

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-102**

**PROPRIETARY NAME REVIEW(S)**

**CONSULTATION RESPONSE**

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

<b>DATE RECEIVED:</b> May 18, 2007	<b>DESIRED COMPLETION DATE:</b> June 8, 2007	<b>OSE REVIEW #:</b> 2007-1128
<b>DATE OF DOCUMENT:</b> January 22, 2007	<b>PUDFA DATE:</b> July 27, 2007	

**TO:** Mary Parks, MD  
Director, Division of Metabolism and Endocrinology Products  
HFD-510

**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:** CaloMist Nasal Spray  
(Cyanocobalamin Nasal Spray)  
25 mcg/0.1 mL

**ADA#:** 22-102

**SPONSOR:** Fleming & Company, Pharmaceuticals

**RECOMMENDATIONS:**

1. DMETS has no objections to the use of the proprietary name, CaloMist Nasal Spray. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval 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, CaloMist Nasal Spray, 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 Sammie Beam, Project Manager, at 301-796-0080.

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: June 13, 2007  
NDA #: 22-102  
NAME OF DRUG: CaloMist Nasal Spray (Cyanocobalamin Nasal Spray), 25 mcg/0.1 mL  
NDA HOLDER: Fleming & Company, Pharmaceuticals

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

I. INTRODUCTION:

This review was written in response to a request from the Division of Metabolism and Endocrinology Products (HFD-510), for assessment of the proposed proprietary name CaloMist Nasal Spray, regarding potential name confusion with other proprietary or established drug names. The first name submitted for this product was "\_\_\_\_\_ Nasal Spray", however, the name was withdrawn by the sponsor before the DMETS name review was completed. Subsequently, the sponsor has submitted the name "CaloMist Nasal Spray" for review and comment. Container labels, carton and insert labeling were provided for review and comment. This NDA is a 505(b)(2) submission. The reference listed drug is Nascobal (Cyanocobalamin) Nasal Spray (NDA 21-642).

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PRODUCT INFORMATION

CaloMist Nasal Spray (Cyanocobalamin, USP) is a synthetic form of vitamin B<sub>12</sub> with equivalent B<sub>12</sub> activity. CaloMist is indicated: \_\_\_\_\_

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\_\_\_\_\_ The recommended dose is one spray in each nostril daily (25 mcg per nostril, total daily dose 50 mcg). CaloMist Nasal Spray should be administered at least \_\_\_\_\_ CaloMist Nasal Spray will be available as a metered dose spray in 30 mL plastic bottles containing 18 mL of solution. Each actuation (0.1 mL) supplies 25 mcg Cyanocobalamin, USP. One bottle will deliver 30 doses (60 sprays).

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## II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of the internet, several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3,4</sup> for existing drug names which sound-alike or look-alike to CaloMist Nasal Spray to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted<sup>5</sup>. The Saegis<sup>6</sup> 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 post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of a drug must be considered in the overall safety evaluator risk assessment.

### A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name CaloMist Nasal Spray. 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, CaloMist Nasal Spray, acceptable from a promotional perspective.
2. The Expert Panel identified ten proprietary names and two herbal products that were thought to have the potential for confusion with CaloMist Nasal Spray. These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage.

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<sup>1</sup> MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> 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.

<sup>4</sup> Phonetic and Orthographic Computer Analysis (POCA)

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

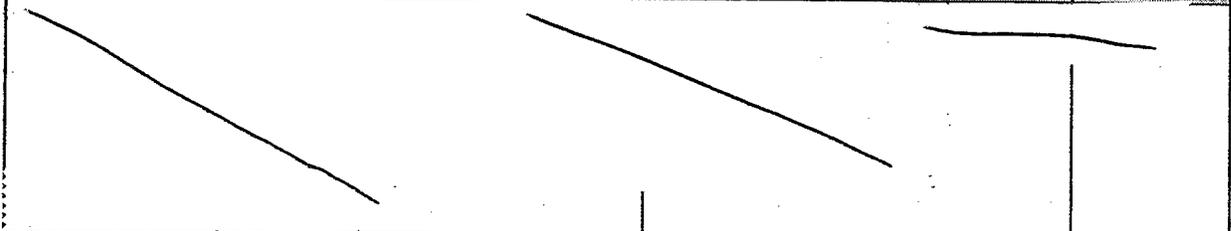
<sup>6</sup> Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

