IGI LABORATORIES

January 15, 2013

0888 13 JAN 28 P4:28

Division of Dockets Management, HFA-305
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Citizen Petition

The undersigned respectively submits this Citizen Petition under 21 USC 355, 21CFR§ 314.93 and 314.161 to request that the Commissioner of the Food and Drug Administration ("FDA") determine whether the drug product Cordran (flurandrenolide) Ointment USP, 0.05% was withdrawn from sale for reasons of safety or efficacy.

A. Action Requested

This petition requests the Commissioner of the FDA to determine whether Cordran (flurandrenolide) Ointment USP, 0.05% (NDA# 12-806 – NDA Holder Aqua Pharmaceuticals) has been voluntarily withdrawn from sale for safety or effectiveness reasons.

B. Statement of Grounds

1. The above referenced New Drug Application ("NDA") for the drug product Cordran (flurandrenolide) Ointment USP, 0.05%, NDA # 12-806, was originally approved on October 16, 1965. At that time the FDA, under the same NDA, approved a 0.025% ointment, and 0.025% and 0.05% creams. The two cream products Cordran SP (flurandrenolide) Cream USP, 0.025%, and 0.05% appear in the active section of FDA's Orange Book and appear to be actively marketed. Additionally, a 0.05% lotion product, Cordran (flurandrenolide) Lotion USP, 0.05%, NDA # 13-790 – NDA Holder Aqua Pharmaceuticals) is currently listed in the Orange Book as active, and appears to be actively marketed.
The Cordran (flurandrenolide) Ointment USP, 0.05% from what can be determined was listed in the Orange Book until 2011, but is currently listed in the Orange Book in the "Discontinued" section. To the best knowledge, information and belief of this Petitioner, the innovator has chosen not to market this product for commercial reasons.

2. The NDA holder for this product, Aqua Pharmaceuticals, has not withdrawn its Cordran SP (flurandrenolide) Cream USP 0.025% and 0.05%, or Cordran (flurandrenolide) Lotion USP, 0.05%, which contain the same active drug and dosage strength as the discontinued product.

3. Although marketing has been discontinued in the United States, the package insert (revised February 2006) for Cordran SP (flurandrenolide) Cream USP, 0.05% as found on the FDA's Daily Med website still contains references to the ointment product.

IGI Laboratories Inc., 105 Lincoln Ave. P.O. Box 687 Buena, NJ 08310 Phone: 856.697.1441 Fax: 856.697.2259

FDA-2013-P-0113 2013-677 CP

4. Under FDA regulations, an abbreviated new drug application ("ANDA") seeking approval of a generic product referencing a discontinued product must be accompanied by a Citizen Petition for FDA's determination that the discontinued reference listed drug was not voluntarily withdrawn for safety or effectiveness reasons.

5. This Petition requests a determination that Cordran (flurandrenolide) Ointment USP, 0.05% was not voluntarily withdrawn for safety or effectiveness reasons.

Conclusion

For the above stated reasons, this Citizen Petition should be granted.

C. Environmental Impact

Petitioner believes that this petition does not require an environmental impact analysis report under 21CFR§25.31(a).

D. Economic Impact

An economic impact report is required only when requested by the Administration and such report has not been requested. 21CFR§10.30(b).

CERTIFICATION

The undersigned certifies that, to the best of its knowledge and belief of the undersigned, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to the Petitioner which are unfavorable to the Petition.

Respectfully submitted,
IGI Labs, Inc.

Virginia Carman

Virginia Carman
Associate Director,
Regulatory Affairs

IGI Labs, Inc.
105 Lincoln Ave.
PO Box 687
Buena, NJ 08310
(856) 697-1441 ext. 299

List of Enclosures:

1. Proprietary Name Search Results from OB_Rx table for query on Cordran
2. Proprietary Name Search Results from OB_Disc table for query on Cordran
3. Copy of Package Insert from Daily Med for Cordran SP Cream and Cordran Ointment

U.S. Food & Drug Administration

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

-  [1]

 [2][3]

FDA Home

Proprietary Name Search Results from "OB_Rx" table for query on "cordran."

