Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Sterax Cutaneous Emulsion 0.05% w/w

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Desonide 0.05% w/w.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Cutaneous emulsion
White to off-white soft, smooth emulsion.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the cutaneous treatment of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses suc as psoriasis, eczema, and other mainly inflammatory dermatoses.

4.2 Posology and method of administration

For external use only.

Tip the bottle gently to place a quantity of cutaneous emulsion on the fingertips sufficient to cover the area to be treated. Wash hands thoroughly and replace the cap tightly after use.

Adults, children and the elderly:
To be applied once or twice a day depending on the severity of the condition.

4.3 Contraindications

Hypersensitivity to any of the components of the formulation.

Ulcerated lesions.

Acne and rosacea.

Conditions for which cutaneous corticosteroid therapy is contra-indicated, notably skin infections of bacterial, viral, fun and parasitic origin, even when these include an inflammatory response.

4.4 Special warnings and precautions for use

Several preclinical studies were performed to establish the safety of cutaneous application of desonide. From these studies and based on the general knowledge of the adverse reactions associated with the use of topical corticosteroids, particularly their potential systemic action on the hormonal system, it is recommended that the application of Sterax on large areas or under occlusive dressings should be limited.

In paediatric use, patients may demonstrate greater susceptibility to topical-induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio, thus in infants and young children the duration of a daily treatment regimen should be short and limited to the least amount compatible with an effective therapeutic regimen. Particular attention must be given to the likelihood of spontaneous occlusion.

If any local irritation or toxicity, including atrophy, of the skin occurs with desonide, it is normally reversible, and its intensity is dependent on the dose applied and frequency of use. Treatment must be interrupted and the cause investigated.

Whilst it is expected that only minimal effects will be observed when treating areas adjacent to the epithelial mucosa, including the eye, these effects are readily reversed by washing.

The use of Sterax during the first trimester of pregnancy and during breast-feeding should be avoided unless the benefit outweighs any potential risks (see also section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

None known. However, to avoid the potential for increased frequency and severity of side-effects, other corticosteroids or drugs with a similar mode of action should not be used concurrently with desonide.

The main pillars of medical treatment of eczematous alterations are the application of cutaneous preparations containing corticosteroids and intermittent treatment consisting of the application of suitable oil-in-water, water-in-oil or fatty preparations for the care of dry skin. To combat itching, antihistamines may be given and antibiotics may be used systemically to treat infectious forms. Other adjuvant treatment possibilities include climatotherapy, UV radiation or treatment with tar preparations.

Following topical application of a corticosteroid such as desonide to most areas of normal skin, only minimal amounts of the drug reach the dermis and subsequently the systemic circulation; therefore interaction with systemic medications is unlikely.

4.6 Pregnancy and lactation

Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after cutaneous application in laboratory animals.

There are no adequate and well controlled studies to date in pregnant women concerning the teratogenic affects from cutaneously applied corticosteroids. Therefore, cutaneous corticosteroids should be avoided during pregnancy and only used if the potential benefit justifies the perceived risk to the foetus.

Corticosteroids such as desonide should not be used extensively on pregnant patients, in large amounts, on large surface areas or for prolonged periods of time.

It is not known whether topical corticosteroids affect fertility. It is not known whether topical corticosteroids are distributed into milk. Systemic corticosteroids are however distributed into milk. Topical corticosteroids should therefore be used with caution in nursing women.

4.7 Effects on ability to drive and use machines

Based upon the pharmacodynamic profile and clinical experience, performance related to driving and using machines should not be affected.

4.8 Undesirable effects

Side effects have been extremely rare and consist mainly of local burning, irritation and itching. When this occurs, the possibility of sensitisation must be kept in mind. Because skin atrophy, striae, hypertrichosis and adrenal suppression have been shown to occur with prolonged and indiscriminate use of cutaneous corticosteroids, similar phenomena could conceivably occur with prolonged and excessive use of Sterax ointment.

It should be remembered that adrenal suppression is less important with non-halogenated corticosteroids such as desonide than it is for the corresponding fluorinated compounds. The systemic safety of Sterax was investigated in a study on paediatric patients where no influence on desonide plasma levels was observed with or without ACTH stimulation after 28 days of treatment.

