SYN®-AKE is a small peptide that mimics the activity of Waglerin 1, a polypeptide that is found in the venom of the Temple Viper, *Tropidolaemus wagleri*. Clinical trials have shown that SYN®-AKE is capable of reducing mimic wrinkles by inhibiting muscle contractions. To get a real Age Killing Effect, try SYN®-AKE.

**PRODUCT DESCRIPTION**

SYN®-AKE is a synthetic tri-peptide derivative that was developed based on the combined expertise of PENTAPHARM in snake venom research and peptide synthesis. Targeting neuromuscular activity, PENTAPHARM has developed a new snake venom-like active compound which is an antagonist of the muscular nicotinic acetylcholine receptor (nmAChR).

SYN®-AKE has excellent smoothing and fast anti-wrinkle properties that have been proved *in vivo* in a short term study (1 month).

**BACKGROUND**

Mimic wrinkles are part of the visible face wrinkles. As time passes, these wrinkles persist permanently and get deeper and deeper: frown lines, laughter lines and crows feet lines appear more and more due to the repeated movements of facial muscles.

SYN®-AKE has been developed as efficient smoothing and anti-wrinkle care particularly effective against expression lines by relaxing facial muscles. This active tri-peptide acts in a manner similar to Waglerin 1, a neuromuscular blocking compound of the venom of the Temple Viper. Acting at the post-synaptic membrane, SYN®-AKE is a reversible antagonist of the muscular nicotinic acetylcholine receptor (mnAChR). We assume that the tri-peptide is binding to the epsilon subunit of the mnAChR which prevents binding of acetylcholine to the receptor; consequently it remains closed. In the closed state, there is no uptake of sodium ions (Na+) and the muscles stay relaxed.

Chemical structure of the SYN®-AKE molecule
EFFICACY

SMOOTHING AND ANTI WRINKLE EFFECT OF SYN®-AKE

The study was performed on 45 volunteers. SYN®-AKE has been compared against placebo and against a reference substance. Both products have been used at the recommended use level. The study lasted 28 days with a twice-daily application.

SIGNIFICANT DECREASE OF EXPRESSION LINES ON THE FOREHEAD

Both products have been used at the recommended use level. SYN®-AKE at 4% and the reference substance acetyl hexapeptide-3 at 10%. SYN®-AKE clearly showed a higher efficacy for all tested parameters.

Ra: average roughness
Rt: maximum difference between the highest peak and the deepest furrows
Rz: mean value of these different maxima
A decrease of the Ra expresses a smoothed relief.
A decrease of the Rt and Rz expresses a decrease of the wrinkles' depth.

Using the PRIMOS® technique, parallel stripe patterns are projected on the sample with successive phase shift. The analysis of fringe deformations provided a qualitative as well as quantitative evaluation of each height profile.

The skin relief of Volunteer #9 is shown on the illustration on the right. The red profile presents the relief observed on the print at Day 0 and the green profile the relief at Day 28. We can observe a decrease of depth of the deepest wrinkles.
WRINKLES DECREASE UP TO 52% ON THE FOREHEAD

Measurements on Volunteer #29 showed that SYN®-AKE was able to reduce the wrinkles on the forehead by up to 52% (Parameter Rt).

ADDITIONAL INFORMATION

*In vitro* measurements showed that SYN®-AKE (at a concentration of 0.5mM) was able to reduce the frequency of contractions of innervated muscle cells by 82% (p<0.05) after 2 hours treatment.

Additional *in vivo* measurements have been made on the crow’s foot. These results confirmed the smoothing and anti-wrinkle effect of SYN®-AKE on this face area.

TECHNICAL INFORMATION

PRODUCT SPECIFICATIONS

- Appearance : Clear, colorless to yellowish, viscous liquid
- Peptide content : 2400-2600 ppm
- pH : 4.5-5.5
- Relative density (20°C) : 1.15-1.22
- Refractive index (25°C) : 1.40-1.46
- Microbial count : < 100 CFU/ml
- Specified pathogens : absent

PRESERVATION AND MICROBIOLOGY

SYN®-AKE contains no preservative. SYN®-AKE is free of specified pathogens. The amount of non-pathogenic microorganisms with less than 100 CFU per ml of SYN®-AKE meets the CTFA microbiology guidelines.

SAFETY AND ECOLOGY

Standard and well-defined safety testing has been performed on SYN®-AKE which has proved the product to be safe for cosmetic use. The data available do not indicate any environmental risks. The manufacturing process is designed to meet the criteria for the assessment of safety, health and protection of people and of the environment set out in the Responsible Care Program.

PROCESSING AND DOSAGE

SYN®-AKE could be processed either warm (for maximum 2 hours at 70°C) or cold. SYN®-AKE is stable in the pH-range of 3.0 to 5.5. In formulations, SYN®-AKE is compatible with ethanol at concentrations of up to 50% (maximally tested concentration). For skin care preparations, we recommend the addition of 1 to 4% SYN®-AKE. Basic Guide Formulations are available upon request.
STORAGE AND SHELF LIFE
SYN®-AKE should be stored in the original sealed container protected from light in a clean place at a temperature between 15 and 25°C. If stored under the recommended conditions, SYN®-AKE remains stable for at least 1 year. In order to avoid secondary microbial contamination, following opening, the content of the containers should be used immediately since SYN®-AKE does not contain any preservative.

GENERAL PRODUCT INFORMATION

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>SYN®-AKE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Code</td>
<td>800628</td>
</tr>
<tr>
<td>INCI Name (listed in the CTFA Dictionary)</td>
<td>Water, Glycerin, Dipeptide Diaminobutyroyl Benzylamide Diaceta</td>
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<tr>
<td>EU-Labelling Name</td>
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<td>Chemical Name</td>
<td>H-β-Ala-Pro-Dab-NHBzl x 2 AcOH</td>
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<tr>
<td>Shelf life</td>
<td>at least 1 year</td>
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</tbody>
</table>

COMPOSITION

A) Ingredient(s) | INCI Name # | Amount *
As listed in the CTFA Dictionary
Dipeptide Diaminobutyroyl | F |
Benzylamide Diacetate

B) Additives | INCI Name # | Amount *
Solvents
Water | B |
Glycerin | A |
Preservative
None | --- |
Others (buffers, antioxidants, colorants)
None | --- |

** CTFA Dictionary
* FDA-Code (A = > 50%, B = 25-50%, C = 10-25%, D = 5-10%, E = 1-5%, F = 0.1-1%, G = < 0.1%)

REMARK
Although these data and information have been prepared with the utmost possible care, we reserve the right to make changes due to product improvement and other considerations.

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