REGISTERED PACKAGE INSERT

SCHEDULING STATUS S4

PROPRIETARY NAME AND DOSAGE FORM

ADVANTAN SCALP SOLUTION

Corticoid skin preparations

COMPOSITION

1 ml Advantan contains methylprednisolone aceponate (21-acetoxy-11β-hydroxy-6α-methyl-17-propionyloxy-1,4-pregnadiene-3,20-dione) 1 mg.

PHARMACOLOGICAL CLASSIFICATION

A. 13.4.1 Corticosteroids without anti-infective agents.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

After topical application, Advantan Scalp Solution suppresses inflammatory and allergic skin reactions as well as reactions associated with hyperproliferation, leading to regression of the objective symptoms (erythema, oedema, weeping) and the subjective complaints (itching, burning, pain).

The mechanism of action of methylprednisolone aceponate is not completely understood. It is known that methylprednisolone aceponate itself binds to the intracellular glucocorticoid receptor and this is especially true for the principal metabolite methylprednisolone-17-propionate, which is formed after cleavage in the skin.

The steroid receptor complex binds to certain regions of DNA, thereby triggering a series of biological effects.

The understanding of the mechanism of the anti-inflammatory action is more precise. Binding of the steroid receptor complex results in induction of macrocortin synthesis. Macrocortin inhibits the release of arachidonic acid and thus the formation of inflammatory mediators such as prostaglandins and leukotrienes.

The immunosuppresive action of glucocorticoids can be explained by inhibition of cytokine synthesis and an antimitotic effect, which so far is not well understood.

Inhibition of the synthesis of vasodilating prostaglandins or potentiation of the vasoconstrictive effect of adrenalin finally results in the vasoconstrictive activity of glucocorticosteroids.

Pharmacokinetic properties

Methylprednisolone aceponate becomes available in the skin after application of the Advantan formulations. The concentration in the stratum corneum and living skin decreases from the outside to the inside.

Methylprednisolone aceponate is hydrolised in the epidermis and dermis to the main metabolite 6α-methylprednisolone-17-propionate which binds more firmly to the corticoid receptor than the parent drug.

The rate and extent of percutaneous absorption of a topical corticosteroid depends on a series of factors: chemical structure of the compound, the composition of the vehicle, the concentration of the compound in the vehicle, the conditions of exposure (area dose, duration of exposure, open or occlusion) and the skin status (kind and severity of skin disease, anatomical site, etc).

The percutaneous absorption of methylprednisolone aceponate from Advantan Scalp Solution was investigated after single application to volunteers and after once daily application for 4 weeks in patients with psoriasis capitis. $\leq$ 5 ml of the solution were applied once or daily onto the hairy scalp. A percutaneous absorption of methylprednisolone aceponate through the skin of the hairy scalp could not be demonstrated using a radioimmunological method for determination of methylprednisolone aceponate in the plasma.

Taking into consideration the detection limit of the radioimmunological method the systemic corticosteroid load caused by percutaneous absorption through the scalp in both trials was assessed to be less than 4 ng and 7 ng methylprednisolone aceponate equivalent/kg body weight and day, respectively.

After reaching the systemic circulation, the primary hydrolysis product of methylprednisolone aceponate, 6α-methyl-17-propionate is quickly conjugated with glucuronic acid and as a result, inactivated.

The metabolites of methylprednisolone aceponate (main metabolite: 6α-methylprednisolone-17-propionate-21-glucuronide) are eliminated primarily via the kidneys with a half-life of about 16 hours. Following intravenous administration, excretion of the ^{14}C-labelled substances with the urine and faeces was complete within 7 days. No accumulation of substance or metabolites takes place in the body.

INDICATIONS

Treatment of inflammatory and pruritic dermatoses of the hairy scalp, e.g. endogenous eczema (atopic dermatitis, neurodermatitis), seborrhoeic eczema, contact eczema, nummular eczema, vulgar eczema.

CONTRA-INDICATIONS

Tuberculous or syphilitic processes in the area to be treated, chicken-pox, zoster and other viral infections, rosacea, perioral dermatitis and post-vaccination skin reactions.

Corticosteroids have been shown to be teratogenic in animals following dermal application. As these agents are absorbed percutaneously, teratogenicity following topical application cannot be excluded. Therefore Advantan should not be used during pregnancy.

DOSAGE AND DIRECTIONS FOR USE

For external use only.

Advantan Scalp Solution is to be applied dropwise once daily to the affected areas and rubbed in lightly.

In general, the duration of use should not exceed 4 weeks.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

Occasionally, the alcohol content of the Advantan Scalp Solution may lead to local skin irritations such as a mild transient burning sensation. Less frequently, itching, erythema, dry skin, scaling and folliculitis may arise.

Hypersensitivity reactions to the components may occur.

Long-term continuous treatment with topical corticosteroids should be avoided as far as possible as this may cause atrophic changes in the skin leading to thinning, loss of elasticity, dilatation of superficial blood vessels, telangiectasiae and ecchymoses. These changes are particularly likely to occur on the face and when occlusive dressings are used.

Systemic absorption of topically applied corticosteroids may occur, particularly under the following conditions: when large quantities are used, or when application is made to wide areas of the body, or to damaged skin, when potent topical corticosteroids are used, and when the occlusive dressing technique is applied. Depression of the hypothalamic-pituitary-adrenal axis with consequent suppression of the adrenal gland may occur. These effects are most likely to be severe in children. Growth may be retarded and a Cushingoid state may be produced. Benign increased intracranial pressure has been rarely reported.

Additional, specific therapy is required in bacterially infected skin diseases and/or in fungus infections.

To date, no clinical data are available for the use of Advantan Scalp Solution in children.

Care must be taken when using Advantan Scalp Solution to avoid contact with the eyes.

The clinical indication for treatment with Advantan Scalp Solution must be very carefully reviewed and the benefits weighed against the risks in lactating women.

Topical corticosteroids should be used with particular caution in facial dermatoses, and only for short periods. A steroid rosacea-like facies may be produced.

Regular review should be made of the necessity for continuing therapy.

This corticosteroid preparation should not be used in the nappy areas in infants for flexural eruptions, and ideally it should not be applied to infants and young children.

The treatment of psoriasis with potent topical corticosteroids may provoke the pustular form of the disease.

Advantan should not be applied to skin crease areas.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Please refer to the paragraph "Side-effects and special precautions". If any symptoms of overdosage occur, treatment must be discontinued.

IDENTIFICATION

Clear, colourless, non-aqueous solution.

PRESENTATION

Polyethylene dropper bottles of 20 or 50 ml.

STORAGE INSTRUCTIONS

Store below 30°C. Keep well closed. Keep out of reach of children.

REGISTRATION NUMBER

32/13.4.1/0361

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DATE OF PUBLICATION OF THE PACKAGE INSERT

26 September 2001