CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76067

DRAFT FINAL PRINTED LABELING

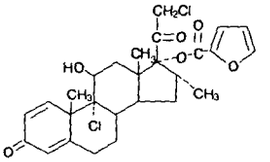
Mometasone Furoate Ointment USP, 0.1%

For Dermatologic Use Only
Not for Ophthalmic Use

℞ only

DESCRIPTION Mometasone Furoate Ointment USP, 0.1% contains mometasone furoate for dermatologic use. Mometasone furoate is a synthetic corticosteroid with anti-inflammatory activity.

Chemically, mometasone furoate is 9α,21-Dichloro-11β,17-dihydroxy-16α-methylpregna-1,4-diene-3,20-dione 17-(2-furoate), with the empirical formula $C_{27}H_{30}Cl_2O_6$, a molecular weight of 521.4 and the following structural formula:



Mometasone furoate is a white to off-white powder practically insoluble in water, slightly soluble in octanol, and moderately soluble in ethyl alcohol.

Each gram of Mometasone Furoate Ointment USP, 0.1% contains: 1 mg mometasone furoate in an ointment base of hexylene glycol, phosphoric acid, propylene glycol stearate, white wax, white petrolatum, and purified water.

CLINICAL PHARMACOLOGY Like other topical corticosteroids, mometasone furoate has anti-inflammatory, anti-pruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A_2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A_2.

Pharmacokinetics The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Occlusive dressings with hydrocortisone for up to 24 hours have not been demonstrated to increase penetration; however, occlusion of hydrocortisone for 96 hours markedly enhances penetration. Studies in humans indicate that approximately 0.7% of the applied dose of Mometasone Furoate Ointment USP, 0.1% enters the circulation after 8 hours of contact on normal skin without occlusion. Inflammation and/or other disease processes in the skin may increase percutaneous absorption.

Studies performed with Mometasone Furoate Ointment USP, 0.1% indicate that it is in the medium range of potency as compared with other topical corticosteroids.

In a pediatric trial, 24 atopic dermatitis patients, of which 19 patients were age 2 to 12 years, were treated with Mometasone Furoate Cream USP, 0.1% once daily. The majority of patients cleared within 3 weeks.

INDICATIONS AND USAGE Mometasone Furoate Ointment USP, 0.1% is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Mometasone Furoate Ointment USP, 0.1% may be used in pediatric patients 2 years of age or older, although the safety and efficacy of drug use for longer than 3 weeks have not been established (see **PRECAUTIONS - Pediatric Use**). Since safety and efficacy of Mometasone Furoate Ointment USP, 0.1% have not been established in pediatric patients below 2 years of age, its use in this age group is not recommended.

CONTRAINDICATIONS Mometasone Furoate Ointment USP, 0.1% is contraindicated in those patients with a history of hypersensitivity to any of the components in the preparation.

PRECAUTIONS ***General*** Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Patients applying a topical steroid to a large surface area or areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free cortisol tests.

In a study evaluating the effects of mometasone furoate ointment on the hypothalamic-pituitary-adrenal (HPA) axis, 15 grams were applied twice daily for 7 days to six adult patients with psoriasis or atopic dermatitis. The ointment was applied without occlusion to at least 30% of the body surface. The results show that the drug caused a slight lowering of adrenal corticosteroid secretion.

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 corticosteroid.

Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur requiring supplemental systemic corticosteroids. For information on systemic supplementation, see Prescribing Information for those products.

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios (see **PRECAUTIONS - Pediatric Use**).

If irritation develops, Mometasone Furoate Ointment USP, 0.1% should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing failure to heal rather than noting a clinical exacerbation as with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic patch testing.

If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favorable response does not occur promptly, use of Mometasone Furoate Ointment USP, 0.1% 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. This medication should not be used 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 so as to be occlusive unless directed by the physician.

4. Patients should report to their physician any signs of local adverse reactions.
5. Parents of pediatric patients should be advised not to use Mometasone Furoate Ointment USP, 0.1% in the treatment of diaper dermatitis. Mometasone Furoate Ointment USP, 0.1% should not be applied in the diaper area as diapers or plastic pants may constitute occlusive dressing (see **DOSAGE AND ADMINISTRATION**).
6. This medication should not be used on the face, underarms, or groin areas unless directed by the physician.
7. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician.

