

Fillerina[®] 12 HA

D E N S I F Y I N G - F I L L E R

First dermo-cosmetic filler
for at-home use

14 doses (2 ml) of Gel Filler
14 doses (2 ml) of Nourishing Film
2 precision applicators

For skin depressions (age wrinkles and expression lines)

For the volume of cheekbones and lips

Cosmetic product for topical use

TECHNICAL MANUAL

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FILLERINA 12HA DENSIFYING - FILLER

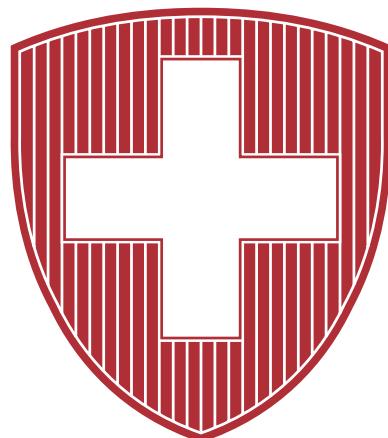
Fillerina: The Patents

SWISS PATENT CH 705 713 - Fillerina Complex

SWISS PATENT CH 711 466 - Transdermic Technology

SWISS PATENT CH 695 412 - Precision Applicator

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FILLERINA 12HA DENSIFYING - FILLER

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Graduated precision applicator
with truncated tip.

Swiss Patent No. CH 695 412 A5

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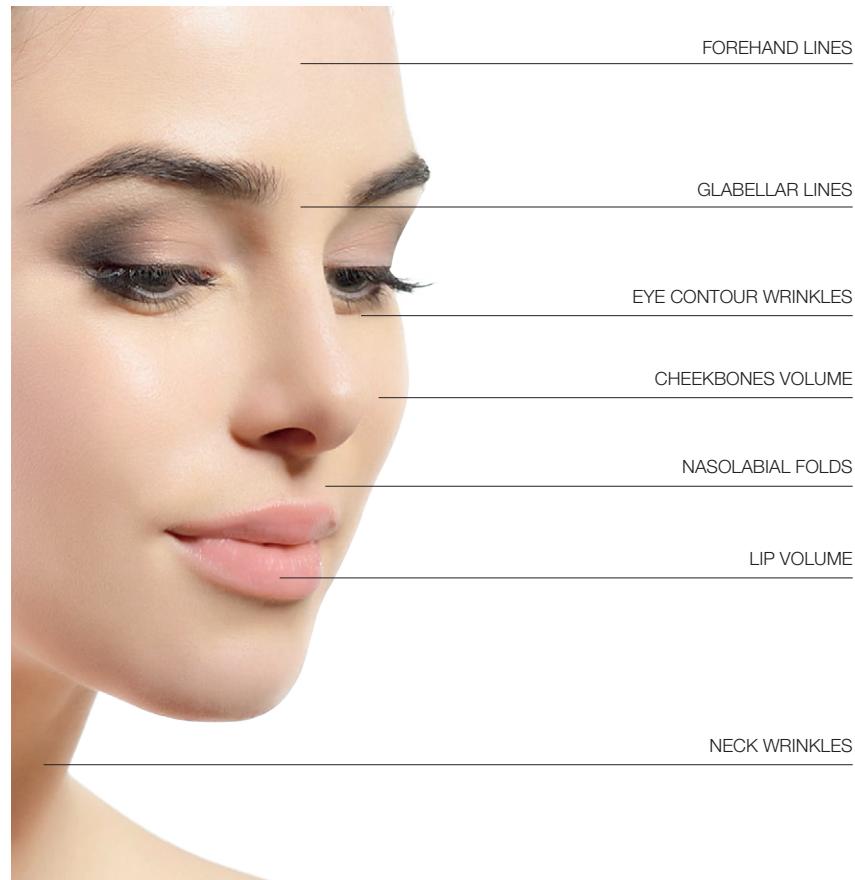


1. Fillerina Hyaluronic Acid And Filler Action



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Fillerina Product Concept

Injection dermal fillers based on hyaluronic acid are used to fill and give volumes to areas of the face showing signs of aging, skin depressions, hollow cheeked facial features, etc.

The filling properties of hyaluronic acid are based on its strong ability to swell and form inside the skin tissues a soft and easily malleable gel by combining with large quantities of water molecules.

Fillerina was developed to satisfy the need to bring in the deepest layers of the skin important quantities of hyaluronic acid (like the injections of aesthetic medicine) but **without the use of a needle** and therefore **without invasive procedures**.

To achieve this goal, several researches have been carried out for 5 years. As a result, the researchers obtained a diversification of the molecular weights of Hyaluronic Acid so to allow its penetration deep into the skin.

Thanks to this achievement, Fillerina overcomes the standard cosmetic products containing hyaluronic acid, which can claim only a good hydration of the most superficial layers of the skin.

Fillerina becomes a real alternative to the aesthetic medicine injections, being able to produce a remarkable **filler action on wrinkles and sagging**, as well as filling and **volumizing particular areas of the face such as cheekbones and lips**.

Fillerina is an intensive treatment to be used for 14 days.

The box contains:

14 doses of 2 ml of Gel Filler

14 doses of 2 ml of Nourishing Film

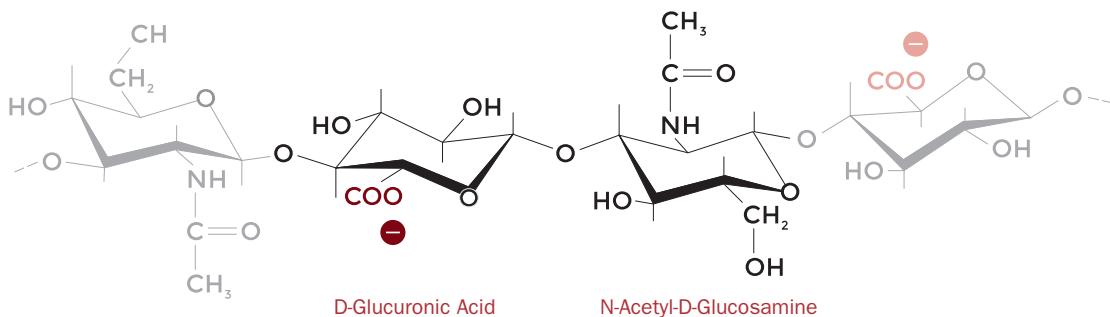
2 Precision applicators to distribute the preparations on the areas of the face where the filler and the volumizing effect is desired



Hyaluronic Acid in the Third Millennium

Since its first identification dated 1934 hyaluronic acid (HA) has been studied in a variety of research areas.

This unbranched glycosaminoglycan, consisting of repeated disaccharide units composed of N-Acetyl-D-Glucosamine and D-Glucuronic Acid, is almost ubiquitous in humans and other vertebrates.



Hyaluronic acid is involved in many key processes, including cellular signaling and communication, wound healing, tissue regeneration, morphogenesis, matrix organization and filling and has unique physico-chemical properties, such as biocompatibility, biodegradability, mucoadhesiveness, hygroscopicity and viscoelasticity. Hyaluronic acid is gaining an exponentially growing interest in the world for many pharmaceutical, medical, aesthetic and cosmetic applications.

Evolution and Filler Action of the Hyaluronic Acids of Fillerina

The first formulation of Fillerina consisted of 6 molecules of Hyaluronic Acids with molecular weights ranging from 1000 Daltons to 2 million Dalton.

Experimental tests performed with the Franz Cells method (see page 17) highlighted their *ex vivo* penetration capability (on skin membranes) in inversely proportional percentages compared to the Dalton weight of the single molecules.

Based on these results and thanks to the collaboration with international biotechnological production laboratories, Labo research team created new molecules with infinitesimal eights: 2 Hyaluronic Acids weighing 800 Dalton and 400 Dalton respectively. These components have shown a total penetration (100%) into the skin layers.

With the passing of time, the core formulation of Fillerina has been enriched with 4 additional medium-weight Hyaluronic Acid molecules up to a system composed of **12 molecules of HA**, all with different molecular weights with excellent fillin , resistance and volumizing performances.

FILLERINA 12HA DENSIFYING - FILLER



Franz Diffusion Cell: tool used to conduct Fillerina molecules *ex vivo* penetration tests

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Transdermic Technology and Ex Vivo Penetration Studies

Since 2007, Labo has carried out extensive researches in the field of de mo-cosmetic substances absorption with the aim of achieving similar effects to those of aesthetic medicine. A first result was achieved with Fillerina: to reach a true filling penetration efficacy through the skin without the use of a needle Labo developed hyaluronic acid molecules with different molecular weights. To understand their true penetration capabilities, they underwent an ex vivo test with Franz cells: it was thus possible to establish, for each hyaluronic acid molecule, with specific functions contained in the preparation, if it really penetrates the cutaneous layers, and eventually, the precise percentage that penetrated. Results highlighted the importance of the molecular weight: the lower the molecular weight of the substance, the more it can penetrate the stratum corneum and reach epidermis and dermis where it can act.

