FERNDALE
LABORATORIES INC
ETHICAL PHARMACEUTICALS SINCE 1897

February 14, 2001

6336 '01 FEB 26 A10:41

Dockets Management Branch (HFA-305)
Food and Drug Administration
Room I-23
12420 Parklawn Drive
Rockville, MD 20857

CITIZEN'S PETITION

The undersigned submits this Petition pursuant to Section 505 of the Federal Food, Drug and Cosmetic Act and 21 CFR 314.93, 10.25(a) and 10.30 of the Food and Drug Administration's regulations, to request the Commissioner of Food and Drugs to make a determination of ANDA suitability for a topical corticosteroid drug product.

A. Action Requested

Petitioner request that the Commissioner of Food and Drugs makes a determination that an abbreviated new drug application (ANDA) is suitable for a topical cream containing 2% hydrocortisone acetate.

B. Statement of Grounds

The Drug Price Competition and Patent Term Restoration Act of 1984 ("The Waxman-Hatch Act") extend eligibility for the submissions of ANDAs to certain drug products identical to those approved via new drug applications, as identified in the Approved Drug Products with Therapeutic Equivalence Evaluations ("The Orange Book") issued by the Food and Drug Administration. Where the proposed product differs from the "reference listed drug" in one or more aspects, a person may petition the Agency, under Section 505(j)(2)(c) of the Act, for a determination of ANDA suitability as a similar or related drug product.

The reference listed drug product which forms the basis for this petition is a topical cream containing hydrocortisone acetate 2.5% (Hydrocortisone Acetate Cream USP 2.5%, manufactured by Ferndale Laboratories, Inc.). Exhibit A contains the printout from the Electronic Orange Book when prescription products are queried for hydrocortisone acetate.

To the best of the petitioner's knowledge, applicable U.S. patents with respect to the drug substance, hydrocortisone acetate have expired.

01P-0085

CP1

780 West Eight Mile Road • Ferndale, Michigan 48220 • 248.548.0900 • 800.621.6003

The proposed drug differs from the reference listed drug product (Hydrocortisone Acetate Cream USP 2.5%) with regard to strength (2% versus 2.5%) and is identical with respect to dosage form, route of administration, and conditions of use. Labeling for the listed drug is included in Exhibit B.

Petitioner intends to request a waiver of bioequivalence based on the DESI status of hydrocortisone acetate.

The healthcare community would benefit from having an alternate choice via the availability of a topical cream product with the potency of 2%. The proposed product contains the same active ingredient (hydrocortisone acetate), at the same route of administration and would be labeled with the same conditions of use as the reference listed drug, Hydrocortisone Acetate Cream USP 2.5%.

Draft labeling for Hydrocortisone Acetate Cream USP 2% is enclosed in Exhibit C and is based on the labeling for the reference listed drug, Hydrocortisone Acetate Cream USP 2.5%. The finished product will be packaged in an appropriate container/closure system.

Based on the above, Petitioner believes that a hydrocortisone acetate cream 2% warrants finding of ANDA suitability and that the Commissioner should grant permission for the filing of an ANDA for a hydrocortisone acetate cream 2%.

C. Environmental Impact

Petitioner hereby claims a categorical exclusion from the requirement of an Environmental Impact Analysis. The approval of this petition will result in an abbreviated new drug application (ANDA) for a drug product that will be excluded for the requirement of an Environmental Impact Analysis, pursuant to 21 CFR §25.24(c)(1).

D. Economic Impact

Information under this section will be submitted if requested by the Commissioner following review of this petition.

E. Certification

The undersigned certifies, that, to the best 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.

Enclosures:

Exhibit A	Printout of the Orange Book found on the FDA website when queried for the active ingredient, Hydrocortisone Acetate.
Exhibit B	Labeling for the listed drug (Hydrocortisone Acetate Cream USP 2.5%)
Exhibit C	Draft labeling (Package insert, carton and canister labels)

Sincerely,
Ferndale Laboratories, Inc.

