PRODUCT MONOGRAPH

PrNERISONE®

(diflucortolone valerate)

Oily Cream 0.1% w/w

GSK Standard

Topical Corticosteroid

GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4

Date of Revision:
January 26, 2017

Submission Control No: 200095

TABLE OF CONTENTS

PAGE

[Pr]NERISONE®

(diflucortolone valerate)

Oily Cream 0.1% w/w

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Topical use	Oily Cream 0.1% w/w	For a complete listing see DOSAGE FORMS, COMPOSITION AND PACKAGING section.

INDICATIONS AND CLINICAL USE

NERISONE® (diflucortolone valerate) is indicated for the topical treatment of corticosteroid-responsive acute and chronic skin diseases, where anti-inflammatory, anti-allergic and anti-pruritic action is required for a maximum duration of 4 weeks.

Pediatrics (< 18 years of age): NERISONE® is contraindicated in pediatric patients less than one year of age. Safety and effectiveness of NERISONE® in pediatric patients less than 18 years of age have not been established [see WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics (< 18 years of age)].

Geriatrics (> 65 years of age): Safety and effectiveness of NERISONE® in geriatric patients over 65 years of age have not been established [see WARNINGS AND PRECAUTIONS, Special Populations, Geriatrics (> 65 years of age)].

CONTRAINDICATIONS

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section of the product monograph.
- Patients who are hypersensitive to other corticosteroids.
- Skin diseases in infants under one year of age.

- Patients with viral (e.g. herpes, varicella, or vaccinia) lesions of the skin, bacterial or fungal skin infections, parasitic infections, skin manifestations relating to tuberculosis or syphilis, eruptions following vaccinations.
- Patients with rosacea.
- Patients with pruritus without inflammation.
- Patients with perianal and genital pruritus.
- Patients with perioral dermatitis.
- Patients with acne vulgaris.
- Topical application to the eye.

WARNINGS AND PRECAUTIONS

General
Patients should be advised to inform subsequent physicians of the prior use of corticosteroids.

NERISONE® should not be used under occlusion due to increased risk of systemic exposure and infection. When used under occlusive dressing, over extensive areas, on the face, scalp, axillae, or scrotum, sufficient absorption may occur to result in adrenal suppression and other systemic effects (see WARNINGS AND PRECAUTIONS – Endocrine and Metabolism, Immune and Ophthalmologic).

Carcinogenesis and Mutagenesis
Long term animal studies have not been performed to evaluate the carcinogenic potential of NERISONE®.

Cardiovascular
Suitable precautions should be taken when using topical corticosteroids in patients with stasis dermatitis and other skin diseases associated with impaired circulation.

Use of corticosteroids around chronic leg ulcers may be associated with a higher occurrence of local hypersensitivity reactions and an increased risk of local infection.

Endocrine and Metabolism
Manifestations of hypercortisolism (Cushing's Syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency, can occur in some individuals as a result of increased systemic absorption of topical corticosteroids. Hyperglycemia and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids (see ADVERSE REACTIONS).

Conditions which augment systemic absorption include the formulation and potency of the topical corticosteroid, the application of topical corticosteroids over large body surface areas, application to intertriginous areas (such as the axillae), frequency of application, prolonged use, or the use of occlusive dressings. Other risk factors for increased systemic effects include increasing hydration of the stratum corneum, use on thin skin areas (such as the face), and use on broken skin or in conditions where the skin

barrier may be impaired.

If patients must be treated over large body surface areas, they should be evaluated periodically for evidence of HPA axis suppression (see WARNINGS AND PRECAUTIONS – Monitoring and Laboratory Tests). If HPA axis suppression or Cushing's syndrome is observed, an attempt should be made to withdraw the drug by reducing the frequency of application. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency (see ADVERSE REACTIONS).

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 corticosteroid supplementation, see the prescribing information for those products.

Pediatric patients may absorb larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity from equivalent doses because of their larger skin surface to body mass ratios as compared with adult patients (see WARNINGS AND PRECUATIONS – Special Populations, Pediatrics).

Immune
Topical corticosteroids may increase the risk of infections, including aggravation of cutaneous infection and masked infection. In particular, bacterial infection is encouraged by the warm, moist conditions within skin-fold areas, or caused by occlusive dressings. If concomitant skin infections develop, NERISONE® should be discontinued and antimicrobial therapy should be administered.

