1 NERISONE®
NERISONE® Diflucortolone valerate 0.1 % fatty ointment
NERISONE® Diflucortolone valerate 0.1 % cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
NERISONE® Cream:
1 g white cream contains 1 mg (0.1 %) diflucortolone valerate. The cream is an oil-in-water emulsion containing approximately 70% water.

NERISONE® Fatty Ointment:
1 g white single-phase fatty ointment contains 1 mg (0.1 %) diflucortolone valerate.
NERISONE® Fatty Ointment contains methyl parahydroxybenzoate and propyl parahydroxybenzoate. For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Topical cream
Topical fatty ointment

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
All skin diseases which respond to topical corticoid therapy (e.g.): contact dermatitis, contact eczema, occupational eczema vulgar, nummular, degenerative and seborrhoeic eczema, dyshidrotic eczema, eczema in varicose syndrome (but not directly onto lower limb ulcers), anal eczema, eczema in children, neurodermatitis (endogenous eczema, atopic dermatitis), psoriasis, lichen ruber planus et verrucosus, lupus erythematosus discoides, first degree burns, sunburn, insect bites.

4.2 Dose and method of administration
At the beginning of treatment, the NERISONE® preparation best suited to the skin condition is applied thinly two or perhaps three times per day. Once the clinical picture has improved, one application per day usually suffices.

NERISONE® is available as a cream and a fatty ointment. Which form should be used in the individual case will depend on the appearance of the skin: NERISONE® CREAM in weeping skin conditions and NERISONE® FATTY OINTMENT in very dry skin conditions.

NERISONE® CREAM has a high water and low fat content. In weeping skin diseases it allows secretions to drain away, thus providing for rapid subsidence and drying up of the skin. It is also suitable for application to moist, exposed and hairy areas of the body.

If the skin dries out too much under protracted use of NERISONE® CREAM, the patient should be switched to a form which contains more fat (NERISONE® FATTY OINTMENT).
NERISONE® FATTY OINTMENT is for very dry conditions and chronic stages demand an anhydrous fatty base. The occlusive effect of the NERISONE® FATTY OINTMENT base promotes the healing process.

Occlusive dressings
An occlusive dressing may be called for in unusually refractory cases. When it is, it should be managed as follows: After application of the appropriate NERISONE® preparation, the area under treatment should be covered with a plastic foil which should then be fixed firmly on all edges to healthy skin by means of adhesive plaster. Plastic gloves can be used to occlude the hands. The dressing should be kept in place for as long as can be expected of the patient, but generally not for longer than 24 hours. If the occlusive treatment is expected to be prolonged, it is advisable to change the dressing every 12 hours. If an infection develops under the dressing, occlusive treatment must be terminated.

Paediatric population
Babies and children up to the age of 4 years should not be treated with NERISONE® for longer than 3 weeks, particularly on skin areas covered by nappies.

4.3 Contraindications
Tuberculous or syphilitic processes in the area to be treated; virus diseases (e.g. vaccinia, varicella, herpes zoster); rosacea; perioral dermatitis; and post-vaccination skin reactions in the area to be treated; hypersensitivity to the active substances or to any of the excipients listed in Section 6.1.

4.4 Special warnings and precautions for use
Additional specific therapy is required for bacterially infected skin diseases and/or for fungal infections.

NERISONE® should not be allowed to come into contact with the eyes when being applied to the face.

Extensive application of topical corticosteroids to large areas of the body, for prolonged periods of time, under occlusion, or around the eyes can significantly increase the risk of side effects (see ‘Undesirable Effects’) and may lead to the development of glaucoma.

4.5 Interaction with other medicines and other forms of interaction
None so far known.

4.6 Fertility, pregnancy and lactation
As a general rule, topical preparations containing corticoids should not be applied during the first trimester of pregnancy. In particular, application to large areas of the body or for prolonged periods must be avoided.

4.7 Effects on ability to drive and use machines
Not known.

4.8 Undesirable effects
Local symptoms such as itching, burning, erythema or vesiculation may occur in isolated cases under treatment with NERISONE®.
The following reactions may occur when NERISONE® is applied to large areas of the body (about 10% and more) and/or for long periods of time (more than 4 weeks), particularly when the fatty ointment or an occlusive dressing is used: local concomitant symptoms such as atrophy of the skin, telangiectasia, striae, acneform changes of the skin, and systemic effects of the corticoid due to absorption. In rare cases allergic skin reactions, perioral dermatitis, skin discolouration, increased growth of body hair (hypertrichosis) or folliculitis may occur.

Side effects cannot be excluded in neonates whose mothers have been treated extensively or for a prolonged period of time during pregnancy or while lactating (for example, reduced adrenocortical function, when applied during the last weeks of pregnancy).

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions [https://nzphvc.otago.ac.nz/reporting/](https://nzphvc.otago.ac.nz/reporting/).

4.9 Overdose

On the basis of results from acute toxicity studies with both diflucortolone valerate and the NERISONE® preparations no acute risk of intoxication is to be expected either after a single dermal application of an overdose (application over a large area under conditions favouring resorption) or even after inadvertent oral intake of a whole package.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

NERISONE® suppresses inflammation in inflammatory and allergic skin conditions and alleviates subjective complaints such as itching, burning and pain.

Capillary dilatation, intercellular oedema and tissue infiltration regress; capillary proliferation is suppressed. This leads to fading of inflamed skin surfaces.

