

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

8026799-9093

## HALONOVA

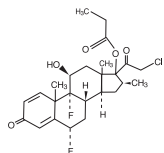
(Halobetasol Propionate Cream 0.05 % w/w)

### COMPOSITION :

Halobetasol Propionate U.S.P. 0.05 % w/w  
Chlorocresol I.P. 0.1 % w/w  
In a cream 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 anti-inflammatory 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)-(6 $\alpha$ ,11 $\beta$ ,16 $\beta$ )-; 21-chloro-6 $\alpha$ ,9-difluoro-11 $\beta$ ,17-dihydroxy-16 $\beta$ -methyl-pregna-1,4-diene-3,20-dione-17-propionate with the empirical formula C<sub>25</sub>H<sub>31</sub>ClF<sub>2</sub>O<sub>5</sub>. 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.

### CLINICAL PHARMACOLOGY

#### Mechanism of Action

Like other topical corticosteroids, halobetasol propionate has anti-inflammatory, antipruritic and vasoconstrictive actions. The mechanism of the anti-inflammatory activity of the topical corticosteroids, in general, is unclear. However, cortico-steroids 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 leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

#### Pharmacokinetics

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle and the integrity of the epidermal barrier. Occlusive dressings with hydrocortisone for up to 24 hours have not been demonstrated to increase penetration, however, occlusion of hydrocortisone for 96 hours markedly enhances penetration. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and or other disease processes in the skin may increase percutaneous absorption. 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. Studies performed on the halobetasol propionate cream indicate that it is in the super-high range of potency as compared with other topical corticosteroids.

#### INDICATIONS

Halobetasol propionate cream is an ultra high-potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

### CONTRAINDICATIONS

Halobetasol propionate cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

Halobetasol propionate cream is contraindicated in viral diseases of the skin including herpes simplex, vaccinia and varicella.

### WARNINGS AND PRECAUTIONS

#### General

Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of 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, AM 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.

Halobetasol propionate cream produced HPA axis suppression when used in divided doses at 7 g day for 1 week in patients with psoriasis. These effects 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. Use in children under 12 years of age is not recommended. If irritation develops, halobetasol propionate cream 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 antibacterial agent should be used. If a favorable response does not occur promptly, use of halobetasol propionate cream should be discontinued until the infection has been adequately controlled. Halobetasol propionate cream 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, hypersensitive patients and patients with glaucoma. Patients should be advised to inform subsequent physician of the prior use of corticosteroids.

#### Information for the Patient

**Patients using topical corticosteroids 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.
- 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 or 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.

#### Laboratory Tests

The following tests may be helpful in evaluating patients for HPA axis suppression : ACTH-stimulation test, AM plasma-cortisol test; urinary free-cortisol test.

#### Carcinogenesis, Mutagenesis and Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of halobetasol propionate. Positive mutagenicity effects were observed in two genotoxicity assays. Halobetasol propionate was positive in a Chinese hamster micronucleus test, and in a mouse lymphoma gene mutation assay in vitro.

Studies in the rat following oral administration at dose levels up to 50g/kg day indicated no impairment of fertility or general reproductive performance.

In other genotoxicity testing, halobetasol propionate was not found to be genotoxic in the Ames Salmonella assay, in the sister chromatid exchange test in somatic cells of the Chinese hamster, in chromosome aberration studies of germinal and somatic cells of rodents, and in a mammalian spot test to determine point mutations.

#### Pregnancy, Teratogenic Effects

##### Pregnancy Category C

Corticosteroids have been shown to be teratogenic, in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application to laboratory animals.

Halobetasol propionate has been shown to be teratogenic in SPF rats and chinchillatype rabbits when given systemically during gestation at doses of 0.04-0.1 mg/kg in rats and 0.01 mg/kg in rabbits. These doses are approximately 13,33 and 3 times, respectively, the human topical dose of halobetasol propionate cream Halobetasol propionate was embryotoxic in rabbits but not in rats.

Cleft palate was observed in both rats and rabbits. Omphalocele was seen in rats, but not in rabbits. There are no adequate and well-controlled studies of the teratogenic potential of halobetasol propionate in pregnant women. Halobetasol propionate cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

#### Nursing Mothers

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 halobetasol propionate cream is administered to a nursing woman.

#### Pediatric Use

Safety and effectiveness of halobetasol propionate cream 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 risk of adrenal insufficiency during or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate 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 responses to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

#### Geriatric Use

Of approximately 400 patients treated with halobetasol cream in clinical studies, 25% were 61 years and over and 6% were 71 years and over. No overall differences in safety or effectiveness were observed between these patients and younger patients; and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

#### ADVERSE REACTIONS

In controlled clinical trials, the most frequent adverse events reported for halobetasol propionate included stinging, burning or itching in 4.4% (cream) of the patients. Less frequently reported adverse reactions were: Cream: dry skin, erythema, skin atrophy, leukoderma, vesicles and rash; Cream : 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, but may occur more frequently with high potency corticosteroids, such as halobetasol propionate cream. These reactions are listed in an approximate decreasing order of occurrence: folliculitis, hypertrichosis, acneiform eruptions, hypo-pigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae, and miliaria.

#### OVERDOSAGE

Topically applied halobetasol propionate cream can be absorbed in sufficient amount to produce systemic effects.

#### DOSAGE AND APPLICATION

Apply a thin layer of halobetasol propionate cream to the affected skin once or twice daily, as directed by your physician, and rub in gently and completely.

Halobetasol propionate cream is an ultra high-potency corticosteroid; therefore, treatment should be limited to 2 weeks, and amounts greater than 50 g/week should not be used. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, reassessment of diagnosis may be necessary. Halobetasol propionate cream should not be used with occlusive dressings.

#### EXPIRY DATE

Do not use later than the date of expiry.

#### STORAGE

**Do not freeze. Protect from light.**  
**Store at a temperature not exceeding 25° C.**

Keep out of reach of children  
Keep the cap tightly closed after use  
FOR EXTERNAL USE ONLY

#### PRESENTATION

HALONOVA is available in tube of 15 gm.



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.)  
Village Malpur, P.O. Bhud, Tehsil Nalagarh,  
Baddi, Dist. Solan, (H.P.) -173 205.