PRODUCT MONOGRAPH

MYLAN-CLOBETASOL SCALP APPLICATION

(Clobetasol 17-propionate 0.05% w/w in aqueous-alcohol base)

(60 ml bottles)

Topical Corticosteroid

Mylan Pharmaceuticals ULC

85 Advance Road Etobicoke,

Ontario M8Z 2S6

DATE OF PREPARATION:

June 5, 2009

DATE OF REVISION:

Control#: 129665

NAME OF DRUG

MYLAN-CLOBETASOL SCALP APPLICATION

(Clobetasol 17-propionate 0.05 %w/w)

(60 mL bottles)

THERAPEUTIC CLASSIFICATION

Topical Corticosteroid

ACTIONS AND CLINICAL PHARMACOLOGY

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) is a very potent topical corticosteroid with anti-inflammatory, antipruritic, and vasoconstrictive actions.

Pharmacokinetics

In man, the extent of percutaneous absorption of topical corticosteroids, including clobetasol 17-propionate, is determined by many factors, including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressing.

As with all topical corticosteroids, clobetasol 17-propionate can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids.

Once absorbed through the skin, topical corticosteroids enter pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids, including clobetasol 17-propionate and its metabolites, are also excreted in the bile.

Bioavailability

The relative potency of corticosteroids is usually assayed by the vasoconstriction test which reflects the potency of the steroid molecule, its topical activity as well as its bioavailaility from the particular formulation. The vascoconstrictor response of MYLAN-CLOBETASOL SCALP APPLICATION was compared with Dermovate Scalp Application as well as a placebo in a randomised and double blind study involving twelve healthy subjects. The summated frequencies of the skin blanching scores recorded by all the observers, for all the subjects, are presented in the table below as the Percentage Possible Score (%TPS) versus time after initial application:

Summated %TPS Values Recorded for All Observers and. All Subjects

J OBSERVATIONS TIME (hours after application)												
Preparation	7	8	9	10	12	113	(14	115	16	17	18	128
Dermovate	13.3	20.0	25.9	33.5	43.9	50.2	57.1	58.4	58.2	56.3	52.4	30.2
Mylan	15.2	20.3	27.0	34.4	44.2	50.3	58.3	59.7	59.8	56.9	52.2	30.3
Placebo	4.8	6.2	5.6	5.7	3.5	3.6	3.2	2.6	2.0	1.0	1.8	1.2

The results demonstrate that Mylan's 0.05% clobetasol 1 7-propionate scalp

application is topically equivalent in skin blanching potential (drug delivery potential) to Glaxo's (Dermovate) 0.05% clobetasol 17-propionate scalp application.

INDICATIONS AND CLINICAL USE

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) is indicated for short-term topical treatment of recalcitrant corticosteroid responsive dermatoses, including severe cases of psoriasis and seborrhoeic dermatitis.

CONTRAINDICATIONS

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) should not be used in the treatment of acne; infected skin lesions if no anti-infective agent is used simultaneously; fungal and viral infections of the skin, including herpes simplex, vaccinia and varicella; pregnancy and lactation; hypersensitivity to any of the ingredients. Topical corticosteroids are also contraindicated in tuberculous lesions of the skin. Clobetasol propionate should not be used in the treatment of rosacea and perioral dermatitis.

WARNINGS

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) should not be used in the eye. When used over extensive areas for prolonged periods, it is possible that sufficient absorption may take place to give rise to systemic effects. Because of the potential of potent corticosteroids to suppress the hypothalamic-pituitary adrenal

(HPA) it is advisable, therefore, to use MYLAN-CLOBETASOL for brief periods only, and to discontinue its use as soon as the lesions have cleared up. Do not use more than fifty millilitres of MYLAN-CLOBETASOL SCALP APPLICATION per week. Patients should be advised to inform subsequent physicians of the prior use of corticosteroids.

PRECAUTIONS

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) 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 observations of the patient is important if these areas are to be treated.

Although hypersensitivity reactions are rare with topically-applied steroids, the drug should be discontinued and appropriate therapy initiated if there are signs of hypersensitivity.