4.9 Overdose

Sterax is for cutaneous use only. If the medication is applied excessively, no more rapid or better results will be obtained and the undesirable effects described above may be increased and intensified.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The well known pharmacodynamic properties of the corticosteroids are vasoconstrictor, anti-inflammatory, anti-proliferative and immuno-suppressive effects.

The vasoconstrictor effects of corticosteroids on the small capillary blood vessels of the skin lessens the erythema of treated lesions. This effect correlates well with the clinical potency of a corticosteroid and is frequently used to assay the clinical activity of corticosteroid compounds. The exact mechanism of blanching as produced by corticosteroids is not yet fully understood. Based on the vasoconstrictor assay, desonide is classified as a mid-potent (group III) corticosteroid by the European classification, and is classified as a mild (group VI) corticosteroid by the American classification.

Corticosteroids interfere with the synthesis of prostaglandins and leukotrienes by inhibiting phospholipase A2 activity. This enzyme releases arachidonic acid from the phospholipids of cellular membranes, and is thus directly involved in inflammation. The anti-inflammatory effects of corticosteroids are additionally due to their ability to reduce the number of polymorphonuclear leucocytes and monocytes and to interfere with their function at the site of inflammation. The corticosteroids stop the release of histamine, and the ability of the target cell to be stimulated by histamine. Desonide is very active on non-immune inflammation induced by cantharidine; also on non-immune and delayed-hypersensitivity reactions induced by picryl chloride on mouse ear.

The anti-proliferative effects of topical corticosteroids include reduction in the number of mitoses in the basal cell layer of the epidermis, as well as a reduction in fibroblastic activity of the dermis caused by retardation of DNA synthesis. This inhibition of epidermal and dermal growth is responsible for the most common cutaneous adverse effect of all topical corticosteroids, namely local atrophy at the application sites.

Most of the immuno-suppressive effects of corticosteroids are seen with their systemic use rather that their topical use. Corticosteroids primarily suppress cell mediated immunity, but they also exhibit some effects on humoral immunity by interfering with passage of immune complexes through cells. The use of topical steroids is associated with Langerhans cell-associated inhibition of T-cell activation.

5.2 Pharmacokinetic properties

Percutaneous absorption of topical drugs, particularly topical corticosteroids, has been investigated for about twenty years.

In summary, the percutaneous absorption of topical corticosteroids is generally low and depends on the following

factors: amounts and concentrations applied, pharmacological activity of the drug or vehicle components in the skin, skin occlusion, vehicle, loss of barrier function in the case of cutaneous disease status or environmental factors, age of the patient, number of applications per day, and anatomical site of application.

5.3 Preclinical safety data

Acute animal toxicity / safety studies have been performed with desonide in rats. At the higher dose tested (20 ml/kg), no pharmacotoxicity or gross pharmaceutical lesions were observed. The oral LD50 in rats was greater than 20 ml/kg. Based on this result, desonide is practically non-toxic by the oral route of administration.

The acute irritant potential of desonide has been determined in rabbits. At a treatment dose of 2 mg/kg desonide, in either abraded or normal skin, or in the presence or absence of occlusion, no pharmacotoxic signs were induced in any animals which had a minor dermal irritation. Subacute cutaneous route toxicity of desonide was investigated in rabbits in two preclinical studies for respectively 3 and 32 consecutive days. Only a minimal dermal irritation potential for rabbit skin, even under the exaggerated test conditions was observed in the 3 day irritation test.

When the application was performed for 32 days, minimal to moderate erythema and minimal oedema were observed, indicating a good tolerance of the animals to the desonide. Systemic effects determined during the 32 day toxicity study (i.e. depressed growth curves, significant changes in clinical chemistries and organ weights) were attributable to the exaggerated cutaneous treatment (2 g/kg) applied. Furthermore, these conditions which produced only minimal toxic effects in rabbits are not common for corticosteroids administered by the cutaneous route.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tetrasodium edetate tetrahydrate
Sodium laurilsulfate
Mineral oil 15 - 25 mPa.s
Self-emulsifying glyceryl monostearate
Sorbitan monostearate
Cetyl alcohol
Stearyl alcohol
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Propylene glycol
Sodium hydroxide (10% solution)
and/or Citric acid anhydrous (25% solution)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Store below 25^{o}C.

6.5 Nature and contents of container

HDPE bottles with polypropylene caps containing 10, 30, 60 or 100 ml of lotion.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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