For the use of Dermatologists or a Hospital or a Laboratory only.

8026805-9093

HALONOVA-S

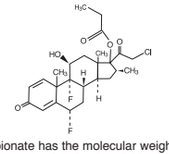
Halobetasol Propionate 0.05 % w/w &
Salicylic Acid 3.0 % w/w Ointment

COMPOSITION :

Halobetasol Propionate U.S.P.	0.05 % w/w
Salicylic Acid I.P.	3.0 % w/w
In a ointment base	q.s.

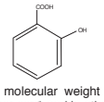
DESCRIPTION

Halobetasol propionate, is an ultra high-potency corticosteroid for topical dermatological use. The corticosteroids constitute a class of primarily synthetic steroids used topically as an antiinflammatory and anti-pruritic. Chemically, Halobetasol Propionate is Pregna-1,4-diene-3,20-dione,21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-,(6α,11β,16β)-; 21-chloro-6α,9-difluoro-11β,17-dihydroxy-16β-methyl-pregna-1,4-diene-3,20-dione17-propionate with the empirical formula $C_{25}H_{31}ClF_2O_5$. It has the following structural formula :



Halobetasol propionate has the molecular weight of 484.96. It is white to off-white powder. It is freely soluble in dichloromethane and in acetone; practically insoluble in water.

Salicylic Acid is 2-hydroxy benzoic acid with the empirical formula $C_7H_6O_3$. It has the following structural formula :



Salicylic Acid has the molecular weight of 138.1. It is freely soluble in *ethanol* (95 *per cent*) and in ether, sparingly soluble in *chloroform*; slightly soluble in water.

CLINICAL PHARMACOLOGY

Pharmacological Actions

Halobetasol

Halobetasol propionate is a synthetic corticosteroid for topical dermatological use. The corticosteroids constitute a class of primarily synthetic steroids used topically as an anti-inflammatory and antipruritic agent. Like other topical corticosteroids, halobetasol propionate has antipruritic, and vasoconstrictive actions. The mechanism of the anti-inflammatory activity of the topical corticosteroids, in general, 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 prostaglandins and leukortrienes by inhibiting the release of their common precursor arachidonic acid.

Salicylic acid

Salicylic Acid has been shown to produce desquamation of the horny layer of skin while not effecting qualitative or quantitative changes in the structure of the viable epidermis. The mechanism of action has been attributed to a dissolution of intercellular cement substance.

Pharmacokinetic Profile

Topical corticosteroids can be absorbed from normal intact skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Inflammation and/or other disease processes in the skin may increase percutaneous absorption. Occlusive dressings with hydrocortisone for up to 24 hours have not been demonstrated to increase penetration. Human and animal studies indicate that less than 6% of the applied dose of halobetasol propionate enters the circulation within 96 hours following topical administration of the ointment.

Salicylic acid exerts only local action after topical application. Salicylates are distributed in the extracellular space. Fifty to eighty percent of salicylate is protein bound to albumin. Almost 95 % of a single dose of salicylate is excreted within 24 hours of its entrance into the extracellular space. The major metabolites identified in the urine after topical administration are salicyluric acid, salicylate, glucuro-nides and free salicylic acid.

INDICATIONS

Indicated for topical treatment of Chronic plaque Psoriasis.

Application

Apply a thin layer of ointment to the affected skin areas once or twice daily as directed by your physician and rub in gently and completely. For some patients, adequate maintenance therapy may be achieved with less frequent application. Ointment should not be used with occlusive dressings.

CONTRAINDICATIONS

Halonova-S ointment is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.It is also contraindicated in viral diseases of the skin including herpes simplex, vaccinia and varicella.

WARNINGS AND PRECAUTIONS

Halobetasol

General

Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for gluco- corticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment. Patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free-cortisol tests. Patients receiving super potent corticosteroids should not be treated for more than 2 weeks at a time and only small areas should be treated at any one time due to the increased risk of HPA suppression. These effect were reversible upon discontinuation of treatment. 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 corticosteroid. 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.

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. If irritation develops, Halonova-S ointment should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing failure to heal rather than noting a clinical exacerbation as with most topical products not containing corticosteroids.

Such an observation should be corroborated with appropriate diagnostic patch testing.

If concomitant skin infections are present or develop, an appropriate antifungal or anti-bacterial agent should be used. If a favorable response does not occur promptly, use of Halonova-S ointment should be discontinued until the infection has been adequately controlled. Halonova-S ointment should not be used in the treatment of rosacea or perioral dermatitis, and it should not be used on the face, groin, or in the axillae.

Prolonged use of topical corticosteroid products may produce atrophy of the skin and subcutaneous tissues. If this occurs, treatment should be discontinued. Topical corticosteroids should be used with caution in patients with stasis dermatitis and other skin diseases associated with impaired circulation, hyper sensitive patients and patients with glaucoma. Patients should be advised to inform subsequent physician of the prior use of corticosteroids.

Use in children

Safety and effectiveness of Halonova-S ointment in pediatric patients have not been established and use in pediatric patients under 12 is not recommended. 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 or after withdrawal of treatment.