Deborah L. Theres
Manager, Regulatory Affairs

Exhibit A

Active Ingredient Search Results from "Rx" table for query on "hydrocortisone acetate."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
062166		Yes	BACITRACIN; HYDROCORTISONE ACETATE; NEOMYCIN SULFATE; POLYMYXIN B SULFATE	Ointment; Ophthalmic	400 UNITS/GM; 1%; EQ 3.5MG BASE/GM; 10,000 UNITS/GM	BACITRACIN-NEOMYCIN-POLYMYXIN W/ HYDROCORTISONE ACETATE	PHARMADERM
050202		Yes	CHLORAMPHENICOL; HYDROCORTISONE ACETATE	Powder For Reconstitution; Ophthalmic	12.5MG/VIAL; 25MG/VIAL	CHLOROMYCETIN HYDROCORTISONE	PARKEDALE
050356		Yes	COLISTIN SULFATE; HYDROCORTISONE ACETATE; NEOMYCIN SULFATE; THONZONIUM BROMIDE	Suspension/Drops; Otic	EQ 3MG BASE/ML; 10MG/ML; EQ 3.3MG BASE/ML; 0.5MG/ML	COLY-MYCIN S	PARKEDALE
017351		Yes	HYDROCORTISONE ACETATE	Aerosol, Metered; Rectal	10%	CORTIFOAM	SCHWARZ PHARMA
081274		Yes	HYDROCORTISONE ACETATE	Cream; Topical	1%	HEMSOL-HC	ABLE
040259		Yes	HYDROCORTISONE ACETATE	Cream; Topical	2.5%	HYDROCORTISONE ACETATE	FERNDALE LABS
008228	BP	No	HYDROCORTISONE ACETATE	Injectable; Injection	25MG/ML	HYDROCORTONE	MERCK
008228		Yes	HYDROCORTISONE ACETATE	Injectable; Injection	50MG/ML	HYDROCORTONE	MERCK
083128	BP	No	HYDROCORTISONE ACETATE	Injectable; Injection	25MG/ML	HYDROCORTISONE ACETATE	STERIS
086207		Yes	HYDROCORTISONE ACETATE	Lotion; Topical	0.5%	DRICORT	INGRAM PHARM
080828		Yes	HYDROCORTISONE ACETATE	Ointment; Ophthalmic	0.5%	HYDROCORTISONE ACETATE	ALTANA
083205		No	HYDROCORTISONE ACETATE	Paste; Topical	0.5%	ORABASE HCA	COLGATE
085981		No	HYDROCORTISONE ACETATE	Powder; For Rx Compounding	100%	HYDROCORTISONE ACETATE	PHARMA TEK
060751		Yes	HYDROCORTISONE ACETATE; NEOMYCIN SULFATE	Ointment; Topical	1%; EQ 3.5MG BASE/GM	NEO-CORTEF	PHARMACIA AND UPJOHN

060188		Yes	HYDROCORTISONE ACETATE; NEOMYCIN SULFATE	Suspension/Drops; Ophthalmic	1.5%; EQ 3.5MG BASE/ML	COR-OTICIN	AKORN
050218		Yes	HYDROCORTISONE ACETATE; NEOMYCIN SULFATE; POLYMYXIN B SULFATE	Cream; Topical	0.5%; EQ 3.5MG BASE/GM; 10,000 UNITS/GM	CORTISPORIN	MONARCH PHARMS
061016		Yes	HYDROCORTISONE ACETATE; OXYTETRACYCLINE HYDROCHLORIDE	Suspension/Drops; Ophthalmic	1.5%; EQ 5MG BASE/ML	TERRA-CORTRIL	PFIZER
089440	BX	No	HYDROCORTISONE ACETATE; PRAMOXINE HYDROCHLORIDE	Aerosol, Metered; Topical	1%; 1%	HYDROCORTISONE ACETATE 1% AND PRAMOXINE HCL 1%	COPLEY PHARM
086195	BX	No	HYDROCORTISONE ACETATE; PRAMOXINE HYDROCHLORIDE	Aerosol, Metered; Topical	1%; 1%	PROCTOFOAM HC	SCHWARZ PHARMA
086457	BX	No	HYDROCORTISONE ACETATE; PRAMOXINE HYDROCHLORIDE	Aerosol, Metered; Topical	1%; 1%	EPIFOAM	SCHWARZ PHARMA
083778		No	HYDROCORTISONE ACETATE; PRAMOXINE HYDROCHLORIDE	Cream; Topical	0.5%; 1%	PRAMOSONE	FERNDALE LABS
085368		No	HYDROCORTISONE ACETATE; PRAMOXINE HYDROCHLORIDE	Cream; Topical	1%; 1%	PRAMOSONE	FERNDALE LABS
085980		No	HYDROCORTISONE ACETATE; PRAMOXINE HYDROCHLORIDE	Lotion; Topical	1%; 1%	PRAMOSONE	FERNDALE LABS
085979		No	HYDROCORTISONE ACETATE; PRAMOXINE HYDROCHLORIDE	Lotion; Topical	2.5%; 1%	PRAMOSONE	FERNDALE LABS
080505	AT	Yes	HYDROCORTISONE ACETATE; UREA	Cream; Topical	1%; 10%	CARMOL HC	KENWOOD LABS
089472	AT	No	HYDROCORTISONE ACETATE; UREA	Cream; Topical	1%; 10%	U-CORT	THAMES

