Fujisawa

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CYCLOCORT®

(amcinonide)

DESCRIPTION

The topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and antipruritic agents.

TOPICAL LOTION 0.1%

Each gram of CYCLOCORT (amcinonide) Topical Lotion contains 1 mg of the active steroid amcinonide in AQUATAIN,* a white, smooth, homogeneous, opaque emulsion composed of Benzyl Alcohol 1% (wt/wt) as preservative, Emulsifying Wax, Glycerin, Isopropyl Palmitate, Lactic Acid, Purified Water and Sorbitol Solution. In addition, contains Polyethylene Glycol 400.

Sodium hydroxide may be used to adjust pH to approximately 4.4 during manufacture.

TOPICAL CREAM 0.1%

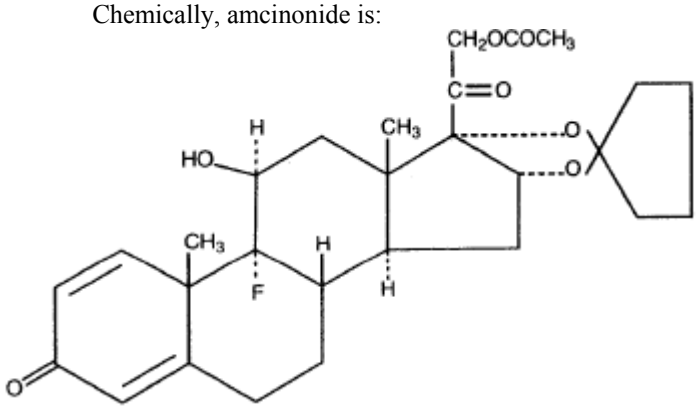
Each gram of CYCLOCORT (amcinonide) Topical Cream contains 1 mg of the active steroid amcinonide in AQUATAIN,* a white, smooth, homogeneous, opaque emulsion composed of Benzyl Alcohol 2% (wt/wt) as preservative, Emulsifying Wax, Glycerin, Isopropyl Palmitate, Lactic Acid, Purified Water and Sorbitol Solution.

*AQUATAIN™ is non-staining, water-washable, paraben-free, spermaceti-free, and has a light texture and consistency.

TOPICAL OINTMENT 0.1%

Each gram of CYCLOCORT (amcinonide) Topical Ointment contains 1 mg of the active steroid amcinonide in a specially formulated base composed of Benzyl Alcohol 2% (wt/wt), White Petrolatum, Emulsifying Wax, and Tenox II (Butylated Hydroxyanisole, Propyl Gallate, Citric Acid, Propylene Glycol).

Chemically, amcinonide is:



$C_{28}H_{35}FO_7$ **Molecular Weight 502.58**

Pregna-1, 4-diene-3,20-dione, 21-(acetyloxy)-16,17-[cyclopentylidenebis (oxy)] -9-fluoro-11-hydroxy-, (11β, 16α).

CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, antipruritic 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 (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.

CONTRAINDICATONS

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 that 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.

Pediatric patients 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.

The products are not for ophthalmic use.

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 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 since 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.

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 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, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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 pediatric patients.

ADVERSE REACTIONS

In the clinical trials with CYCLOCORT Lotion, the investigators reported a 4.7% incidence of side effects. In a weekly acceptability evaluation, approximately 20% of the patients treated with CYCLOCORT Lotion or placebo reported itching, stinging, soreness, or burning at one or more of the visits.

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
Acneiform eruptions
Hypopigmentation
Perioral dermatitis
Allergic contact dermatitis
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 from two to three times daily depending on the severity of the condition.

The lotion may be applied topically to the specified lesions, particularly to those in hairy areas, two times per day. The lotion should be rubbed into the affected area completely, and the area should be protected from washing, clothing, rubbing, etc. until the lotion has dried.

Occlusive dressings may be a valuable therapeutic adjunct 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

CYCLOCORT® (amcinonide) Topical Lotion 0.1% (1 mg/g) with AQUATAIN™ hydrophilic base

NDC 0469-7404-20 Product Code 740420
20 mL (19.6 g) bottle

NDC 0469-7404-60 Product Code 740460
60 mL (58.8 g) bottle

CYCLOCORT® (amcinonide) Topical Cream 0.1% (1 mg/g) with AQUATAIN™ hydrophilic base

NDC 0469-7054-15 Product Code 705415
15 g tube

NDC 0469-7054-30 Product Code 705430
30 g tube

NDC 0469-7054-60 Product Code 705460
60 g tube

CYCLOCORT® (amcinonide)Topical Ointment 0.1% (1 mg/g)

NDC 0469-7115-15 Product Code 711515
15 g tube

NDC 0469-7115-30 Product Code 711530
30 g tube

NDC 0469-7115-60 Product Code 711560
60 g tube

Store at Controlled Room Temperature 15º-30ºC (59º-86ºF).
DO NOT FREEZE.

Rx only

Manufactured for
Fujisawa Healthcare, Inc.,
Deerfield, IL 60015

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jonathan Wilkin
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