Ophthalmologic
Topical corticosteroids should be used with caution on lesions close to the eye because systemic absorption may cause increased intraocular pressure, cataract, or glaucoma.

Sensitivity
Local hypersensitivity reactions (see ADVERSE REACTIONS) may resemble symptoms of the condition under treatment. If hypersensitivity reactions occur, NERISONE® should be discontinued and appropriate therapy should be initiated.

Allergic contact dermatitis with corticosteroids is usually diagnosed by observing a failure to heal rather than noticing a clinical exacerbation. Such an observation should be corroborated with appropriate diagnostic patch testing.

Sexual Function/ Reproduction
There are no data in humans to evaluate the effect of topical corticosteroids on fertility. Corticosteroids have been shown to impair fertility in animal studies.

Skin
Topical corticosteroids should be used with caution in psoriasis as rebound relapses, development of tolerances, risk of generalised pustular psoriasis, and development of local or systemic toxicity due to impaired barrier function of the skin have been reported in some cases. If used in psoriasis careful patient supervision is important.

If significant irritation develops, NERISONE® should be discontinued and appropriate therapy should be instituted.

Prolonged use of topical corticosteroid preparations may produce striae or atrophy of the skin or subcutaneous tissue. Topical corticosteroids should be used with caution on lesions of the face, groin, and axillae as these areas are more prone to atrophic changes than other areas of the body. Frequent observation is important if these areas are to be treated. If skin atrophy is observed, treatment should be discontinued.

Special Populations

Pregnant Women: Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development (see TOXICOLOGY). NERISONE® has been shown to be teratogenic after dermal application in laboratory animals at doses similar to human therapeutic doses.

There are no adequate and well controlled studies of NERISONE® in pregnant women. Administration of NERISONE® during pregnancy should only be considered if the expected benefit to the mother outweighs the potential risk to the fetus. The minimum quantity should be used for the minimum duration.

Nursing Mothers: The safe use of topical corticosteroids during lactation has not been established.

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 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 NERISONE® is administered to a nursing mother. Administration of NERISONE® during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

If used during lactation, NERISONE® should not be applied to the breasts to avoid accidental ingestion by the infant.

Pediatrics (< 18 years of age): The safety of NERISONE® has not been studied in pediatric patients. **NERISONE® is contraindicated in patients less than one year of age.**

There are no adequate and well-controlled studies of NERISONE® in pediatric patients. Administration of topical corticosteroids to children under 18 years of age should be limited to the least amount and for the shortest duration compatible with an effective therapeutic regimen (see DOSAGE AND ADMINISTRATION).

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 the use of topical corticosteroids in infants and children. HPA axis suppression, Cushing's 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. Chronic corticosteroid therapy may interfere with the growth and development of children.

Geriatrics (> 65 years of age): The safety of NERISONE® has not been studied in geriatric patients.

In general, topical corticosteroids should be used cautiously in elderly patients, reflecting their increased skin fragility and greater frequency of hepatic, renal, or cardiac dysfunction, and of concomitant disease or other drug therapy. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs.

There are no adequate and well-controlled studies of NERISONE® in geriatric patients.

For geriatric patients over 65 years of age, the minimum quantity should be used for the minimum duration (see DOSAGE AND ADMINISTRATION).

Patients with renal / hepatic impairment: The safety of NERISONE® has not been studied in patients with renal or hepatic impairment.

In case of systemic absorption, metabolism and elimination may be delayed leading to increased risk of systemic toxicity.

There are no adequate and well-controlled studies of NERISONE® in patients with renal or hepatic impairment. For patients with renal or hepatic impairment, the minimum quantity should be used for the minimum duration (see DOSAGE AND ADMINISTRATION).

Monitoring and Laboratory Tests

The cosyntropin (ACTH $_{1-24}$) stimulation test may be helpful in evaluating patients for HPA axis suppression.