Prolonged use of topical corticosteroids may produce atrophy of the skin and of subcutaneous tissues. If this is noted, discontinue the use of this product.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If it is considered necessary, the topical corticosteroid may be used as an adjunct to control inflammation, erythema and itching. If a symptomatic response is not noted within a few days to a week, the local application of corticosteroid should be discontinued until the infection has been brought under control.

Significant systemic absorption may occur when steroids are applied over large areas of the body, especially under occlusive dressings. Because the degree of absorption of clobetasol 17-propionate when applied under occlusive dressing has not been measured, its use in this fashion is not recommended.

Use in Pregnancy:

The safety of MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) in pregnancy has not been established. If used, the expected benefits should be weighed against the potential hazard to the fetus, particularly during the first trimeter of pregnancy. Infants born of mothers who have received substantial doses of glucocoticosteroids during pregnancy should be carefully observed for hypoadrenalism.

Like other glucocoticosteroids, Clobetasol 17-propionate is teratogenic to rodent species (see under TOXICOLOGY). The relevance of these findings to humans has not yet been established.

Use in Nursing Mothers:

It is not known whether topical adrenocorticoids are excreted in breast milk, however, systemic adrenocorticoids are excreted in breast milk and may cause growth suppression in the infant. Therefore, MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) should not be used during the course of breastfeeding.

Use in Geriatrics:

Caution is recommended in the use of adrenocorticoids in the elderly because purpura and skin lacerations may be more likely. Therefore, topical adrenocorticoids should be used infrequently, for brief periods, or under close medical supervision in patients with evidence of pre-existing skin atrophy.

Use in Pediatrics :

Because the safety and effectiveness of MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) has not been established in children, its use in children 12 years old and younger is not recommended. Adrenal suppression , Cushing syndrome, intracranial hypertension and growth retardation due to the systemic absorption of topical adrenocorticoids have been documented in children.

ADVERSE REACTIONS

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) is generally well tolerated during short-term treatment. The most frequent adverse reactions reported have been local and have included, dryness of skin, local burning, irritation, itching, skin atrophy, striae, change in pigmentation, secondary infection, and hypertrichosis.

Systemic absorption of topical corticosteroids has produced reversible HPA axis suppression, manifestations of Cushing syndrome, hyperglycemia, and glucosuria in some patients. In rare instances, treatment (or withdrawal of treatment) of psoriasis with corticosteroids may provide the pustular form of the disease.

OVERDOSE: SYMPTOMS AND TREATMENT

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) therapy should be discontinued when the typical signs of hypercorticism appear.

For treatment of chronic topical overdose, no specific antidote exists, however, treatment is symptomatic, supportive and consists of discontinuance of the topical adrenocorticoid therapy. Gradual withdrawal of the preparation may be necessary.

DOSAGE AND ADMINISTRATION

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) is applied once or twice daily to the affected areas of the scalp and rubbed in gently. The total dose applied weekly should not exceed 50 millilitres.

Therapy should be discontinued if no response is noted after one week or as soon as the lesion heals. It is advisable to use MYLAN-CLOBETASOL SCALP APPLICATION for brief periods only.

PHARMACEUTICAL INFORMATION

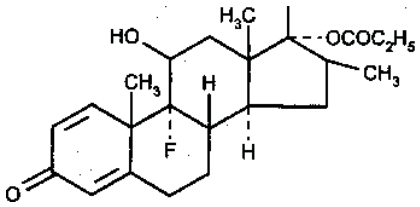
DRUG SUBSTANCE

Proper Name: Clobetasol 17-propionate

Chemical Name: 21 -Chloro-9a-fluoro-1 1 6, 1 7a-dihydroxy-1 60-methylpregna-1 $_1$4-diene-3,20-dione 17-propionate.

Structural Formula:

CH_2Cl C = 0



Molecular Formula: $C_{25}H_{32}0$ CIF

Molecular Weight: 467

Description: Clobetasol 17-propionate is a white-to-cream-coloured crystalline powder. It is insoluble in water, with a melting point of 195.5 to 197°C.

COMPOSITION: MYLAN-CLOBETASOL SCALP APPLICATION contains 0.05% w/w of clobetasol 17-propionate in an aqueous-alcohol base. The non-medicinal ingredients are carbomer, isopropyl alcohol, purified water and sodium hydroxide.

STABILITY AND STORAGE RECOMMENDATIONS:

Store between 15°C and 30°C in a tight container.

