# Prescribing Information

# Ultralan
## Cream, Ointment

1. **NAME OF THE MEDICINAL PRODUCT**

U L T R A L A N

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Ointment: 1 g contains 2.5 mg (0.25%) fluocortolone and 2.5% (0.25%) fluocortolone caproate.

Cream: 1 g contains 2.5 mg (0.25%) fluocortolone pivalate and 2.5 mg (0.25%) fluocortolone caproate.

**3. PHARMACEUTICAL** FORM

Ointment
Cream

**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 seborrheic eczema
- dishidrotic 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 Dosage and method of administration**

At the commencement of treatment, the Ultralan preparation best suited to the skin condition is applied thinly twice or, in more severly affectd skin areas, three times per day. Once the clinical picture has improvedone application per day usually suffices.

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

Ultralan Ointment

Skin conditions which are neither weeping nor very dry require a base with balanced proportions of fat and water. Ultralan Ointment makes the skin slightly greasy without retaining heat or fluid. Of the four different forms of Ultralan, the ointment has the widest range of use.

Ultralan Cream

Ultralan 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. Ultralan Cream is also suitable for application to moist, exposed and hairy areas of the body.

Occlusive dressings

In refractory cases an occlusive dressing may improve the efficacy of Ultralan and should be managed as follows: After application of the appropriate Ultralan preparation, the area under treatment should be covered with a plastic foil which should then be fixed firmly all round 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 interrupted and a specific therapy instituted. (See also SPECIAL WARNINGS below).

**4.3 Contra-indications**

Not suitable for the treatment of ophthalmic conditions.

Tuberculous or syphilitic processes in the area to be treated; virus diseases (e.g. vaccinia, chickenpox, shingles). Acne vulgaris, undiagnosed perianal and genital pruritus, napkin eruptions, primary bacterial or fungal infections of the skin.

Secondary infections in the absence of appropriate anti-infective therapy.

**4.4 Special warnings and special precautions for use**

As with all topical steroids, there is a risk of skin atrophy following extensive therapy.

Long-term continuous therapy should be avoided irrespective of age. Occlusion should be restricted to dermatoses involving limited areas. Adrenal suppresion can occur even without occlusion.

If the skin dries out too much under protracted use of Ultralan Cream, the patient should be switched to a form which contains more fat (Ultralan Ointment).

Ultralan should not be allowed to come into contact with the eyes being applied to the face. If rosacea or perioral dermatitis is present, Ultralan must not be applied to the face.

Topical corticosteroids may be hazardous in psoriasis for a number of reasons including rebound relapses following development of tolerance, risk of generalised pustular psoriasis, and local and systemic toxicity due to impaired barrier function of the skin. Steroids may have a place in psoriasis of the scalp and chronic plaque psoriasis of the hands and feet. Careful patient supervision is important in psoriasis.

**4.5 Interaction with other medicaments and other forms of interaction**

None so far known.

**4.6 Pregnancy and lactation**

Topical administration of corticosteriods to pregnant animals can cause abnormalities of foetal development, including cleft palate and intra-uterine growth retardation.

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 applicable.

**4.8 Undesirable effects**

The following reactions may occur when Ultralan 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 occlusive dressings are used: local concomitant symptoms such as atrophy of the skin, telangiectasia, striae, acneform changes of the skin, perioral dermatitis, increased growth of body hair (hypertrichosis) and systematic effects of the corticoid due to absorption. In rare cases allergic skin reactions 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).

**4.9 Overdose**

None stated.

**5. PHARMACOLOGICAL PROPERTIES**

## 5.1 Pharmacodynamic properties

Ultralan suppresses inflammation in inflammatory and allergic skin conditions and alleviates subjective complains such as itching, burning and pain. Owing to the different speeds with which the two forms of its corticoid component take effect, Ultralan is both fast-acting and long-lasting in its effectiveness.

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

## 5.2 Pharmacokinetic properties

A combination of two corticosteroids (steroid alcohol with ester or two different esters of the same steroid) in a dermatological preparation is pharmacokinetically meaningful, since a higher concentration of corticosteroids can be achieved and maintained over a longer period of time in the skin after application of a combination as compared with a single compound. Due to a different lipophilicity two compounds distribute in a different way into the horny layer and diffuse at different rates through the skin, leading to a rapid onset of action but also to a protracted activity.

