PRODUCT INFORMATION

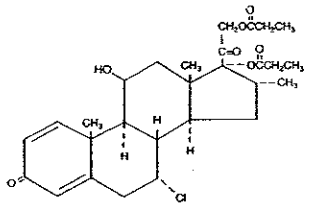
ACLOVATE® (alclometasone dipropionate cream) Cream, 0.05%

ACLOVATE® (alclometasone dipropionate ointment) Ointment, 0.05%

For Dermatologic Use Only— Not for Ophthalmic Use.

DESCRIPTION: ACLOVATE Cream and Ointment contain alclometasone dipropionate (7α-chloro-11β,17,21-trihydroxy-16α-methylpregna-1,4-diene-3,20-dione 17,21-dipropionate), a synthetic corticosteroid for topical dermatologic use. The corticosteroids constitute a class of primarily synthetic steroids used topically as anti-inflammatory and antipruritic agents.

Chemically, alclometasone dipropionate is $C_{28}H_{37}ClO_7$. It has the following structural formula:



Alclometasone dipropionate has the molecular weight of 521. It is a white powder, insoluble in water, slightly soluble in propylene glycol, and moderately soluble in hexylene glycol.

Each gram of ACLOVATE Cream contains 0.5 mg of alclometasone dipropionate in a hydrophilic, emollient cream base of propylene glycol, white petrolatum, cetearyl alcohol, glyceryl stearate, PEG 100 stearate, Ceteth-20, monobasic sodium phosphate, chlorocresol, phosphoric acid, and purified water.

Each gram of ACLOVATE Ointment contains 0.5 mg of alclometasone dipropionate in an ointment base of hexylene glycol, white wax, propylene glycol stearate, and white petrolatum.

CLINICAL PHARMACOLOGY: Like other topical corticosteroids, alclometasone dipropionate has anti-inflammatory, antipruritic, 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. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption. A study utilizing a radiolabeled alclometasone dipropionate ointment formulation was performed to measure systemic absorption and excretion. Results indicated that approximately 3% of the steroid was absorbed during 8 hours of contact with intact skin of normal volunteers.

Studies performed with ACLOVATE Cream and Ointment indicate that these products are in the low to medium range of potency as compared with other topical corticosteroids.

INDICATIONS AND USAGE: ACLOVATE Cream and Ointment are low to medium potency corticosteroids indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. ACLOVATE Cream and Ointment may be used in pediatric patients 1 year 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 the safety and efficacy of ACLOVATE Cream and Ointment have not been established in pediatric patients below 1 year of age, their use in this age-group is not recommended.

CONTRAINDICATIONS: ACLOVATE Cream and Ointment are contraindicated in those patients with a history of hypersensitivity to any of the components in these preparations.

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 to 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.

The effects of ACLOVATE Cream and Ointment on the HPA axis have been evaluated. In one study, ACLOVATE Cream and Ointment were applied to 30% of the body twice daily for 7 days, and occlusive dressings were used in selected patients either 12 hours or 24 hours daily. In another study, ACLOVATE Cream was applied to 80% of the body surface of normal subjects twice daily for 21 days with daily 12-hour periods of whole body occlusion. Average plasma and urinary free cortisol levels and urinary levels of 17-hydroxysteroids were decreased (about 10%), suggesting suppression of the HPA axis under these conditions. Plasma cortisol levels have also been demonstrated to decrease in pediatric patients treated twice daily for 3 weeks without occlusion.

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 area to body mass ratios (see PRECAUTIONS: Pediatric Use).

If irritation develops, ACLOVATE Cream or Ointment should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing a *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 ACLOVATE Cream or Ointment 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, 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 ACLOVATE Cream or Ointment in the treatment of diaper dermatitis. ACLOVATE Cream or Ointment 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, Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids.

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. There are no adequate and well-controlled studies in pregnant women. ACLOVATE Cream or Ointment 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 topical 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 ACLOVATE Cream or Ointment is administered to a nursing woman.

Pediatric Use: ACLOVATE Cream and Ointment may be used with caution in pediatric patients 1 year of age or older, although the safety and efficacy of drug use for longer than 3 weeks have not been established. Use of ACLOVATE Cream and Ointment is supported by results from adequate and well-controlled studies in pediatric patients with corticosteroid-responsive dermatoses. Since the safety and efficacy of ACLOVATE Cream and Ointment have not been established in pediatric patients below 1 year 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 adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects, including striae, have been reported with inappropriate use of topical corticosteroids in infants and children. Pediatric patients applying ACLOVATE Cream or Ointment to >20% of the body surface area are at higher risk for HPA axis suppression.

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

ACLOVATE Cream or Ointment should not be used in the treatment of diaper dermatitis.

Geriatric Use: A limited number of patients at or above 65 years of age have been treated with ACLOVATE Cream and Ointment in US clinical trials. The number of patients is too small to permit separate analysis of efficacy and safety. No adverse events were reported with ACLOVATE Ointment in geriatric patients, and the single adverse reaction reported with ACLOVATE Cream in this population was similar to those reported by younger patients. Based on available data, no adjustment of dosage of ACLOVATE Cream and Ointment in geriatric patients is warranted.

ADVERSE REACTIONS: The following local adverse reactions have been reported with ACLOVATE Cream in approximately 2% of patients: itching and burning, erythema, dryness, irritation, and papular rashes.

The following local adverse reactions have been reported with ACLOVATE Ointment in approximately 1% of patients: itching, burning, and erythema.

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 approximate decreasing order of occurrence: folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and miliaria.

OVERDOSAGE: Topically applied ACLOVATE Cream and Ointment can be absorbed in sufficient amounts to produce systemic effects (see PRECAUTIONS).

DOSAGE AND ADMINISTRATION: Apply a thin film of ACLOVATE Cream or Ointment to the affected skin areas two or three times daily; massage gently until the medication disappears.

ACLOVATE Cream and Ointment may be used in pediatric patients 1 year of age or older. Safety and effectiveness of ACLOVATE Cream or Ointment in pediatric patients for more than 3 weeks of use have not been established. Use in pediatric patients under 1 year 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.

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

Geriatric Use: In studies where geriatric patients (65 years of age or older, see PRECAUTIONS) have been treated with ACLOVATE Cream or Ointment, safety did not differ from that in younger patients; therefore, no dosage adjustment is recommended.

HOW SUPPLIED: ACLOVATE Cream, 0.05% is supplied in 15-g (NDC 0173-0401-00), 45-g (NDC 0173-0401-01), and 60-g (NDC 0173-0401-06) tubes.

ACLOVATE Ointment, 0.05% is supplied in 15-g (NDC 0173-0402-00), 45-g (NDC 0173-0402-01), and 60-g (NDC 0173-0402-06) tubes.

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

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July 2000 RL-846