The methodology for evaluating the hyaluronic acid quantities that penetrate into the different layers of the skin is the same used in medicine and pharmacology to test the drug release through the skin tissues. The designated tool is called Franz Diffusion Cells and it consists in two chambers between which the skin membrane is placed. At preset experimental times, the percentages of active substances penetrated in the membrane are detected: at first, the data referring to epidermis and dermis penetration are kept separate and then the total quantity absorbed by the two skin layers is evaluated.

Labo patented this method and applied it to several active molecules for dermo-cosmetic use to make them similar, in their penetration into epidermis and dermis, to those injected by the aesthetic doctor (Transdermic Technology Swiss Patent CH 711 466).

The 12 Hyaluronic Acids of Fillerina

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HYALURONIC ACID INCI NAME		MOLECULAR WEIGHT (in Dalton)	FUNCTION
1	Hydrolyzed Glycosaminoglicans	400 Da	
2	Sodium Hyaluronate	800 Da	Immediate and complete (100%) penetration to the median and deep layers of the skin (ex vivo test). Help swelling of the tissues and smoothing of wrinkles.
3	Hyaluronic Acid	1,000 Da	
4	Hydrolyzed Sodium Hyaluronate	5,000 Da	Immediate penetration to the median and deep layers of the skin (ex vivo test). Help swelling of the tissues and smoothing of wrinkles.
5	Sodium Hyaluronate	20,000 Da	
6	Hydrolyzed Hyaluronic Acid	50,000 Da	
7	Sodium Hyaluronate	80,000 Da	Penetrate the median and deep layers of the skin (ex vivo test), filling wrinkles and depressions from the inside.
8	Sodium Hyaluronate	100,000 Da	Quickly penetrates the superficial and median layers of the skin filling wrinkles and skin micro-relief
9	Sodium Hyaluronate	200,000 Da	Penetrate the superficial and middle deep layers of the skin (ex vivo test) in comparable quantity where they bind large quantities of water. Help leveling out the cutaneous microrelief.
10	Sodium Hyaluronate	500,000 Da	
11	Sodium Hyaluronate	2,000,000 Da	Penetrates the surface layers of the (ex vivo test). Helps keeping tissues plumped up.
12	Sodium Hyaluronate	Reticulated Hyaluronic Acid	Guarantees a slow, continual hyaluronic acid release into the skin (ex vivo test). Helps keeping tissues



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Ex Vivo Penetration Test of the 12 Hyaluronic Acids

Fillerina 12 Hyaluronic Acids were tested ex vivo with Franz Cells to establish both their penetration capability, and the consequent efficacy potential for a high filler and volumizing effect in the skin layers.

The following charts show the transdermic penetration percentages at different experimental times (3 times or 6 times) of the 12 tested hyaluronic acid molecules, detected on epidermis, dermis and on epidermis + dermis together.

Ex vivo Test TV.01.C_2012 / 1600-1605, July 2012 (6 HA molecules)
Ex vivo Test TV.01.C_2013 / 1845-1846, August 2013 (2 HA molecules)
Ex vivo Test TV.01.C_2015 / 3264b, March 2016 (1 HA molecules)
Ex vivo Test E.EX.070-MS04_2019 / 333 February 2019 (3 HA molecules)

Penetration Chart 12 Hyaluronic Acid Molecules

Epidermis

Experimental Times	Molecular Weight in Dalton	400 Da	800 Da	1,000 Da	5,000 Da	20,000 Da	50,000 Da	80,000 Da	100,000 Da	200,000 Da	500,000 Da	2,000,000 Da	Crosspolymer
15 min		5.73 %	5.58 %	5.05 %	3.58 %		5.11 %			2.94 %		1.01 %	3.06 %
30 min		11.49 %	9.91 %	9.64 %	9.60 %	11.10 %	10.83 %	10.50 %	15.30 %	11.17 %	10.10 %	7.86 %	4.03 %
2 h		24.74 %	13.61 %	18.95 %	30.32 %		20.55 %			20.36 %		14.69 %	4.75 %
4 h		30.70 %	19.17 %	27.02 %	36.35 %		24.48 %			24.55 %		19.64 %	5.67 %
8 h		31.82 %	22.09 %	31.19 %	38.34 %	31.60 %	27.42 %	27.10 %	32.40 %	26.59 %	25.30 %	24.73 %	6.42 %
24 h		30.56 %	27.08 %	33.87 %	38.86 %	37.30 %	28.06 %	27.20 %	39.60 %	27.07 %	26.90 %	29.94 %	7.49 %

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Dermis

Experimental Times	Molecular Weight in Dalton	400 Da	800 Da	1,000 Da	5,000 Da	20,000 Da	50,000 Da	80,000 Da	100,000 Da	200,000 Da	500,000 Da	2,000,000 Da	Crosspolymer
15 min		7.32 %	6.75 %	7.28 %	13.33 %		5.24 %			2.53 %		1.52 %	2.45 %
30 min		15.26 %	17.06 %	16.75 %	19.00 %	18.40 %	17.06 %	16.90 %	14.00 %	9.44 %	10.20 %	2.73 %	4.05 %
2 h		43.89 %	33.86 %	30.12 %	47.45 %		46.71 %			16.61 %		4.18 %	5.83 %
4 h		67.42 %	71.64 %	46.79 %	60.85 %		64.19 %			21.67 %		5.90 %	9.94 %
8 h		69.18 %	78.65 %	60.01 %	62.88 %	68.60 %	75.33 %	72.60 %	25.70 %	27.78 %	28.70 %	7.92 %	14.28 %
24 h		73.90 %	78.77 %	63.11 %	66.50 %	68.60 %	75.97 %	73.00 %	29.60 %	28.59 %	28.40 %	9.98 %	19.86 %

Epidermis + Dermis

Experimental Times	Molecular Weight in Dalton	400 Da	800 Da	1,000 Da	5,000 Da	20,000 Da	50,000 Da	80,000 Da	100,000 Da	200,000 Da	500,000 Da	2,000,000 Da	Crosspolymer
15 min		13.05 %	12.32 %	12.32 %	16.91 %		10.35 %			5.47 %		2.53 %	5.51 %
30 min		26.74 %	26.97 %	26.39 %	28.60 %	29.50 %	27.89 %	27.50 %	29.30 %	20.61 %	20.30 %	10.59 %	8.08 %
2 h		68.64 %	47.49 %	49.07 %	77.77 %		67.26 %			36.97 %		18.87 %	10.58 %
4 h		98.12 %	90.81 %	73.81 %	97.20 %		88.67 %			46.23 %		25.54 %	15.61 %
8 h		100.99 %	100.74 %	91.20 %	101.22 %	100.10 %	102.75 %	99.80 %	58.10 %	54.36 %	54.10 %	32.65 %	20.70 %
24 h		104.47 %	105.84 %	96.98 %	105.35 %	105.80 %	104.03 %	100.20 %	69.20 %	55.65 %	55.20 %	39.93 %	27.36 %



Fillerina
Penetration Chart of
the 12 Hyaluronic Acids

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In Vivo Efficacy Study

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Efficacy Studies on Fillerina

In vivo test

FU.04.C.SL_2012 / 1842
November 2012

An *in vivo* test was conducted to evaluate the efficacy of Fillerina treatment to fill skin depressions (wrinkles), to reshape the cheekbones and give volume to lips.

This clinical-instrumental, randomized and placebo-controlled study of the filling effect for facial wrinkles and plumping for cheekbones and lips involved 40 female volunteers (20 treated with the product and 20 with placebo), aged between 25 and 55 years. The volunteers' skin was characterised by signs of chronological ageing: roughness, a decrease in volume due to emptying of tissues, especially on cheekbones and lips.

After periods of use of 7, 14 and 30 days, and also after only 3 hours, the effects of Fillerina treatment were evaluated by non-invasive skin bioengineering techniques capable of quantifying the filling of wrinkles and the improvement of the facial contours, and the volume of the cheekbones and lips.

The products of Fillerina treatment and the placebo were applied according to Labo instructions:

- Use the gel every day for 14 days, in the morning or evening, by applying 2 ml of gel on the wrinkles and expression lines, on the cheekbones and on the surface of the lips.
- Let the gel act for 10 minutes, then gently pat the product using the palm of the hands to allow it to be completely absorbed;
- Once the gel has been absorbed, draw up 1 to 2 ml of Nourishing Film and apply it all over face and neck, massaging until completely absorbed.
- Apply day, night and lip creams from day 15 to day 30.