AVAILABILITY OF DOSAGE FORMS

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) is available in 20 and 60 ml white, opaque, plastic bottles.

INFORMATION FOR THE PATIENT

MYLAN-CLOBETASOL SCALP APPLICATION

(Clobetasol 17-propionate)

GENPHARM ULC

MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) is a very high potency topical corticosteroid with anti-inflammatory, antipruritic, and vasoconstrictive actions. MYLAN-CLOBETASOL SCALP APPLICATION (Clobetasol 17-propionate) is indicated for short-term topical treatment of difficult to treat corticosteroid responsive dermatoses, including severe cases of psoriasis and seborrhoeic dermatitis.

Instructions for use:

MYLAN-CLOBETASOL SCALP APPLICATION should be applied sparingly once or twice daily to only the affected areas of the scalp after being applied to the scalp MYLAN-CLOBETASOL SCALP APPLICATION should be rubbed in gently the total dose applied weekly should not exceed 50 millilitres therapy should be discontinued if no response is noted after one week or as soon as lesions heal. check with your physician if symptoms do not improve within one week or if condition becomes worse

This medication is to be used as directed by the physician and should not be used longer than the prescribed time period. It is for external use only. Avoid contact with the eyes.

This medication should not be used for any disorder other than the one for which it is prescribed.

Do not exceed the prescribed dose.

Do not use occlusive wrapping/bandages on treated sites unless directed by a physician.

5. Inform your physician of the following points:

if you are pregnant, intend to become pregnant or are breast feeding or intend to breast feed.

any current use of corticosteroids for treatment of skin disorders

any allergic reactions, arthritis or asthma, in particular if you have developed an allergy or intolerance to corticosteroids Report any signs of local adverse reactions to your physician.

Notify your physician if infection appears at treatment site. Appropriate antifungal or antibacterial agent should be instituted in the presence of dermatological infections with discontinuation of topical corticosteroids.

8. Children may absord proportionally larger amounts than adults. MYLAN-CLOBETASOL SCALP APPLICATION is not recommended for children less than 12 years old because they are more suseptible than adults to adrenal suppression.

STORAGE AND STABILITY RECOMMENDATIONS:

Store between 15oC and 30oC in well closed containers

COMPOSITION:

MYLAN-CLOBETASOL SCALP APPLICATION contains 0.05% w/w of clobetasol 17-propionate in an aqueous-alcohol base. The non-medicinal ingredients are carbomer, isopropyl alcohol, purified water and sodium hydroxide.

PHARMACOLOGY

Animals:

Thymolytic activity was determined in mice in comparison with betamethasone 12alcohol. Activity of clobetasol 17-propionate was two to ten times greater, depending upon route of administration.

Anti-granuloma activity of clobetasol 17-propionate was determined in mice, using cotton wool pellets soaked in carregeenin. Clobetasol 17-propionate was five times as potent as betamethasone alcohol, when given subcutaneously. In rats, both steroids had approximately equal activity in both tests.

Mineralocorticoid activity was determined in rats and compared with betamethasone alcohol, both steroids showing equally weak activity.

Androgenic-anabolic activities were tested in female mice. Clobetasol 1 7-propionate showed no such effects, as judged by preputial gland and growth rate measurements. In male rats, using the seminal vesicle, levator ani and growth rate measurements, clobetasol 17-propionate was equally inactive.

Anti-estrogenic activity was determined in mice by measuring the uterine weight after estrone and clobetasol 17-propionate administration. Clobetasol 17-propionate showed anti-estrogenic activity. In ovariectomized rats, it showed marked anti-estrogenic activity when compared with progesterone.

Estrogenic activity in weanling rats was about one five-hundredth that of estrone.

Progestational activity of subcutaneously-given clobetasol 17-propionate in rabbits, was about five times that of betamethasone 1 7-valerate, while orally, it had only one-half the activity of the latter steroid .

Antigonadotropic activity was tested in weanling male rats and revealed no such effect exerted by clobetasol 17-propionate.

Human:

In volunteers, the potency of clobetasol 17-propionate was compared with that of fluocinolone acetonide and betamethasone 1 7-valerate, using the vasoconstrictor test of McKenzie and Atkinson. The results showed clobetasol 17-propionate to be eighteen times as potent as fluocinolone acetonide, and six times as potent as betamethasone 1 7-valerate.

