LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Miniderm
glycerol

SE/H/572/01/MR

This module reflects the scientific discussion for the approval of Miniderm. The procedure was finalised at 2006-04-11. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

ACO Hud AB has applied for marketing authorisation for Miniderm 20% cream. The active substance is glycerol, an osmotic dehydrating agent with moisturising properties, often included in topical preparations, both medicinal products and cosmetics. The product is indicated for the treatment of dry skin, and can be used both in adults and children.

II. QUALITY ASPECTS

II.1 Introduction

Miniderm is presented in the form of a cream containing 20 % glycerol. The excipients are white petrolatum, hydrogenated canola oil, light liquid paraffin, glycerol monostearate, macrogol stearate, cetostearyl alcohol, hard paraffin, dimeticone, cholesterol, propyl parahydroxybenzoate, methyl parahydroxybenzoate and purified water. The cream is filled in plastic tubes with 100 g cream or plastic jars with 500 mg cream.

II.2 Drug Substance

Glycerol has a monograph in the Ph Eur.

Glycerol is a clear, colourless, hygroscopic syrupy liquid which is miscible with water and alcohol, slightly soluble in acetone and practically insoluble in chloroform, ether and in fatty and essential oils. The structure of glycerol has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on chirality is presented. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The active substance specification includes relevant tests and the limits for impurities/degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Miniderm cream is formulated using excipients described in the current Ph Eur, except for hydrogenated canola oil and the mixture of glyceryl stearate and macrogol stearate which are controlled according to acceptable in house specifications. White petrolatum is currently controlled according to USP but the manufacturer has committed to apply for a type IB variation to comply with white soft paraffin in Ph Eur. All raw materials used in the product are of vegetable origin.

The product development has taken into consideration the physico-chemical characteristics of the active substance. The pH of the product and the conservative system has been especially described.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, when stored below 25°C.

III. NON-CLINICAL ASPECTS

The pharmacodynamics, pharmacokinetics and toxicology of glycerol are considered well known. Glycerol is present in a large number of medicinal products, both for topical administration and administration via other routes.

Two excipients of Miniderm are not described in pharmacopoeias, glyceryl and macrogol stearate (trade name: Arlacel 165) and hydrogenated canola oil (trade name: Akorex L). Both excipients are well known ingredients in other ACO products on the Swedish market, and have not given cause for any safety concerns.

IV. CLINICAL ASPECTS

The submitted bibliography indicates some efficacy of glycerol for the hydration of the skin. Best effect has been demonstrated for higher concentrations >25 %. However, there seem to be some effects also from lower concentrations of 10-20 % of glycerol.

One study has been submitted including 197 patients with atopic dermatitis and out of these 195 completed the study. The study was randomised, double-blind with three parallel arms, multicenter and involved five Swedish centres. Miniderm 20 % glycerol was compared with its vehicle and the active comparator Fenuril, a cream with 4 % urea and 4 % sodium chloride and previously approved for the treatment of dry skin. According to the results the applied product appears to have the same effect upon skin dryness when assessed by patients and investigators compared with a previously approved moisturizer, Fenuril. However, a higher dryness severity score of a selected dry skin area and a lower skin hydration by the use of technical measures (TEWL) was also seen by the use of Miniderm compared with Fenuril. There was no significant difference upon skin dryness of Miniderm measured as VAS, DASI or by technical measures compared with the vehicle but the degree of improvement when evaluated by the patient was reported to be higher for Miniderm. A significantly less smarting sensation for the applied product compared to the active comparator Fenuril, was demonstrated. There was no difference in smarting potential between Miniderm and its vehicle.

In summary: A reduced efficacy is demonstrated for some of the secondary end-points compared with Fenuril. On the other hand a better tolerance measured as smarting sensation and comparative efficacy for other secondary efficacy endpoints have been demonstrated. It should also be noted that no great advantages of either efficacy or tolerance was demonstrated in the submitted study report for the applied product when compared with the vehicle alone. However, an additional beneficial effect of the active ingredient glycerol for the treatment of dry skin is to some extent supported by the findings reported in the bibliography.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User consultation of the package leaflet has not been performed. The applicant has made a commitment to perform user testing during 2006.

The risk/benefit ratio is considered positive and Miniderm 20% cream is recommended for approval.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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