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Efficacy Studies On Fillerina

In vivo test

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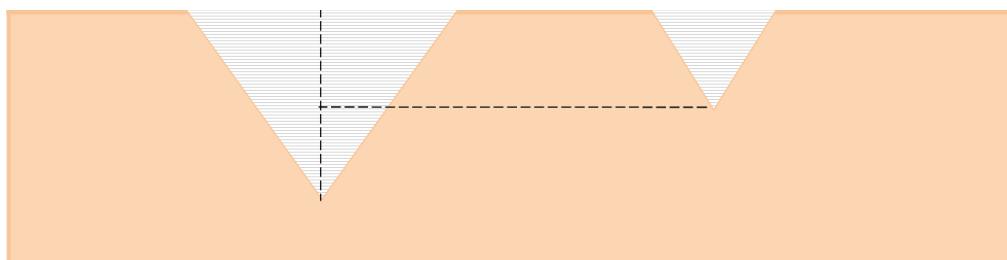
November 2012

REDUCTION IN WRINKLE DEPTH

For the *in vivo* evaluation of the skin, the cutaneous relief (wrinkles and furrows) was evaluated by Primos D, using profilometric measurements (measurement of the profile of the skin folds) taken with a 3D scanner. The instrument acquires a cloud of points on the surface of the object to be measured in a three-dimensional coordinated system. The depth of the wrinkles is calculated inside the line of measurement.

The wrinkle depth is the linear measurement of the skin surface at the innermost point, expressed in micro-millimetres.

The filling action of Fillerina reduces wrinkle depth by an average of 21.8%, and up to 54.8%



RESULTS

GROUP		T3 h	T7 d	T14 d	T30 d
ACTIVE	Average	-1,1%	-8,4%	-14,5%	-21,8%
	Up to	-13,3%	-36,5%	-40,1%	-54,8%

Treatment with the Fillerina active ingredient results in an average reduction in the wrinkle depth of -8.4%, -14.5% and -21.8%, respectively after 7, 14 and 30 days of treatment. 95% of subjects had positive results at 14 and 30 days.

GROUP		T3 h	T7 d	T14 d	T30 d
PLACEBO	Average	+3,2%	-0,2%	+0,3%	+1,3%
	Up to	-8,6%	-5,9%	-6,2%	-7,1%

Efficacy Studies on Fillerina

In vivo test

FU.04.C.SL_2012 / 1842

November 2012

FILLING OF WRINKLE VOLUME

For the *in vivo* testing of the skin, the cutaneous relief was evaluated by Primos D using profilometric measurements (measurement of the profile of the skin folds) then with a 3D scanner. The instrument acquires a cloud of points on the surface of the object to be measured in a three-dimensional coordinated system.

The wrinkle volume is calculated below the reference plane of the cross-section image along the entire length of the wrinkle.

The wrinkle volume is represented by the empty space left by the depressions of the wrinkles and furrows, measured in mm³

The Fillerina effect allows decreasing the volume of the wrinkle by an average of 26.3%, and up to 48.8%, filling the empty space



RESULTS

GROUP		T7	T14	T30	T30 d
ACTIVE	Average	-11,3%	-18,4%	-26,3%	-21,8%
	Up to	-32,9%	-37,8%	-48,8%	-54,8%

The treatment with the Fillerina active ingredient results in an average reduction of the wrinkle volume of -11.3%, -18.4% and -26.3%, respectively after 7, 14 and 30 days of treatment. 95% of subjects had positive results at 14 and 30 days.

GROUP		T7	T14	T30	T30 d
PLACEBO	Average	-1,1%	-0,8%	+1,7%	+1,3%
	Up to	-9,5%	-8,2%	-9,9%	-7,1%



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Efficacy Studies on Fillerina

In vivo test

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LIFTING OF FACIAL FEATURES

Fillerina's effect on the lifting of facial features was evaluated using morphometric image analysis conducted on frontal images of the face.

The following 5 vertical measurements were taken on each image: a) 2 measurements passing through the internal and external side of the eye, on each side of the face, and b) 1 measurement passing through the centre of the nose.

RESULTS in millimetres

GROUP		T7	T14	T30	T30 d
ACTIVE	Average	-0,443	-1,124	-1,326	-21,8%
	Up to	-1,051	-1,961	-2,871	-54,8%

In all the areas measured, the treatment with the Fillerina active ingredients results in a lifting of the facial contours (expressed as a reduction in the distance between the measured points). Instead, the treatment with placebo resulted in a sagging of the skin tissues of the face.

94% of subjects had positive results at 14 days, and 97% at 30 days.

GROUP		T7	T14	T30	T30 d
PLACEBO	Average	+0,151	+0,157	+0,112	+1,3%
	Up to	-0,296	-0,300	-0,315	-7,1%

Efficacy Studies on Fillerina

In vivo test

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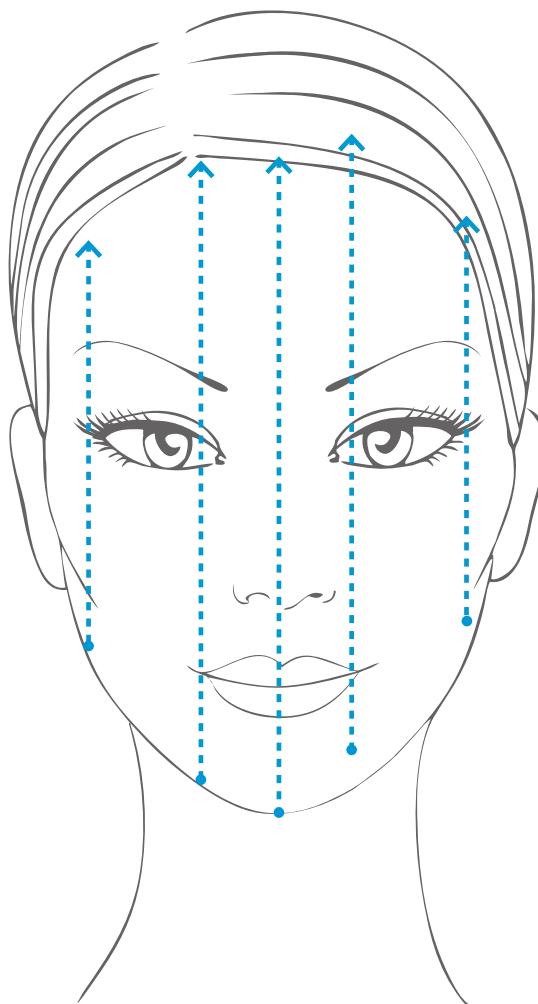
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LIFTING OF FACIAL FEATURES

Lifting of the features

Average: -1.32 mm

Up to: -2.87 mm



The data measure the distance between the upper part (front) and lower part of the face (jawline) in 5 points and are expressed in millimetres.

Negative number = reduction in distance = remodelling action of the oval.



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Efficacy Studies on Fillerina

In vivo test

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INCREASE IN CHEEKBONE VOLUME

The plumping effect is evaluated as the ability of the product to cause a spatial change in the contour of the cheekbones along the x axis (line 3).

The evaluation is performed on 2D digital images: a line tangent to the nose (1) is drawn, two lines are drawn to define the upper (2) and lower (3) limits of the skin area around the cheekbones, then the distance (red lines) of the contours of the cheekbones are evaluated from line 1 in 5 points (within region 2 to 3).

The treatment with the Fillerina product results in an increase in the volume of the cheekbones.

This action means an increase in the distance between a tangent line passing through the nose and the contour of the cheekbone.

RESULTS in millimetres

GROUP		T7	T14	T30	T30 d
ACTIVE	Average	+0,875	+2,186	+2,275	-21,8%
	Up to	+1,68	+3,034	+3,392	-54,8%

The treatment with the Fillerina active ingredients results in greater prominence of the cheekbone contours (up to 3.39 millimetres more) at all times.

99% of subjects had positive results at 14 days, and 100% at 30 days.