An international controlled trial on eleven hundred and fifty patients with bilateral lesions of psoriasis or eczema, showed that clobetasol propionate cream and ointment were effective.

Thirty commercial topical steroid preparations were compared, and the results have shown that clobetasol propionate cream had high activity.

The effect of clobetasol propionate ointment on adrenocortical function was studied in thirty-five patients with various skin conditions using the steroid for two to four weeks. No adrenocortical suppression was observed in thirty cases. Two patients had subnormal plasma corticosteroid level at the beginning. Three patients showed adrenocortical suppression during therapy, using 8 g, 40 g and 100 g ointment per week. Four other patients using about 100 g of ointment weekly showed no plasma corticosteroid depression.

TOXICOLOGY

Acute Toxicity:

In mice, the LD_{50} (oral) is > 4 g/kg; LD_{50} (s.c.) is > 4 g/kg. In rats, the LD_{50} (s.c.) is > 1 g/kg.

After a single subcutaneous injection of 1, 2 or 4 g/kg of clobetasol 17-propionate, most mice developed hepatic necrosis, thymic atrophy and some developed interstitial nephritis.

Rats received a single subcutaneous injection of 1 g/kg of clobetasol 17-propionate. Histological examination showed fatty liver necrosis and nephrocalcinosis. An oral dose of 1 g/kg gave similar results.

In guinea pigs, a single subcutaneous injection of 60 mg/kg of clobetasol 17-propionate caused no drug-related histological changes.In rabbits, a single intramuscular injection of 60 mg/kg of clobetasol 17-propionate caused no death. There was intra-alveolar hemmorhage and thymus involution in three out of four animals. All animals had foamy periportal cells with increased glycogen content. Some of the injection sites showed small foci of muscle necrosis.

In cats, a single intramuscular injection of 60 mg/kg of clobetasol 17-propionate caused no death. There were some cytoplasmic changes in the hearts and livers, with lipid infiltration. The thymus glands were involuted.

In dogs, a single intramuscular injection of 15 mg/kg of clobetasol 17-propionate caused increased liver glycogen content, weight loss and melena. One dog had salivary gland inflammation. A dose of 60 mg/kg caused a local abscess at the injection site in one day. Histologically, there was lipid infiltration in the heart and liver, as well as thymus involution. One dog became moribund at the highest dose.

Subacute Toxicity:

In rats, daily subcutaneous injections of clobetasol 17-propionate were given for twelve weeks at doses from 1.44 mcg to 180 mcg/kg. Results showed growth reduction, increased hemoglobin concentration, leucopenia, SGOT elevation, reduction of thymus weight, reduced blood glucose and adrenal atrophy. The females had decreased uterine weight and bone marrow hypoplasia. Some animals had chronic respiratory disease and interstitial nephritis.

In dogs, daily intramuscular injections of 1.44, 7.2, 36.0 or 180 mcg/kg of clobetasol 17-propionate were given for thirteen weeks. One dog died after forty injections of the highest dose. In others there was reduced hemoglobin, leucopenia, increased serum protein, increased liver and kidney weights, adrenal atrophy and increased alkaline phosphatase.

Teratology:

Although studies in humans have not been done, studies in animals have shown that topical adrenocorticoids are systemically absorbed and may cause fetal abnormalities. For example, clobetasol propionate appears to be fairly well absorbed percutaneously, and when administered subcutaneously, it proved to be a relatively potent teratogen in both the rabbit and mouse.

Mice were treated with subcutaneous injections of 0.03, 0.1, 0.3 or 1.0 mg/kg of clobetasol 17-propionate from day seven to day sixteen of pregnancy. There was no maternal mortality. The number of live fetuses decreased and resorption sites increased at the highest dose. Cleft palate, skeletal immaturity and abnormalities occurred at doses from 0.1 to 1.0 mg/kg, the incidence being dose-related.

In rabbits, daily subcutaneous injections of clobetasol 17-propionate at doses of 1, 3 or 10 mcg/kg, from day six to day eighteen of pregnancy caused decreased weight gain of the mothers receiving the highest dose. A dose of 3 mcg/kg increased skeletal maturity and caused cleft palate. The highest dose caused a reduced number of live fetuses and of litter weight, as well as an increased incidence of cleft palate and skeletal abnormalities.

