PRESCRIBING INFORMATION

PrSARNA HC®

Hydrocortisone USP

Lotion, 1% and 2.5% (w/v)

Topical Corticosteroid

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Topical use	Lotion, 1% and 2.5% w/v	Preservative: Glydant Excipients: Camphor, Menthol For a complete listing see DOSAGE FORMS, COMPOSITION AND PACKAGING section.

INDICATIONS AND CLINICAL USE

SARNA HC® (hydrocortisone USP) Lotion is indicated for topical therapy of corticosteroid responsive dermatoses for a maximum duration of 4 weeks in patients 2 years of age and older, where an anti-inflammatory and antipruritic activity is required in the topical management of these conditions.

Geriatrics (> 65 years of age): Safety and effectiveness of SARNA HC® Lotion in geriatric patients over 65 years of age have not been established. Some published studies of 1% hydrocortisone creams have reported that clinical outcomes in geriatric patients over 65 years of age were consistent with those of the general adult population (see WARNINGS AND PRECAUTIONS, Special Populations, Geriatrics (> 65 years of age)).

Pediatrics (<18 years of age): Safety and effectiveness of SARNA HC® Lotion in pediatric patients less than 18 years of age have not been established. Some published studies of 1% hydrocortisone creams have reported that clinical outcomes in pediatric patients less than 18 years of age were consistent with those of the general adult population (see WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics (<18 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 PRESCRIBING INFORMATION.
- Patients who are hypersensitive to other corticosteroids, camphor, or menthol.
- Infants and children under 2 years of age.
- Patients with bacterial, tubercular, or fungal infections involving the skin, viral diseases (such as herpes simplex, chicken pox, and vaccinia), parasitic infections, skin manifestations relating to tuberculosis or syphilis, eruptions following vaccinations, rosacea, acne vulgaris, and pruritus without inflammation.
- Topical application to the eye.

WARNINGS AND PRECAUTIONS

General

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

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

Avoid application to large areas of the body due to increased risk of systemic camphor toxicity, as camphor (an excipient in SARNA HC® Lotion) is readily absorbed after topical application. Symptoms of systemic camphor toxicity include the development of convulsions and CNS depression (see OVERDOSAGE).

Avoid contact with nostrils, mouth, or other mucous membranes, as camphor and menthol (excipients in SARNA HC® Lotion) have an irritant effect. Application to mucous membranes may also increase absorption and the risk of development of camphor systemic toxicity (see OVERDOSAGE). In case of accidental contact with mucous membranes, rinse well with water.

Keep out of the reach and sight of children.

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 PRECAUTIONS – Special Populations, Pediatrics).

Immune

Topical corticosteroids may increase the risk of infections including aggravation of cutaneous infection, masked infection, and secondary infections. 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, SARNA HC® Lotion 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, cataracts, or glaucoma.

Camphor and menthol (excipients in SARNA HC® Lotion) may cause eye irritation. Avoid contact with the eyes. In case of accidental contact with the eyes, rinse well with water.

Sensitivity

Local hypersensitivity reactions (see ADVERSE REACTIONS) may resemble symptoms of the condition under treatment. If hypersensitivity reactions occur, SARNA HC® Lotion 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.

Avoid use on sensitive areas, such as broken or very inflamed skin, as the irritant effects of camphor and menthol (excipients in SARNA HC® Lotion) may be exacerbated.

SARNA HC® Lotion contains the excipient Glydant which contains traces of formaldehyde. Formaldehyde may cause allergic sensitization or irritation upon contact with the skin.

Skin

If significant irritation develops, SARNA HC® Lotion 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: There are no adequate and well-controlled studies of SARNA HC® Lotion in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development (see TOXICOLOGY). Subcutaneous administration of hydrocortisone to mice at doses of ≥30 mg/kg/day, to rabbits at a dose of 675 µg/kg/day, and the administration of a single intramuscular injection of ≥25 mg to hamsters during pregnancy produced fetal abnormalities including cleft palate. The relevance of this finding to human beings has not been established.

