

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

75-374

APPROVED DRAFT LABELING



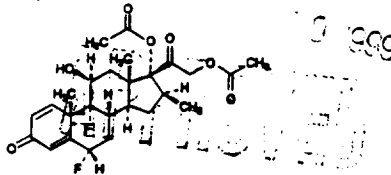
fougera®

DIFLORASONE DIACETATE OINTMENT USP, 0.05%

R only

FOR EXTERNAL USE ONLY NOT FOR OPHTHALMIC USE

DESCRIPTION: Diflorasone diacetate ointment contains 0.5 mg diflorasone diacetate in an ointment base.
Chemically, diflorasone diacetate is 6α,9-difluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 17,21-diacetate with the molecular formula $C_{28}H_{32}F_2O_7$ and a molecular weight of 484.54. The structural formula is represented below:



Each gram of diflorasone diacetate ointment, for topical administration, contains 0.5 mg diflorasone diacetate in an ointment base consisting of propylene glycol, glyceryl monoacetate and white petrolatum.

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. They 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 steroids 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

(over)

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 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 dressings.
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.

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 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 children.

ADVERSE REACTIONS: The following local adverse reactions have been reported 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:

- | | |
|------------------------|---------------------------------|
| 1. Burning | 9. Perioral dermatitis |
| 2. Itching | 10. Allergic contact dermatitis |
| 3. Irritation | 11. Maceration of the skin |
| 4. Dryness | 12. Secondary infections |
| 5. Folliculitis | 13. Skin atrophy |
| 6. Hypertrichosis | 14. Striae |
| 7. Acneiform eruptions | 15. Milaria |
| 8. Hypopigmentation | |

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

DOSAGE AND ADMINISTRATION: Diflurasone diacetate ointment should be applied to the affected area as a thin film from one to three times daily depending on the severity or resistant nature 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 initiated.

HOW SUPPLIED: Diflurasone Diacetate Ointment USP, 0.05% is available in the following size tubes:
NDC 0188-0243-15 15 gram tube
NDC 0188-0243-30 30 gram tube
NDC 0188-0243-60 60 gram tube

Store at controlled room temperature 15° to 30°C (59° to 86°F). Keep tightly closed.

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747

1243
#188
R10/98





N 0168-0243-60 3

NDC 0168-0243-60

fougera®

R only

**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

**FOR EXTERNAL USE ONLY
NOT FOR OPHTHALMIC USE**
WARNING: Keep out of reach
of children.

NET WT 60 grams

DIARY
#233
M004

fougera®
**DIFLORASONE
DIACETATE
OINTMENT
USP, 0.05%**

USUAL DOSAGE: Apply to affected area 1 to 3 times daily.
See package insert for full prescribing information.
Store at controlled room temperature 15°-30°C (59°-86°F). Keep tightly
closed.
IMPORTANT: The opening of this product is covered by a metal tamper-
resistant seal. If this seal has been punctured or is not visible, do not use
and return product to place of purchase.
E. FOUGERA & CO.
a division of Altana Inc., MELVILLE, NEW YORK 11747

TO OPEN: To puncture the seal, reverse
the cap and place the puncture-top onto
the tube. Push down firmly until seal is
open.
To close, screw the cap back onto the
tube.

NDC 0168-0243-60

fougera®

R only

**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

Each gram contains: 0.5 mg
diflorasone diacetate in a vehicle
consisting of propylene glycol,
glyceryl monostearate and white
petrolatum.

NET WT 60 grams

1-3/8 X 1-3/8 X 5-3/16
PRINT SIDE

Item# :IX4487
Pharma : #233
Die SIZE: 1.375" x 1.375" x 6.187"
Colors :Black Process Yellow



N 0168-0243-60 3

NDC 0168-0243-60

fougera[®]

R only

**DIFLORASONE DIACETATE
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DI487
233
Phar

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NDC 0168-0243-60

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PRINT SIDE
1-3/8 X 1-3/8 X 5-3/16

Item# :IX4487
Pharma :#233
Die SIZE: 1.375" x 1.375" x 6.167"
Colors :Black Process Yellow



0168-0243-30

APPROVE

WALLEN
0168
Pharma

NDC 0168-0243-30

R only

fougera®

**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

**FOR EXTERNAL USE ONLY
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NET WT 30 grams

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E. FOUGERA & CO.
a division of Allana Inc., MELVILLE, NEW YORK 11747

TO OPEN: To puncture the seal, reverse
the cap and place the puncture-top onto
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open.

To close, screw the cap back onto the
tube.

NDC 0168-0243-30

R only

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petrolatum.

NET WT 30 grams

0168-0243-30

Item# :IW4486
Pharma :#189
Die SIZE:1.2187" x 1.0" x 5.3125"
Colors: Black, Process Yellow



N 0168-0243-30 6

APPROX

FRONT
SIDE
FRONT

NDC 0168-0243-30

R only

fougera[®]

**DIFLORASONE DIACETATE
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E. FOUGERA & CO.
a division of Altana Inc., MELVILLE, NEW YORK 11747

TO OPEN: To puncture the seal, reverse
the cap and place the puncture-top onto
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To close, screw the cap back onto the
tube.

NDC 0168-0243-30

R only

fougera[®]

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petrolatum.

