LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Karbamid Evolan
(urea)

SE/H/1954/01/MR

This module reflects the scientific discussion for the approval of Karbamid Evolan. The procedure was finalised on 2018-10-09. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Evolan Pharma AB has applied for a marketing authorisation for Karbamid Evolan 50mg/g cream. Karbamid Evolan is moisturizing creams that contain urea as active substance.

For approved indications, see the Summary of Product Characteristics.

The marketing authorisation has been granted pursuant to Article 10(3) of Directive 2001/83/EC.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83 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

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. Overview based on literature review is, thus, appropriate.

III.1 Ecotoxicity/environmental risk assessment

Since Karbamid Evolan is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

There are no objections to approval of Karbamid Evolan from a non-clinical point of view.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

No pharmacokinetic studies have been performed for this product. Karbamid Evolan is a product for topical application. Hence, conventional pharmacokinetic bioequivalence studies are not relevant due to low systemic exposure to urea. The absence of pharmacokinetic studies is acceptable.

IV.2 Pharmacodynamics

Urea is considered a well-known constituent of moisturizing creams. The mode of action of urea in Karbamid Evolan 50 mg/g cream is the same as in the reference product Canoderm 5% cream. The water-binding and barrier- strengthening ability of the creams contributes to normalization of dry skin and prevention of eczema relapses.

IV.3 Clinical efficacy

The efficacy of urea in the treatment of dry skin of different origin is considered well known. Studies demonstrating beneficial efficacy of the reference product Canoderm® on the recurrence of atopic eczema are briefly described in the Clinical Overview. Since the pharmaceutical composition of Karbamid Evolan and Canoderm® are similar, the same efficacy profiles of the two products can be anticipated.

IV.4 Clinical safety

The safety profile of urea 5% when used in moisturizing creams is considered well known. The labelling of clinical safety in the SmPC of Karbamid Evolan 5% is considered to adequately reflect the safety data available.

IV.5 Risk Management Plans

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 Karbamid Evolan.
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 SE/H/556/01 and Natriumklorid Evolan 500 mg capsules. The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Karbamid Evolan, is found adequate. There are no objections to approval of the product from a non-clinical and clinical point of view. The pharmaceutical composition of the product is not completely identical with the reference product Canoderm 5% cream, but very similar, the marginal difference was assessed of no clinical relevance. Therefore, Karbamid Evolan received the same labelling as the reference product. The product information is acceptable.

The application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83 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

Karbamid Evolan, 50mg/g cream was approved in the national procedure on 2018-10-09.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
	Initial Mutual Recognition Procedure	N/A	2019-09-11	2018-10-09	N/A

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

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