There are no data available on the use of camphor and menthol (excipients in SARNA HC® Lotion) during pregnancy. Oral doses of camphor and menthol administered to animals have not been associated with abnormalities of fetal development (see TOXICOLOGY). Camphor is readily absorbed after topical application and is known to cross the placenta; however, it has not been associated with teratogenic effects when applied topically during pregnancy. High oral doses of camphor in humans are implicated in foetal and neonatal death and are known to induce abortions.

Pregnant women should seek medical advice before using SARNA HC® Lotion. Administration of SARNA HC® Lotion 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.

Fertility: There are no data in humans to evaluate the effect of topical corticosteroids on fertility. No studies have been conducted with camphor or menthol (excipients in SARNA HC® Lotion) to specifically investigate reproductive toxicity.

Nursing Mothers: The safe use of topical corticosteroids or of camphor and menthol (excipients in SARNA HC® Lotion) 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 or camphor and menthol (excipients in SARNA HC® Lotion) 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 SARNA HC® Lotion is administered to a nursing woman. Administration of SARNA HC® Lotion during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

Breast-feeding women should seek medical advice before using SARNA HC® Lotion. If used during lactation, SARNA HC® Lotion should not be applied to the breasts to avoid accidental ingestion by the infant.

Pediatrics (<18 years of age): The safety of SARNA HC® Lotion has not been studied in pediatric patients.

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.

There are no adequate and well-controlled studies of SARNA HC® Lotion in pediatric patients. Some published studies of 1% hydrocortisone creams have reported that clinical outcomes in pediatric patients less than 18 years of age were consistent with those of the general adult population.[1, 2, 3, 5] 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).

The safety and efficacy of SARNA HC® Lotion has not been established in children under 2 years of age. Camphor (an excipient in SARNA HC® Lotion) is readily absorbed after topical application. Infants and children under 2 years of age are at increased risk of developing systemic camphor toxicity because of their higher ratio of skin surface area to body mass and their immature barrier function. Application of camphor containing products to the nostrils of infants, even in small quantities, has been associated with serious adverse events such as convulsions. Do not use SARNA HC® Lotion in children under 2 years of age (see CONTRAINDICATIONS and DOSAGE AND ADMINISTRATION, Pediatrics (<18 years of age)).

Geriatrics (>65 years of age): The safety of SARNA HC® Lotion 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.

Camphor (an excipient in SARNA HC® Lotion) is readily absorbed after topical application, metabolised in the liver, and excreted in urine. Renal or hepatic impairment in the elderly may delay metabolism and elimination of systemically absorbed camphor and increase the risk of developing systemic camphor toxicity (see OVERDOSAGE).

There are no adequate and well-controlled studies of SARNA HC ® Lotion in geriatric patients. Some published studies of 1% hydrocortisone creams have reported that clinical outcomes in geriatric patients over 65 years of age were consistent with those of the general adult population.[1, 3, 4, 5] 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 SARNA HC® Lotion has not been studied in patients with renal or hepatic impairment.

In case of systemic corticosteroid absorption, renal or hepatic impairment may delay metabolism and elimination leading to increased risk of systemic corticosteroid toxicity (see OVERDOSAGE).

Camphor (an excipient in SARNA HC® Lotion) is readily absorbed after topical application, metabolised in the liver, and excreted in urine. Renal or hepatic impairment may delay metabolism and elimination of systemically absorbed camphor leading to increased risk of developing systemic camphor toxicity (see OVERDOSAGE).

There are no adequate and well controlled studies of SARNA HC® Lotion 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 have been identified during the post-approval use of SARNA HC® Lotion. 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), increased weight/obesity, delayed weight gain/growth retardation in children, decreased endogenous cortisol levels, hyperglycemia/glucosuria, hypertension, osteoporosis, and steroid withdrawal syndrome.

Eye Disorders: Cataract, glaucoma.

General Disorders and Administrative Site Reactions: application site irritation/pain and swelling.

Immune System Disorders: Local hypersensitivity.

Infections and infestations: Secondary infection.