GROUP		T7	T14	T30	T30 d
PLACEBO	Average	-0,221	-0,217	-0,230	+1,3%
	Up to	+0,315	+0,424	+0,469	-7,1%

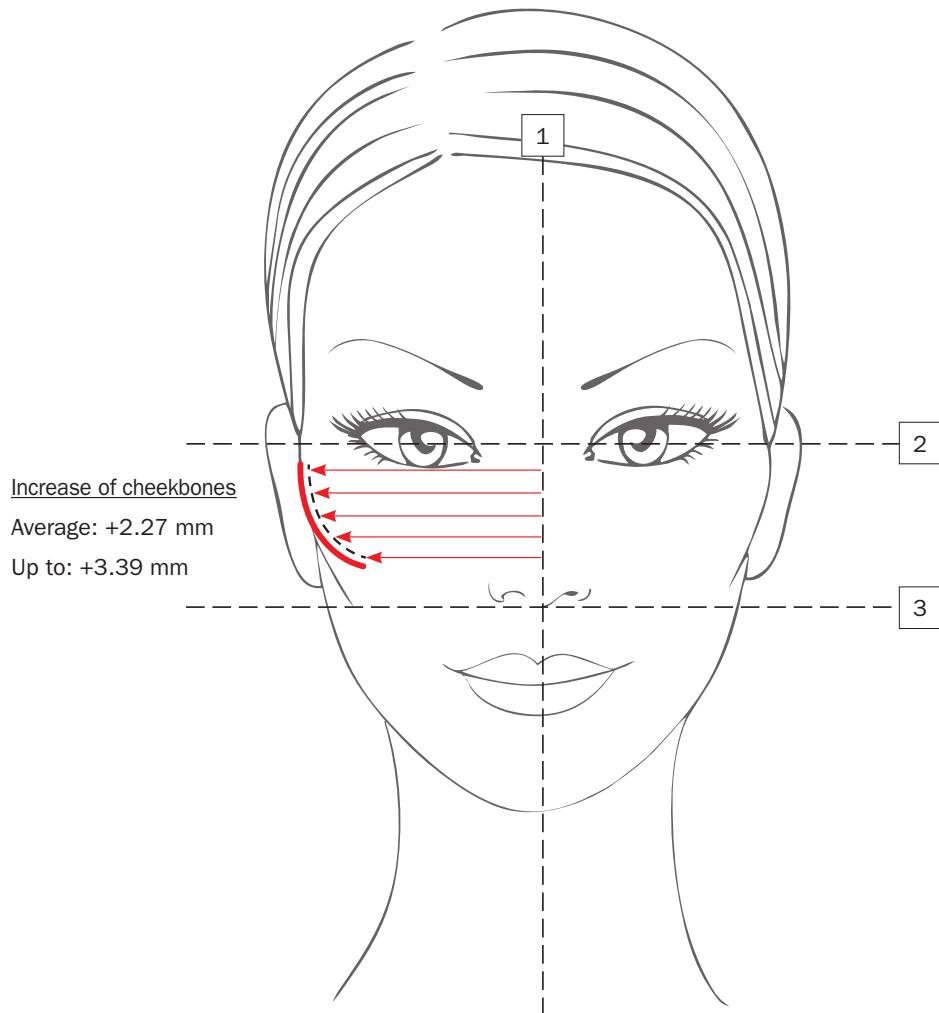
Efficacy Studies on Fillerina

In vivo test

FU.04.C.SL_2012 / 1842

November 2012

INCREASE IN CHEEKBONE VOLUME



The data measure the variation in the distance between the contours of the cheekbones and a line tangent to the nose, expressed in millimetres.

Efficacy Studies on Fillerina

In vivo test

FU.04.C.SL_2012 / 1842

November 2012

LIFTING OF CHEEKBONES

The lifting of the cheekbones is evaluated as the ability of the product to result in a spatial change in the contour of the cheekbones along the y axis (line 1).

The evaluation is performed on 2D digital images as follows: a line is drawn intersecting the eyes (2), and then the distance, in millimetres, of the contours of the cheekbones from line 2 in 3 points (green lines) is evaluated.

Negative number = reduction in the distance = lifting of cheekbones

RESULTS in millimetres

GROUP		T7	T14	T30	T30 d
ACTIVE	Average	-0,989	-2,500	-2,517	-21,8%
	Up to	-2,057	-3,430	-3,672	-54,8%

The treatment with the Fillerina active ingredients results in a progressive lifting of the contours of the cheekbones. This action means a reduction in the distance between the contours of the cheekbones and a horizontal line intersecting the eyes. Average lifting results of -2.5 mm, and up to -3.6 mm.

93.3% of subjects had positive results at 14 days, and 96.6% at 30 days.

GROUP		T7	T14	T30	T30 d
PLACEBO	Average	+0,199	+0,241	+0,265	+1,3%
	Up to	-0,085	-0,097	-0,114	-7,1%

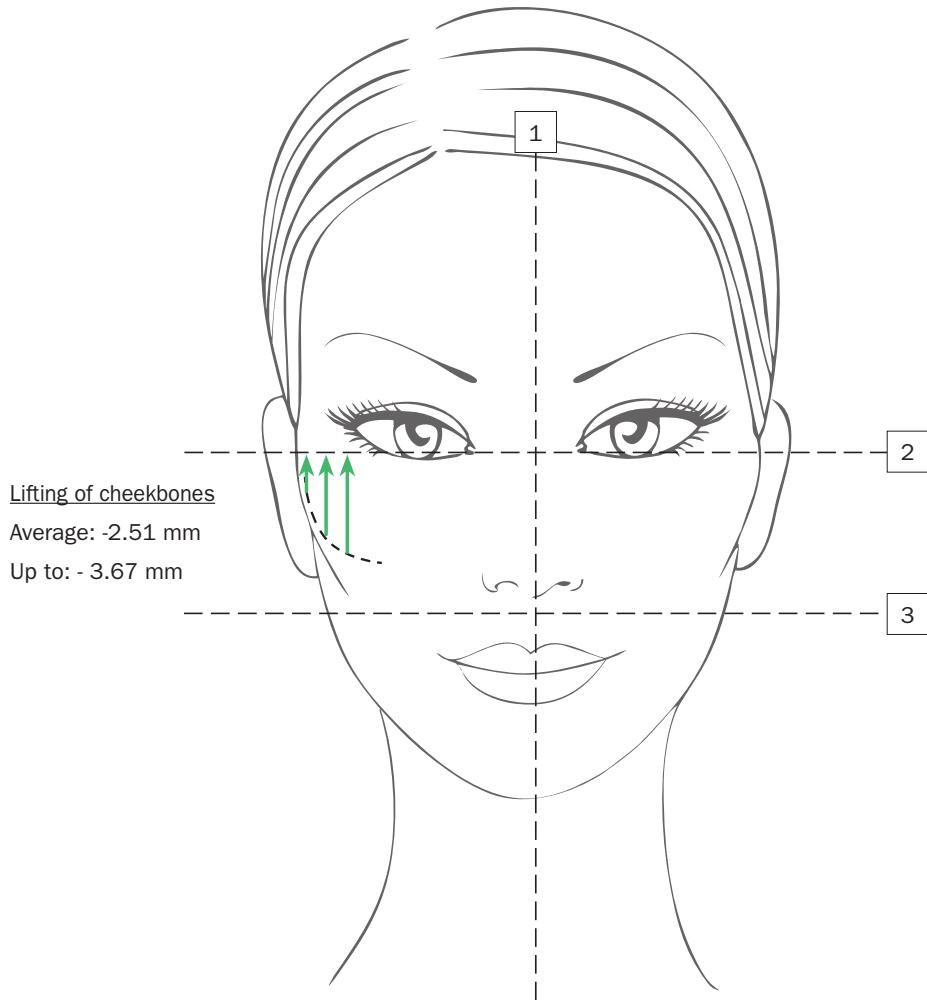
Efficacy Studies on Fillerina

In vivo test

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November 2012

LIFTING OF CHEEKBONES



The measurement of the cheekbone lift is a reduction (in millimetres) of the distance between the contours of the cheekbones and a horizontal line intersecting the eyes.

Efficacy Studies on Fillerina

In vivo test
FU.04.C.SL_2012 / 1842
November 2012

INCREASE IN LIP VOLUME

RESULTS in millimetres

GROUP		T3 h	T7 d	T14 d	T30 d
ACTIVE	Average	+8,5%	+11,3%	+12,8%	+14,2%
	Up to	+45,9%	+40,9%	+42,4%	+44,7%

The treatment with the Fillerina active ingredient results in an increase in the volume of the lips at all times. After 3 hours of the first application, an increase of +8.5% was already reported.

95% of subjects had positive results at 14 days, and 100% at 30 days.

GROUP		T3 h	T7 d	T14 d	T30 d
PLACEBO	Average	-1,4%	-1,2%	-1,7%	-2,5%
	Up to	+10,7%	+17,6%	+10,5%	+4,1%

Efficacy Studies on Fillerina

In vivo test

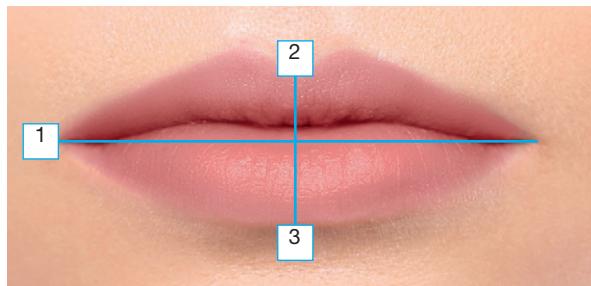
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November 2012

INCREASE IN LIP VOLUME

The plumping effect of the lips is evaluated using morphometric image analysis on digital photos of the face.

The plumping effect of the lips was calculated based on mathematical interpolation of the following parameters: 1) length of the labial rim, 2) height of the upper lip and 3) height of the lower lip.



