

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !

IND # _____ YES /___/ ! NO /___/ Explain: _____
! _____
!

Investigation #2 !

IND # _____ YES /___/ ! NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !

YES /___/ Explain _____ ! NO /___/ Explain _____
! _____
! _____
!

Investigation #2 !

YES /___/ Explain _____ ! NO /___/ Explain _____
! _____
! _____
!

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES / /

NO / /

If yes, explain: _____

 / S / 2/9/00
Signature/ Date
Title: Project Manager

 / S / 2-11-00
Signature of Office/ Date
Division Director

cc: Original NDA

Division File HFD-93 Mary Ann Holovac

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from 1.1 volume.
SD = 6.29.99

1.2. Patent Information
Item 13

Time Sensitive Patent Information

**Patent Information Pursuant to 21 C.F.R. § 314.53
for**

Alosetron hydrochloride Tablets

NDA 21-107

The following is provided in accord with the Drug Price Competition and Patent Term Restoration Act of 1984:

Active Ingredient: Alosetron hydrochloride
Dosage Form: oral tablet
Strength(s): 1 mg

U.S. Patent 5,360,800

<u>Expiration Date</u>	<u>Type of Patent</u>	<u>Patent Owner</u>	<u>U.S. Agent</u>
2 February 2010	Drug Drug Product Composition/ Formulation Method of Use	Glaxo Group Limited	Glaxo Wellcome Inc.

The undersigned declares that U.S. Patent 5,360,800 covers the drug, formulation, composition and method of use of Alosetron hydrochloride tablets. This product is the subject of this application for which approval is being sought.

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MCNEIL
REQUEST FOR TRADEMARK REVIEW

907

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530), 9201 Corporate Blvd, Room N461
FEB - 2 1998

From: Division of Gastrointestinal and Coagulation Drug Products		HFD-180
Attention: Melodi McNeil, Project Manager		Phone: (301) 443-0483
Date: October 16, 1997		
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product		
Proposed Trademark: Lotronex		IND
Established name, including dosage form: alosetron Tablets		
Other trademarks by the same firm for companion products: N/A		
Indications for Use (may be a summary if proposed statement is lengthy): Treatment of patients with irritable bowel syndrome (IBS)		
Initial Comments from the submitter (concerns, observations, etc.): Note: This consult request is being sent during the IND stage, as opposed to the NDA stage.		

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

cc: Original IND HFD-180/division file; HFD-180/M.McNeil; HFD-180/Duffy

Rev. December 95



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MM 11/16/97

Consult #907 (HFD-180)

LOTRONEX

alosetron tablets

The Committee noted sound-alike/look-alike conflicts with the following marketed products: LOTREL, LOTRISONE, LACTINEX, and LOTRIMIN. The committee felt there was a low potential for mix-up with these products since they have differing strengths, dosage forms, dosing regimens and therapeutic indications. There were no misleading aspects found.

The Committee has no reason to find the proposed proprietary name unacceptable.

ISI 2/28/98, Chair
CDER Labeling and Nomenclature Committee

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Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm 15B03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

Date of Review: 2/3/00
NDA#: 21-107
Name of Drug: Lotronex®
(alosetron HCl)
NDA Holder: GlaxoWelcome

I. INTRODUCTION

This consult was written in response to a request from the Division of Gastro-Intestinal and Coagulation Drug Products (HFD-180) on January 10, 2000, to review the proposed proprietary drug name, Lotronex® in regard to potential name confusion with existing proprietary/generic drug names. The Division would like a decision by January 12, 2000. However, in order to render an opinion on the name, medication error staff would like more time to do a more thorough review on the proposed name. The Division comes back on 2/1/00 with a request for a definitive decision by 2/4/00.

The Labeling and Nomenclature Committee (LNC) had reviewed this proprietary name and concluded that the proposed proprietary name Lotronex® was acceptable on 11/25/99. This consult was forwarded to OPDRA for final clearance prior to approval of NDA.

PRODUCT INFORMATION

Lotronex® tablets contain 1.124 mg alosetron HCl equivalent to 1 mg of alosetron. It is indicated for the treatment of irritable bowel syndrome (IBS). The usual dose is 1 mg twice a day.

Alosetron is a potent and highly selective 5-HT₃ receptor antagonist. 5-HT₃ receptors are nonselective cation channels that are extensively distributed on enteric neurons in the human gastrointestinal tract, as well as other peripheral and central locations. Alosetron inhibits activation of non-selective cation channels which results in the modulation of the enteric nervous system. Alosetron is rapidly absorbed after administration with a mean absolute bioavailability of approximately 50-60% (approximate range _____). It is metabolized by human microsomal cytochrome P450 system and excreted

mainly through the renal route.

Lotronex® will be supplied as 1 mg tablets in bottles of 60 and 120.