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

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Calomist Nasal Spray	Cyanocobalamin, USP Nasal spray solution 25 mcg/0.1 mL	Maintenance of normal hematologic status in pernicious anemia patients who are in remission following intramuscular vitamin B <sub>12</sub> therapy and who have no nervous system involvement, as a supplement to other vitamin B <sub>12</sub> deficiencies. One spray in each nostril once daily.	N/A
Coldmist DM	Dextromethorphan 32 mg, guaifenesin 595 mg, and pseudoephedrine hydrochloride 48 mg Extended-release tablets	Unable to find product specific dosing information.	LA
Coldmist Jr	Pseudoephedrine hydrochloride 48 mg and guaifenesin 595 mg Extended-release capsules	1 or 2 capsules every 12 hours, up to 4 capsules per day.	
Coldmist LA	Pseudoephedrine hydrochloride 85 mg and guaifenesin 795 mg Extended-release tablets	1 tablet every 12 hours, up to 2 tablets per day.	
Calohist Skin Protectant  (OTC product)	Calamine 8% and Pramoxine 1% Lotion	Temporary relief of itching and pain associated with rashes due to poison ivy, poison oak, poison sumac, insect bites, and minor irritations. Dries the oozing and weeping of poison ivy, poison oak, and poison sumac: Apply to affected area no more than 3 to 4 times daily.	LA/SA
Alamast	Pemirolast potassium Ophthalmic solution 0.1%	Prevention of itching of the eye due to allergic conjunctivitis: 1 or 2 drops in each affected eye four times per day	LA/SA
Calamine Lotion  (OTC product; multiple products available, this info is for the CVS house brand)	Calamine 6.97% and Zinc oxide 6.97% Lotion	Used for relief of itching, oozing and weeping due to poison ivy, oak and sumac: Apply to the affected area 3 to 4 times per day.	LA/SA
Colocort	Hydrocortisone Rectal Suspension, USP Suspension 100 mg/60 mL	Adjunctive therapy in the treatment of ulcerative colitis: One rectal enema nightly for 21 days. Difficult cases may require 2 or 3 months of treatment.	LA
Codehist DH	Pseudoephedrine, chlorpheniramine maleate, codeine phosphate  Unable to find product specific information.	Unable to find product specific dosage information.	LA

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Calomist Nasal Spray	Cyanocobalamin, USP Nasal spray solution 25 mcg/0.1 mL	Maintenance of normal hematologic status in pernicious anemia patients who are in remission following intramuscular vitamin B <sub>12</sub> therapy and who have no nervous system involvement; as a supplement to other vitamin B <sub>12</sub> deficiencies: One spray in each nostril once daily	N/A
Lemohist Plus	Chlorpheniramine 2 mg, guaifenesin 100 mg, and pseudoephedrine 32.4 mg Capsule	Temporary relief of sinus congestion, runny nose, sneezing, and throat and airway irritation due to colds, upper respiratory tract infections, and allergies.  Unable to find product specific dosing information.	LA
Thalomid  [Has a restricted distribution program: System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.)]	Thalidomide Capsules 50 mg, 100 mg, and 200 mg	Multiple myeloma: Administer in combination with dexamethasone in 28-day treatment cycles: 200 mg once daily at least 1 hour after evening meal. Erythema nodosum leprosum: Initiate dosing at 100 mg to 300 mg per day, at least 1 hour after the evening meal. In severe cases dosing may be initiated at 400 mg per day.	SA  (Note: Telephone orders for Thalomid are not permitted)
Carbihist  (Product has been discontinued; other generic products are available)	Carbinoxamine Oral liquid 4 mg/5 mL	Treatment of allergic rhinitis, allergic conjunctivitis, rhinorrhea, pruritis, sneezing and urticaria: 5 mL to 10 mL, three to four times per day.	LA
Calamus	Calamus Herb  Some products identified: Calamus Root: 450 mg capsules Calamus Root Cream Calamus Root Powder Calamus Root Ointment Calamus Root Liquid Extract/Tincture: (1:5) Calamus Root Pure Essential Oil Calamus Root Tea	Used orally for digestive disorders, to stimulate appetite and digestion. Also used as a sedative; to induce sweating; and for rheumatoid arthritis and stroke. Chewed: to remove the smell of tobacco, as a stimulant, as an euphoric and as a hallucinogen. Used topically for skin disease. <i>ORAL: 1-3 grams of the rhizome has been used three times daily. As a tea, one cup of tea, prepared by steeping 1-3 grams of the rhizome in 150 mL of boiling water for 5-10 minutes, has been used three times daily. 1-3 mL of the liquid extract, 1:1 in 60% alcohol, has been used three times daily. 2-4 mL of the tincture, 1:5 in 60% alcohol, has been used three times daily.<sup>7</sup></i>	LA/SA
Calamint	Herb  Does not appear to be available in a pharmaceutical dosage form	Used orally for respiratory illnesses and colds with fever. Also used to promote sweating and as an expectorant.	LA/SA