Thank you for searching the Electronic Orange Book

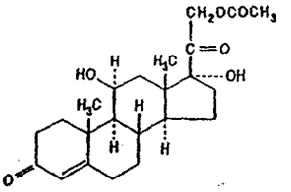
Return to Electronic Orange Book Home Page

Exhibit B

HYDROCORTISONE ACETATE CREAM USP, 2.5%

DESCRIPTION

The topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and anti-pruritic agents. Hydrocortisone acetate is a member of this class. Hydrocortisone Acetate has a molecular formula of $C_{23}H_{32}O_6$, a molecular weight of 404.50 and a CAS registry number of 50-03-3. The chemical name is: Pregn-4-ene-3,20-dione,21-(acetyloxy)-11, 17-dihydroxy-, (11β)- and the chemical structural formula is presented below:



Each gram of the cream contains hydrocortisone acetate 25 mg (2.5% w/w) in a water washable cream containing the following inactive ingredients: aquaphor, isopropyl palmitate, stearic acid, cetyl alcohol, polyoxyl 40 stearate, potassium sorbate, triethanolamine lauryl sulfate, propylene glycol and purified water.

CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. 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.

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. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE

Topical corticosteroids are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS

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

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 which augment systemic absorption include the 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 by using the 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, requiring supplemental systemic corticosteroids.

Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. (See PRECAUTIONS—Pediatric Use.)

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted. In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

Labeling
Hydrocortisone Acetate Cream USP, 2.5% — Insert

Information for Patients: 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 for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed 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 child being treated in the diaper area, as 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, 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.

Pregnancy. Teratogenic Effects. 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 on pregnant patients, in large amounts, or for prolonged period 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 mature patients because of a larger skin surface to body weight ratio.*

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children 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 children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

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	Hypertrichosis	Maceration of the skin
Itching	Acneiform eruptions	Secondary infection
Irritation	Hypopigmentation	Skin atrophy
Dryness	Perioral dermatitis	Striae
Folliculitis	Allergic contact dermatitis	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 effected area as a thin film two to four times daily depending on the severity of the condition.

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.

HOW SUPPLIED

Hydrocortisone Acetate Cream, USP 2.5% is supplied in the following:
1 oz (28.4 g) tubes (NDC 0496-0791-04)
2 oz (57 g) tubes (NDC 0496-0791-03)

℞ Only.

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

FERNDALE LABORATORIES, INC.
FERNDALE, MICHIGAN 48220

Iss. 0998
MG #14144

Exhibit C

Proposed Labeling

Ferndale Laboratories proposed labeling for Hydrocortisone Acetate Cream USP 2% is enclosed on the following pages.

Tube Labeling
- Professional Sample
- 1 oz tube

Carton Labeling
- Professional Sample
- 1 oz tube

Package Insert

Proposed Labeling -
tube text, Professional Sample, Hydrocortisone Acetate Cream USP 2%

NDC

Hydrocortisone Acetate Cream USP 2%

Professional Sample

℞ Only.