Skin and Subcutaneous Tissue Disorders: Contact dermatitis /dermatitis, erythema, rash, urticaria, pruritus, blisters, skin irritation, skin burning, skin pain, skin exfoliation, skin atrophy*, atrophy of subcutaneous tissues, skin dryness*, skin striae*, change in pigmentation*, hypertrichosis, telangiectasia*, and exacerbation of underlying symptoms. The following have been observed with the use of occlusive dressings: pustules, miliaria, folliculitis, and pyoderma.

*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 SARNA HC® Lotion.

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.

Menthol (an excipient in SARNA HC® Lotion) has been shown to interact with warfarin when administered to the oral cavity in a "cough drop" formulation containing 7 mg of menthol. The potential interaction between menthol and warfarin is related to the potential for significant systemic absorption from the gastrointestinal tract rather than through topical absorption of menthol.

Drug-Drug Interactions

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 SARNA HC® Lotion 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).
- If the condition worsens or does not improve within 2-4 weeks, treatment and diagnosis should be re-evaluated.
- SARNA HC® Lotion is for topical use only and not for ophthalmic use.
- SARNA HC® Lotion is contraindicated in infants and children under two years of age (see CONTRAINDICATIONS). Pediatric patients may be more susceptible to local and systemic toxicity from equivalent doses of topical corticosteroids because of their larger skin surface to body weight ratios, and may require shorter courses of treatment than adults.
- Geriatric patients may be more susceptible to percutaneous absorption and the potential effects of systemic absorption. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs.

Recommended Dose and Dosage Adjustment

A thin layer should be applied topically to affected skin area(s) with gentle massage once or twice a day for a maximum of 4 weeks. 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): SARNA HC® Lotion is contraindicated in infants and children under two years of age. Application of camphor containing products to the nostrils of infants, even in small quantities, has been associated with serious adverse events such as convulsions. In older children, care should be taken when using SARNA HC® Lotion. The minimum quantity should be used for the shortest duration to achieve the desired therapeutic benefit (see CONTRAINDICATIONS and WARNINGS AND PRECAUTIONS – Special Populations, Pediatrics (< 18 years of age)).

Geriatrics (>65 years of age): SARNA HC® Lotion should be used with caution in geriatric patients due to increased risk of renal or hepatic impairment in this population. 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: SARNA HC® Lotion should be used with caution in patients with renal/hepatic impairment as metabolism and elimination maybe delayed leading to increased risk of systemic corticosteroid toxicity or systemic camphor toxicity. In patients with renal or hepatic impairment, the minimum quantity should be used for the shortest duration to achieve the desired therapeutic benefit (see WARNINGS AND PRECAUTIONS – Special Populations, Patients with renal / hepatic impairment).

Missed Dose

In the event of missed dose, SARNA HC® Lotion 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.

OVERDOSAGE

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

Topically applied corticosteroids, camphor, and menthol can be absorbed in sufficient amounts to produce systemic effects (see WARNINGS AND PRECAUTIONS).

Excessive prolonged use or misuse of corticosteroids may suppress hypothalamic-pituitary-adrenal (HPA) axis function, resulting in secondary adrenal insufficiency. If symptoms of HPA axis suppression occur, SARNA HC® Lotion should be withdrawn gradually by reducing the frequency of application. Further management should be as clinically indicated. If toxic effects occur, SARNA HC® Lotion treatment should be discontinued and symptomatic therapy should be administered.

Camphor is readily absorbed from sites of application. Accidental ingestion, excessive use, or misuse of topical camphor may increase the risk of developing camphor systemic toxicity. Overdose after topical application or due to accidental ingestion of camphor is associated with the development of convulsions and CNS depression that may involve respiratory depression leading, ultimately, to respiratory failure. In the event of overdose, supportive care may be required. Further management should be as clinically indicated or as recommended by the regional poisons centre, where available.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

SARNA HC® Lotion belongs to a class of topical drugs called topical corticosteroids. It is considered to be a mild or low potency corticosteroid. Topical corticosteroids share anti-inflammatory, antipruritic and vasoconstrictive actions. 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.