2. Fillerina Densifying Action and Additional Components



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Fillerina Densifying Action and Additional Components

In order to support a densifying action on the skin layers, Fillerina Filler Gel contains **3 Collagen molecules** with different molecular weights (2,000 Dalton, 12,000 Dalton, 300,000 Dalton) and **2 Elastin molecules** with different molecular weights (1,400 Dalton and 2,200 Dalton). Collagen is the main fibrous element of the skin responsible for its density and compactness. Elastin provides the skin with more elasticity and plasticity. They interact with Fillerina 12 Hyaluronic Acids thus carrying out a strong densifying action.

Fillerina Filler Gel is enriched also with additional components that assist the filling and volumizing action of hyaluronic acids, acting more gradually and supporting their biological function at skin level structures: Palmitoyl Tripeptide-38 (Matrifull) and Acetyl Hexapeptide-37. Finally, Chondroitin Sulfate helps create a 3D scaffold with Hyaluronic Acid molecules.

Fillerina Densifying Action and Additional Components

DENSIFYING MOLECULES INCI NAME		MOLECULAR WEIGHT (in Dalton)	FUNCTION
1	Hydrolyzed Collagen	2,000 Da	Collagen is the main fibrous element of the skin, responsible for its density and compactness. It creates in the dermis a supporting structure that is filled with Hyaluronic Acid. Very low molecular weight Collagen molecules penetrate up to the deepest layers of the dermis, while the biggest molecule guarantees a progressive and modulated penetration of Collagen in the dermis.
2	Hydrolyzed Collagen	12,000 Da	
3	Hydrolyzed Collagen	300,000 Da	
4	Hydrolyzed Elastin	1,400 Da	Very low molecular weight Elastin molecules that penetrate up to the deep layers of the dermis where they interact with collagen and fibroblasts, providing the skin with more elasticity and plasticity.
5	Hydrolyzed Elastin	2,200 Da	

ADDITIONAL MOLECULES INCI NAME		MOLECULAR WEIGHT (in Dalton)	FUNCTION
1	Palmitoyl Tripeptide-38 (Matrifull)	675 Da	Stimulates the synthesis of Collagen I, Collagen III and Fibronectin to gradually reconstruct the extracellular matrix of the dermis.
2	Acetyl Hexapeptide-37	525 Da	Regulates the water transportation through the skin by stimulating the production of Aquaporins, that are membrane proteins involved in the water flow through the different layers of the skin.
3	Chondroitin Sulfate	10,000 Da	At dermis level, it binds itself to Hyaluronic Acids creating a 3D molecular scaffold, which will be resistant to skin hyaluronidases depolymerization action over time, thus prolonging Hyaluronic Acid effects.



Fillerina Densifying Action and Additional Components

Thanks to Labo transdermic technology also the additional components of Fillerina have been tested to check and evaluate their capability to penetrate through the skin.

The following charts show the percentages reported for each molecule at the experimental times of 30 minutes, 8 hours and 24 hours, on epidermis, dermis and epidermis + dermis.

Ex vivo Test TV.01.C_2015/3264a, March 2016 (Matrifull, Hexapeptide)

Ex vivo Test TV.01.C_2014/869, April 2014 (Chondroitin sulfate)

Ex vivo Test E.EX.070-MS04_2016/3687, December 2016 (3 Collagen molecules)

Ex vivo Test E.EX.070-MS04_2017/3666B, December 2017 (2 Elastin molecules)

Epidermis

	Molecules	Hydrolyzed Collagen	Hydrolyzed Collagen	Hydrolyzed Collagen	Hydrolyzed Elastin	Hydrolyzed Elastin	Matrifull Palmitoyl Tripeptide-38	Acetyl Hexapeptide-37	Chondroitin Sulfate
Experimental Times	Molecular Weight in Dalton	2,000 Da	12,000 Da	300,000 Da	1.400 Da	2.200 Da	670 Da	520 Da	10,000 Da
15 min									24.60 %
30 min		17.60 %	13.20 %	7.30	16.70 %	15.20 %	8.10 %	12.30 %	29.57 %
2 h									32.46 %
4 h									37.19 %
8 h		47.30 %	38.60 %	31.70 %	39.80 %	37.70 %	28.40 %	37.10 %	39.39 %
24 h		63.50 %	63.50 %	57.20 %	38.40 %	67.40 %	53.70 %	61.40 %	40.82 %

Dermis

	Molecules	Hydrolyzed Collagen	Hydrolyzed Collagen	Hydrolyzed Collagen	Hydrolyzed Elastin	Hydrolyzed Elastin	Matrifull Palmitoyl Tripeptide-38	Acetyl Hexapeptide-37	Chondroitin Sulfate
Experimental Times	Molecular Weight in Dalton	2,000 Da	12,000 Da	300,000 Da	1.400 Da	2.200 Da	670 Da	520 Da	10,000 Da
15 min									1.12 %
30 min		18.80 %	15.70 %	15.90	18.70 %	18.60 %	5.50 %	14.10 %	2.48 %
2 h									2.81 %
4 h									16.33 %
8 h		34.10 %	34.40 %	30.80 %	37.20 %	42.10 %	13.20 %	15.50 %	21.29 %
24 h		37.80 %	38.40 %	36.10 %	31.00 %	28.80 %	21.20 %	21.80 %	40.04 %

Epidermis + Dermis

	Molecules	Hydrolyzed Collagen	Hydrolyzed Collagen	Hydrolyzed Collagen	Hydrolyzed Elastin	Hydrolyzed Elastin	Matrifull Palmitoyl Tripeptide-38	Acetyl Hexapeptide-37	Chondroitin Sulfate
Experimental Times	Molecular Weight in Dalton	2,000 Da	12,000 Da	300,000 Da	1.400 Da	2.200 Da	670 Da	520 Da	10,000 Da
15 min									25.72 %
30 min		36.50 %	28.90 %	23.20 %	35.40 %	33.80 %	13.60 %	26.40 %	32.05 %
2 h									35.27 %
4 h									53.52 %
8 h		81.40 %	73.00 %	62.50 %	76.90 %	79.80 %	41.60 %	52.60 %	60.68 %
24 h		101.30 %	95.50 %	74.60 %	98.38 %	97.06 %	74.90 %	83.20 %	80.86 %



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3. The Dosages



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Fillerina Densifying-Filler Classification of grades and dosages



FILLERINA 12 DENSIFYING-FILLER
GRADE 3



FILLERINA 12 DENSIFYING-FILLER
GRADE 4



GRADE 5

- Very deep wrinkles and expression lines
- Age wrinkles with very marked and uneven microrelief
- Severe depression and depletion of the tissues
- Skin with insufficient thickness, density and plasticity
- Marked sagging signs
- Need for more volume to cheekbones and lips



FILLERINA 12 DENSIFYING-FILLER
GRADE 5



FILLERINA 12 DENSIFYING-FILLER
GRADE 3



FILLERINA 12 DENSIFYING-FILLER
GRADE 4

- Initial wrinkles and expression lines
- Initial age wrinkles and uneven microrelief
- Initial depression and depletion of the tissues
- Skin with decreasing thickness, density and plasticity
- Initial sagging signs
- Need for more volume to cheekbones and lips

Fillerina Dosages

Fillerina 12 Densifying-Filler dermo-cosmetic treatments for at-home use come in three different concentrations, in order to provide the most effective, suitable treatment for the conditions of the skin and the cutaneous tissues of the face and neck and enhance the volume of cheekbones and lips.

Grade 3: Initial wrinkles and expression lines. Initial age wrinkles and uneven microrelief. Initial depression and depletion of the tissues. Skin with decreasing thickness, density and plasticity. Initial sagging signs. Need for more volume to cheekbones and lips.

Grade 4: Deep wrinkles and expression lines. Age wrinkles with visible, marked and uneven microrelief. Conspicuous depression and depletion of the tissues. Skin with poor thickness, density and plasticity. Visible sagging signs. Need for more volume to cheekbones and lips.

Grade 5: Very deep wrinkles and expression lines. Age wrinkles with very marked and uneven microrelief. Severe depression and depletion of the tissues. Skin with insufficient thickness density and plasticity. Marked sagging signs. Need for more volume to cheekbones and lips.

To help choose the most suitable dosage for each individual's condition, Labo has created a photographic scale, the Fillerimeter: consumers can compare themselves with the pictures and decide what grade better suits their skin needs and the most evident signs of aging. Photos are followed by a clear and explanatory description of the phases through which the chrono- and photo-aging processes occur.