<sup>7</sup> Natural Medicines Comprehensive Database. Available at: [www.naturaldatabase.com](http://www.naturaldatabase.com). Accessed June 27, 2007.

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Calomist Nasal Spray	Cyanocobalamin, USP Nasal spray solution 25 mcg/0.1 mL	Maintenance of normal hematologic status in pernicious anemia patients who are in remission following intramuscular vitamin B <sub>12</sub> therapy and who have no nervous system involvement, as a supplement to other vitamin B <sub>12</sub> deficiencies. One spray in each nostril once daily.	N/A
			
<p>*Frequently used, not all-inclusive.  **L/A (look-alike), S/A (sound-alike)  ***Name pending approval. Not FOI releasable.</p>			

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**B. PRESCRIPTION ANALYSIS STUDIES**

**I. Methodology:**

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of CaloMist Nasal Spray with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 123 health care professionals (pharmacists, physicians, and nurses). 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 CaloMist Nasal Spray (see page 7). 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 that were surveyed responded to these studies.

**APPEARS THIS WAY ON ORIGINAL**

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p>Outpatient RX:</p> <p><i>Calomist Nasal Spray</i>  <i>#1</i>  <i>1 spray into each nostril</i>  <i>daily</i></p>	<p>“CaloMist Nasal Spray, 25 mcg  Dispense number one  One spray into each nostril daily.”</p>
<p>Inpatient RX:</p> <p><i>Calomist Nasal Spray 25mcg + spray 1x daily</i></p>	

2. Results:

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

C. SAFETY EVALUATOR RISK ASSESSMENT

In evaluating the name “CaloMist Nasal Spray”, we considered how the product will be scripted in real world practice. The proposed proprietary name is “CaloMist Nasal Spray”, however, the “Nasal Spray” portion of the name may not be specified in a written or verbal prescription for the product. Furthermore, the capital letter “M” may be written in lowercase on a prescription. These factors must be considered in our assessment of the name “CaloMist Nasal Spray”.

In reviewing the proprietary name, CaloMist Nasal Spray, ten proprietary names and two herbs were identified to have the potential to sound and/or look similar to CaloMist Nasal Spray. They are: Coldmist DM/Jr/LA, Calohist Skin Protectant, Alamast, Calamine Lotion, Colocort, Codehist DH, Lemohist Plus, Thalomid, Carbihist, Calamus, Calamint, and : \_\_\_\_\_

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

Upon analysis of the names Lemohist Plus, Codehist DH, Carbihist, Thalomid, Calamus, Calamint, \_\_\_\_\_ Alamast, Calamine, and Colocort it was determined that these names would not be considered further because they lack convincing look-alike and/or sound-alike similarities with CaloMist Nasal Spray in addition to having numerous differentiating product characteristics such as the product strength, indication of use, route of administration and dosage form. Additionally, Carbihist has been discontinued (other generic products are available);

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

Calamus and Calamint are herbs and Calamint does not appear to be available in a pharmaceutical dosage form; Thalomid has a restricted distribution program; and only limited product information could be found concerning the strength and/or dosing of Lemohist Plus and Codehist DH. The remaining names are discussed in detail below.

