

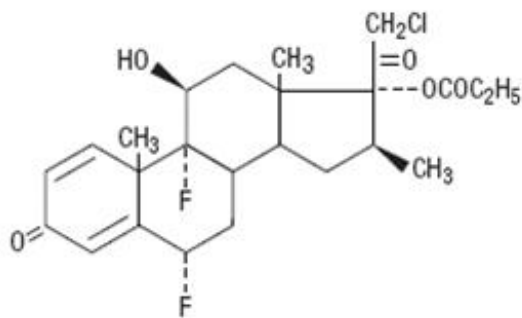
ULTRAVATE X- halobetasol propionate
Ranbaxy Laboratories Inc.

ULTRAVATE X
(halobetasol propionate ointment) Ointment, 0.05%
For Dermatological Use Only. Not for Ophthalmic Use.
Rx only

DESCRIPTION

Ultravate® (halobetasol propionate) ointment, 0.05% contains halobetasol propionate, 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.

Chemically halobetasol propionate is 21-chloro-6 α , 9-difluoro-11 β , 17-dihydroxy-16 β -methylpregna-1, 4-diene-3-20-dione, 17-propionate, C₂₅H₃₁ClF₂O₅. It has the following structural formula:



Halobetasol propionate has the molecular weight of 485. It is a white crystalline powder insoluble in water.

Each gram of Ultravate Ointment contains 0.5 mg/g of halobetasol propionate in a base of aluminum stearate, beeswax, pentaerythritol cocoate, petrolatum, propylene glycol, sorbitan sesquioleate, and stearyl citrate.

CLINICAL PHARMACOLOGY

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, 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 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 of the ointment.

Studies performed with Ultravate Ointment indicate that it is in the super-high range of potency as compared with other topical corticosteroids.

INDICATIONS AND USAGE

Ultravate Ointment 0.05% is a super-high potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. Treatment beyond two 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. Use in children under 12 years of age is not recommended.

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.

CONTRAINDICATIONS

Ultravate Ointment is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

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, 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.

Ultravate Ointment produced HPA axis suppression when used in divided doses at 7 grams per day for one 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. For information on systemic supplementation, see prescribing information for those products.

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios (see **PRECAUTIONS: Pediatric Use**).

If irritation develops, Ultravate 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 antibacterial agent should be used. If a favorable response does not occur promptly, use of Ultravate Ointment should be discontinued until the infection has been adequately controlled.

Ultravate 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.

Information for Patients

Patients using Ultravate® Ointment should receive the following information and instructions:

1. The medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. The medication should not be used for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged, otherwise covered or wrapped, so as to be occlusive unless directed by the physician.
4. 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; A.M. 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 50 mcg/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 in laboratory animals.

Halobetasol propionate has been shown to be teratogenic in SPF rats and chinchilla-type rabbits when given systemically during gestation at doses of 0.04 to 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 Ultravate Ointment. 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. Ultravate Ointment 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 Ultravate Ointment is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of Ultravate 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 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.

Geriatric Use

Of approximately 400 patients treated with Ultravate® Ointment 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 Ultravate Ointment included stinging or burning in 1.6% of the patients. 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, such as Ultravate Ointment. These reactions are listed in an approximate decreasing order of occurrence: folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae and miliaria.

OVERDOSAGE

Topically applied Ultravate Ointment can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS**).

DOSAGE AND ADMINISTRATION

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

Ultravate (halobetasol propionate) Ointment is a super-high potency topical corticosteroid; therefore, treatment should be limited to two weeks, and amounts greater than 50 g/wk 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.

Ultravate Ointment should not be used with occlusive dressings.

HOW SUPPLIED

Ultravate® (halobetasol propionate) Ointment, 0.05% is supplied in the following tube size:

50 g (NDC 10631-102-50)

STORAGE

Store between 15°C and 30°C (59°F and 86°F).