ADVERSE REACTIONS

Post-Marketing Adverse Drug Reactions

The following adverse reactions are reported when topical corticosteroids are used as recommended. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Endocrine Disorders: Hypothalamic-pituitary adrenal (HPA) axis suppression, cushingoid features (e.g. moon face, central obesity), delayed weight gain/growth retardation in children, osteoporosis, hyperglycemia/glucosuria, hypertension, increased weight/obesity, decreased endogenous cortisol levels, and steroid withdrawal syndrome.
Eye Disorders: Glaucoma, cataract.
General Disorders and Administration Site Conditions: Application site irritation/pain.
Immune System Disorders: Local hypersensitivity.
Infections and Infestations: infection.
Skin and Subcutaneous Tissue Disorders: Pruritus, local skin burning /skin pain, allergic contact dermatitis/dermatitis, dryness folliculitis, acneiform eruptions, perioral dermatitis, erythema, rash, urticaria, pustular psoriasis, skin thinning*/skin atrophy*, skin wrinkling*, skin dryness*, striae*, telangiectasias*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, alopecia, trichorrhexis, and miliaria.
**Skin features secondary to local and/or systemic effects of hypothalamic-pituitary adrenal (HPA) axis suppression.*

DRUG INTERACTIONS

Overview

No clinical trials were specifically designed to assess potential drug-drug, drug-food, drug-herb, or drug-laboratory interactions with NERISONE®.

Drug-Drug Interactions

Co-administered drugs that can inhibit CYP3A4 (e.g., ritonavir, itraconazole) have been shown to inhibit the metabolism of corticosteroids leading to increased systemic exposure. The extent to which this interaction is clinically relevant depends on the dose and route of administration of the corticosteroids and the potency of the CYP3A4 inhibitor.

Interactions with other drugs have not been established.

Drug-Food Interactions

Interactions with food have not been established.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Interactions
Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Dosing Considerations
- Patients/caregivers should be instructed to use the minimum quantity of NERISONE® for the shortest duration of time necessary to achieve the desired therapeutic benefit because of the potential for corticosteroids to suppress the hypothalamic-pituitary-adrenal (HPA) axis and cause skin atrophy (see WARNINGS AND PRECAUTIONS).

Recommended Dose and Dosage Adjustment
Apply a thin layer and gently rub in using only enough to cover the affected area once or twice a day for a maximum of 4 weeks. Once daily applications may be considered for mild-moderate eczematous dermatoses. In the more steroid-resistant lesions, it should be applied two times daily for initiating treatment, tapering off to once daily for up to 4 weeks.

Allow adequate time for absorption after each application before applying an emollient.

If the condition worsens or does not improve within 2-4 weeks, treatment and diagnosis should be re-evaluated.

Avoid abrupt discontinuation of topical corticosteroids when control is achieved, as rebound of pre-existing dermatoses can occur. Continue an emollient as maintenance therapy.

Pediatrics (< 18 years of age): NERISONE® is contraindicated in children under one year of age (see CONTRAINDICATIONS). Care should be taken when using NERISONE® in pediatric patients over one year of age.

Pediatric patients are more likely to develop local and systemic toxicity from equivalent doses of topical corticosteroids because of their larger skin surface to body weight ratios, and, in general, require shorter courses of treatment and less potent agents than adults.

The minimum quantity should be used for the shortest duration to achieve the desired therapeutic benefit [see WARNINGS AND PRECAUTIONS — Special Populations, Pediatrics (< 18 years of age)].

Geriatrics (> 65 years of age): NERISONE® should be used with caution in geriatric patients due to increased risk of renal or hepatic impairment in this population. Geriatric patients may be more susceptible to percutaneous absorption and the potential effects of systemic absorption. The minimum quantity should be used for the shortest duration to achieve the desired therapeutic benefit [see WARNINGS AND PRECAUTIONS — Special Populations, Geriatrics (> 65 years of age)].

Renal/Hepatic Impairment: In patients with renal or hepatic impairment the minimum quantity should be used for the shortest duration to achieved the desired therapeutic benefit (see WARNINGS AND PRECAUTIONS — Special Populations, Patients with renal / hepatic impairment).

Missed Dose

In the event of missed dose, NERISONE ® should be applied as soon as possible after the missed dose is remembered. If this is close to the scheduled application time or the next dose, the patient should wait and apply the next scheduled dose. The usual schedule should be resumed thereafter.

