which the dose may be decreased to 2,000 units three times per week for an additional 3 months. <u>Induction of ovulation in pregnancy</u> : 5,000 to 10,000 units one day following the last dose of menotropins.	LA <i>No overlap</i> • Dose : ➢500 units to 10,000 units vs. inexact dose • Dosage form : ➢Powder for injection vs. solution for irrigation • Product strength : ➢10,000 units/vial vs. multiple ingredient strengths • Route of administration : ➢Intramuscular vs. intraocular • Indication of use : ➢Prepubertal cryptorchidism, hypogonadism, and induction of ovulation in pregnancy vs. intraocular irrigation • Context of use : ➢Navstel use will likely be limited to areas where ophthalmic surgical procedures are performed.
Nasarel	Flunisolide Nasal spray 0.025% (29 mcg/actuation)	<u>Allergic rhinitis</u> : 2 sprays each nostril twice daily, may increase to 2 sprays three times per day.	LA <i>No overlap</i> • Dose : ➢2 sprays vs. inexact dose • Product strength : ➢(29 mcg/actuation) vs. multiple ingredient strengths • Route of administration : ➢Intranasal vs. intraocular • Frequency of administration : ➢Two or three times per day vs. once Indication of use : ➢Allergic rhinitis vs. intraocular irrigation • Context of use : ➢Navstel use will likely be limited to areas where ophthalmic surgical procedures are performed

the risk for the reconstitution step to be omitted.

4. The Applicant markets BSS Plus (balanced salt solution enriched with bicarbonate, dextrose, and glutathione), a sterile intraocular irrigating solution that is similar to Navstel. If the Applicant plans to continue to market BSS Plus, ensure that the labels for Navstel are clearly differentiated from those of BSS Plus in order to minimize any look-alike similarities between the products in order to minimize product selection errors.

B. CONTAINER LABEL (Part I, 250 mL and 500 mL)

1. See General Comments A-1, A-2 and A-4.
2. When the bottle is hung, all of the written information will appear upside down (except for the red block area where "SINGLE PATIENT USE ONLY" is printed. We recommend that information identifying the product (e.g., proprietary name, established name, volume, etc.) also be presented such that when the bottle is hung, the information appears right side up.



b(4)

C. INSERT LABELING

1. In the Dosage and Administration section under "Reconstitution Instructions" there are 10 steps that describe the process, yet there is only one diagram and that diagram shows little detail. The diagram needs to be more detailed in order to effectively show the proper reconstitution method. Additionally, we recommend that additional detailed diagrams be added in order to clearly demonstrate what is described in the written instructions. Furthermore, include pictures and text that identify the items included with the product (e.g., the Vacuum Transfer Device).
2. The "Reconstitution Instructions" state that a "Vacuum Transfer Device" is supplied. However, the "How Supplied/Storage and Handling" section, does not list this item. Please state all of the items supplied with this product in the "How Supplied/Storage and Handling" section of the insert labeling.

Appendix A. Prescription Study Results for Navstel

Inpatient	Outpatient	Verbal
Narstel, or Nabstel	Narstel	Nafcil
naustel	Narstel	Nafcil
Naustel	Narstel	Nafcil
Navstel	Naustel	Nafsil
Navstel	Navstel	Nafto
Navstel	Navstel	Nasdel
Navstel	Navstel	Nasdel
Navstel	Navstel	Nastel
Navstil	Navstel	Nastel
	Navstel	Nastell
	Navstel	Nastil
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		Navsil
		Navstel
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Loretta Holmes
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DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
3/14/2008 04:28:07 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
3/14/2008 04:45:45 PM
DRUG SAFETY OFFICE REVIEWER