To report SUSPECTED ADVERSE REACTIONS, contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

5090133 (Flat), 5090134 (Folded)

Revised November 2011

PACKAGE LABEL. PRINCIPAL DISPLAY PANEL



Non Varnish Area

Rx only

Ultravate® Ointment
(halobetasol propionate 0.05%)
NET Wt. 50 g
Packaged* with complimentary
Lac-Hydrin® Ten Plus
(moisturizing cream)



Ointment



Ultravate® Ointment
(halobetasol propionate 0.05%)
NET Wt. 50 g

Packaged* with complimentary
Lac-Hydrin® Ten Plus
(moisturizing cream)

Ointment

NDC 10631-119-01



Ultravate® Ointment
(halobetasol propionate 0.05%)
NET Wt. 50 g

Packaged* with complimentary
Lac-Hydrin® Ten Plus
(moisturizing cream)

Ointment



Ultravate® Ointment
(halobetasol propionate 0.05%)
NET Wt. 50 g

Packaged* with complimentary
Lac-Hydrin® Ten Plus
(moisturizing cream)

Ultravate® Ointment
(halobetasol propionate 0.05%)
NET Wt. 50 g

Each gram contains 0.5 mg halobetasol propionate in a base of aluminum stearate, beeswax, pentaerythritol coccoate, petrolatum, propylene glycol, sorbitan sesquioleate and stearyl citrate.

Store at controlled room temperature 15° C - 30° C (59° F - 86° F).

Lot no. and exp. date on carton and crimp of tube.

WARNING: Keep out of reach of children.

For topical use only. Not for use in eyes.

Usual Dosage: Apply once or twice daily, or as directed by physician. See insert for complete information.



*Not been studied for use as a combination therapy with Ultravate® Ointment.

A combination of lactic acid with COSMEDERM-38™ Technology makes LAC-HYDRIN® Ten Plus a moisturizer like no other. It is dermatologically tested and guaranteed to soften and smooth rough and dry skin - yet it's gentle enough to use on the face.

Physician-Tested. Allergy Tested. Fragrance-Free.

Instructions: For best results, apply to dry skin twice a day.

Avoid contact with eyes. For external use only.

Caution: For external use only. Avoid contact with eyes, and broken or irritated skin. If contact occurs, rinse thoroughly with water. If excessive stinging or redness develops, discontinue use and consult your physician.

Sunburn Alert: This product contains an alpha hydroxy acid (AHA) that may increase your skin's sensitivity to the sun and particularly the possibility of sunburn. Use a sunscreen, wear protective clothing, and limit sun exposure while using this product and for a week afterwards.

Ingredients: Water, Lactic Acid, Sodium Hydroxide, Strontium Nitrate, Glycerin, Stearyl Alcohol, Propanediol, C12-15 Alkyl Benzoate, Cetearyl Isononanoate, Capric/Caprylic Triglyceride, Cyclopentasiloxane, Cetyl Alcohol, Behentrimonium Methosulfate, Mineral Oil, Tocopherol Acetate, Xanthan Gum, PPG-18/18 Dimethicone, Polysorbate 20, Phenoxethanol, Silica, Potassium Sorbate, Ethylhexylglycerin, Disodium EDTA, CAB Oxy K (Ppg-8, Rosmarinus Officinalis Leaf Extract CO2, Ascorbyl Palmitate, Caprylic/Capric Triglycerides, Ascorbic Acid, Tocopherol and Citric Acid).

COSMEDERM-38™ is a registered trademark of COSMEDERM Bioscience, Inc. Protected by U.S. Patents 5,716,625; 5,804,203; 6,139,850; 7,404,967

RANBAXY
Jacksonville, FL 32257 USA
06311901A 0212



Dispense as a Complete Package

Rx only



Net Wt. 225 g (8 oz.)



Net Wt. 225 g (8 oz.)



Net Wt. 225 g (8 oz.)