Administration

- NERISONE ® is for topical use only.
- Use with occlusive dressings is not recommended (see WARNINGS AND PRECAUTIONS).
- NERISONE ® is not for use in or near the eye or on other mucous membranes.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (see WARNINGS AND PRECAUTIONS). In the event of overdose or misuse, the features of hypercortisolism may occur (see ADVERSE REACTIONS).

Excessive prolonged use or misuse may suppress hypothalamic-pituitary-adrenal (HPA) axis function, resulting in secondary adrenal insufficiency. If symptoms of HPA axis suppression occur, NERISONE® should be withdrawn gradually by reducing the frequency of application, or by substituting a less potent corticosteroid because of the risk of glucocorticosteroid insufficiency. Further management should be as clinically indicated.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

NERISONE® contains diflucortolone valerate, which belongs to a class of topical drugs called topical corticosteroids. It is considered to be a mid-potency corticosteroid. Topical corticosteroids share anti-inflammatory, antipruritic and vasoconstrictor actions.

Both diflucortolone valerate and its split ester are topically active.

The mechanism of anti-inflammatory activity of topical corticosteroids is unclear. However, corticosteroids are thought to act by the induction of phospholipase A2

inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostagladins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Pharmacodynamics

The pharmacodynamics of NERISONE® has not been specifically investigated in any clinical studies. Topical corticosteroids have anti-inflammatory, antipruritic, and vasoconstrictive properties.

Pharmacokinetics

The pharmacokinetics of NERISONE® (absorption, distribution, excretion, and metabolism) has not been specifically investigated in any clinical studies. Pharmacokinetic properties of the drug class of topically applied corticosteroids remain incompletely understood.

Absorption: Topical corticosteroids can be systemically absorbed from intact healthy skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the product formulation, potency, vehicle, frequency and duration of application, as well as the integrity of the epidermal barrier, skin thickness, application to intertriginous areas (such as the axillae) and to large skin surface areas. Occlusion, hydration of the stratum corneum, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Distribution: The use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids is necessary because circulating levels are well below the level of detection.

Metabolism: Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. They are primarily metabolized in the liver.

Excretion: Topical corticosteroids are excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

STORAGE AND STABILITY

Store between 15ºC and 25ºC. Do not freeze. Keep out of the sight and reach of children.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Medicinal Ingredients: NERISONE® contains 0.1% w/w of diflucortolone valerate.

Non-medicinal Ingredients: NERISONE® is a water-in-oil emulsion with about 30% water. The external, lipophilic phase contains white petrolatum, mineral oil, aluminum

stearates, cera alba (EU); beeswax (PCPC), dicocoyl pentaerythrityl distearyl citrate, hydrogenated palm glycerides citrate, sorbitan sesquioleate, tocopherol, and white wax. NERISONE® is available in 30g and 60g tubes.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

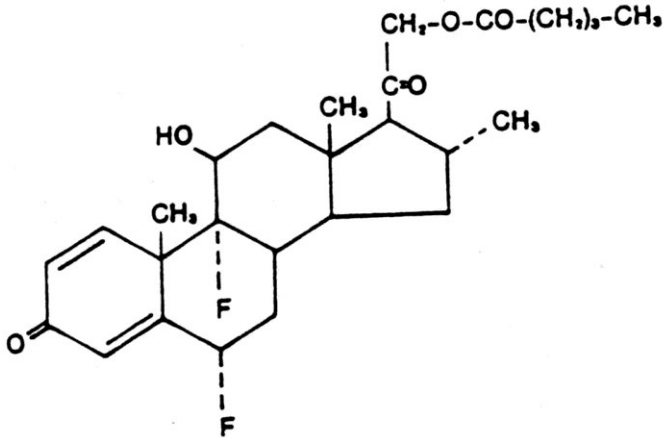
Common name: diflucortolonevalerate

Chemical name: 6α, 9-difluoro-11ß, 21-dihydroxy-16 α-methyl-pregna-1, 4-diene-3, 20 dione 21-valerate

Molecular formula: $C_{27}H_{36}F_2O_5$

Molecular mass: 478.58

Structural formula:



Physicochemical properties: Diflucortolone valerate is a white to slightly cream-white crystalline, odorless powder, easily soluble in chloroform, slightly soluble in methanol and sparingly soluble in ether. It melts between 200°C and 205°C and has a specific rotation within +98° to +103° in dioxane.

