

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-076

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

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

DATE RECEIVED: November 29, 2006	DESIRED COMPLETION DATE: March 1, 2007 PDUFA DATE: May 20, 2007	OSE REVIEW #: 2006-916
--	--	-------------------------------

TO: Susan J. Walker, MD
Director, Division of Dermatology and Dental Products
HFD-540

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: Denise V. Baugh, PharmD, BCPS, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME:
Locoid (Hydrocortisone butyrate) Lotion, 0.1%

NDA#: 22-076

SPONSOR: Ferndale Laboratories, Inc.

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Locoid. 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 to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name, Locoid, 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 Angela Robinson Project Manager, at 301-796-2284.

**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: November 29, 2006
NDA# 22-076
NAME OF DRUG: Locoid (Hydrocortisone Butyrate) Lotion, 0.1%
NDA HOLDER: Ferndale Laboratories, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Dermatology and Dental Products (HFD-540), for assessment of the proprietary name, "Locoid", regarding potential name confusion with other proprietary or established drug names. Locoid (Hydrocortisone Butyrate) Lotion, 0.1% is a new addition to the Locoid product line. The sponsor currently markets Locoid as a 1% solution, cream, lipocream and ointment (see below). Draft container labels, carton and insert labeling were provided for review and comment.

Name & Container Size	Strength	Directions
Locoid Lotion, 2 fl. oz. (59 ml) and 4 fl. oz. (118 ml) (proposed product)	0.1%	Apply to affected area two — times daily.
Locoid Solution, 60 ml	0.1%	Apply to affected area two to three times daily.
Locoid Ointment, 15 g	0.1%	Apply to affected area two to three times daily.
Locoid Cream, 15 g	0.1%	Apply to affected area two to three times daily.
Locoid Lipocream, 45 g	0.1%	Apply to affected area two to three times daily.

PRODUCT INFORMATION

Locoid Lotion, (Hydrocortisone Butyrate) 0.1% is indicated for _____ in patients 3 months of age or older. It is applied to the affected area(s) 2 — times daily, depending on severity of the condition. It will be available as 2 fluid ounce and 4 fluid ounce bottles.

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 Locoid 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 components, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of the 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, Locoid. 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, Locoid, acceptable from a promotional perspective.
2. The Expert Panel identified identified four (4) proprietary names thought to have the potential for confusion with Locoid. These products are listed in Table 1 (see page 4) along with the dosage forms available and usual dosage.

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

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

Product Name	Dosage Form(s), Established name	Usual adult dose	Other**
Locoid	Hydrocortisone butyrate 0.1% ointment, 0.1% cream, 0.1% lipocream, 0.1% solution	Apply to affected area(s) 2-3 times daily	
Lopid	Gemfibrozil 600 mg film coated tablet	600 mg twice daily	LA
Duvoid (Canada)	Bethanecol 5 mg, 10 mg, 25 mg, 50 mg tablet	Urinary retention, neurogenic bladder, and/or bladder atony: 10 mg to 50 mg 2 to 4 times per day	LA
Lorcet 10/650	Hydrocodone 10 mg/acetaminophen 650 mg tablet	Take 2.5 mg to 10 mg every 4 to 6 hours not to exceed 4 grams of acetaminophen per day and 60 mg of hydrocodone per day	LA
Lorcet Plus	Hydrocodone 7.5 mg/acetaminophen 650 mg tablet		
Lorcet HD	Hydrocodone 5 mg/acetaminophen 650 mg		
Locoid	Hydrocortisone butyrate Ointment: 0.1% Cream: 0.1% Lipocream: 0.1% Solution: 0.1%	Apply to affected area(s) two to three times daily.	SA/LA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

b(4)

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Locoid 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. Each study 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 Locoid (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: <i>Locoid 0.1% Lotion</i>	"Locoid 0.1% lotion Dispense 1 bottle and apply to the affected area of skin twice daily —
Inpatient RX: <u><i>Locoid 0.1% Lotion</i></u>	

b(4)

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. ADVERSE EVENT REPORTING SYSTEM (AERS)

Since Locoid products are currently in the market, the Adverse Event Reporting System (AERS) was searched for all post-marketing safety reports concerning medication errors associated with Locoid. The MEDDRA High Level Group Term (HLGT): "medication errors", "pharmaceutical product complaint" and the term "Locoid" and "hydrocortisone butyrate" were used as search criteria. The AERS search did not retrieve any pertinent medication error reports.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Locoid, the primary concerns relating to look-alike and sound-alike confusion with Locoid (Hydrocortisone butyrate) Lotion, 0.1% are Lopid, Duvoid, Lorcet, and the currently marketed dosage forms of Locoid.

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, Locoid.

Upon further review, the name, Duvoid (Bethanecol) will not be reviewed further because it is a foreign name (from Canada) and there is a lack of convincing look-alike and sound-alike similarities along with different product characteristics such as dosage form (lotion vs. tablet), route of administration (topical vs. oral) and strength (0.1% vs. 5 mg, 10 mg, 25 mg, and 50 mg).

The remaining names of concern are discussed in detail below.

1. Locoid lotion is a product extension of the Locoid product line. This product is currently marketed as a 0.1% ointment, cream, lipocream, and solution. The proposed Locoid Lotion shares the same product strength (1%) and dosing frequency (i.e, apply to affected area two — times daily) as the existing Locoid product line. Other than the dosage form, the proposed name is exactly identical in respect to the root name, Locoid. Due to the fact that the proposed Locoid lotion and the existing Locoid product lines are identical in active ingredient, product strength, and dosing frequency, it is unlikely that a patient would face significant adverse effects if one was to get the wrong dosage form. However, every effort should be made to have the labels of this dosage form look different to minimize selection errors. b(4)
2. Lopid was identified as a name that looks like Locoid when scripted. Lopid is indicated for treatment of hypertriglyceridemia in patients who are at great risk for pancreatitis and who have not responded to dietary intervention. It is available as a 600 mg tablet.