Ultravate® Ointment
(halobetasol propionate 0.05%)
NET Wt. 50 g

Packaged* with complimentary
Lac-Hydrin® Ten Plus
(moisturizing cream)

Rx only

ULTRAVATE X

halobetasol propionate kit

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:10631-119
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Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:10631-119-01	1 in 1 KIT		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 TUBE	50 g
Part 2	1 TUBE	225 g

Part 1 of 2

ULTRAVATE

halobetasol propionate ointment

Product Information

Item Code (Source)	NDC:10631-102
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Route of Administration	TOPICAL
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Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HALOBETASOL PROPIONATE (UNII: 91A0K1TY3Z) (HALOBETASOL - UNII:9P6159HM7T)	HALOBETASOL PROPIONATE	0.50 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
ALUMINUM STEARATE (UNII: U6XF9NP8HM)	
YELLOW WAX (UNII: 2ZA36H0S2V)	
PETROLATUM (UNII: 4T6H12BN9U)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
MONOSTEARYL CITRATE (UNII: YWW937R1QR)	
SORBITAN SESQUIOLEATE (UNII: 0W8RRI5W5A)	
PENTAERYTHRITOL (UNII: SU420W1S6N)	

Product Characteristics

Color	white	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:10631-102-50	50 g in 1 TUBE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA019967	07/09/2012	

Part 2 of 2

LAC-HYDRIN TEN PLUS

ammonium lactate cream

Product Information

Item Code (Source)	NDC:10631-114
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
AMMONIUM LACTATE (UNII: 67M901L9NQ) (AMMONIUM CATION - UNII:54S68520I4)	AMMONIUM LACTATE	100 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
ALKYL (C12-15) BENZOATE (UNII: A9EJ3J61HQ)	
ALPHA-TOCOPHEROL ACETATE (UNII: 9E8X80D2L0)	
ASCORBIC ACID (UNII: PQ6CK8PD0R)	
ASCORBYL PALMITATE (UNII: QN83US2B0N)	
BEHENTRIMONIUM METHO SULFATE (UNII: 5SHP745C61)	
CETEARYL ISONONANOATE (UNII: P5O01U99NI)	
CETYL ALCOHOL (UNII: 936JST6JCN)	
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
CYCLOMETHICONE (UNII: NMQ347994Z)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
ETHYLHEXYLGLYCERIN (UNII: 147D247K3P)	
GLYCERIN (UNII: PDC6A3C0OX)	

LACTIC ACID (UNII: 33X04XA5AT)
MINERAL OIL (UNII: T5L8T28FGP)
PHENOXYETHANOL (UNII: HIE492ZZ3T)
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)
POLYSORBATE 20 (UNII: 7T1F30V5YH)
POTASSIUM SORBATE (UNII: 1VPU26JZZ4)
PROPANEDIOL (UNII: 5965N8W85T)
ROSEMARY (UNII: IJ67X351P9)
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)
SODIUM HYDROXIDE (UNII: 55X04QC32I)
STEARYL ALCOHOL (UNII: 2KR89I4HIY)
STRONTIUM NITRATE (UNII: BDG873AQZL)
TOCOPHEROL (UNII: R0ZB2556P8)
TRICAPRYLIN (UNII: 6P92858988)
WATER (UNII: 059QF0K00R)
XANTHAN GUM (UNII: TTV12P4NEE)

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:10631-114-05	225 g in 1 TUBE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020508	07/09/2012	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA019968	07/01/2012	

Labeler - Ranbaxy Laboratories Inc. (169932519)

Registrant - Ranbaxy Laboratories Inc. (169932519)

Establishment

Name	Address	ID/FEI	Business Operations
Contract Pharmaceuticals Limited		248761249	manufacture(10631-114)

Establishment

Name	Address	ID/FEI	Business Operations
CA-BOTANA INTERNATIONAL		106276728	manufacture(10631-102, 10631-119)