SARNA HC® Lotion contains the excipients camphor and menthol. The anti-pruritic and/or analgesic effect of camphor is thought to be via transient receptor potential vanilloid 3/1(TRPV3/TRPV1) activation and/or inhibition of nociceptive-sensing transient receptor potential ankyrin 1 (TRPA1). The anti-pruritic and/or analgesic action of menthol is thought to be via transient receptor potential melastatin 8 (TRPM8) activation and/or inhibition of nociceptive- sensing TRPA1. Anti-pruritic and/or analgesic activity may be due to menthol's direct activation of Ca^{2+} currents.

Pharmacodynamics

The Pharmacodynamics of SARNA HC® Lotion have not been specifically investigated in any clinical studies. Topical corticosteroids have anti-inflammatory, antipruritic, and vasoconstrictive properties.

When applied topically, camphor has an anti-pruritic and surface anaesthetic effect, creating a feeling of coolness. Menthol has a cooling-anesthetising effect when applied to the skin. Thermoreception channels, TRPM8 and TRPV3 are activated by menthol; TRPA1 is inhibited

by menthol. The topical application of menthol to the skin is commonly associated with a cooling sensation (by activation of TRPM8), which may control itching.

Pharmacokinetics

The pharmacokinetics of SARNA HC® Lotion (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.

Camphor is readily absorbed from all administration sites. There are no clinical data available on the absorption of menthol.

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 metabolised in the liver.

Camphor is hydroxylated in the liver to yield hydroxycamphor metabolites which are then conjugated with glucuronic acid. Menthol is glucuronidated in the liver.

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

Glucuronide metabolites of camphor and menthol are excreted in the urine.

STORAGE AND STABILITY

Store between 15° and 30° C. Keep out of the reach and sight of children.

DOSAGE FORMS, COMPOSITION AND PACKAGING

SARNA HC® Lotion is an off-white lotion.

SARNA HC® Lotion contains hydrocortisone USP 1% or 2.5% w/v in an emollient base containing Camphor 0.525% w/v, citric acid anhydrous, cetyl alcohol, edetate disodium, Aerosil 200, Arlacel 165, Parfum Bouget MR 564 (fragrance), isopropyl myristate, menthol crystals 0.525% w/v, PEG 400 monostearate, purified water, stearic acid, white petrolatum, xantham gum, and Glydant as the preserving agent.

SARNA HC® 1% Lotion is available in a 150 mL bottle and SARNA HC® 2.5% Lotion is available in a 75 mL tube.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

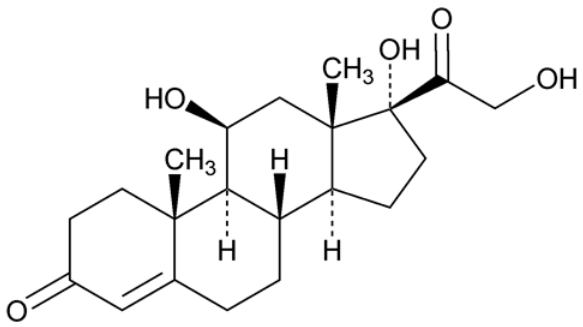
Common name: hydrocortisone

Chemical name: Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11β)-

Molecular formula: $C_{21}H_{30}O_5$

Molecular mass: 362.46

Structural formula:



Physicochemical properties: hydrocortisone is a white to practically white, odourless, crystalline powder.

TOXICOLOGY

Carcinogenesis

Long term animal studies have not been performed to evaluate the carcinogenic potential of topical corticosteroids. Subcutaneous injection of hydrocortisone at 50 mg/kg once per week for 52 weeks was not carcinogenic in male rats. [6]

No animal studies have been conducted with camphor and menthol in combination.

Camphor has not been evaluated in a carcinogenicity study.

A racemic mixture of menthol (50:50 mixture of L and D isomer) demonstrated no evidence of tumourgenic effects in a rat carcinogenicity study.

Genotoxicity

Hydrocortisone was not mutagenic in a bacterial mutagenicity assay (*Salmonella typhimurium*) in the absence or presence of metabolic activation, and was not genotoxic in an unscheduled DNA synthesis (UDS) assay in rat primary hepatocytes. Hydrocortisone was genotoxic in a chromosome aberration assay in human lymphocytes, and a mouse bone marrow micronucleus/sister chromatid exchange assay.