DETAILED PHARMACOLOGY

Human

On dermal application of diflucortolone valerate, both the un-split ester and the free diflucortolone arising from cleavage of the ester exert anti-inflammatory, anti-proliferative and pharmaco-logical effects.

In the vasoconstriction test on human skin, in which hyperemia has been experimentally induced, a water/oil emulsion with 0.001% diflucortolone valerate is as effective as a similar preparation containing 0.1% fluocortolone.

Animal

In experimentally produced inflammation of the rat ear, the anti-inflammatory effect of diflucortolone valerate is about three times greater than that of fluocortolone. In the same trial-design, the local anti-inflammatory effect of diflucortolone valerate is equal to that of fluocinolone acetonide and betamethasone-17-valerate but greater than that for beclomethasone dipropionate.

On subcutaneous administration in the rat adjuvant-paw-edema test, the anti-inflammatory effect of diflucortolone valerate is about 30 times greater than that of fluocortolone and about three times more than dexamethasone. In contrast in this type study, fluocinolone acetonide, which is almost equipotent topically with diflucortolone valerate, is systemically twenty times more active in its anti-inflammatory effect.

Diflucortolone valerate is about ten times as active as fluocortolone in the ring-granuloma test.

On oral administration to adrenalectomized rats, the effect of diflucortolone is equal to that of dexamethasone as measured by a decrease in body weight, elevation of blood sugar and the increased elimination of potassium, phosphorus and nitrogen via urine and faeces.

Endocrinological action on systemic administration is characterized by the absence of estrogenic, anabolic androgenic and anti-androgenic properties. Exceptions are progestational effect in the Clauberg test in the rabbit and an anti-estrogenic effect in the mouse uterus test.

TOXICOLOGY

Acute Toxicology

A summary of acute toxicology studies of diflucortolone valerate in various species is shown in Table 1.

Table 1 Results of Acute Toxicology Studies in Various Species

Drug	Species	Route	LD_{50} (g/kg)	Symptoms
Diflucortolone valerate (DFV)	Mouse	Oral	>4.0	Transient apathy
	Rat	Oral	3.1	Cachexia pronounced apathy Ventricumbence
	Dog	Oral	>1.0	None
DFV Oily Cream 0.1%	Rat	Oral	>38.1	None

Subacute Toxicity

Following daily subcutaneous administration of diflucortolone valerate over six weeks, the tolerance limit for rats was 0.4 µg/kg/day and for dogs 40 µg/kg/day. All side effects observed at these or higher doses, such as thymolysis and atrophy of the adrenal cortex, correspond to those produced by subcutaneous administration of any systemically potent corticoid.

In topical tolerance studies over 28 days on the intact and scarified skin of the beagle dog and rabbit, no macroscopic or histological differences were seen when a daily application of 0.25g of oily cream were compared with the corresponding bases.

Following daily application of the oily cream to the shaved and scarified skin of dogs over a period of 13-14 weeks, systemic corticoid effects occurred only after application of amounts of cream in excess of 100 mg/kg.

Teratology

Following dermal application of the diflucortolone valerate ointment preparation to scarified skin during the phase of organogenesis in pregnancy, embryotoxic and typical steroidal teratogenic effects occurred at doses in excess of 500 mg/kg/day of ointment containing 0.1% diflucortolone valerate in rats and 50 mg/kg/day of the 0.1% ointment in rabbits. Effects included delayed ossification, umbilical hernia, caudal aplasia, reduced fetal weights, increased perinatal mortality, cleft palate and shortened limbs.

REFERENCES

1. Grejs J. Vergleichende Prufung von Diflucortolon-21-valerat Creme und Hydrocortison-17butyrat Creme bei Hautkranken. Therapie der Gegenwart 1978;117,12:1930-37.

2. Hoppe G. Treating skin diseases in Asia with diflucortolone valerate. Modern Medicine of Asia 1977;13,7:17-22

3. Hoppe G. A multicentric clinical trial with diflucortolone valerate in S-E Asia (with comparison to the results obtained worldwide). Filipino Family Physician 1977;15,2:32-38

4. Langen M, Sastre Y, Hernandez M. Results of a multicentre, multinational clinical trial of diflucortolone valerate (Nerisona) (trans.) Zeitschrift fur Hautkrankheiten 1976;51,(Suppl 1):1-16.