NET WT 30 grams

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Item# :IW4486
Pharma :#189
Die SIZE:1.2187" x 1.0" x 5.3125"
Colors: Black, Process Yellow

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APPROVED

MAKES
A NEW
FRAME

NDC 0168-0243-15 **R** only
fougera[®]
**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

**FOR EXTERNAL USE ONLY
NOT FOR OPHTHALMIC USE**
WARNING: Keep out of reach
of children.
NET WT 15 grams

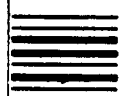
fougera[®]
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DIACETATE
OINTMENT
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IMPORTANT: The opening of this product is covered by a metal temper-resistant seal. If this seal has been punctured or is not visible, do not use and return product to place of purchase.
E. FOUGERA & CO.
a division of Allergan Inc., MELVILLE, NEW YORK 11747

TO OPEN: To puncture the seal, reverse the cap and place the puncture-top onto the tube. Push down firmly until seal is open.
To close, screw the cap back onto the tube.

NDC 0168-0243-15 **R** only
fougera[®]
**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

Each gram contains: 0.5 mg diflorasone diacetate in a vehicle consisting of propylene glycol, glyceryl monostearate and white petrolatum.
NET WT 15 grams



7604
PRINT SIDE SHOWN
1-1/16 x 7/8 x 4-1/4

Item# :IU4485
Die Size:1.063" x .875" x 4.250"
Pharma: #188
Colors: Black, Process Yellow

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APPROVED

11445
2128
1808

NDC 0168-0243-15

only

fougera[®]

**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

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F. FOUGERA & CO.
a division of **Alkermes Inc.**, MELVILLE, NEW YORK 11747

TO OPEN: To puncture the seal, reverse
the cap and place the puncture-top onto
the tube. Push down firmly until seal is
open.
To close, screw the cap back onto the
tube.

NDC 0168-0243-15

only

fougera[®]

**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

Each gram contains: 0.5 mg
diflorasone diacetate in a vehicle
consisting of propylene glycol,
glyceryl monostearate and white
petrolatum.

NET WT 15 grams

T604
PRINT SIDE SHOWN
1-1/16 x 7/8 x 4-1/4

Item#: IU4485
Die Size: 1.063" x .875" x 4.250"
Pharma: #188
Colors: Black, Process Yellow

12/90

NDC 0168-0243-60

fougera[®]

**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

FOR EXTERNAL USE ONLY
NOT FOR OPHTHALMIC USE

R only

Each gram contains: 0.5 mg diflorasone diacetate in a vehicle consisting of propylene glycol, glyceryl monostearate and white petrolatum.

NET WT 60 grams

USUAL DOSAGE: Apply to affected area 1 to 3 times daily.

See package insert for full prescribing information.

WARNING: Keep out of reach of children.

TO OPEN: Use cap to puncture seal.

IMPORTANT: Do not use if seal has been punctured or is not visible.

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

Keep tightly closed.

See crimp of tube for

Lot No. and Exp. Date

X4487

R9/98

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747



3.468

Item# :X4487
Die Size: 1.125" x 6.00"
Pharma :#233
Colors: Black, Process Yellow

6.000

mayo

NDC 0168-0243-60

fougera[®]

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Keep tightly closed.

See crimp of tube for Lot No. and Exp. Date

X4487

R9/98

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747



3.468

Item#: X4487
Die Size: 1.125" x 6.00"
Pharma: #233
Colors: Black, Process Yellow

6.000

2.687

NDC 0168-0243-30

fougera

**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

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WARNING: Keep out of reach of children.
TO OPEN: Use cap to puncture seal.
IMPORTANT: Do not use if seal has been punctured or is not visible.

E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747

R only

Each gram contains: 0.5 mg diflorasone diacetate in a vehicle consisting of propylene glycol, glyceryl monostearate and white petrolatum.

NET WT 30 grams

Store at controlled room temperature 15°-30°C (59°-86°F).
Keep tightly closed.
See crimp of tube for Lot No. and Exp. Date

W4486 R2/08



0168-0243-30

Item# W4486
Die Size: .875" x 5.25"
Pharma #189
Colors Black, Process Yellow

5.250

ujs

NDC 0168-0243-30

fougera®

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OINTMENT USP, 0.05%**

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E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747



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NET WT 30 grams

Store at controlled room temperature 15°-30°C (59°-86°F).
Keep tightly closed.
See crimp of tube for Lot No. and Exp. Date

W4486 R2/96



3 0168-0243-30 6

2.687

Item# W4486
Die Size: .875" x 5.25"
Pharma #189
Colors Black, Process Yellow

5.250

NDC 0188-0243-15

fougera

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E. FOUGERA & CO.
a division of *Alana Inc.*
MELVILLE, NEW YORK 11747

R only **APR** 20 1999

Each gram contains 0.05 mg
diflurasone diacetate in a
vehicle consisting of propylene
glycol, glyceryl monostearate
and white petrolatum.

NET WT 15 grams

Store at controlled room temperature
15°-25°C (59°-77°F).
Keep tightly closed.
See strip of tube for
Lot No. and Exp. Date

U4485 0188-0243-153

2.281

Item# U4485
Die Size: .750" x 4.0"
Pharma #188
Colors Black, Process Yellow

4.000

2.281

NDC 0168-0243-15

fougera

**DIFLORASONE DIACETATE
OINTMENT USP, 0.05%**

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E. FOUGERA & CO.
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MELVILLE, NEW YORK 11747

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Store at controlled room temperature
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Keep tightly closed.
See stamp of tube for
Lot No. and Exp. Date

APR 20 1999

U4485

0168-0243-15 3

Item# U4485
Die Size: .750" x 4.0"
Pharma #188
Colors Black, Process Yellow

4.000