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

1. Urinary free cortisol test
2. Hydrocortisone suppression test
3. Dexamethasone suppression test
4. ACTH stimulation test
5. 24-hour urinary free cortisol test
6. PRA (plasma renin activity)
7. Plasma aldosterone level

Information for Patients:

This medication should not be used in the diaper areas as diapers or plastic pants may constitute occlusive dressings. Use on the face, underarms, or skin creases may be associated with skin atrophy. Nasal and ocular irritation may occur. Do not use on puncture wounds, cuts, infections, orayed areas.

Contraindications:

Hydrocortisone valerate cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the product.

Precautions:

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 relative adrenal insufficiency, which generally develop gradually, may include weakness, easy fatigability, reduced tolerance to stress, low blood pressure, and reduced skin thickness. The incidence of HPA axis suppression increases with the duration of use and higher potency of topical corticosteroids.

Drug Interactions:

Hydrocortisone valerate cream may cause adrenal suppression, which may affect the effectiveness of other medications taken by the patient.

Pediatric Use:

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios compared to adults.

Clinical Pharmacology:

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 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.

255069 LFLT PI HYDRCRTISN VALRT CREAM USP 2% US (FRONT)
Carcinogenesis, Mutagenesis, and Impairment of Fertility
Long-term animal studies have not been performed to evaluate the carcinogenic potential of hydrocortisone valerate. Hydrocortisone valerate cream was shown to be non-mutagenic in the Ames-Salmonella/Microsome Plate Test. There are no studies which assess the effects of hydrocortisone valerate on fertility and general reproductive performance.

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 application in laboratory animals. Dermal embryofetal developmental studies were conducted in rabbits and rats with hydrocortisone valerate cream. 0.2%, Hydrocortisone valerate cream, 0.2%, was administered topically for 4 hours/day, rather than the preferred 24 hours/day, during the period of organogenesis in rats (gestational days 6 to 16) and rabbits (gestational days 6 to 10). Topical doses of hydrocortisone valerate up to 0.8 mg/kg/day (54 mg/kg/day) were administered to rats and 0.4 mg/kg (60 mg/kg/day) were administered to rabbits. In the absence of maternal toxicity, a significant increase in delayed skeletal ossification in fetuses was noted at 9 mg/kg/day (2X the Maximum Recommended Human Dose [MRHD] based on body surface area [BSA]) comparisons) in the rabbit study. No malformations in the fetuses were noted at 5 mg/kg/day (2X MRHD based on BSA) were noted in the rabbit study. A significant increase in delayed skeletal ossification in fetuses was noted at 5 mg/kg/day (2X the MRHD based on BSA comparisons) in the rabbit study. Increased numbers of fetal malformations (e.g., cleft palate, omphalocele and clubfoot) were noted 3 mg/kg/day (3X MRHD based on BSA comparisons) in the rabbit study.

There are no adequate and well-controlled studies in pregnant women. Hydrocortisone valerate cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
Systemic corticosteroids administered to human milk may 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 hydrocortisone valerate cream is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established. There is no data on adrenal suppressive and/or growth suppression. 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 Cushings syndrome when they are treated with topical corticosteroids. They are therefore at a 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 (see PRECAUTIONS). HPA axis suppression, Cushings 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 an absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Geriatric Use
Clinical studies of hydrocortisone valerate cream did not include sufficient numbers of subjects aged 65 and over to determine whether they responded differently from younger subjects. Other reported clinical experiences has not identified differences in responses between the elderly and younger patients.

ADVERSE REACTIONS
The following local adverse reactions have been reported with topical corticosteroids, and they 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, hirsuties, hypopigmentation, acneiform eruptions, hyperpigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria. In controlled clinical studies involving pediatric patients one month to 12 years of age (n=153), the incidence of adverse experiences, regardless of relationship to the use of hydrocortisone valerate cream, was approximately 21%. Reported reactions included stinging (10%), eczema (7%), fungal infection (5%), and gastrointestinal disorder (3%). In controlled clinical studies involving pediatric patients 2 to 12 years of age (n=153), the incidence of adverse experiences, regardless of relationship to the use of hydrocortisone valerate cream, was approximately 10%. Reported reactions included stinging (10%), eczema (7%), fungal infection (5%), and gastrointestinal disorder (3%). 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 Cushings syndrome when they are treated with topical corticosteroids. They are therefore at a 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 (see PRECAUTIONS). HPA axis suppression, Cushings syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids.

ADVERSE REACTIONS
The following local adverse reactions have been reported with topical corticosteroids, and they 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, hirsuties, hypopigmentation, acneiform eruptions, hyperpigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria. In controlled clinical studies involving pediatric patients one month to 12 years of age (n=153), the incidence of adverse experiences, regardless of relationship to the use of hydrocortisone valerate cream, was approximately 21%. Reported reactions included stinging (10%), eczema (7%), fungal infection (5%), and gastrointestinal disorder (3%). In controlled clinical studies involving pediatric patients 2 to 12 years of age (n=153), the incidence of adverse experiences, regardless of relationship to the use of hydrocortisone valerate cream, was approximately 10%. Reported reactions included stinging (10%), eczema (7%), fungal infection (5%), and gastrointestinal disorder (3%).

OVERDOSE
Topically applied hydrocortisone valerate cream can be absorbed in sufficient amounts to produce systemic effects (see PRECAUTIONS).

TOXICITY AND HARMFUL EFFECTS
Hydrocortisone valerate cream should be applied to the affected area as thin film two or three times daily depending on the severity of the condition. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, management of the diagnosis may be necessary. Hydrocortisone valerate cream should not be used for prolonged periods of time, unless directed by a physician. Hydrocortisone valerate cream should not be applied to the diaper area if the patient requires diapers or plastic pants as these garments may constitute occlusive dressing.

HOW SUPPLIED
Hydrocortisone valerate cream USP, 0.2%, is supplied in 15 g (NDC 68180-954-01), 45 g (NDC 68180-954-02) and 60 g (NDC 68180-954-03) tube sizes.

Storage
Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Manufactered for: Lupin Pharmaceuticals, Inc., Buildings, Marksburg 21782, United States.

Manufactured by: Lupin Limited, Pithampur (M.P.) - 464 775, India.

June 2018

ID#: 255069