Investigation on the time course of the vasoconstriction in volunteers as well as investigations on the percutaneous absorption indicate that fluocortolone and fluocortolone pivalate penetrate more rapidly into and through human skin than fluocortolone caproate, giving evidence that the above mentioned principles have been realized with the Ultralan dermatological preparations.

Measurement of the drug recovery on the skin surface at the end of the exposure time in healthy skin volunteers as well as in eczema and psoriasis patients overestimate the extent of the percutaneous absorption and are therefore only of limited value for an assessment of the systemic drug load and for risk assessment. Pharmacodynamic investigations of the effect on the pituitary adrenal axis show only a small risk of systematic effects if not large areas of the body are treated over a long time.

Fluocortolone-21-monoesters are hydrolized like a series of other 21-esters of corticosteroids most probably already in the skin, at the latest immediately after percutaneous absorption, into fluocortolone and the corresponding fatty acid. Fluocortolone itself possesses the shortest plasma half-life of all synthetic corticosteroids (approx. 75 - 90 minutes determined after i.v. administration) comparable to that of the endogenous cortisol.

Fluocortolone is inactivated in the human organism via a series of reduction, oxidation and conjugation reactions with glucoronic and sulfuric acid and is excreted as metabolites mainly with the urine.

## 5.3 Preclinical safety data

In systemic tolerance studies following repeated oral and parenteral administration the effect of fluocortolone , fluocortolone caproate and fluocortolone pivalate was that of a typical

glucocorticoid. It can be derived from these results that no systematic side effects further to those which are typical of glucocorticoids are to be expected following therapeutic use of the Ultralan preparations even under extreme conditions such as application over large areas and\or occlusion.

Specific embryotoxicity studies with the active substances contained in Ultralan preparations 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 Ultralan preparations. However, taking animal-experimental results into consideration particular care should be taken when deciding to use Ultralan.

Investigation of floucortolone in a bacterial test system for the detection of pointmutagenic effects gave no indications of a genotoxic potential. Since no relevant indications of genotoxic effects have been found for any of the glucocorticoids, such effects are not to be expected from the active substances in Ultralan.

Specific tumorigenicity studies have not been carried out with the active substances contained in Ultralan. On the basis of knowledge concerning the structures, the pharmacological action pattern and the results of systemic tolerance studies with chronic administration, there is no suspicion of a tumorigenic potential. Since systematically effective immunosuppressive dosages will not be reached after dermal application of Ultralan if used as directed, no influence on the occurrence of tumors is to be expected.

Following repeated dermal administration of fluocortolone and the two esters in different combinations and preparations, no substance-related dermal changes were observed.

## 6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ointment

Amphocerin KS
White soft paraffin
Heavy liquid paraffin
lanolin
White wax
Dehymulus E (mixture of dioctadecyl citrate, pentaerythritol dicoco esters, beeswax, aluminium stearate)
Perfume oil citrus rose
Purified water

Cream

White soft paraffin
Heavy liquid paraffin
Stearyl alcohol
Polyoxyl 40 stearate

Polyacrylic acid
Disodium edetate
Perfume oil citrus rose
Sodium hydroxide
Methyl and propyl parahydroxybenzoate
Purified water.

6.2 Incompatibilities
None so far known.

6.3 Shelf life

Cream

5 years.

Ointment

2 years

6.4 Special precautions for storage

Cream
Store below 30° C.

Ointment

Store below 25° C.

6.5 Nature and contents of container

Cream
Standard tubes with 5, 10, 15, 20, 30, 50, 100 and 200 g with membrane closure and screw cap (tube material aluminium, internal coating done with epoxide, end seal band made of polyamide-based compound, external coating made of polyester, screw cap made of high-density polyethylene).
Thread jar with 300 g made of opal glass and a sealing disk of polyethylene, screw cap made of polystyrene.

6.6 Instructions for use \ handling

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

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