Local Irritancy:

A comparative skin irritation evaluation on rabbits was performed for MYLAN-CLOBETASOL SCALP APPLICATION 0.05% (Mylan) with Dermovate Scalp Application 0.05%

(Glaxo, Can.). Each test article was topically applied in 0.5 ml portions to a group of six rabbits by patch application to an abraded and intact surface of the skin. The samples remained covered and in contact with the skin for a period of 24 hours and then were removed by washing each site with 200 millilitres of tepid water. An evaluation of irritancy was conducted one hour following the 24 hour exposure. The Primary Irritation scores were determined at 1, 24 and 48 hours, and the results obtained were 0.03 ± 0.07 for MYLAN-CLOBETASOL SCALP APPLICATION 0.05% and 0.05% for Dermovate Scalp Application 0.05%. Therefore, both tested articles have essentially the same non-irritating potential to rabbit skin

BIBLIOGRAPHY

1. Adrenocorticoids (Topical). The United States Pharmacopoeia Dispensing Information. Tenth Edition 1990; 60-84.
2. Allenby, C.F. et al. Effect on adrenal function of topically applied clobetasol propionate (Dermovate). Brit Med *J* 1975; 619-621.
3. Bjornberg, A. and L. Hellgren. Treatment of psoriasis with clobetasol propionate: a double-blind comparison with betamethasone valerate. Curr Med Res Opin 1975;3:36-38.
4. Bachmann-Buffle, B. Allergy to clobetasol-17-propionate (Dermovate®) Dermatologica 1983; 167: 104.
5. Carruthers, J.A., August, P.J. and R.C.D. Staughton. Observations on the systemic effect of topical clobetasol propionate (Dermovate). Brit Med J 1975; 4:203-204.
6. Chalmers, R.J.G., Beck, M.H. and H.L. Muston. Simultaneous hypersensitivity to clobetasone butyrate and clobetasol propionate. Contact Dermatitis 1983; 9(4):317-318.
7. Clement, M. et al. The effect on epidermal DNA synthesis of a combination of topical steroid with either dithranol or tar as used for psoriasis. Brit *J* Derm 1983; 109:327-335.
8. Clobetasot Propionate. Martindale, the extra pharmacopoeia, 29th edition. James E.F. Reynolds (ed). London, The Pharmaceutical Press, 1989;885.
9. Comparative skin irritation study of alpha-clobetasol propionate scalp application 0.05 % (Genpharm) vs dermovate scalp application 0.05% (Glaxo Can.).
   Nucro Technics, Scarborough, Ontario. June 8, 1990.

10. Dooms-Goossens, A. et al. Allergic contact dermatitis to topical corticosteroids: clobetasol propionate and clobetason butyrate. Contact Dermatitis 1983: 9:470-478.
11. Du Vivier, A., Marshall, R.C. and L.G. Brookes. An animal model for evaluating the local and systemic effects of topically applied corticosteroids on epidermal DNA synthesis. Brit J Derm 1978; 98:209-215.
12. Gip, L. and A. Hamfelt. Studies on the efficacy and adrenal effects of Diprolene ointment 0.05% and Dermovate ointment 0.05% in patients with psoriasis or other resistant dermatoses. Cutis 1984; 33(2):215-224.
13. Gip, L. and A. Hamfelt. A double-blind clinical trial of diprolene ointment versus dermovate ointment for resistant psoriasis and atopic dermatoses. Curr Ther Res 1981 ;30:895-904.
14. Harst, L.C.A. v.d. et al. Comparison of two application schedules for clobetasol 17 propionate. Acta Dermatovener 1982;62(3):270-273.
15. Hillstrom, L., Pettersson, L. and L. Svensson. Comparison of betamethasone dipropionate lotion with salicylic acid (Diprosalic®) and clobetasol propionate lotion (Dermovate®) in the treatment of psoriasis of the scalp. Int Med Res 1982; 10:419-422.
16. Hindson, T.C., Hazell, M. and L. Wickramasinghe. Clobetasol propionate ointment as first-aid for burns. Lancet 1987; 1541: 1087-1088.
17. Hradil, E., Lindstrom, C. and H. Moller. Intermittent treatment of psoriasis with clobetasol propionate. Acta Dermatovener 1978;58:375-377.