Laboratory Tests The following tests may be helpful in evaluating patients for HPA axis suppression:

ACTH stimulation test
A.M. plasma cortisol test
Urinary free cortisol test

Carcinogenesis, Mutagenesis, and Impairment of Fertility In studies of the effect of mometasone furoate on fertility, pregnancy, and postnatal development in rats and rabbits, 25 rats were treated with doses up to 1.2 mg/kg of drug topically, and 15 rabbits with doses up to 0.3 mg/kg of drug topically. The drugs were left on the skin for 6 hours daily during gestation. At the highest dosage, the rat dams lost weight. One of the rabbit dams at the highest dosage had wrinkled skin, muscle wasting and aborted 5 fetuses.

Genetic toxicity studies with mometasone furoate, which included the Ames test, mouse lymphoma assay, and a micronucleus test did not reveal any mutagenic potential.

Long term animal studies have not been performed to evaluate the carcinogenic potential of Mometasone Furoate Ointment USP, 0.1%.

Pregnancy Teratogenic effects: Pregnancy Category C Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.

Rat offspring of dams treated with 1.2 mg/kg of mometasone furoate topically (4 times the maximum dose in a 50 kg individual) displayed umbilical hernias, unossified sternebrae and vertebrae, and wavy ribs, as well as markedly depressed fetal growth. Rabbit offspring of dams treated with up to 0.3 mg/kg of mometasone furoate topically (the same dose as the maximum dose in a 50 kg individual) displayed flexed paws, umbilical hernias, and cleft palate. A 50 kg female using 1 gram of Mometasone Furoate Ointment USP, 0.1% would apply approximately 0.023 mg/kg.

There are no adequate and well-controlled studies of the teratogenic potential of mometasone furoate in pregnant women. Therefore, Mometasone Furoate Ointment USP, 0.1% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when Mometasone Furoate Ointment USP, 0.1% is administered to a nursing woman.

Pediatric Use Mometasone Furoate Ointment USP, 0.1% may be used with caution in pediatric patients 2 years of age or older, although the safety and efficacy of drug use for longer than 3 weeks have not been established. Use of Mometasone Furoate Ointment USP, 0.1% is supported by results from adequate and well-controlled studies in pediatric patients with corticosteroid-responsive dermatoses. Since safety and efficacy of Mometasone Furoate Ointment USP, 0.1% have not been established in pediatric patients below 2 years of age, its use in this age group is not recommended. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are, therefore, also at greater risk of gluco-corticosteroid insufficiency during and/or after withdrawal of treatment. Pediatric patients may be more susceptible than adults to skin atrophy, including striae, when they are treated with topical corticosteroids. Pediatric patients applying topical corticosteroids to greater than 20% of body surface are at higher risk of HPA axis suppression.

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

Mometasone Furoate Ointment USP, 0.1% should not be used in the treatment of diaper dermatitis.

ADVERSE REACTIONS In controlled clinical studies involving 812 patients, the incidence of adverse reactions associated with the use of Mometasone Furoate Ointment USP, 0.1% was 4.8%. Reported reactions included burning, pruritus, skin atrophy, tingling/stinging, and furunculosis. Reports of rosacea associated with the use of Mometasone Furoate Ointment USP, 0.1% have been received. In controlled clinical studies (n=74) involving pediatric patients 2 to 12 years of age, the incidence of adverse experiences associated with the use of Mometasone Furoate Cream is approximately 7%. Reported reactions included stinging, pruritus, and furunculosis.

The following additional local adverse reactions have been 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: irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae, and miliaria.

OVERDOSAGE Topically applied Mometasone Furoate Ointment USP, 0.1% can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS**).

DOSAGE AND ADMINISTRATION Apply a thin film of Mometasone Furoate Ointment USP, 0.1% to the affected skin areas once daily. Mometasone Furoate Ointment USP, 0.1% may be used in pediatric patients 2 years of age or older. Safety and efficacy of Mometasone Furoate Ointment USP, 0.1% in pediatric patients for more than 3 weeks have not been established. Use in pediatric patients under 2 years of age is not recommended.

As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, reassessment of diagnosis may be necessary.

Mometasone Furoate Ointment USP, 0.1% should not be used with occlusive dressings unless directed by a physician. Mometasone Furoate Ointment USP, 0.1% should not be applied in the diaper area if the child still requires diapers or plastic pants as these garments may constitute occlusive dressing.

HOW SUPPLIED Mometasone Furoate Ointment USP, 0.1% is supplied in 15 g and 45 g tubes; boxes of one.

Store Mometasone Furoate Ointment USP, 0.1% between 2° and 30°C (36° and 86°F).

Mfg. By: Clay-Park Labs, Inc., Bronx, NY 10457

D119
N0701

Usual Dose: See package insert.

