

# Anusol-HC<sup>®</sup> 2.5%

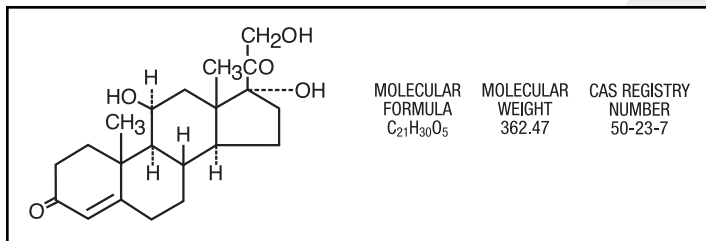
## (Hydrocortisone Cream, USP)

### RX ONLY.

#### DESCRIPTION

The topical corticosteroids constitute a class of primarily synthetic steroids used as antiinflammatory and antipruritic agents. Anusol-HC 2.5% (Hydrocortisone Cream, USP) is a topical corticosteroid with hydrocortisone 2.5% (active ingredient) in a water-washable cream containing the following inactive ingredients: benzyl alcohol, petrolatum, stearyl alcohol, propylene glycol, isopropyl myristate, polyoxyl 40 stearate, carbomer 934, sodium lauryl sulfate, edetate disodium, sodium hydroxide to adjust the pH, and purified water.

Hydrocortisone has the chemical name Pregn-4-ene-3,20-dione, 11,17, 21, trihydroxy-, (11 $\beta$ )- and the chemical structure below.



#### CLINICAL PHARMACOLOGY

Topical corticosteroids share antiinflammatory, antipruritic and vasoconstrictive actions.

The mechanism of antiinflammatory activity of the topical corticosteroids is unclear. Various laboratory methods, including vaso-constrictor 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.

If HPA axis suppression is noted (by using the urinary free cortisol and ACTH stimulation tests) an attempt should be made to withdraw the drug or to reduce the frequency of application.

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.

**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 has been 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 urinary free cortisol test and the ACTH stimulation test may be helpful in evaluating the HPA axis suppression.

**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 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 corticosteroids administered to a nursing woman.

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, caution should be exercised when topical corticosteroids are administered to a nursing woman.

**USE IN PEDIATRIC PATIENTS:** 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

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    | Dryness        | Acneiform eruptions | Allergic contact dermatitis | Skin atrophy |
| Itching    | Folliculitis   | Hypopigmentation    | Maceration of the skin      | Striae       |
| Irritation | Hypertrichosis | Perioral dermatitis | Secondary infection         | Miliaria     |

#### OVERDOSAGE

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

#### DOSAGE AND ADMINISTRATION

Anusol-HC<sup>®</sup> 2.5% (Hydrocortisone Cream, USP) should be applied to the affected area 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

Anusol-HC<sup>®</sup> 2.5% (Hydrocortisone Cream, USP) is supplied in 30 gram tubes (NDC 65649-401-30).

**STORE AT 20°–25°C (68°–77°F). SEE USP CONTROLLED ROOM TEMPERATURE. STORE AWAY FROM HEAT. PROTECT FROM FREEZING.**

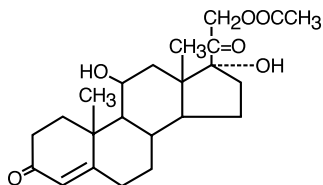
#### PRESCRIBING INFORMATION AS OF OCTOBER 2003.

Manufactured for: Salix Pharmaceuticals, Inc., Morrisville, NC 27560

# Anusol-HC<sup>®</sup> 25 mg Suppository (Hydrocortisone Acetate)

## DESCRIPTION

Each Anusol-HC<sup>®</sup> 25-mg Suppository contains 25 mg hydrocortisone acetate in a hydrogenated vegetable oil base. Hydrocortisone acetate is a corticosteroid. Chemically, hydrocortisone acetate is pregn-4-ene-3, 20-dione, 21-(acetyloxy)-11, 17-dihydroxy (11B)- with the following structural formula:



## CLINICAL PHARMACOLOGY

In normal subjects, about 26 percent of hydrocortisone acetate is absorbed when the hydrocortisone acetate suppository is applied to the rectum. Absorption of hydrocortisone acetate may vary across abraded or inflamed surfaces.

Topical steroids are primarily effective because of their anti-inflammatory, anti-pruritic and vasoconstrictive action.

## INDICATIONS AND USAGE

For use in inflamed hemorrhoids, post-irradiation (facitial) proctitis, as an adjunct in the treatment of chronic ulcerative colitis, cryptitis, other inflammatory conditions of the anorectum, and pruritis ani.

## CONTRAINDICATION

Anusol-HC<sup>®</sup> suppositories are contraindicated in those patients with a history of hypersensitivity to any of the components.

## PRECAUTIONS

Do not use unless adequate proctologic examination is made. If irritation develops, the product should be discontinued and appropriate therapy instituted.

In the presence of an infection, 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.

No long-term studies in animals have been performed to evaluate the carcinogenic potential of corticosteroid suppositories.

## INFORMATION FOR PATIENTS

Staining of fabric may occur with use of the suppository. Precautionary measures are recommended.

## PREGNANCY CATEGORY C

In laboratory animals, topical steroids have been associated with an increase in the incidence of fetal abnormalities when gestating females have been exposed to rather low dosage levels. There are no adequate and well-controlled studies in pregnant women.

Anusol-HC<sup>®</sup> suppositories should only be used during pregnancy if the potential benefit justifies the 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.

It is not known whether this drug is excreted in human milk, and because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Anusol-HC<sup>®</sup> suppositories, 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.

## ADVERSE REACTIONS

The following local adverse reactions have been reported with corticosteroid suppositories.

1. Burning
2. Itching
3. Irritation
4. Dryness
5. Folliculitis
6. Hypopigmentation
7. Allergic contact dermatitis
8. Secondary infection

## DRUG ABUSE AND DEPENDENCE

Drug abuse and dependence has not been reported in patients treated with Anusol-HC<sup>®</sup> suppositories.

## OVERDOSAGE

If signs and symptoms of systemic overdosage occur, discontinue use.

## DOSAGE AND ADMINISTRATION

Usual dosage: One suppository in the rectum morning and night for two weeks, in nonspecific proctitis. In more severe cases, one suppository three times daily; or two suppositories twice daily. In factitial proctitis, recommended therapy is six to eight weeks or less, according to response.

## HOW SUPPLIED

Anusol-HC<sup>®</sup> 25-mg Suppositories are white, cylinder shaped, with one end tapered. Package of 12 suppositories (NDC 65649-411-12) and package of 24 suppositories (NDC 65649-411-24).

Store at 20°–25°C (68°–77°F). See USP controlled room temperature. Store away from heat. Protect from freezing. Rx only.

## PRESCRIBING INFORMATION AS OF OCTOBER 2003.

Manufactured for: Salix Pharmaceuticals, Inc., Morrisville, NC 27560

## OPENING INSTRUCTIONS

Avoid excessive handling of the suppository.

It is designed to melt at body temperature.

1. Separate plastic film at top opening and pull downward.
2. Continue pulling downward to almost the full length of the suppository.
3. Gently remove the suppository from the film pocket.