Appl No	TE Code[4]	RLD[5]	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
N012806		Yes	FLURANDRENOLIDE	CREAM; TOPICAL	0.025%	CORDRAN SP	AQUA PHARMS
N012806		Yes	FLURANDRENOLIDE	CREAM; TOPICAL	0.05%	CORDRAN SP	AQUA PHARMS
N013790		Yes	FLURANDRENOLIDE	LOTION; TOPICAL	0.05%	CORDRAN	AQUA PHARMS
N016455		Yes	FLURANDRENOLIDE	TAPE; TOPICAL	0.004MG/SQ CM	CORDRAN	WATSON PHARMS

Return to Electronic Orange Book Home Page [6]

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through November, 2012
Patent and Generic Drug Product Data Last Updated: January 11, 2013

Links on this page:

1. http://www.addthis.com/bookmark.php?u508=true&v=152&username=fdamain
2. http://www.addthis.com/bookmark.php
3. http://www.fda.gov/default.htm
4. http://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079068.htm#Therapeutic Equivalence-Related Terms
5. http://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079068.htm#Reference Listed Drug
6. ../default.cfm

Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)
Email FDA

U.S. Food & Drug Administration

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

- 1

FDA Home[2] [3]

Proprietary Name Search Results from "OB_Disc" table for query on "cordran.'

Appl No	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
N012806	FLURANDRENOLIDE	OINTMENT; TOPICAL	0.025%	CORDRAN	AQUA PHARMS
N012806	FLURANDRENOLIDE	OINTMENT; TOPICAL	0.05%	CORDRAN	AQUA PHARMS
N050346	FLURANDRENOLIDE; NEOMYCIN SULFATE	CREAM; TOPICAL	0.05%;EQ 3.5MG BASE/GM	CORDRAN-N	LILLY
N050345	FLURANDRENOLIDE; NEOMYCIN SULFATE	OINTMENT; TOPICAL	0.05%;EQ 3.5MG BASE/GM	CORDRAN-N	LILLY

Return to Electronic Orange Book Home Page [4]

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through November, 2012
Patent and Generic Drug Product Data Last Updated: January 11, 2013

Links on this page:

1. http://www.addthis.com/bookmark.php?u508=true&v=152&username=fdamain
2. http://www.addthis.com/bookmark.php
3. http://www.fda.gov/default.htm
4. ../default.cfm

Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

- Accessibility
- Contact FDA
- Careers
- FDA Basics
- FOIA
- No Fear Act

- Site Map
- Transparency
- Website Policies

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)
Email FDA

- USA.gov
-
-
-
-
-
-

- For Government
- For Press

- Combination Products
- Advisory Committees
- Science & Research
- Regulatory Information
- Safety
- Emergency Preparedness
- International Programs
- News & Events
- Training and Continuing Education
- Inspections/Compliance
- State & Local Officials
- Consumers
- Industry
- Health Professionals

U.S.Department of **Health & Human Services**

Links on this page:

1. http://www.addthis.com/bookmark.php?u508=true&v=152&username=fdamain
2. http://www.addthis.com/bookmark.php
3. http://www.fda.gov/default.htm
4. ../default.cfm

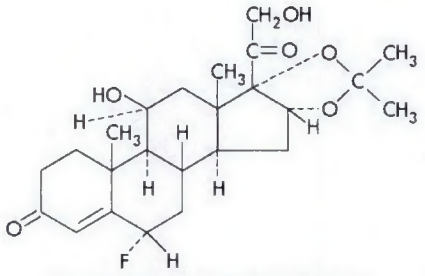
CORDRAN - flurandrenolide cream
CORDRAN - flurandrenolide ointment
Aqua Pharmaceuticals, LLC

Cordran® SP Cream
and
Cordran® Ointment
Flurandrenolide, USP
128401
Revised: February 2006
Rx only

DESCRIPTION

Cordran® (Flurandrenolide, USP) is a potent corticosteroid intended for topical use. Flurandrenolide occurs as white to off-white, fluffy, crystalline powder and is odorless. Flurandrenolide is practically insoluble in water and in ether. One g dissolves in 72 mL of alcohol and in 10 mL of chloroform. The molecular weight of flurandrenolide is 436.52.