1. The root name Coldmist of Coldmist DM, Coldmist Jr, and Coldmist LA was identified as a name with similar appearance to CaloMist. The Coldmist products are extended-release combination products that have different ingredients and strengths (see Table 1, page 4). These products are indicated for the temporary relief of symptoms due to colds, upper respiratory tract infections and allergies. The recommended dose for Coldmist Jr is 1 or 2 capsules every 12 hours and for Coldmist LA the dose is 1 tablet every 12 hours. DMETS was unable to locate product specific dosage information for Coldmist DM.

Coldmist and CaloMist may have a similar appearance because both names contain eight letters and have the same ending letters ("mist"). Additionally, the first three letters of both names may look similar when scripted ("Col" vs. "Cal"). However, Coldmist contains the upstroke letter "d" (when written in lowercase) which may help to differentiate the names.

*Coldmist Calomist*

Coldmist and CaloMist have different product characteristics. Some of the different product characteristics include: indication of use (relief of symptoms due to colds, allergies, etc. vs. treatment of vitamin B<sub>12</sub> deficiencies), route of administration (oral vs. intranasal), dosage form (tablet vs. solution), dose [1 tablet vs. 50 mcg or 1 spray (25 mcg) in each nostril], and frequency of administration (every 12 hours vs. once daily). These product differences may help to differentiate the names. For example, a prescription for Coldmist would likely state the number of tablets to be taken as well as the frequency of administration since it's important that the maximum recommended dose is not exceeded. Additionally, there are three Coldmist products available, so a prescription would have to specify which product is to be dispensed. Although there are some orthographic similarities between the names Coldmist and CaloMist, the product differences will help to minimize potential confusion between the name pair.

2. The root name Calohist of Calohist Skin Protectant was identified as a name with similar sound and appearance to CaloMist. Calohist Skin Protectant contains calamine and pramoxine. It is indicated for the temporary relief of itching and pain associated with rashes due to poison ivy, oak, and sumac, insect bites, and minor irritations. The recommended dose is one application to the affected area(s) 3 or 4 times per day.

Calohist and CaloMist both contain eight letters of which seven are identical and in the same positions in both names (CALOHIST vs. CALOMIST) which makes the names look very similar in appearance. However, the letter "h" in Calohist has an upstroke when scripted which may help to differentiate the name pair. The names may sound similar because they both contain three syllables that may sound similar when spoken (CĀ-LŌ-HĪST vs. CĀL-Ō-MĪST).

## Calohist Calomist

Calohist and Calomist do not have any overlapping product characteristics. These products differ in indication of use (relief of itching, oozing, etc. due to poison ivy, poison oak, etc. vs. treatment of vitamin B<sub>12</sub> deficiencies), route of administration (topical to skin vs. intranasal), frequency of administration (3 to 4 times per day vs. once daily), and method of access (over-the-counter vs. prescription) which may help to differentiate the name pair. For instance, a written or verbal prescription for Calohist is unlikely to be given because it is an over-the-counter product. Additionally, Calohist appears to be a CVS house brand and therefore may have limited distribution which may limit availability and name recognition of this product. Although there are orthographic and phonetic similarities between these names, the different product characteristics will minimize the potential to confuse Calohist and Calomist.

### III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

DMETS notes that the container label and carton labeling were submitted with the name "~~\_\_\_\_\_~~ Nasal Spray", however, this previously proposed trade name was withdrawn by the sponsor. However, DMETS has reviewed the labels and labeling and focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement in the interest of minimizing potential user error and enhancing patient safety. These comments are applicable to Calomist if the sponsor plans to use a similar layout.

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#### A. GENERAL COMMENTS

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2   Page(s) Withheld

       Trade Secret / Confidential (b4)

  ✓   Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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