Each gram contains: 1 mg mometasone furoate in an ointment base of hexylene glycol, phosphoric acid, propylene glycol stearate, white wax, white petrolatum, and purified water.

11945CPL-2X
N0701

NDC 45802-119-42

MOMETASONE FUROATE OINTMENT USP, 0.1%

For Dermatologic Use Only.
Not for Ophthalmic Use.

45 g

MAR 18 2002

℞ only

MOMETASONE FUROATE OINTMENT USP, 0.1%
45 g

Read accompanying directions carefully.

APPROVED

Store between 2° and 30°C (36° and 86°F).

Lot number and Expiration date see crimp of tube or see box.

Mfg. By: **CLAY-PARK LABS, INC.**, Bronx, NY 10457

UPC
0-81642-11942

NDC 45802-119-42

MOMETASONE FUROATE OINTMENT USP, 0.1%

For Dermatologic Use Only.
Not for Ophthalmic Use.

45 g

℞ only

MOMETASONE FUROATE OINTMENT USP, 0.1%
45 g

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AP 3/18/02

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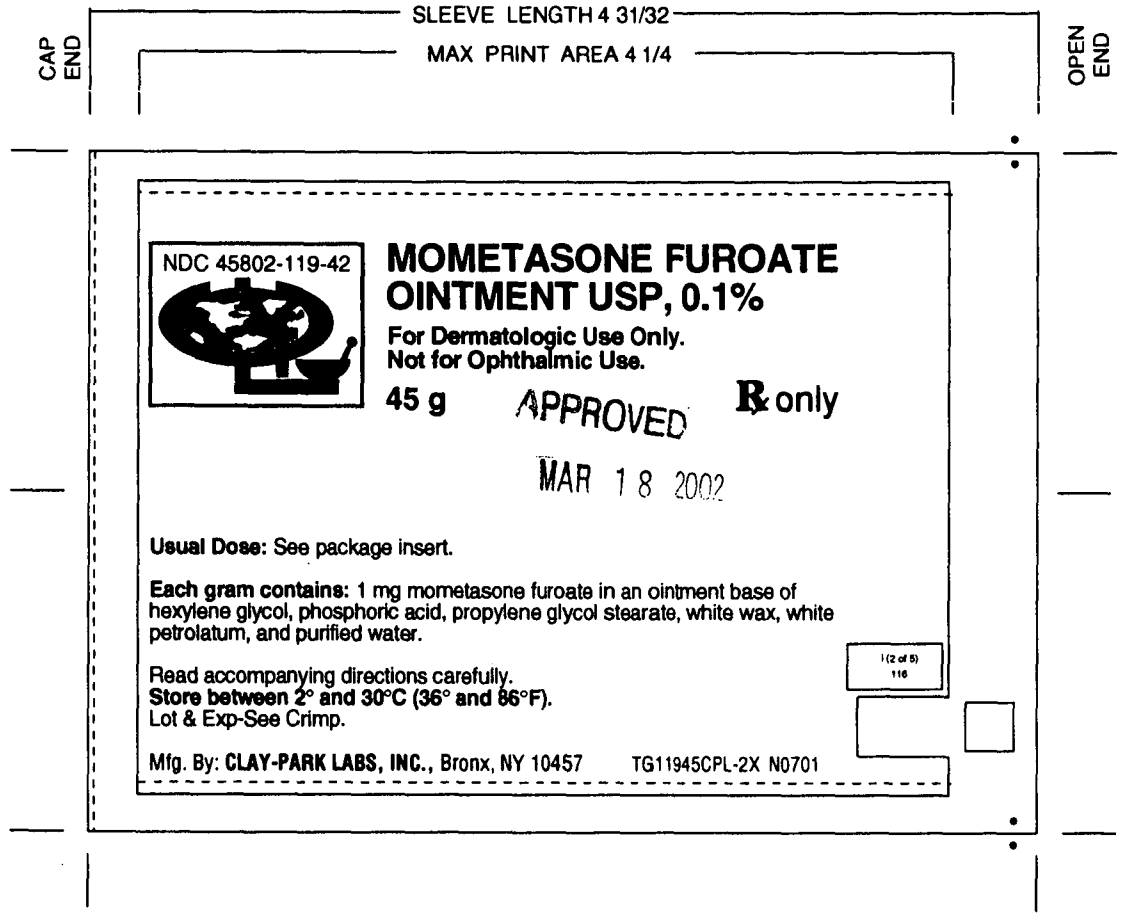

