SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Karbamid Evolan 50 mg/g cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g of cream contains: urea 50 mg.

Excipient(s) with known effect
Ethyl parahydroxybenzoate, methyl parahydroxybenzoate, cetostearyl alcohol, propylene glycol (50 mg/g).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream
White cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For moisturising of dry skin of different origin and for prevention of relapse of atopic eczema.

4.2 Posology and method of administration

For moisturising of dry skin of different origin: The cream can be applied when needed, preferably several times daily and always after contact with water.

For prevention of relapse of atopic eczema: Apply at least twice daily and preferably after contact with water.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Avoid application into eyes, nose, ears or to open wounds or mucous membranes.

Karbamid Evolan cream contains ethyl and methyl parahydroxybenzoate, which may cause allergic reactions (possibly delayed).
Karbamid Evolan cream contains cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).
Karbamid Evolan cream contains propylene glycol, which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Karbamid Evolan can be used during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

There is no indication that Karbamid Evolan has any effect on the ability to drive or use machines.

4.8 Undesirable effects

The cream can give transient, local sensation of burning and heat. The face is most sensitive.

Common (>1/100)	*Skin*: Transient sensations of burning or heat

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.*

4.9 Overdose

Not relevant since the product is for cutaneous use only.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Protectives and emollients. ATC code: D02AE01.

Mode of Action
Karbamid Evolan cream contains 5 % urea in an emollient cream base. The water-binding ability and barrier- strengthening ability of Karbamid Evolan contributes to normalization of dry skin and prevention of eczema relapses. Karbamid Evolan's cream base composition delivers urea into the skin and enhances its therapeutic efficacy i.e. the moisturizing, anti-pruritic and protective effects.

Clinical efficacy
The effect of cream containing 5 % urea on the recurrence of atopic eczema was investigated in clinical studies.

In a randomized, double-blind controlled prospective comparative multi-center study, 198 subjects ≥18 years old, diagnosed with atopic dermatitis with visible atopic eczema of body surface area corresponding to a total area of at least the size of one palm were included in the study. Patients with eczema exclusively on the hands were excluded.
At the screening visit, study area eczemas were defined and the subjects treated their atopic eczemas with a strong glucocorticoid cream (mometasone furoate cream 0.1%) during a

3 weeks stabilization phase. In total 172 patients who became eczema free were randomized to maintenance treatment with either urea cream or reference cream (containing no urea and with a neutral effect on the skin barrier). The maintenance phase lasted for 180± 14 days or until eczema relapse.

At baseline, the median score of disease severity was 6.00 classified as moderate atopic dermatitis according to Rajka and Langeland and the number of relapses during the last year was 4.0.
The primary end-point was to examine the time between randomization and a subsequent event of relapse measured as a hazard ratio. The results of the study can be seen in the table below.

Table 1. Response to Urea Cream Treatment

	Urea cream	**Reference cream**	
Hazard Ratio (95% CI) compared to reference cream	0.634 (0.446, 0.901) (p=0.0110)		
Median Time to Relapse of Atopic Eczema (days) (Kaplan-Meier) Difference vs reference cream	22.0 (p=0.0129) 46.7 %	15.0	
Eczema Free Proportions at Day 180 (Kaplan-Meier)	26.4%	9.9%	
Absolute Risk Reduction			14.0%
Relative Risk Reduction			15.6%
Relative Risk			1.18

In another randomized controlled prospective multi-center clinical study, 55 patients with atopic eczema entered the study and treated defined atopic lesions with a strong steroid cream (betamethasone valerate 0.1% cream) during three weeks. Thereafter, 44 patients with cleared eczema were randomised to either maintenance therapy with urea cream, or with no treatment. The time to relapse of the eczema was measured during 26 weeks. The study showed that urea cream significantly increased the time to eczema relapse ($p<0.01$) compared to no treatment. During the maintenance therapy, 68% of the patients treated with urea cream were eczema-free after 26 weeks (median time to relapse >180 days). In the untreated group, 32% were eczema-free for the corresponding period (median time to relapse 30 days). The absolute risk reduction was 36% and the relative risk reduction 53%.

The effect of urea cream on the recurrence of hand eczema was investigated in a small clinical study. The median time to reappearance of eczema was 20 days in the urea cream group compared to 2 days in the no treatment group ($p = 0.0401$).

5.2 Pharmacokinetic properties

The systemic absorption of urea has not been studied but is assumed to be negligible.

5.3 Preclinical safety data

No preclinical data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Triglycerides, medium-chain
Polysorbate 60
Cetostearyl alcohol
Canola oil, hydrogenated
Propylene glycol (E 1520)
Carbomer
Dimethicone
Paraffin, hard
Glycerol - glycerol polymetacrylate
Ethyl parahydroxybenzoate (E 214)
Methyl parahydroxybenzoate (E 218)
Sodium lactate solution
Citric acid
Stearoyl macrogolglycerides
Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Aluminium laminated plastic tube (polyethylene), 100 g, with snap cap.
Plastic jar (polypropylene) with pump (polypropylene, polyethylene, glass), 500 g.
Twin pack 600 g containing, plastic jar (polypropylene) with pump, 500 g + aluminium laminated plastic tube (polyethylene), 100 g, with snap cap.

Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

Not applicable.

7. MARKETING AUTHORISATION HOLDER

<To be completed nationally>

8. MARKETING AUTHORISATION NUMBER

<To be completed nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<To be completed nationally>

10. DATE OF REVISION OF THE TEXT

2025-02-18

<To be completed nationally>