The chemical name of flurandrenolide is Pregn-4-ene-3,20-dione, 6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis (oxy)]-, (6α, 11β, 16α)-; its empirical formula is $C_{24}H_{33}FO_6$. The structure is as follows:



Flurandrenolide Chemical Structure

Each g of Cordran® SP Cream (Flurandrenolide Cream, USP) contains 0.5 mg (1.145 µmol; 0.05%) or 0.25 mg (0.57 µmol; 0.025%) flurandrenolide in an emulsified base composed of cetyl alcohol, citric acid, mineral oil, polyoxyl 40 stearate, propylene glycol, sodium citrate, stearic acid, and purified water.

Each g of Cordran® Ointment (Flurandrenolide Ointment, USP) contains 0.5 mg (1.145 µmol; 0.05%) or 0.25 mg (0.57 µmol; 0.025%) flurandrenolide in a base composed of white wax, cetyl alcohol, sorbitan sesquioleate, and white petrolatum.

CLINICAL PHARMACOLOGY

Cordran is primarily effective because of its anti-inflammatory, antipruritic, and vasoconstrictive actions.

The mechanism of the anti-inflammatory effect of topical corticosteroids is not completely understood. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man. Corticosteroids with anti-inflammatory activity may stabilize cellular and lysosomal membranes. There is also the suggestion that the effect on the membranes of lysosomes prevents the release of proteolytic enzymes and, thus, plays a part in reducing inflammation.

Pharmacokinetics—The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses (see DOSAGE AND ADMINISTRATION).

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. They are metabolized primarily in the liver and then excreted in the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE

Cordran is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS

Topical corticosteroids are contraindicated in patients with a history of hypersensitivity to any of the components of these preparations.

PRECAUTIONS

General -

Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Conditions that augment systemic absorption include application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area or under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression using urinary-free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, so that supplemental systemic corticosteroids are required.

Pediatric patients may absorb proportionately larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity (see Pediatric Use under PRECAUTIONS).

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

In the presence of dermatologic infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, Cordran should be discontinued until the infection has been adequately controlled.

Information for the Patient -

Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped in order to be occlusive unless the patient is directed to do so by the physician.
4. Patients should report any signs of local adverse reactions, especially under occlusive dressing.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a patient being treated in the diaper area, because these garments may constitute occlusive dressings.

Laboratory Tests -

The following tests may be helpful in evaluating the HPA axis suppression:
Urinary-free cortisol test
ACTH stimulation test

Carcinogenesis, Mutagenesis, and Impairment of Fertility -

Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids.

Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Usage in Pregnancy -

Pregnancy Category C—Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively for pregnant patients or in large amounts or for prolonged periods of time.

Nursing Mothers -

It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities *not* likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use -

Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than do mature patients because of a larger skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in pediatric patients receiving topical corticosteroids. Manifestations of adrenal suppression in pediatric patients include linear growth retardation, delayed weight gain, low

plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to pediatric patients should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of pediatric patients.

ADVERSE REACTIONS

The following local adverse reactions are reported infrequently with topical corticosteroids but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence:

Burning
Itching
Irritation
Dryness
Folliculitis
Hypertrichosis
Acneform eruptions
Hypopigmentation
Perioral dermatitis
Allergic contact dermatitis

The following may occur more frequently with occlusive dressings:

Maceration of the skin
Secondary infection
Skin atrophy
Striae
Miliaria

OVERDOSAGE

Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (see PRECAUTIONS).

DOSAGE AND ADMINISTRATION

Topical corticosteroids are generally applied to the affected area as a thin film 1 to 4 times daily, depending on the severity of the condition.

For moist lesions, a small quantity of the cream should be rubbed gently into the affected areas 2 or 3 times a day. For dry, scaly lesions, the ointment is applied as a thin film to affected areas 2 or 3 times daily.

Occlusive dressings may be used for the management of psoriasis or recalcitrant conditions.

