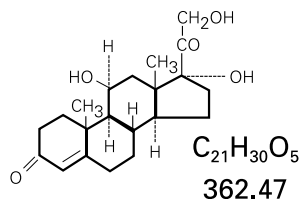


# PROCTOCORT® Cream

## (Hydrocortisone Cream, USP) 1%

### DESCRIPTION

The topical corticosteroids constitute a class of primary synthetic steroids used as anti-inflammatory and antipruritic agents. Hydrocortisone is a member of this class. Chemically hydrocortisone is pregn-4-ene-3, 20-dione, 11, 17, 21-trihydroxy-, (11β)-. Its structural formula is:



Each gram of Proctocort® Cream (Hydrocortisone Cream USP) 1% contains 10mg hydrocortisone USP in a cream base consisting of purified water, cetyl alcohol, glycerin, stearyl alcohol, propylene glycol, sodium lauryl sulfate, cetyl palmitate, and sorbic acid.

### 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. 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

Hydrocortisone cream is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

### CONTRAINDICATIONS

Hydrocortisone cream is 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 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 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, 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, 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, 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 children receiving topical corticosteroids. Manifestations of adrenal suppression in children 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 children 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 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:

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

Proctocort® Cream (Hydrocortisone Cream USP) 1% is supplied in 1 ounce (28.35g) tubes. (NDC 65649-501-30)

Store at 20° to 25° C (68° to 77° F). See USP Controlled Room Temperature. Store away from heat. Protect from freezing.

### RX ONLY.

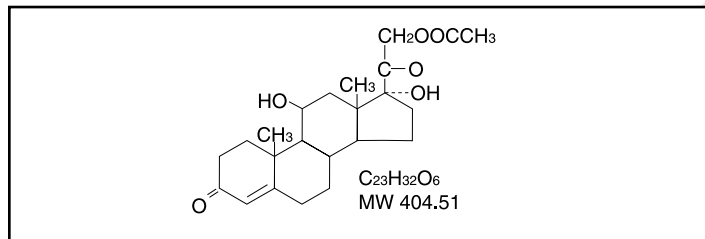
Manufactured for Salix Pharmaceuticals, Inc., Morrisville, NC 27560

# PROCTOCORT<sup>®</sup> Suppository

## (Hydrocortisone Acetate Rectal Suppositories) 30 mg

### DESCRIPTION

Hydrocortisone Acetate is a corticosteroid designated chemically as pregn-4-ene-3, 20-dione, 21-(acetyloxy)-11, 17-dihydroxy-(11b) with the following structural formula:



Each rectal suppository contains hydrocortisone acetate, USP 30 mg in a specially blended hydrogenated vegetable oil base.

### CLINICAL PHARMACOLOGY

In normal subjects, about 26% of hydrocortisone acetate is absorbed when the 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

Proctocort<sup>®</sup> Suppositories are indicated for use in inflamed hemorrhoids, postirradiation (factual) proctitis; as an adjunct in the treatment of chronic ulcerative colitis; cryptitis; and other inflammatory conditions of anorectum and pruritus ani.

### CONTRAINDICATIONS

Proctocort<sup>®</sup> Suppositories are contraindicated in those patients having a history of hypersensitivity to hydrocortisone acetate or any of the components.

### PRECAUTIONS

Do not use Proctocort<sup>®</sup> Suppositories 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 anti-bacterial agent should be instituted. If a favorable response does not occur promptly, Proctocort<sup>®</sup> Suppositories should be discontinued until the infection has been adequately controlled.

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

**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. Proctocort<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 Proctocort<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 hydrocortisone acetate suppositories; burning, itching, irritation, dryness, folliculitis, hypopigmentation, allergic contact dermatitis, secondary infection.

### DRUG ABUSE AND DEPENDENCE

Drug abuse and dependence have not been reported in patients treated with hydrocortisone acetate suppositories.

### OVERDOSAGE

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

### DOSAGE AND ADMINISTRATION

For rectal administration. Detach one suppository from strip of suppositories. Remove the foil wrapper. Avoid excessive handling of the suppository which is designed to melt at body temperature. Insert suppository into the rectum with gentle pressure, pointed end first. Insert one suppository in the rectum twice daily, morning and night for two weeks, in nonspecific proctitis. In more severe cases, one suppository three times a day or two suppositories twice daily. In fistulal proctitis, the recommended duration of therapy is six to eight weeks or less, according to the response of the individual case.

### HOW SUPPLIED

Box of 12 suppositories - NDC 65649-511-12

Box of 24 suppositories - NDC 65649-511-24

### RX ONLY.

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

### PRESCRIBING INFORMATION AS OF DECEMBER 2003.

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