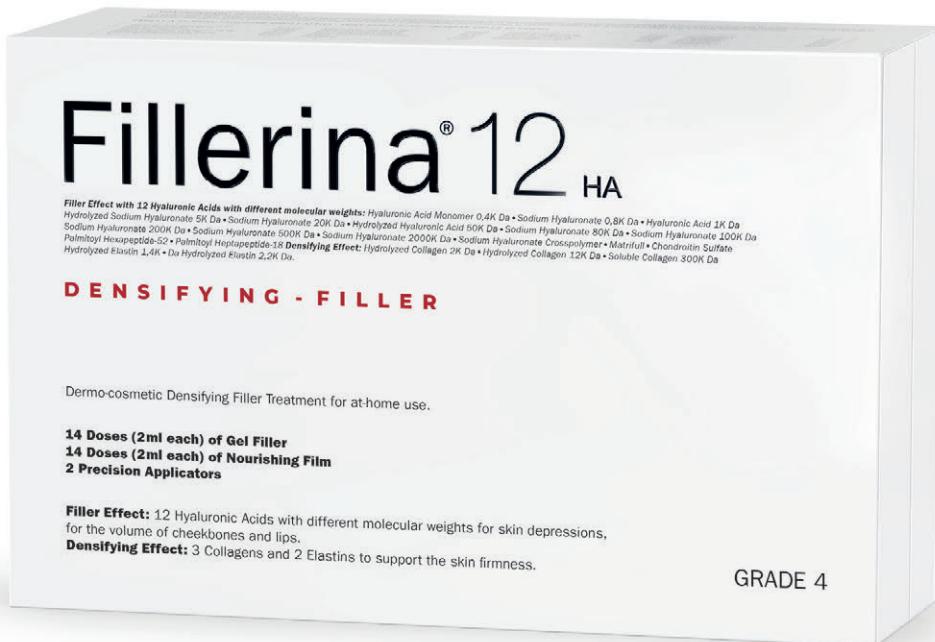


4. The Product



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FILLERINA 12_{HA} DENSIFYING - FILLER



Dermo-cosmetic Densifying Filler Treatment for at-home use.

- 14 Doses (2ml each) of Gel Filler
- 14 Doses (2ml each) of Nourishing Film
- 2 Precision Applicators

Filler Effect: 12 Hyaluronic Acids with different molecular weights: Hyaluronic Acid Monomer 0.4K Da • Sodium Hyaluronate 0.8K Da • Hyaluronic Acid 1K Da
Hydrolyzed Sodium Hyaluronate 5K Da • Sodium Hyaluronate 20K Da • Hydrolyzed Hyaluronic Acid 50K Da • Sodium Hyaluronate 80K Da • Sodium Hyaluronate 200K Da
Sodium Hyaluronate 2000K Da • Sodium Hyaluronate 500K Da • Sodium Hyaluronate 2000K Da • Sodium Hyaluronate Crosspolymer • Matrixyl • Chondroitin Sulfate
Palmitoyl Hexapeptide-52 • Palmitoyl Heptapeptide-18 **Densifying Effect:** Hydrolyzed Collagen 2K Da • Hydrolyzed Collagen 12K Da • Soluble Collagen 300K Da
Hydrolyzed Elastin 1.4K Da • Hydrolyzed Elastin 2.2K Da

GRADE 4

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The Filler Treatment

Fillerina 12 Densifying-Filler Intensive Treatment for at-home use consists in a Densifying-Filler Gel (Bottle No. 1), having a high content of the 12 absorbable Hyaluronic Acids, of the 3 Collagens and 2 Elastins with different molecular weights. Bottle No.2 contains a Nourishing Film to be used after the Gel.

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FILLERINA 12HA DENSIFYING - FILLER



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The Filler Treatment

How to Use

Fillerina 12 Densifying-Filler Treatment shall be used every day for 14 days, in the morning or evening, depending on individual needs and habits, by applying 2 ml of Densifying-Filler Gel (Bottle No. 1) on wrinkles, on the most marked microrelief and on areas that require particular plumping up (cheekbones, lips). To promote Fillerina action, it is recommended to apply the product on clean skin, free from sebum and impurities. The application shall be performed by means of the special Dispenser/Applicator, which allows to draw up two separate 1 ml amounts of product (adding up to a total of 2 ml per application) and accurately release it onto the desired areas. The Densifying-Filler Gel should be left to work for 10 minutes in order for the active ingredients to "fill in" the application areas. Using the palm of the hands or fingers, pat in the remaining product to complete the application. Do not carry out rotating massages or movements to avoid the possible formation of surface residues. Any feeling of tension on the skin is due to the action of the product. Then apply the Nourishing Film (Bottle No. 2) which guarantees a sufficient amount of moisturizing and nourishing substances and allows the filler application to be completed with maximum comfort for the skin of face and neck. Draw up 1 – 2 ml of Film, as required, and apply it all over face and neck.



FOR EXTERNAL USE ONLY

Instructions for opening: Fillerina bottles (No. 1 and No. 2) are sealed by means of special metal seals with plastic opening system. The opening side is marked by two arrows: lift the plastic disc by following the arrows and gently pull it upwards, then sideways till removing the metal seal. Remove the rubber cap and dispose of it, then draw up the desired product. After opening, close the bottle using the plastic cap you find inside the box



How to Use

To facilitate the action of the product, it is advisable to drink two glasses of water before the application of Fillerina Gel.

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FILLERINA 12_{HA} DENSIFYING - FILLER



Daily Treatments

Fillerina 12 Densifying-Filler Daily Treatments are available in the same dosages of Fillerina 12 Densifying-Filler Intensive Treatments.

Fillerina 12 Densifying-Filler Day Cream – Moisturizing and protective, with densifying-filler effect. To be used alone or together with other Fillerina products. In a 50-ml tube. Dosages: Grade 3, Grade 4, Grade 5. Apply the product in the morning onto clean face and neck helping the absorption with a gentle massage.

Fillerina 12 Densifying-Filler Night Cream – Nourishing and restoring, with densifying-filler effect. To be used alone or together with other Fillerina products. In a 50-ml tube. Dosages: Grade 3, Grade 4, Grade 5. Apply the product in the evening onto clean face and neck helping the absorption with a gentle massage.

Fillerina 12 Densifying-Filler Eye Contour Cream – For eye contour, with densifying-filler effect. To be used alone or together with other Fillerina products. In a 15-ml tube. Dosages: Grade 3, Grade 4, Grade 5. Apply the product in the morning and/or in the evening onto the eye contour helping the absorption with a gentle massage.

Fillerina 12 Densifying-Filler Lip Contour Cream – For lips and lip contour, with densifying-filler effect. To be used alone or together with other Fillerina products. In a 15-ml tube. Dosages: Grade 3, Grade 4, Grade 5. Apply the product in the morning and/or in the evening onto the whole lip area helping the absorption with a gentle massage.

The Application Protocol

Recommended treatment protocol for Fillerina:

Fillerina 12 Densifying-Filler Intensive Treatment lasts 14 days and can be repeated every 2-3 months, using daily treatments in the intermediate periods.

Day or night creams can also be used during the 14 days of the basic cycle, alternating their application with the intensive Densifying-Filler treatment.

FILLERINA 12HA DENSIFYING - FILLER

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5. The Patents



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The Patents

Fillerina Treatments can count on 3 patents:

SWISS PATENT CH 705 713 - Fillerina Complex
SWISS PATENT CH 711 466 - Transdermic Technology
SWISS PATENT CH 695 412 - Precision Applicator



Schweizerische Eidgenossenschaft
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Eidgenössisches Institut für Geistiges Eigentum
Institut Fédéral de la Propriété Intellectuelle
Istituto Federale della Proprietà Intellettuale
Institut Federal da Proprietad Intellectuala

Urkunde · Certificat · Certificato

über die Erteilung des Erfindungspatentes Nr.
de délivrance du brevet d'invention n°
di rilascio del brevetto d'invenzione no.

705 713

Nachdem die gesetzlichen Bedingungen erfüllt worden sind, ist für die in der beigefügten Patentschrift dargelegte Erfindung ein Patent mit der oben angegebenen Nummer erteilt worden.
Auf der ersten Seite der Patentschrift sind alle wesentlichen Angaben enthalten, die das vorliegende Erfindungspatent betreffen.
Erfindungspatente werden ohne Gewährleistung des Bundes erteilt. Massgeblich ist der Eintrag im Patentregister.

Bern, Datum der Patenterteilung

Les conditions requises par la loi étant remplies, un brevet portant le numéro susmentionné a été délivré pour l'invention décrite dans le fascicule ci-joint.

Sur la première page du fascicule du brevet figurent toutes les indications essentielles relatives au brevet d'invention considéré.

Les brevets d'invention sont délivrés sans garantie de l'Etat. Seul l'enregistrement dans le registre des brevets fait foi.

Berne, date de la délivrance du brevet

Essendo soddisfatte le condizioni prescritte dalla legge, è stato rilasciato un brevetto contrassegnato dal numero sopraindicato per l'invenzione documentata nel fascicolo allegato.
Sulla prima pagina del fascicolo del brevetto figurano tutte le indicazioni essenziali concernenti il brevetto in questione.
I brevetti d'invenzione sono rilasciati senza garanzia dello Stato. Determinante è l'iscrizione nel registro dei brevetti.