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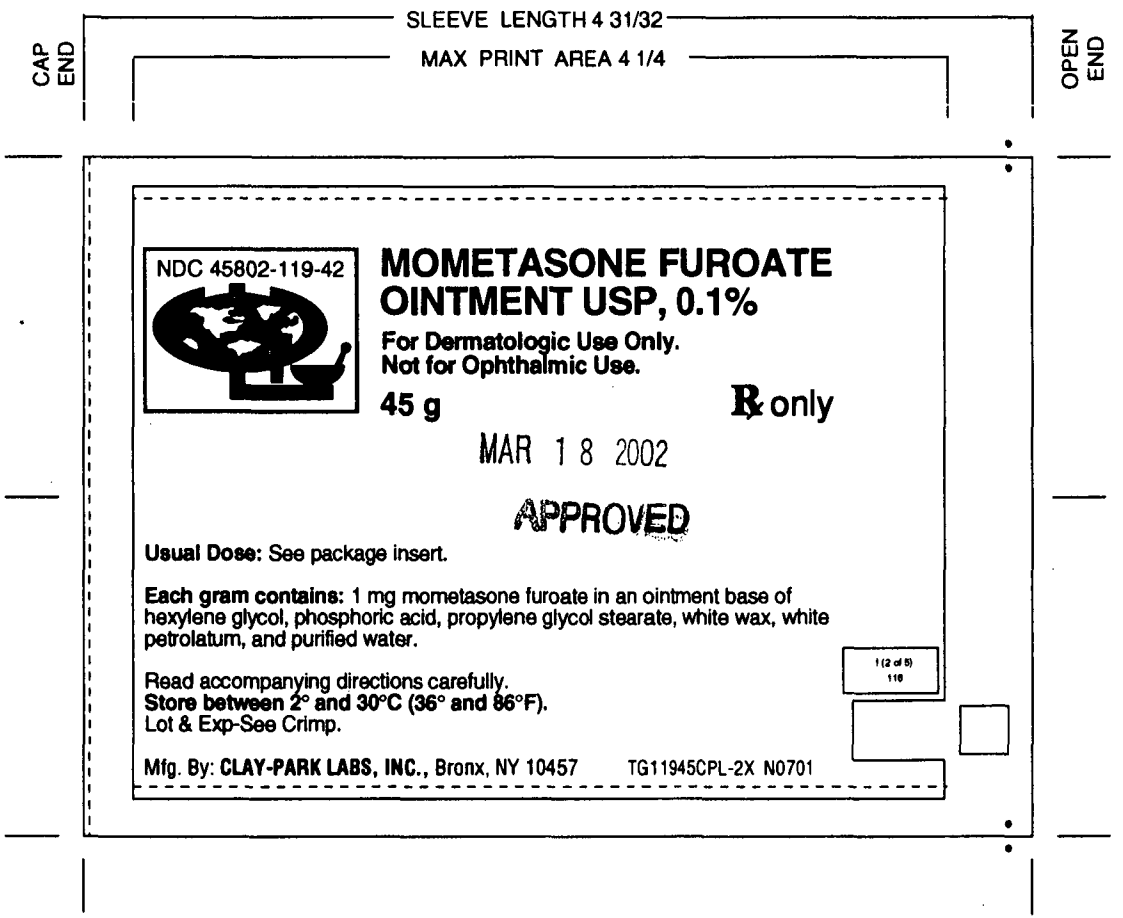