5. Langen ML. Topical treatment of various skin diseases with diflucortolone valerate in 360 patients. Clinical Therapeutics 1979;2,2:124-133

6. Lofferer O. Study of a new topically effective corticosteroid (diflucortolone valerate) using the psoriasis - plaque test (trans.) Dermatologia Venezolana 1975;14,1-2:37-47

7. Mackey JP. Diflucortolone valerate and fluocinolone acetonide in eczema: a double-blind trial. Pharmatherapeutica 1977;1,7:462-465

8. Reckers R, Wendt H. Multicentre clinical trial of the new corticosteroid diflucortolone valerate as a cream, ointment and fatty ointment. Arzneimittel-Forschung (Drug Research) 1976;26,7b:1499-1509

   Part 1: Comparative studies of diflucortolone valerate and fluocortolone, fluocortolone caproate and pivalate applied topically in a double-blind contralateral design.

   Part II: Comparative studies with various commercial preparations. (trans.)

9. Straehl B. Behandlung verschiedener Dermatosen mit Diflucortolon-valerat 0.1% (Nerisona).Schweizerische Rundschau fUr Medizin (Praxis) 1978;67,35:1277-1284

10. Van Zuiden E. Diflucortolonvalerianat und Fluocinolonacetonid bei Ekzem und Dermatitis. Therapie der Gegenwart 1978;117,8:1248-1264

PART III: CONSUMER INFORMATION

PrNERISONE®

diflucortolone valerate 0.1% (w/w) oily cream

This leaflet is part III of a three-part "Product Monograph" and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about NERISONE®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
NERISONE® is used to help relieve the redness, swelling, and itching of certain skin problems for up to 4 weeks.

What it does:
NERISONE® contains diflucortolone valerate which belongs to a group of medicines called steroids. Steroids help to reduce redness, swelling and irritation of the skin.

When it should not be used:
Do not use NERISONE® if you are allergic to diflucortolone, other corticosteroids, or to any other ingredients in NERISONE®.

Do not apply NERISONE® to the areas of the skin that:
- have bacterial, fungal, parasitic, viral skin infections (e.g. cold sores, chicken pox), tuberculosis or syphilis skin lesions, or a skin reaction following a recent vaccination
- have acne
- have rosacea (a facial skin condition where the nose, cheeks, chin, forehead or entire face are unusually red, with or without tiny visible blood vessels, bumps or pus-filled bumps)
- have rashes around the mouth
- have itchy skin which is not inflamed
- have itchy skin around the anus or genitals (penis and vagina)

Do not apply in or near the eye.

Do not use on children under 1 year of age.

If you think any of these apply to you, don't use NERISONE® until you have checked with your doctor or pharmacist.

What the medicinal ingredient is:
Diflucortolone valerate

What the nonmedicinal ingredients are:
aluminum stearates, beeswax (PCPC), cera alba (EU); dicocoyl pentaerythrityl distearyl citrate, hydrogenated palm glycerides citrate, mineral oil, purified water, sorbitan sesquioleate, tocopherol, white petrolatum and white wax.

What dosage forms it comes in:
oily cream, available in 30 g and 60 g tubes

WARNINGS AND PRECAUTIONS

NERISONE® should not be applied over large areas unless advised by a physician. Apply only enough to cover the affected areas.

Only use NERISONE® for as long as your doctor recommends.

Before using NERISONE®, talk to your doctor or pharmacist if:
- you are pregnant or planning to become pregnant.
- you are breastfeeding. If you do use NERISONE® when breastfeeding, do not use on your breast area to ensure that the baby does not accidentally get it in their mouth.
- you have used corticosteroids before
- you have sores in the leg as a result of poor circulation (such as stasis dermatitis).
- you have problems with your kidney or liver. You may need to use a smaller amount of NERISONE® or use it less often.

Other warnings you should know about:
- NERISONE® should be used with caution on the face, or in skin fold areas, such as the groin or the armpit.
- Avoid applying NERISONE® in or near the eye, or other mucous membranes. In case of contact, wash with water. Absorption may cause increased pressure in the eye (glaucoma), or a cloudy lens in the eye (cataracts).
- Do not use airtight dressings such as a bandage, or cover the treated areas tightly.
- If you are over 65 years of age, use NERISONE® with caution. You may need to use a smaller amount of NERISONE® or use it less often
- The skin of children absorbs larger amounts of topical corticosteroids than the skin of adults; and therefore, children may be more likely to develop side effects.
- Topical corticosteroids may increase the risk of an allergic reaction or an infection if applied near ulcers on the legs.