Berna, data del rilascio del brevetto

Der Direktor/Le Directeur/Il Direttore

Dr. Roland Grossenbacher





SCHWEIZERISCHE EidGENOSSENSCHAFT
EIDGENÖSSISCHES INSTITUT FÜR GEISTIGES EIGENTUM

(11) CH

705 713 B1

(51) Int. Cl.: A61K 8/73
A61Q 19/08 (2006.01)
(2006.01)

Erfnungspatent für die Schweiz und Liechtenstein

Schweizerisch-liechtensteinischer Patentschutzvertrag vom 22. Dezember 1978

(12) PATENTSCHRIFT

(21) Anmeldenummer: 01715/12

(22) Anmelddatum: 21.09.2012

(24) Patent erteilt: 15.05.2013

(45) Patentschrift veröffentlicht: 15.05.2013

(73) Inhaber:
Labo Cosprophar AG, St. Jakobs-Strasse 17
4052 Basel (CH)

(72) Erfinder:
Die Erfinder haben auf Nennung verzichtet

(74) Vertreter:
Schmauder & Partner AG Patent- und Markenanwälte
VSP, Zwängiweg 7
8038 Zürich (CH)

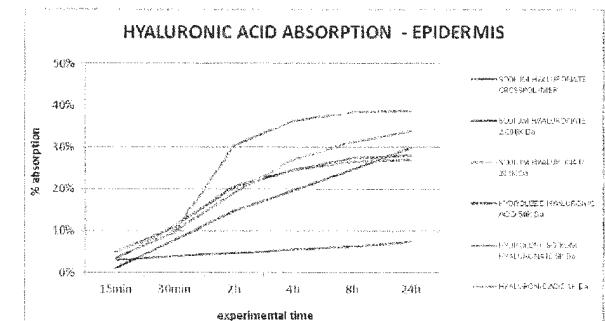
(54) Dermokosmetische Zusammensetzung zur topischen Anwendung.

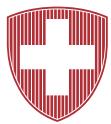
(57) Eine dermokosmetische Zusammensetzung mit füllender Wirkung zur topischen Anwendung beinhaltet eine Mischung auf Basis von Hyaluronsäuren unterschiedlicher Molekulargewichte. Die Mischung umfasst:

- Hyaluronsäure oder ein physiologisch annehmbares Salz davon mit einem Molekulargewicht von 800 bis 1200 Dalton,
- Hyaluronsäure oder ein physiologisch annehmbares Salz davon mit einem Molekulargewicht von 4000 bis 6000 Dalton,
- Hyaluronsäure oder ein physiologisch annehmbares Salz davon mit einem Molekulargewicht von 20.000 bis 70.000 Dalton,
- Hyaluronsäure oder ein physiologisch annehmbares Salz davon mit einem Molekulargewicht von 150.000 bis 250.000 Dalton,
- Hyaluronsäure oder ein physiologisch annehmbares Salz davon mit einem Molekulargewicht von 1.800.000 bis 2.200.000 Dalton,
- Hyaluronsäure-Kreuzpolymer oder ein physiologisch annehmbares Salz davon,

sowie einen kosmetisch annehmbaren Träger.

Die dermokosmetische Zusammensetzung ist insbesondere zum Glätten von Runzeln oder Furchen in der Epidermis mittels topischer Anwendung geeignet.





Schweizerische Eidgenossenschaft • Confédération suisse • Confederazione Svizzera

Urkunde • Certificat • Ce tificate

über die Erteilung des Erfindungspatentes N .
de délivrance du brevet d'invention n°
di rilascio del brevetto d'invenzione no.

695 412

Nachdem die gesetzlichen Bedingungen erfüllt worden sind, ist für die in der beigefügten Patentschrift
dargelegte Erfindung ein Patent mit der oben angegebenen Nummer erteilt worden.

Auf der ersten Seite der Patentschrift sind alle wesentlichen Angaben enthalten, die das vorliegende
Erfindungspatent betreffen.

Erfindungspatente werden ohne Gewährleistung des Bundes erteilt. Massgeblich ist der Eintrag
im Patentregister.

Bern, Datum der Patenterteilung

Les conditions requises par la loi étant remplies, un brevet portant le numéro susmentionné a été délivré
pour l'invention décrite dans le fascicule ci-joint.

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au brevet d'invention considéré.

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des brevets fait foi.

Berne, date de la délivrance du brevet

Essendo soddisfatte le condizioni prescritte dalla legge, è stato rilasciato un brevetto contrassegnato
dal numero sopraindicato per l'invenzione documentata nel fascicolo allegato.

Sulla prima pagina del fascicolo del brevetto figurano tutte le indicazioni essenziali concernenti
il brevetto in questione.

I brevetti d'invenzione sono rilasciati senza garanzia dello Stato. Determinante è l'iscrizione nel registro
dei brevetti.

Berna, data del rilascio del brevetto



Eidgenössisches Institut für Geistiges Eigentum
Institut Fédéral de la Propriété Intellectuelle
Istituto Federale della Proprietà Intellettuale

Der Direktor/Le Directeur/Il Direttore

Dr. Roland Grossenbacher



SCHWEIZERISCHE EIDGENOSSENSCHAFT
EIDGENÖSSISCHES INSTITUT FÜR GEISTIGES EIGENTUM

(19)

Erfolgspatent für die Schweiz und Liechtenstein

Patentschutzvertrag Schweiz-Liechtenstein vom 22. Dezember 1978

(11) CH 695 412 A5

(51) Int. Cl.: A45D 34/04 (2006.01)
A45D 40/26 (2006.01)
A45D 44/00 (2006.01)
A45D 19/00 (2006.01)
A61M 35/00 (2006.01)

(12) **PATENTSCHRIFT**

(21) Anmeldenummer: 01714/04

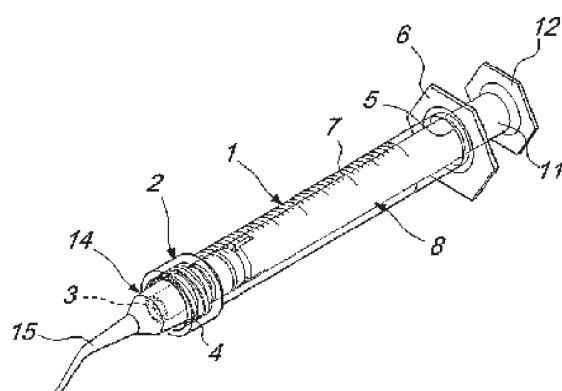
(22) Anmelddatum: 19.10.2004

(24) Erteilungsdatum: 15.05.2006

(45) Veröffentlichung
der Anmeldung: 15.05.2006

(54) **Besondere Methode und Bausatz zur Anwendung von Kosmetikprodukten.**

(57) Es wird eine Methode zur externen Anwendung eines jeglichen Kosmetikprodukts durch die Verwendung einer Spritze und einer Hohlnadel für Außenanwendungen mit stumpfer Spitze beschrieben. Die Kombination von dieser Nadelart mit Spritzen und irgendeinem Kosmetikprodukt ermöglicht eine präzise und sorgfältige und demnach vorteilhafte Anwendung des Kosmetikprodukts sowohl hinsichtlich der Menge des angewandten Produkts als auch der Anwendungsstelle. Ein weiterer Aspekt der Erfahrung besteht aus dem Bausatz, der zumindest eine Spritze und zumindest eine Hohlnadel gemeinsam mit zumindest einem anzuwendenden Kosmetikprodukt besteht, wobei das Kosmetikprodukt entweder bereits in der Spritze oder als Alternative in einem eigenen Behälter enthalten sein kann, der gemeinsam mit dem Bausatz geliefert wird.





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Confederaziun svizra

Eidgenössisches Institut für Geistiges Eigentum
Institut Fédéral de la Propriété Intellectuelle
Istituto Federale della Proprietà Intellettuale
Institut Federal da Proprietad Intellectuala

Urkunde · Certificat · Certificato

über die Erteilung des Erfindungspatentes Nr.
de délivrance du brevet d'invention n°
di rilascio del brevetto d'invenzione no.

711 466

Nachdem die gesetzlichen Bedingungen erfüllt worden sind, ist für die in der beigefügten Patentschrift dargelegte Erfindung ein Patent mit der oben angegebenen Nummer erteilt worden.
Auf der ersten Seite der Patentschrift sind alle wesentlichen Angaben enthalten, die das vorliegende Erfindungspatent betreffen.
Erfindungspatente werden ohne Gewährleistung des Bundes erteilt. Massgeblich ist der Eintrag im Patentregister.

Bern, Datum der Patenterteilung

Les conditions requises par la loi étant remplies, un brevet portant le numéro susmentionné a été délivré pour l'invention décrite dans le fascicule ci-joint.
Sur la première page du fascicule du brevet figurent toutes les indications essentielles relatives au brevet d'invention considéré.
Les brevets d'invention sont délivrés sans garantie de l'Etat. Seul l'enregistrement dans le registre des brevets fait foi.