Camphor was nonmutagenic in bacterial reverse mutation assay and nonclastogenic in both *in vitro* chromosome aberration assays and an *in vivo* micronucleus test.

L-Menthol was considered to be non-genotoxic in a range of *in vitro* and *in vivo* tests.

Fertility

The effect on fertility of Hydrocortisone has not been evaluated in animals.

There are no data available on the reproductive toxicity of camphor.

There are no data available on the reproductive toxicity of menthol.

Pregnancy

Subcutaneous administration of hydrocortisone to mice at doses of ≥30 mg/kg/day, to rabbits at a dose of 675 µg/kg/day, and the administration of a single intramuscular injection of ≥25 mg to hamsters during pregnancy produced fetal abnormalities including cleft palate.

Oral administration of camphor to pregnant rats and rabbits was not associated with developmental toxicity (including fetal viability, growth retardation and malformations) even at doses shown to induce maternal toxicity.

Oral administration of menthol to pregnant rats, mice, rabbits, and hamsters was not associated with developmental toxicity.

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PART III: CONSUMER INFORMATION

PrSARNA HC®

Hydrocortisone USP

Lotion 1% and 2.5% (w/v)

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

ABOUT THIS MEDICATION

What the medication is used for:

SARNA HC® is used to help relieve the redness and itchiness of certain skin problems for up to 4 weeks.

What it does:

SARNA HC® contains hydrocortisone 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 SARNA HC® if you:

- are allergic to hydrocortisone, any component of the container, or to any of the other ingredients in SARNA HC® (see **What the nonmedicinal ingredients are**).
- are allergic to other corticosteroids, camphor, or menthol
- have bacterial, tubercular, fungal, parasitic, viral skin infections (e.g. herpes simplex, chicken pox, vaccinia), tuberculosis or syphilis skin lesions, or a skin reaction following a recent vaccination.
- have acne, 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 (papules) or pus-filled bumps (pustules)), or itchy skin which is not inflamed.

Do not apply in or near the eye.

Do not use on infants and children under 2 years of age.

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

What the medicinal ingredient is:

Hydrocortisone

What the nonmedicinal ingredients are:

The nonmedicinal ingredients in SARNA HC® Lotion are camphor, citric acid anhydrous, cetyl alcohol, edetate disodium, Aerosil 200, Arlacel 165, Parfum Bouget MR 564 (fragrance), isopropyl myristate, menthol crystals, PEG 400 monostearate, purified water, stearic acid, white petrolatum, xantham gum and Glydant as the preserving agent.

What dosage forms it comes in:

SARNA HC® Lotion 1% is available in a 150 mL bottle.
SARNA HC® Lotion 2.5% is available in a 75 mL tube.

WARNINGS AND PRECAUTIONS

Topical corticosteroids when used over large areas, on sensitive areas such as the face, in skin-fold areas like the armpit and groin, on broken skin, for prolonged periods or under an airtight dressing are more likely to be absorbed into the bloodstream and cause side effects. Apply only enough to cover the affected areas. SARNA HC® should not be applied over large areas unless advised by a physician.

Only use SARNA HC® for as long as your doctor recommends.

Inform your doctor if you have previously used corticosteroids.

Before using SARNA HC®, talk to your doctor or pharmacist if:

- you are pregnant or planning to become pregnant.
- you are breastfeeding. If you do SARNA HC® when breastfeeding, do not use on your breast area to ensure that the baby does not accidentally get it in their mouth.
- you have other inflammatory skin diseases in the leg as a result of impaired circulation (such as stasis dermatitis).
- you have problems with your kidney or liver. You may need to use a smaller amount of SARNA HC® or use it less often.