Adverse effects including striae have been reported with inappropriate use of topical cortico- steroids in infants and children.

Use in Pregnant or Lactating Women

There are no adequate and well-controlled studies of the teratogenic potential of halobetasol propionate and salicylic acid in pregnant women. Halonova-S ointment should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. 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. There is a potential for serious adverse reactions in nursing infants from the mother's use of salicylic acid and hence a decision should be made whether to discontinue nursing or to discontinue the ointment, taking into account the importance of the drug to the mother. If used by nursing mothers, it should not be used on the chest area to avoid accidental contamination of the child.

Salicylic acid

Prolonged use over large areas, especially in children and those patients with significant renal or hepatic impairment, could result in salicylism. Concomitant use of other drugs which may contribute to elevated serum salicylate levels should be avoided where the potential for toxicity is present.

In patients with renal or hepatic impairment, the area to be treated should be limited and the patient monitored closely for signs of salicylate toxicity: nausea, vomiting, dizziness, loss of hearing, tinnitus, lethargy, hyperpnea, diarrhea, and psychic disturbances. In the event of salicylic acid toxicity, it should be discontinued. Fluids should be administered to promote urinary excretion. Treatment with sodium bicarbonate (oral or intravenous) should be instituted as appropriate.

Patients should be cautioned against the use of oral aspirin and other salicylate containing medications, such as sports injury creams, to avoid additional excessive exposure to salicylic acid. Where needed, aspirin should be replaced by an alternative non-steroidal anti-inflammatory agent that is not salicylate based.

Patients should be advised not to apply occlusive dressings, clothing or other occlusive topical products such as petrolatum-based ointments to prevent excessive systemic exposure to salicylic acid.

Due to potential risk of developing Reye's syndrome, salicylate products should not be used in children and teenagers with varicella or influenza, unless directed by a Physician.

Information for Patients

Patients using Halonova-S ointment should receive the following information and instructions :

- The medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes and other mucous membranes.
- The medication should not be used for any disorder other than that for which it was prescribed.
- The treated skin area should not be bandaged, otherwise covered or wrapped, so as to be occlusive unless directed by the physician.
- Patients should report to their physician any signs of local adverse reactions.

DRUG INTERACTIONS

Salicylic acid

The following interactions are from a published review and include reports concerning both oral and topical salicylate administration.The relationship of these interactions to the use of salicylic acid (topical) is not known. Due to the competition of salicylate with other drugs for binding to serum albumin the following drug interactions may occour :

Sulfonylureas : Hypoglycemia potentiated.

Methotrexate : Decreases tubular reabsorption; clinical toxicity from methotrexate can result.

Oral Anticoagulants : Increased bleeding Drugs changing salicylate levels by altering renal tubular reabsorption:

Corticosteroids: Decreases plasma salicylate level; tapering doses of steroids may promote salicylism.

Drugs with complicated interactions with salicylates.

Heparin : Salicylate decreases platelet adhesiveness and interferes with hemostasis in heparin-treated patients.

Pyrazinamide:Inhibits pyrazinamideinduced hyperuricemia.

Uricosuric Agents : Effect of probenemide, sulfinpyrazone and phenylbutazone inhibited.

Adverse Reactions

Halobetasol

In some controlled clinical trials, the most frequent adverse events reported with halobetasol use are stinging or burning, Less frequently reported adverse reactions were pustulation, erythema, skin atrophy, leukoderma, acne, itching, secondary infection, telangiectasia, urticaria, dry skin, miliaria, paresthesia, and rash.

The following additional local adverse reactions are reported infrequently with topical corticosteroids, and they may occur more frequently with high potency corticosteroids: Folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae and miliaria.

Salicylic acid

Exessive erythema and scaling conceivably could result from use on open skin lesions.

Overdosage

Topically applied Halonova-S ointment can be absorbed in sufficient amounts to produce systemic effects (see warnings and precautions)

Apply a thin layer of ointment to the affected skin areas once or twice daily as directed by your physician and rub in gently and completely. For some patients, adequate maintenance therapy may be achieved with less frequent application. Ointment should not be used with occlusive dressings.

Treatment beyond 2 consecutive weeks is not recommended, and the total dosage should not exceed 50 g/week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis. As with other highly active corticosteroids, therapy should be discontinued when control has been achieved. If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary.

DOSAGE AND APPLICATION

Apply a thin layer of ointment to the affected skin areas once or twice daily as directed by your physician and rub in gently and completely. For some patients, adequate maintenance therapy may be achieved with less frequent application. Ointment should not be used with occlusive dressings.

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EXPIRY DATE

Do not use later than the date of expiry.

STORAGE

Store at temperature not exceeding 25°C. Do not freeze. Protect from light. Keep container tightly closed. Keep the cap tightly closed after use

FOR EXTERNAL USE ONLY

PRESENTATION

HALONOVA-S ointment is available in tube of 15 gm.

torrent

Marketed by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Manufactured in India by :
Helios Pharmaceuticals
(Div. of P.K.T.P. Pvt. Ltd.)
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