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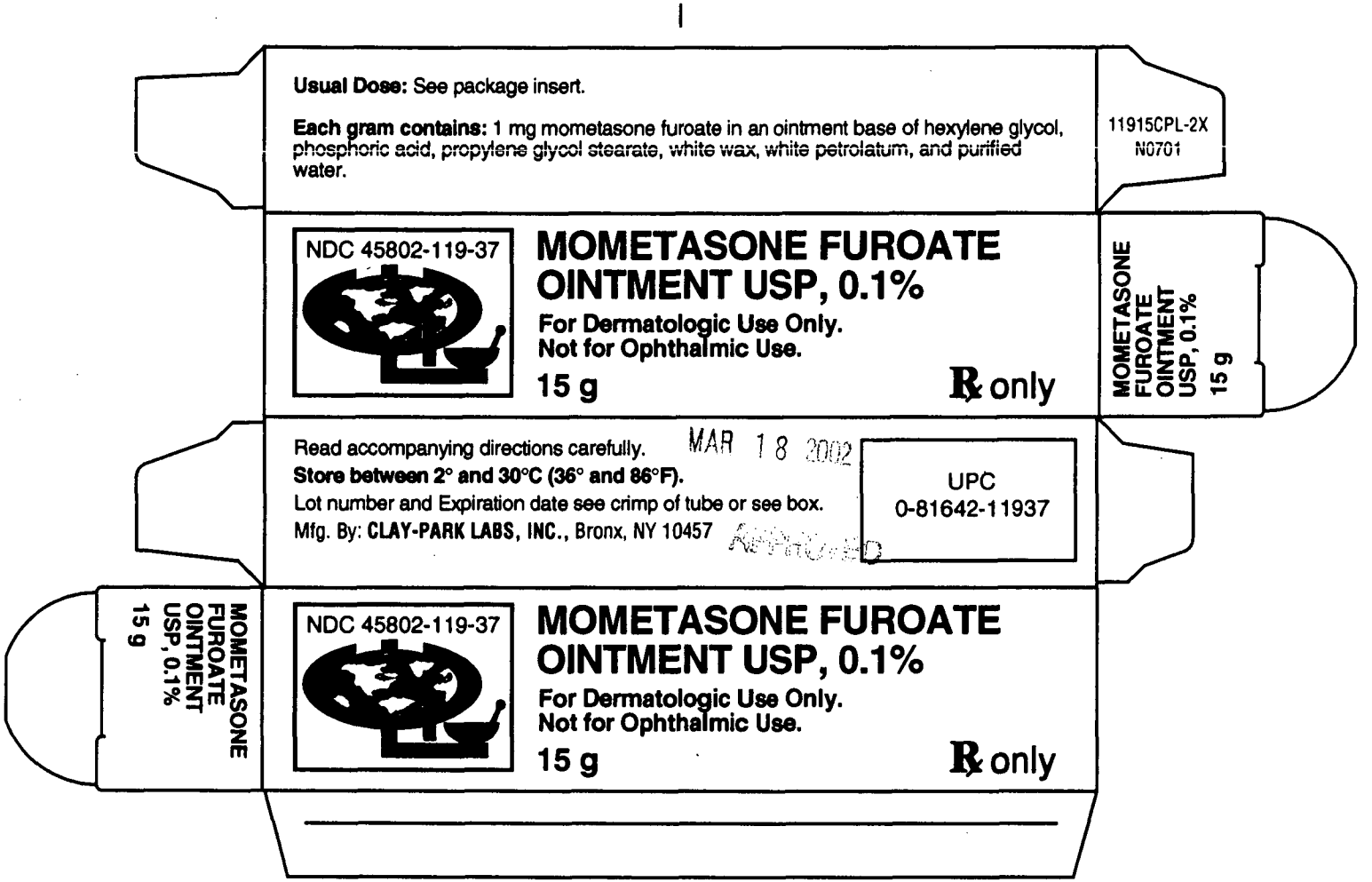

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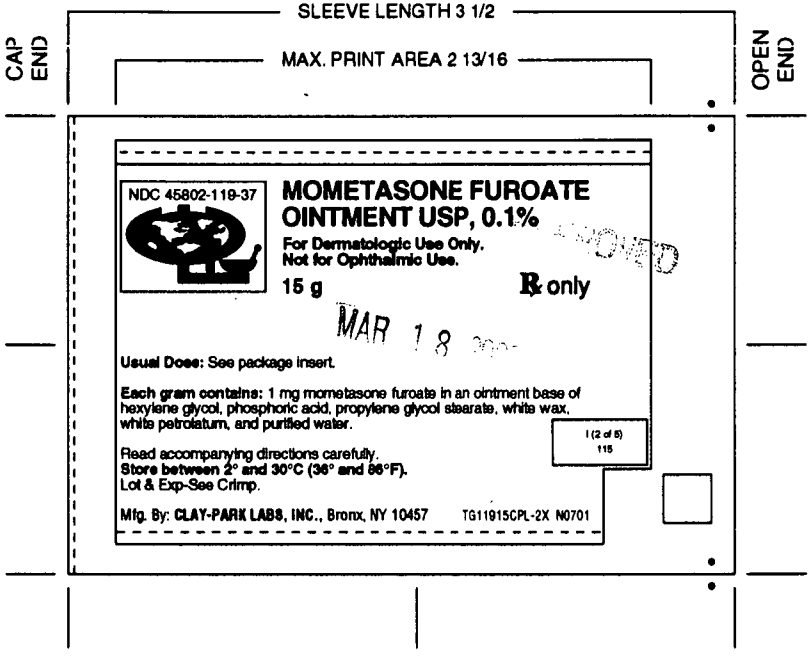

109-6

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