LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Karbolan
(urea)

Asp no: 2020-0285

This module reflects the scientific discussion for the approval of Karbolan. The procedure was finalised on 2021-04-29. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Karbolan, 50 mg/g, cream, is a hybrid application made according to Article 10(3) of Directive 2001/83/EC. The applicant, Evolan Pharma AB, applies through the Swedish National Procedure.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Canoderm, 5%, cream, authorised in Sweden since 1997, with ACO Hud Nordic AB as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

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

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

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 have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of urea are well known. As urea is a widely used, well-known active substance, no further studies are required, and the applicant provides none. The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate and is considered sufficient to support the application.

Environmental Risk Assessment (ERA)
A justification for not performing an ERA has been submitted. Overall, urea is a biomolecule present in most if not all species and is a natural part of the environment. Based on the common presence in the environment, the product is unlikely to alter the concentration or distribution of urea in the environment.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

No pharmacokinetic studies have been performed for this product. Karbolan is a product for topical application. For locally applied products, bioequivalence is generally not a suitable way to show therapeutic equivalence since plasma levels are not relevant for local efficacy, although they may play a role regarding safety. Since the pharmaceutical composition is assessed as essentially similar to the reference product and due to the low systemic exposure to urea, the absence of pharmacokinetic studies is acceptable.

IV.2 Discussion on the clinical aspects

The efficacy and safety of urea in the treatment of dry skin of different origin is considered well known. No formal clinical efficacy and safety study with Karbolan 5% cream has been performed. Studies demonstrating beneficial efficacy of the reference product Canoderm® cream on the recurrence of atopic eczema are briefly described in the Clinical Overview.

The product can be approved from a clinical perspective based on pharmaceutical similarity to the reference product Canoderm® 5% cream. A similar clinical efficacy and safety profile of Karbolan 5% cream and Canoderm® is anticipated.

IV.3 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent, or minimise risks relating to Karbolan.

Routine pharmacovigilance is suggested, and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP
The submitted Risk Management Plan, version 1.0 signed 2017-09-20 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the MPA;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Canoderm 5% cream, non-variation procedure SE/H/556/01/P/01, following the mutual recognition procedure SE/H/556/01/MR with regards to the content and Natriumklorid Evolan 500 mg capsules, national procedure, Dnr 5.4.1-2014-5246 with regards to layout. The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the hybrid product, Karbolan, is found adequate. There are no objections to approval of Karbolan, from a non-clinical and clinical point of view. The product information is acceptable. The benefit/risk ratio is considered positive and Karbolan, 50 mg/g, cream, is recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

Karbolan, 50 mg/g, cream, was approved in the national procedure on 2021-04-29.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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