INTERACTIONS WITH THIS MEDICATION

Some medicines may affect how NERISONE® works, or make it more likely that you'll have side effects. Examples of these medicines include:

- Ritonavir (for HIV)
- Itraconazole (for fungal infections)

Tell your doctor or pharmacist about all your other medications, including medicines that you bought without prescription and natural health products.

PROPER USE OF THIS MEDICATION

NERISONE® is for use on the skin only.

Usual dose:
Use NERISONE® once or twice a day for a maximum of 4 weeks. The number of times you use your medicine may be reduced as your skin gets better or your doctor may prescribe a weaker steroid for you to use instead. If your condition does not improve within 2-4 weeks of treatment, speak to your doctor or pharmacist.

If you use NERISONE® regularly, make sure you talk to your doctor before you stop using it. It is important to not stop using NERISONE® suddenly or your skin condition could flare up again and you could develop steroid withdrawal symptoms.

How to Apply NERISONE®:
- Apply a thin layer and gently rub in, using only enough to cover the entire affected area.
- Wash your hands after use unless treating the hands.
- Excess product should not be returned to the container, since it may cause contamination.
- Your doctor may recommend using a moisturizer as maintenance therapy.If you are also using a moisturizer, allow time for NERISONE® to be absorbed after each application before applying the moisturizer.

NERISONE® should be used for the minimum amount of time required to achieve the desired results, **but always use NERISONE® exactly as your doctor has told you**. Check with your doctor or pharmacist if you are not sure.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:
If you forget to use NERISONE®, apply it as soon as you remember. If it is close to the time scheduled to apply your next dose, wait and apply your next scheduled dose and then continue as before. Do not apply extra NERISONE® to make up for missed doses.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines NERISONE® can have side effects although not everybody gets them.

The following side effects have been reported in patients using topical corticosteroids.

If any of the side effects listed becomes severe or troublesome, tell your doctor or pharmacist.

Common side effects
- itchy skin
- skin burning or pain

Very rare side effects
Use of a topical corticosteroid for a long period of time, over a large body surface, or use under an airtight dressing, may cause the following symptoms:
- skin: thinning, softening, wrinkling, dryness, changes to the colour, the appearance of blood vessels under the surface of your skin, pimples, raised bumps with pus under the skin, allergic contact dermatitis/dermatitis, irritation or pain at the site of application
- increased body hair, hair loss/lack of hair growth/damaged looking hair

In children also look out for the following symptoms:
- delayed weight gain
- slow growth

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if Severe	In all cases	
Allergic reactions: rash, hives, swelling of the skin, chills, fever, muscle aches or pains or flu-like symptoms occurring with or before a skin rash.			✓
No improvement or worsening of condition		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if Severe	In all cases	
Skin infection		✓	
Cushing's syndrome: weight gain, moon face / rounding of the face and obesity.			
Hyperglycemia (increased blood sugar): frequent urination, thirst and hunger.		✓	
Glucosuria (sugar in urine): excessive or sweet smelling urine.		✓	
Hypertension (high blood pressure): headaches, vision disorders, nausea and vomiting.		✓	
Osteoporosis: weakening of the bones, pain, decreased height, bones prone to fracture easily		✓	
Glaucoma or cataracts: blurred vision, increased pressure in your eyes, eye pain.			✓
Low cortisol in your blood or steroid withdrawal: dizziness, weakness, fatigue, weight loss, nausea, diarrhea, and abdominal pain		✓	

This is not a complete list of side effects. For any unexpected effects while taking NERISONE® *contact your doctor or pharmacist.*

HOW TO STORE IT

Store between 15° and 25°C. Do not freeze. Keep out of the sight and reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

http://www.gsk.ca or by contacting the sponsor,

GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4
1-800-387-7374

This leaflet was prepared by GlaxoSmithKline Inc.

Last revised: January 26, 2017

NERISONE is a trademark of Bayer Schering Pharma Aktiengesellschaft, used under license by GSK Inc.