While using SARNA HC®, talk to your doctor or pharmacist if:

- you develop any skin infection
- you have an allergic reaction
- you develop significant skin irritation

- you experience skin thinning or softening
- your condition worsens or does not improve

While using SARNA HC®:

- Avoid use on sensitive areas such as broken or very swollen skin.
- Do not apply SARNA HC® over large areas of the body, as camphor (an ingredient in SARNA HC®) can be absorbed into the body and cause side effects including convulsions.
- SARNA HC® contains traces if formaldehyde which may cause allergic reactions or irritation upon contact with the skin.
- SARNA HC® should be used with caution on the face, or in skin fold areas, such as the groin or the armpit.
- Avoid SARNA HC® from getting in the eye, or other mucous membranes including the nostrils or mouth. In case of contact, wash with water. Absorption in the body may cause increased pressure in the eye (glaucoma), or a cloudy lens in the eye (cataracts).
- Do not use occlusive dressings such as a bandage, nor cover the treated areas tightly.
- If you are over 65 years of age, use SARNA HC® with caution. You may need to use a smaller amount of SARNA HC® or use it less often
- Children absorb larger amounts of topical corticosteroids and therefore, may be more likely to develop side effects. **Do not use SARNA HC® on infants and children less than 2 years of age**.
- If you have any skin disease around a leg ulcer, use of a topical corticosteroid may increase the risk of an allergic reaction or an infection around the ulcer.
- Keep out of the reach and sight of children.

INTERACTIONS WITH THIS MEDICATION

Some medicines may affect how SARNA HC® 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

For topical use only and not for use in the eyes.

Usual dose:
Apply a thin film to the affected areas once or twice a day for a maximum of 4 weeks.

If your condition does not improve within 2-4 weeks of treatment, speak to your doctor or pharmacist. It is important to not stop using SARNA HC® suddenly or your skin condition could flare up again.

If you use SARNA HC® regularly make sure you talk to your doctor before you stop using it.

How to Apply SARNA HC®:

- Apply a thin layer 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.
- A moisturizer should be used as maintenance therapy.

Do not use SARNA HC® on infants and children less than 2 years of age.

SARNA HC® should be used for the minimum amount of time required to achieve the desired results, **but always use SARNA HC® 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 SARNA HC®, 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 SARNA HC® to make up for missed doses.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines SARNA HC® can have side effects although not everybody gets them. Side effects will affect your skin and may have an effect on other parts of your body if a sufficient quantity of medicine is absorbed through the skin and enters your blood stream.

If your skin condition gets worse or your skin becomes swollen during treatment. You may be allergic to the medicine or need other treatment. Stop using SARNA HC® and tell your doctor as soon as possible.

The following side effects have been reported in patients using SARNA HC® and other corticosteroids:

- local hypersensitivity
- contact dermatitis/dermatitis (a type of eczema)
- redness
- rash
- hives
- itching
- blisters
- skin irritation
- skin burning
- skin pain
- skin dryness or flaking
- skin thinning or softening
- stretch marks
- changes in the colour of your skin
- increased body hair
- the appearance of blood vessels under the surface of your skin (telangiectasia)
- worsening of condition
- secondary infection
- application site irritation, pain or swelling

The following have been observed with the use of airtight dressings:

- pus-filled bumps (pustules), heat rash (miliaria), inflammation of the hair follicles (folliculitis), non-healing wounds (pyoderma)

Serious side effects such as Cushing's syndrome may be associated with absorption in the body of topical corticosteroids (for example, from long-term, improper or excessive use). Symptoms include: increased weight, moon face / rounding of the face and obesity. Other side effects may include weight loss, fatigue, nausea, diarrhea and abdominal pain (steroid withdrawal syndrome). Also, look out for delayed weight gain and slow growth in children.

Other symptoms that may only show in blood tests or when your doctor gives you a medical examination are: decreased hormone cortisol levels in your blood, increased sugar levels in your blood or urine, high blood pressure, cloudy lens in the eye (cataract), increased pressure in the eye (glaucoma), as well as weakening of the bones through gradual mineral loss (osteoporosis) and additional tests may be needed after your medical examination to confirm whether you have osteoporosis.

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

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.			✓
Cushing's syndrome: weight gain, moon face / rounding of the face and obesity.			✓

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

HOW TO STORE IT

Store between 15° and 30°C. Keep out of the reach and sight 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.stiefel.ca or by contacting the sponsor,

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