18. Jacobson, C., Cornell, R.C. and R.C. Savin. A comparison of clobetasol propionate 0.05 % ointment and an optimized betamethasone dipropionate 0.05% ointment in the treatment of psoriasis. Cutis 1986; 37(3):213-220.
19. Jegasothy, B. et al. Clobetasol propionate vs fluocinonide creams in psoriasis and eczema. Int J Dermatol 1985;24(7):461-465.
20. Larko, 0., Swanbeck, G. and H. Svartholm. The effect on psoriasis of clobetasol propionate used alone or in combination with UVB. Acta Derm Venereol 1984;64:151-154.
21. Lassus, A. Local treatment of psoriasis of the scalp with clobetasol propionate in alcoholic solution: a comparison of once and twice a day application. Curr Med Res Opin 1976;4:214-217.
22. Miyachi, Y. Adrenal axis suppression caused by a small dose of a potent topical corticosteroid. Arch Dermatol 1982;
23. Oikarinen, A. et al. A local potent glucocorticosteroid decreases the induction of galactosylhydroxylysyl glucosyltransferase in suction blisters but has no effect on basement membrane structures. Brit J Derm 1983;108:171 178.
24. Ponee, M. et al. Effects of glucocorticosteroids on cultured human skin fibroblasts. Influence of anabolic steroids on the inhibitory effects of clobetasol-17-propionate on cell proliferation and collagen synthesis. Arch Dermatol Res 1979; 266:75-82.
25. Priestley, G.C. et al. Proliferative responses of fibroblasts from psoriatic and normal skin to clobetasol propionate. Acta Derm Venereol 1983; 63:393-396.

26. Product Monograph. Dermovate scalp application (clobetasol 17-propionate 0.05%) Liquid 60 ml bottles. Glaxo Canada Ltd. Toronto, Ontario. August 14, 1979.

27. Schwarz, K.J. et al. A double-blind comparison between a new trihalogenated dermatocorticosteroid (Halometasone) cream and clobetasol 17-propionate (Dermovate) cream. Br J Clin Pract 1982; 36(5):192-196.

28. 28 Serup, J. and P. Holm. Domoprednate (Stermonid®), a topical D-homocorticosteroid, skin atrophy and telangiectasia. A double-blind, randomized comparison with hydrocortisone butyrate, betamethasone valerate, clobetasole propionate and placebo. Dermatologica 1985; 170: 189- 194.

29. Sparkes, C.G. and L. Wilson. The clinical evaluation of a new topical corticosteroid, clobetasol propionate. An international controlled trial. Brit J Derm 1974; 90:197-203.

30. Spiro, J.G. and C.M. Lawrence. Contact sensitivity to clobetasol propionate. Contact Dermatitis 1986; 14(2):116 117.

31. Stahle, M. and 0. Hagermark. Effects of topically applied clobetasol-17-propionate on histamine release in human skin. Acta Derm Venereol 1984; 64:239-242.

32. Stankler, L. A double-blind comparison of quarter strength clobetasol propionate in unguentum merck with betamethasone valerate in psoriasis. Brit J. Clin Pract 1983; 389-391.

33. Staughton, R.C.D, and P.J. August. Cushing's syndrome and pituitary-adrenal suppression due to clobetasol propionate. Brit Med J 1975; 2:419-421.

34. Svartholm, H., Larsson, L. and B. Frederiksen. Intermittent topical treatment of psoriasis with clobetasol propionate (Dermovate). Curr Med Res Opin 1982; 8(3):154-157.
35. Van Ketel, W.G. and A.F. Swain. Allergy to clobetasol-17 propionate (dermovate). Contact Dermatitis 1981; 7(5):278 279.
36. Verdich, J. and T. Karlsmark. Betamethasone dipropionate cream for the treatment of psoriasis. A double-blind comparison with clobetasol propionate cream. Dermatologica 1985; 170: 152-155.
37. Walker, S.R. et al. The effect of plasma corticosteroid levels of the short term topical application of clobetasol propionate. Br J Derm 1974;91 :339-343.
38. Zheng, P. et al. Morphologic investigations on the rebound phenomenon after corticosteroid-induced atrophy in human skin. J Invest Derm 1984; 82:345-352.