Berne, date de la délivrance du brevet

Essendo soddisfatte le condizioni prescritte dalla legge, è stato rilasciato un brevetto contrassegnato dal numero sopraindicato per l'invenzione documentata nel fascicolo allegato.
Sulla prima pagina del fascicolo del brevetto figurano tutte le indicazioni essenziali concernenti il brevetto in questione.
I brevetti d'invenzione sono rilasciati senza garanzia dello Stato. Determinante è l'iscrizione nel registro dei brevetti.

Berna, data del rilascio del brevetto

Leiter Patente / chef des Brevets / capo dei Brevetti

Dr. Alban Fischer





SCHWEIZERISCHE EIDGENOSSENSCHAFT
EIDGENÖSSISCHES INSTITUT FÜR GEISTIGES EIGENTUM

(11) CH 711 466 B1

(51) Int. Cl.: A61K 8/34 (2006.01)

Erfindungspatent für die Schweiz und Liechtenstein

Schweizerisch-liechtensteinischer Patentschutzvertrag vom 22. Dezember 1978

(12) PATENTSCHRIFT

(21) Anmeldenummer: 01675/15

(73) Inhaber:
Labo Cosprophar AG, St. Jakobs-Strasse 17
4052 Basel (CH)

(22) Anmeldedatum: 17.11.2015

(72) Erfinder:
Die Erfinder haben auf Nennung verzichtet

(24) Patent erteilt: 28.02.2017

(74) Vertreter:
Schmauder & Partner AG, Patent- und Markenanwälte
VSP, Zwängiweg 7
8038 Zürich (CH)

(45) Patentschrift veröffentlicht: 28.02.2017

(54) Dermokosmetische Zusammensetzung zur topischen Anwendung mit penetrationsverstärkenden Eigenschaften und Verfahren zu deren Herstellung.

(57) Eine dermokosmetische Zusammensetzung zur topischen Anwendung und mit penetrationsverstärkenden Eigenschaften umfasst ein penetrationsverstärkendes System, welches Decylenglykol, Pentyleneglykol und Caprylylglykol enthält, sowie eine oder mehrere dermokosmetisch aktive Substanzen und einen kosmetisch annehmbaren Träger. Eine Technologie bzw. ein transdermales Verfahren zur Penetration von dermokosmetischen Substanzen durch die Haut umfasst das Auswählen von kosmetisch aktiven Substanzen mit einem Molekulargewicht von ≤ 2000 Dalton; das Testen der kosmetisch aktiven Substanzen mit einem MG ≤ 2000 Dalton mittels einer Franz-Diffusionszelle und das Auswählen der kosmetisch aktiven Substanzen mit einem Absorptionsgradienten in die Dermis von weniger als 20% in 24 Stunden; das Zufügen eines vorzugsweise Decylenglykol, Pentyleneglykol und Caprylylglykol umfassenden penetrationsverstärkenden Systems zu den ausgewählten kosmetisch aktiven Substanzen unter Bildung eines Gemisches; und das Zufügen eines kosmetisch annehmbaren Trägers zum besagten Gemisch.

FILLERINA 12HA DENSIFYING - FILLER

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6. Points of Sale



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Fillerina Display at the Pharmacy



Points of Sale

Technical data for pharmacists only. All reproduction on medias, Web included, is forbidden.



LCX, Hong Kong



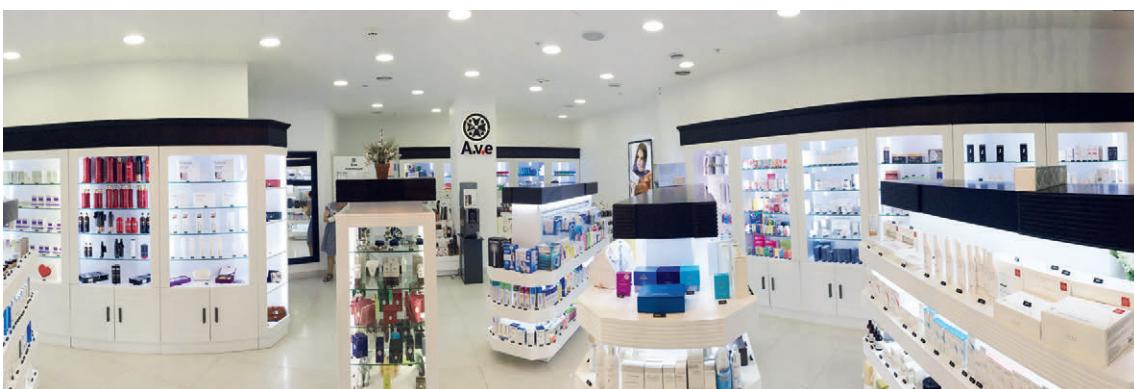
Lord & Taylor, New York



Counter at Pondok Indah Mall, Jakarta



Beautiqa Store, Manila



Ave Pharmacy, Moscow



SWISS
PATENT
CH 705 713

L A B O
LABO COSPROPHAR

FILLERINA 12HA DENSIFYING - FILLER

Points of Sale



Ave Pharmacy, Moscow



Sensiblu Pharmacy, Bucharest



BinSina Pharmacy, Dubai



Ave Pharmacy, Moscow



Kanaki Fotini Pharmacy, Athens



Zaytouna Pharmacy, Beirut

LABO
LABO COSPROPHAR


SWISS
PATENT
CH 705 713

Points of Sale



John Bell & Croyden, London



Apotheek Libra, Houthalen



Kanaki Fotini Pharmacy, Athens



Drogaria Iguatemi, São Paulo



The SM Store at Aura Premier, Manila



Kohl's, New York

8. P.O.S. Materials



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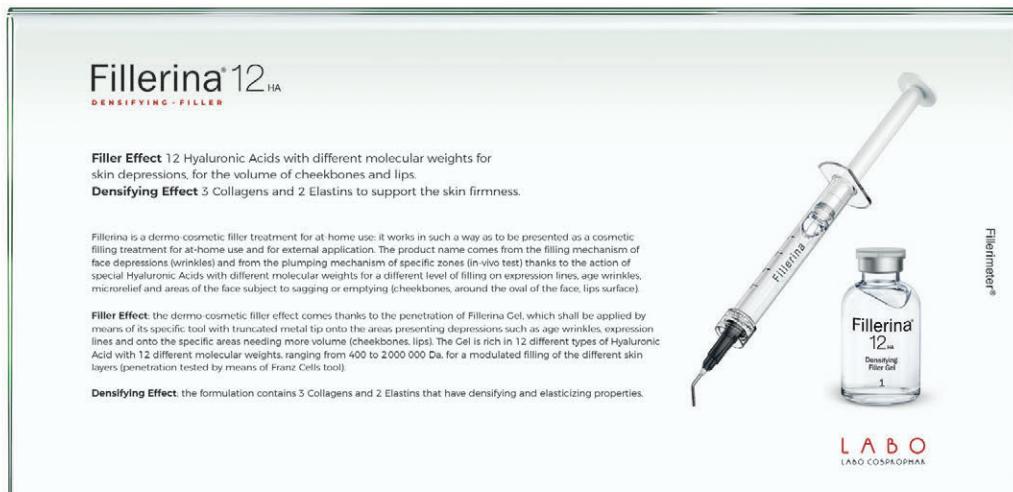
FILLERINA 12_{HA} DENSIFYING - FILLER

P.O.S. Materials

Fillerimeter

The Fillerimeter shows a general description of the cutaneous and aesthetic aspects for which the single dosages of Fillerina (3 - 4 - 5) have been formulated.

The description is completed by two different photographic examples of women faces for each grade to allow greater ease of advice and choice of the most suitable dosage for each condition.



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FILLERINA 12HA DENSIFYING - FILLER

P.O.S. Materials

Window Card

Size: 162 x 130 cm

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Consumer Leaflet



P.O.S. Materials

Free Samples Pre-Filled Applicators

Fillerina 12 Densifying-Filler pre-filled applicato s (1 ml).

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Fillerina 12 Densifying-Filler
free pre-filled applicator,
base formulation



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Sample Sachets

Fillerina 12 Densifying-Filler daily treatments are available in free samples sachets:

- Day Cream: 3-ml sachet
- Eye Contour Cream: 1-ml sachet
- Lip Contour Cream: 1-ml sachet

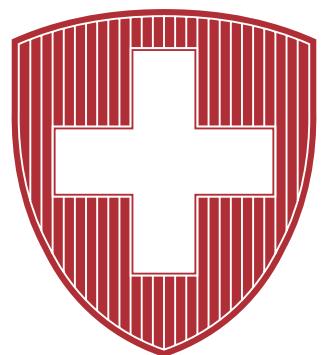
Fillerina 12 Densifying-Filler Gel is also available in a 2-ml sample sachet.

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