II. RISK ASSESSMENT

In order to determine the potential for medication errors and to find out the degree of confusion of the proposed proprietary name, ® with other drug names, the medication error staff of OPDRA searched Micromedex online, PDR (1999 Edition), American Drug Index (43rd Edition), Drug Facts and Comparison (update monthly), the Electronic Orange Book, and US Patent and Trademark Office online database. In addition, OPDRA also searched several FDA databases for potential sound-alike and look-alike names to approved/unapproved drug products through DPR, Medline online, Decision Support System (DSS), Establishment Evaluation System, and LNC database. An expert panel discussion was conducted to review all the findings from the searches. OPDRA also conducted studies of written and verbal analysis of the proposed proprietary name employing health practitioners within FDA to evaluate potential errors in handwriting and verbal communication of the name. This exercise was conducted to simulate the prescription order process.

A. EXPERT PANEL DISCUSSION:

The panel discussed the sound-alike and look-alike names such as Lotrimin, Lotrisone, Lovenox, and Lotrel. Members of the panel voiced concern on the existing drug currently on the market by the proprietary name, Lotemax® which was approved after LNC decision was provided. Lotemax does sound and look-alike to Lotronex. The dosage form for Lotemax comes as topical ophthalmic eye drops whereas Lotronex is supplied as 1 mg oral tablets.

B. STUDY CONDUCTED BY OPDRA

Methodology:

This study involved 92 health professionals consisting of physicians, nurses and pharmacists within FDA to determine the degree of confusion of Lotronex® with other drug names due to the similarity in handwriting and verbal pronunciation of the name. OPDRA staff member wrote three outpatient prescriptions, each consisting of a known drug product and a prescription for Lotronex®. These prescriptions were scanned into the computer and a random sample of the written orders were then delivered to the participating health professionals via e-mail. Outpatient prescriptions were sent to 31 participants and inpatient orders were also sent to 31 participants for review and interpretation. In addition, one pharmacist student recorded

the outpatient orders on voice mail. The voice mail messages were then sent to 30 participating health professionals for their review and interpretation. 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. We understand that our sampling number is small and the study is designed to increase the likelihood of detecting failures.

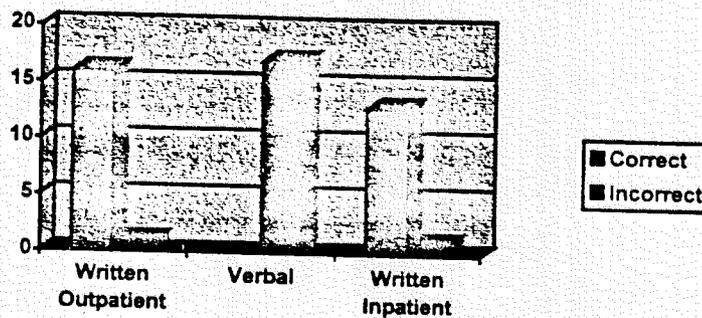
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The results are summarized in Table I.

Table I

<u>Study</u>	<u># of Sample</u>	<u># of Responses (%)</u>	<u>Correctly Interpreted</u>	<u>Incorrectly Interpreted</u>
Written Outpatient	31	17 (55%)	16	1
Verbal	30	17 (57%)	0	17
Written Inpatient	31	14 (45%)	13	1
total	92	48 (52%)	29	19



Sixty percent of the participants responded with the correct name Lotronex®. The incorrect written and verbal responses are as follows in Table II :

Table II

<u>Written</u>	<u>Incorrectly Interpreted</u>
	Lotropex
	Voltronex
<u>Verbal</u>	<u>Phonetic Variables Responses</u>
	Voltranex
	Lotrimex
	Lotrimax (5)
	Voltramax (3)
	Fosamax*
	Lotrinex
	Ultramax (2)

	Votrimax (2)
	Loetronex

C. CONTAINER LABEL, CARTON AND INSERT LABELING:

There is no container label nor carton and insert labeling available for review from the Division.

D. CONCLUSIONS:

The results of the verbal and written analysis studies showed twenty-nine participants interpreted the proprietary name Lotronex® correctly. However, the inaccurate interpretation of the proposed name did overlap with an existing approved drug product, Fosamax® in verbal prescription study. That was not what we predicted in the expert panel discussion. Fosamax® is indicated for osteoporosis for postmenopausal women and comes in three different strengths of oral tablets; 5 mg, 10 mg, and 40 mg. Lotronex® comes as single strength of 1 mg oral tablets. Though these drug names may sound similar, they are not look-alike in written orders. Hence, OPDRA believes that the likelihood of these two names being confused, is low.

The majority of respondents provided misspelled variations of the drug name, but these responses generally were phonetic variations of the study name. These responses pose little concern since they are not proprietary names that currently marketed.

III. RECOMMENDATIONS

OPDRA has no objections to the use of the proprietary name Lotronex®. However, OPDRA has some reservations which should be conveyed to the applicant holder. In addition, we would recommend that the firm provide us a commitment to monitor all Lotronex® postmarketing reports of medication errors or reports of potential errors as Expedited (15-day) reports, regardless of patient outcome.

OPDRA would appreciate feedback of the final outcome of this consult. We are willing to meet with the Division for further discussion.

Should you have any questions concerning this review, please contact Peter Tam at 301-827-3241

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/s/

Peter Tam, RPh.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur

/s/

2/4/2000

Jerry Phillips, RPh.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

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