If an infection develops, the use of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

Use With Occlusive Dressings

The technique of occlusive dressings (for management of psoriasis and other persistent dermatoses) is as follows:

1. Remove as much as possible of the superficial scaling before applying Cordran SP Cream or Cordran Ointment. Soaking in a bath will help soften the scales and permit easier removal by brushing, picking, or rubbing.
2. Rub Cordran SP Cream or Cordran Ointment thoroughly into the affected areas.
3. Cover with an occlusive plastic film, such as polyethylene, Saran Wrap™, or Handi-Wrap®. (When Cordran SP Cream is used, added moisture may be provided by placing a slightly dampened cloth or gauze over the lesion before the plastic film is applied.)
4. Seal the edges to adjacent normal skin with tape or hold in place by a gauze wrapping.
5. For convenience, the patient may remove the dressing during the day. The dressing should then be reapplied each night.
6. For daytime therapy, the condition may be treated by rubbing Cordran SP Cream or Cordran Ointment sparingly into the affected areas.
7. In more resistant cases, leaving the dressing in place for 3 to 4 days at a time may result in a better response.
8. Thin polyethylene gloves are suitable for treatment of the hands and fingers; plastic garment bags may be utilized for treating lesions on the trunk or buttocks. A tight shower cap is useful in treating lesions on the scalp.

Occlusive Dressings Have the Following Advantages—

1. Percutaneous penetration of the corticosteroid is enhanced.
2. Medication is concentrated on the areas of skin where it is most needed.
3. This method of administration frequently is more effective in very resistant dermatoses than is the conventional application of Cordran.

Precautions to Be Observed in Therapy With Occlusive Dressings—Treatment should be continued for at least a few days after clearing of the lesions. If it is stopped too soon, a relapse may occur. Reinstitution of

treatment frequently will cause remission.

Because of the increased hazard of secondary infection from resistant strains of staphylococci among hospitalized patients, it is suggested that the use of occlusive plastic films for corticosteroid therapy in such cases be restricted.

Generally, occlusive dressings should not be used on weeping, or exudative, lesions.

When large areas of the body are covered, thermal homeostasis may be impaired. If elevation of body temperature occurs, use of the occlusive dressing should be discontinued.

Rarely, a patient may develop miliaria, folliculitis, or a sensitivity to either the particular dressing material or a combination of Cordran and the occlusive dressing. If miliaria or folliculitis occurs, use of the occlusive dressing should be discontinued. Treatment by inunction with a corticosteroid such as Cordran may be continued. If the sensitivity is caused by the particular material of the dressing, substitution of a different material may be tried.

Warnings—Some plastic films are readily flammable. Patients should be cautioned against the use of any such material.

When plastic films are used on pediatric patients, the persons caring for the patients must be reminded of the danger of suffocation if the plastic material accidentally covers the face.

HOW SUPPLIED

Cream:
0.025%, 30 g, NDC 16110-034-30; 60 g, NDC 16110-034-60
0.05%, 15 g, NDC 16110-035-15; 30 g, NDC 16110-035-30;
60 g, NDC 16110-035-60

Ointment:
0.025%, 30 g, NDC 16110-024-30; 60 g, NDC 16110-024-60
0.05%, 15 g, NDC 16110-026-15; 30 g, NDC 16110-026-30;
60 g, NDC 16110-026-60

Store at controlled room temperature, 59°-86°F (15°-30°C).
Rx only.

Literature revised February 2006

Marketed by:
Aqua Pharmaceuticals, LLC
Malvern, PA 19355

Under License from:
Oclassen Dermatologics
A Division of Watson Pharma, Inc.
Corona, CA 92880 USA

Manufactured by:
DPT Laboratories, Ltd.
San Antonio, TX 78215

PRINTED IN USA
128401

PRINCIPAL DISPLAY PANEL

Cordran® SP 0.05%
Flurandrenolide Cream, USP
15 g Tube Carton
NDC 16110-035-15

IGI LABORATORIES
105 Lincoln Avenue
P.O. Box 687
Buena, New Jersey 08310-0687

OF THE RETURN ADDRESS. FOLD AT DOTTED LINE

CERTIFIED MAIL™

7012 2210 0000 7509 9179

UNITED STATES POSTAL SERVICE

1000

20852

U.S. POSTAGE
PAID
BUENA, NJ
08310
JAN 17, 13
AMOUNT

$7.80

00089456-01

RETURN RECEIPT REQUESTED

Division of Dockets Management, HFA-305
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RETURN RECEIPT REQUESTED