FERNDALE LABORATORIES, INC.
Ferndale, MI 48220 USA
Toll free (888) 548-0900

Iss: 0201

Each gram of the cream contains: hydrocortisone acetate 20 mg (2% w/w) in a water washable cream containing the following inactive ingredients: cetostearyl alcohol, ceteth 20, light mineral oil, white petrolatum, propylparaben, butylparaben, citric acid, sodium citrate, and purified water.

USUAL DOSAGE: Apply a thin film to the affected area two to four times daily. See package insert for additional information. **KEEP OUT OF REACH OF CHILDREN. FOR EXTERNAL USE ONLY. NOT FOR OPHTHALMIC USE.** Keep tightly closed. Store at controlled room temperature 15°C - 30°C (59°F - 86°F).

Proposed Labeling -
tube text, 1 oz, Hydrocortisone Acetate Cream USP 2%

NDC

Net Wt. 1 oz (28.4 g)

Hydrocortisone Acetate Cream USP 2%

Each gram of the cream contains: hydrocortisone acetate 20 mg (2% w/w) in a water washable cream containing the following inactive ingredients: cetostearyl alcohol, ceteth 20, light mineral oil, white petrolatum, propylparaben, butylparaben, citric acid, sodium citrate, and purified water.

USUAL DOSAGE: Apply a thin film to the affected area two to four times daily. See package insert for additional information.

Iss: 0201

KEEP OUT OF REACH OF CHILDREN.
FOR EXTERNAL USE ONLY. NOT FOR OPHTHALMIC USE.
Keep tightly closed. Store at controlled room temperature 15°C - 30°C (59°F - 86°F).

℞ Only.

FERNDALE LABORATORIES, INC.
Ferndale, MI 48220 USA
Toll free (888) 548-0900

Proposed Labeling -
carton text, 1 oz, Hydrocortisone Acetate Cream USP 2%

NDC 0496-0834-04

Hydrocortisone Acetate Cream USP 2%

Net Wt. 1 oz (28.4 g)

℞ Only.

Hydrocortisone Acetate Cream USP 2%

USUAL DOSAGE: Apply a thin film to the affected area two to four times daily. See package insert for additional information.
KEEP OUT OF REACH OF CHILDREN.
FOR EXTERNAL USE ONLY. NOT FOR OPHTHALMIC USE.
Keep tightly closed. Store at controlled room temperature 15°C - 30°C (59°F - 86°F).

Bar Code

Hydrocortisone Acetate Cream USP 2%

NDC 0496-0834-04

Hydrocortisone Acetate Cream USP 2%

Net Wt. 1 oz (28.4 g)

℞ Only.

Each gram of the cream contains: hydrocortisone acetate 20 g (2% w/w) in a water washable cream containing the following inactive ingredients: cetostearyl alcohol, ceteth 20, light mineral oil, white petrolatum, propylparaben, butylparaben, citric acid, sodium citrate, and purified water.
Iss: 0201

FERNDALE LABORATORIES, INC.
Ferndale, Michigan 48220 USA

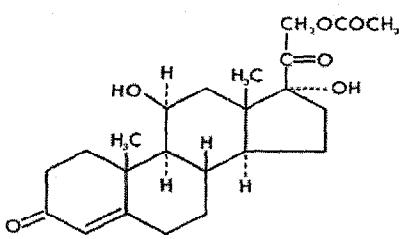
Toll free: (888) 548-0900

Proposed Labeling -
Package Insert

Hydrdocortisone Acetate Cream 2%

DESCRIPTION

The topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and anti-pruritic agents. Hydrocortisone acetate is a member of this class. Hydrocortisone Acetate has a molecular formula of $C_{23}H_{32}O_6$, a molecular weight of 404.50, and a CAS registry number of 50-03-3. The chemical name is: Pregn-4-ene-3,20-dione,21-(acetyloxy)-11, 17-dihydroxy-, (11β)- and the chemical structural formula is presented below:



Hydrocortisone Acetate Cream is a topical preparation containing hydrocortisone acetate 2% w/w in a water washable cream containing the following inactive ingredients: cetostearyl alcohol, ceteth 20, light mineral oil, white petrolatum, propylparaben, butylparaben, citric acid, sodium citrate, and purified water.

CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, anti-pruritic, and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. 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.

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 dressing substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressing may be a valuable therapeutic adjunct for the 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. Corticosteroid are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE

Topical corticosteroids are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS

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

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 which augment systemic absorption include the 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 by using the 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, requiring supplemental systemic corticosteroids.

Children may absorb proportionally larger amounts of topical corticosteroid and thus be more susceptible to systemic toxicity. (See PRECAUTIONS - Pediatric Use.)

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted. In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

information for Patients: 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 used this medication for any disorder other than for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed 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 child being treated in the diaper area, as these garment 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, 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.

Pregnancy. Teratogenic Effects. Pregnancy Category C: Corticosteroids are generally teratogenic in laboratory animals when administered systemically ate 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 on pregnant patients, in large amounts, or for prolonged period of time.

Nursing Mothers: It is not know 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 mature patients because of a larger skin surface to body weight ratio.*

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasm cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

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

ADVERSE REACTIONS:

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

Burning	Hypertrichosis	Maceration of the skin
Itching	Acneiform eruptions	Secondary infection
Irritation	Hypopigmentation	Skin atrophy
Dryness	Perioral dermatitis	Striae
Folliculitis	Allergic contact dermatitis	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 effected areas as a thin film two to four time daily depending on the severity of the condition.

Occlusive dressing may be used for the management of psoriasis or recalcitrant conditions. If an infection develops, the used of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

HOW SUPPLIED

Hydrocortisone Acetate Cream USP 2% 1 oz (28.4 g) tubes NDC

℞ Only.

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

FERNDALE LABORATORIES, INC.
Ferndale, Michigan 48220

Iss. 0201

▲ To seal envelope, remove liner to expose adhesive, close envelope and press firmly ▲

Please place special services sticker here if necessary

CDR

PLEASE TYPE OR PRINT

FOR SHIPMENTS WITHIN U.S. ONLY

FROM

DEBORAH THERES 248-548-0900

TO

FDA: DOCKETS MANAGEMENT BRANCH (HFA-305)
12420 PARKLAWN DRIVE
Rockville MD 20857
ROOM I-23

Payment

Bill to:

Receiver ☐ 3rd Party ☐

☐ Paid in Advance

Origin PTK 4028354643

AIRBORNE EXPRESS

EXP (Letter - 150 lbs) ☒

NAS (Letter - 5 lbs)

SDS (Letter - 150 lbs)

Billing Reference will appear on invoice: HCA USP 2.5%

# of Pkgs	Weight (LBS)	Packaging: One box must be checked — Letter Express	Express Pack	Other Packaging
1	1	☒	☐	☐

Special Instructions

☐ SAT ☐ HAA

☐ LAB ☐

402 835 4643

4 0 2 8 3 5 4 6 4 3

402 835 4643

001 (9/99)M-07 PACKAGE LABEL

MLDA-4X

United States Shipping

1. Complete applicable white sections of the U.S. Airbill. Sign and date the Airbill at the Sender's Signature line. Please press hard.
2. Peel off protective covering from back of Airbill.
3. Affix Airbill to envelope within dotted lines shown.
4. **When using a Drop Box – follow special instructions on the Drop Box.**

International Shipping

Includes Canada & Puerto Rico

Must be typed

1. Complete applicable white sections of the International Express Airbill. Sign and date the Airbill at the Sender's Signature line.
2. Place Airbill in plastic sleeve.
3. Peel off bottom portion from back of plastic sleeve. **Do not seal top**

Limitation on Contents

The maximum acceptable contents of a Letter Express is forty (40) 8-1/2 x 11 pages. If the gross weight of the contents, envelope and airbill exceeds 1/2 pound, the next higher rate will apply. Contents must be of a size and shape which fit the envelope and allow it to be securely sealed without damage. Cash or cash equivalent should not be shipped. Items of high intrinsic value should not be shipped in Letter Express packaging.

Limitations of Liability

Liability of Airborne Express is limited on Letter Express to $100.00 U.S.D., unless a higher value is declared for carriage on our airbill. The maximum declared value on the Letter Express is $500.00 U.S.D. Airborne Express shall not be liable in any event for special incidental ...