5.2 Pharmacokinetic properties

The NERISONE® product line contains as its active ingredient diflucortolone valerate, the 21-monoester of diflucortolone with valeric acid, in a concentration of 0.1%.

So that the NERISONE® formulations are able to exert their therapeutic antiproliferative and anti-inflammatory effects in the skin, it is necessary for diflucortolone valerate to diffuse from the respective formulations into the living epidermis or upper corium. In-vitro penetration studies have shown that diflucortolone valerate quickly penetrates human skin from all galenic formulations.

The following highest substance levels were found in the horny layer 4 hours after application: approx. 300 µg/ml (around 600 µmol/ml) after treatment with fatty ointment and approx. 500 µg/ml (around 1000 µmol/ml) after application of the cream. The corticoid concentration falls in the horny layer from distally to proximally by around 1.5-2 powers of 10. After application to damaged skin - as the model for diseased skin - the local corticoid concentrations in the living skin were far higher at all time points studied than after application to intact skin.
Diflucortolone valerate is partially hydrolysed to diflucortolone while still in the skin. Diflucortolone binds even stronger to the corticoid receptor than the parent drug. Some of the corticosteroid applied to the skin is absorbed percutaneously and distributed in the organism; it then undergoes further metabolic breakdown before being eliminated.

The degree of percutaneous absorption and the resulting systemic load depend on a number of factors such as the nature of the vehicle, the exposure conditions (skin area dose, size of the treated area, duration of treatment), the nature of the treatment (open/occlusive), the condition of the skin barrier and the area of the body to be treated.

After simultaneous dermal application of the radioactively labelled cream, and fatty ointment to different fields of skin on the backs of six volunteers with healthy skin, the amounts of the applied dose absorbed within a mean period of exposure of 4 hours were approx. 0.2 % via intact skin and approx. 0.4 % via "stripped" skin. Extrapolated to a whole day, this results in a mean percutaneous absorption of approx. 1.2 % in the case of an intact penetration barrier and of approx. 2.4 % in the case of a removed barrier.

Following absorption, diflucortolone valerate is hydrolysed extremely quickly to diflucortolone and the corresponding fatty acid. In addition to diflucortolone, 11-keto-diflucortolone and two other metabolites were recovered in plasma. Diflucortolone is eliminated from plasma with a half-life of around 4-5 hours, all metabolites with a half-life of around 9 hours (half-lives were determined after i.v. administration), and excreted with urine and faeces in the proportion 75 : 25.

5.3 Preclinical safety data
In systemic tolerance studies following repeated dermal and subcutaneous administration the effect of diflucortolone valerate was that of a typical glucocorticoid. It can be derived from these results that no side effects further to those which are typical of glucocorticoids are to be expected following therapeutic use of NERISONE® preparations under extreme conditions such as application over large areas and/or occlusion.

Specific embryotoxicity studies with diflucortolone valerate following subcutaneous and dermal administration led to results typical of glucocorticoids, i.e. following sufficiently high exposure embryolethal and/or teratogenic effects could be induced given the appropriate test systems. Since epidemiological studies have as yet given no indications of embryotoxic effects due to systemic glucocorticoid therapy, no embryotoxic effects are to be expected following the therapeutic use of NERISONE® preparations. However, taking animal-experimental results into consideration, particular care should be taken when prescribing NERISONE®.

In vitro investigations for detection of gene mutations in bacteria and mammalian cells as well as in vitro and in vivo examinations for detection of chromosome and gene mutations have not given any indications of a mutagenic potential of diflucortolone valerate.

Specific tumorigenicity studies have not been carried out with diflucortolone valerate. On the basis of the pharmacodynamic action pattern, the lack of evidence of a genotoxic potential, the structural properties and the results of chronic toxicity tests (no indication of proliferative changes), there is no suspicion of a tumorigenic potential of diflucortolone valerate. Since systemically effective immunosuppressive dosages will not be reached after dermal application of NERISONE® if used as directed, no influence on the occurrence of tumours is to be expected.
According to the results from local tolerance studies following repeated dermal administration, no dermal changes further to the side-effects already known for topical preparations containing glucocorticoids are to be expected from therapy with NERISONE®.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cream: White soft paraffin, liquid paraffin, stearyl-alcohol, polyoxyl 40 stearate, polyacrylic acid, sodium hydroxide, disodium edetate dihydrate, methyl parahydroxybenzoate, propyl parahydroxybenzoate, purified water.

Fatty Ointment: White soft paraffin, liquid paraffin, microcrystalline wax, hydrogenated castor oil.

6.2 Incompatibilities

No incompatibilities have been reported.

6.3 Shelf life

NERISONE® Cream - 3 years. NERISONE® Fatty Ointment - 5 years.

NERISONE® cream should be used within 3 months of opening.

6.4 Special precautions for storage

NERISONE® Cream: Store below 25 °C.

NERISONE® Fatty Ointment: Store below 25 °C

Store all drugs properly and keep them out of reach of children.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Tubes made of pure aluminium, interior wall coated with epoxy resin, and with a polyester-based external coating. Fold seal ring is made of polyamide-based heat-sealable material. The screw cap is made of high density polyethylene.

6.6 Special precautions for disposal <and other handling>

None

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

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Auckland
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Toll Free No.: 0800 497 456

9 DATE OF FIRST APPROVAL

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10 DATE OF REVISION OF THE TEXT
December 2019

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