Although these names share the first two letters 'Lo-' and the last two letters '-id', the 'p' in Lopid provides a downstroke which is prominent when scripted (see below). Also, Locoid has six (6) letters whereas Lopid has five (5) making Locoid slightly longer in length when scripted. These orthographic differences make confusion between these two products unlikely. Additionally, there have been no postmarketing reports of confusion with this name pair.

Moreover, both products do not have any overlapping product characteristics. For example the products have the following differences: dosage form (tablet vs. lotion), route of administration (oral vs. topical), and dosing frequency (twice daily vs. — times daily), product strength (600 mg vs. 0.1%). Orthographic differences along with differences in product characteristics between this name pair minimizes the potential for name confusion. Thus the addition of this dosage form to the Locoid product line doesn't seem to pose a problem. b(4)

Lopid Locoid

3. The root name, Lorcet was identified as a name that looks like Locoid when scripted. Lorcet is indicated for the relief of moderate to severe pain. It is a combination product available as Lorcet HD (hydrocodone 5 mg/acetaminophen 650 mg); Lorcet Plus (hydrocodone 7.5 mg/acetaminophen 650 mg); and Lorcet 10/650 (hydrocodone 10 mg/acetaminophen 650 mg).

Both names start with the same two letters (Lo-) which contributes to their look-alike similarities when scripted. Additionally, both names share an upstroke with the last letter in the name (-t vs. -d). However, the middle portion in their names (-ce- vs -oi-) looks different when scripted. Furthermore, because Lorcet is available in three different strength combinations, the specific formulation of Lorcet would have to be indicated on an order which can minimize the potential for confusion between this name pair. Additionally, there have been no postmarketing reports of confusion between Lorcet and Locoid.

Lorcet and Locoid also do not share product characteristics. The route of administration (oral vs. topical), and frequency of administration (every 4 to 6 hours as necessary vs. 2 to 3 times per day) and product strength (hydrocodone 5 mg/acetaminophen 650 mg; hydrocodone 7.5 mg /acetaminophen 650 mg; and hydrocodone 10 mg/acetaminophen 650 mg vs. 0.1%) are different. Therefore, orthographic differences coupled with different product characteristics will decrease the confusion between Lorcet and Locoid. Thus the addition of this dosage from to the Locoid product line doesn't seem to pose a problem.

Lorcet Locoid

II. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

DMETS has reviewed the draft container label, carton labeling, and package insert labeling focusing on safety issues to prevent possible medication errors. However, copies of the labels and labeling for Locoid Lotion 0.1% were provided in black and white, and may not represent the true color of the labels and labeling. Therefore, DMETS cannot assess if there are any safety concerns due to the colors utilized on the labels and labeling. Also the copies of the labels and labeling provided did not contain a scale for size. Please provide the revised copies of the label, carton labeling and package insert labeling so that a proper assessment for safety issues and the potential for medication errors can be performed.

Following review of the draft labels and container labels, DMETS has identified the following areas of improvement which may minimize potential user error.

A. CONTAINER LABEL (4 g Physician Sample (tube), 2 fl. oz. (59 ml) and 4 fl. oz. (118 ml))

1. Ensure that the established name is at least half the size of the proprietary name in accordance with 21 CFR 201.10 (g) (2).
2. Revise the statement, "Sample – Not for Sale" to "Physician's Sample – Not for Sale" to maintain consistent information on the label.
3. Ensure that the sponsor logo is not more prominent than the proprietary name, established name and strength.
4. Relocate the 'Rx only' statement after the stated Net quantity. As currently presented, it appears immediately below the NDC number. Optimally, the proprietary name, established name, and the strength should appear immediately after the NDC number since this is the most important information on the principal display panel.

B. CARTON LABELING

1. Ensure that the net quantity statement appears away from the product strength and has less prominence on the professional samples. Postmarketing experience has shown that medication errors may result when the strength is located closely to the net quantity.
2. Delete the statement _____ to avoid excessive and distracting information on the label. If healthcare practitioners need information on the active and/or inactive ingredients, they can look on the back panel.

b(4)

C. INSERT LABELING

The product strength should be the same throughout the text of the package insert. Please change all references to Locoid and hydrocortisone butyrate to Locoid (Hydrocortisone butyrate) Lotion, 0.1%.

APPENDIX A. – PRESCRIPTION ANALYSIS STUDY

Inpatient	Outpatient	Voice
Locoid	Locoid	Locoid
Locoid	Locoid	Locoid
Locaid	Locoid	Locoid
Locaid	Locoid	Locoid
Locaid	Locoid	Lokoid
Locoid	Locoid	Loquoid
Locoid	Locard	Alocoid
Locaid	Locoid	Locoid
Locoid	Locoid	Wilcoid
Locaid		Locoid
Locaid		Loquoid
Locoid		Lokoy
Locaid		Locoid
		Locoid

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

/s/

Linda Kim-Jung
3/5/2007 01:25:17 PM
DRUG SAFETY OFFICE REVIEWER
Also signing for Denise Baugh.

Carol Holquist
3/5/2007 01:34:12 PM
DRUG SAFETY OFFICE REVIEWER