Technical Information

HyaCare® Filler CL

The topical wrinkle smoother

Intended use

Active for skin care

Benefits at a glance

- Is a topically applied dermal filler
- Contains unique, cross-linked hyaluronic acid particles & is preservative free
- Has super-absorbing properties
- Has improved stability to enzymatic degradation
- Shows improved and longer lasting moisturization
- Recommended usage level: 0.5 – 5%

INCI (PCPC name)

Aqua; Ethylhexyl Stearate; Sodium Hyaluronate Crosspolymer; Polyglyceryl-4 Diisostearate/Polyhydroxystearate/ Sebacate; Sodium Isostearate

Chemical and physical properties (not part of specifications)	
Form	white to off-white W/O emulsion
Active matter	approx. 4% cross-linked Hyaluronic Acid spheres

Cross-linked Hyaluronic Acid is well known for its use as a dermal filler. Dermatologists inject it directly into the skin to physically fill up wrinkles from within. Many consumers do not like such an invasive and expensive approach. Therefore, many consumers are looking for cosmetics alternatives based on formulations which mimic the immediate wrinkle reducing properties of dermal fillers. HyaCare® Filler CL is a W/O emulsion containing small particles of cross-linked Hyaluronic Acid. The average particle size is approx. 700 nm. Due to the cross-linking of Hyaluronic Acid HyaCare® Filler CL has superior water binding properties comparable to that of a super-absorbing polymer.

Properties

- **Super-absorbing properties of HyaCare® Filler CL**

The super-absorbing properties of HyaCare® Filler CL can be demonstrated by adding 1.5 volumes water to 1 volume of the emulsion. The water is completely absorbed accompanied with an increased viscosity and an increase in the particle size.

In contrast, the same W/O emulsion containing noncross-linked Hyaluronic Acid is not able to take up water.

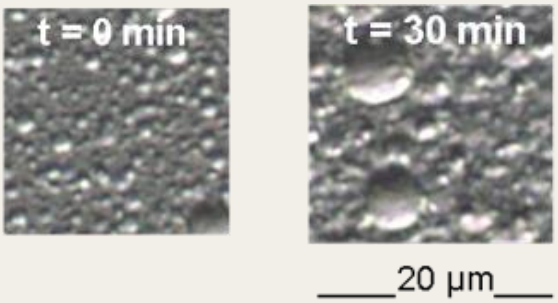

Fig. 1: Particle size of HyaCare® Filler CL before (t = 0 min) and after the addition of water (t = 30 min)

- ***In vitro* stability of HyaCare® Filler CL against enzymatic degradation**

Method: To investigate the stability of HyaCare® Filler CL against degradation by mammalian hyaluronidase (a HA degrading enzyme), cross-linked Hyaluronic Acid was isolated from HyaCare® Filler CL by ethanolic precipitation, repeatedly washed with ethanol and finally freeze-dried. 5 mg/ml of such isolated cross-linked Hyaluronic Acid were incubated in a phosphate buffer with 0.41 mg/ml of a mammalian hyaluronidase from bovine testes (Type I-S, 400 – 1 000 U/mg, Sigma-Aldrich). Linear Hyaluronic Acid at the same concentration was used as control. Enzymatic degradation was quantified photometrically by determination of liberated reducing sugars.

Results: Whereas linear Hyaluronic Acid was prone to degradation by the enzyme, no significant degradation of cross-linked Hyaluronic Acid occurred. Cross-linking thus offers the benefit of superior stability against enzymatic degradation. This supports the longer lasting moisturization capability of HyaCare® Filler CL.

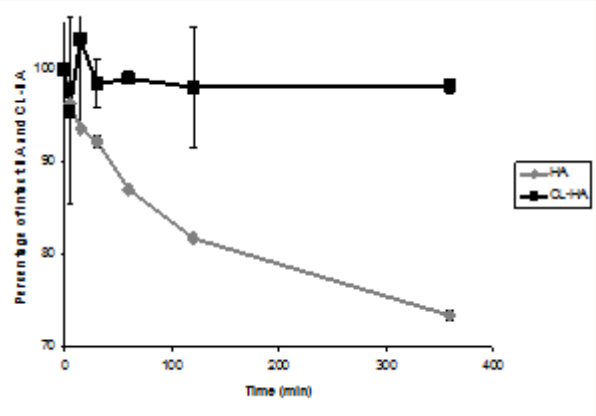

Fig. 2: Stability of HyaCare® Filler CL against enzymatic degradation compared to non-cross linked Hyaluronic Acid (HA)

- ***In vitro* evaluation of protection effect of HyaCare® Filler CL from drying out**

To investigate the hydration effect of HyaCare® Filler CL, artificially dried skin models were analyzed with and without application of HyaCare® Filler CL.

Method: SkinEthic skin models were topically treated either with a formulation containing 0.1% HyaCare® Filler CL or a vehicle formulation for 1 h at 37 °C, 5% CO2. In order to mimic dry skin conditions, the skin models were afterwards incubated under a sterile bench without plate cover for 8 h.

At the end of the incubation time, cell viability was analyzed by a MTT-assay, and the physiological condition of the skin models was evaluated by histological images after Hematoxylin and Eosin staining.

Results: Drying of vehicle-treated skin models under the laminar flow led to a significant decrease of cell viability by 40% compared to the control that was protected with the plate cover. When skin models were treated with HyaCare® Filler CL prior to the drying-step, this effect was dramatically reduced. The cell viability in this case after 8 h of drying was only slightly reduced by 10% compared to the control skin models. Monitoring of cell viability over 8 hrs revealed that HyaCare® Filler CL even provides a superior long term effect compared to the vehicle.

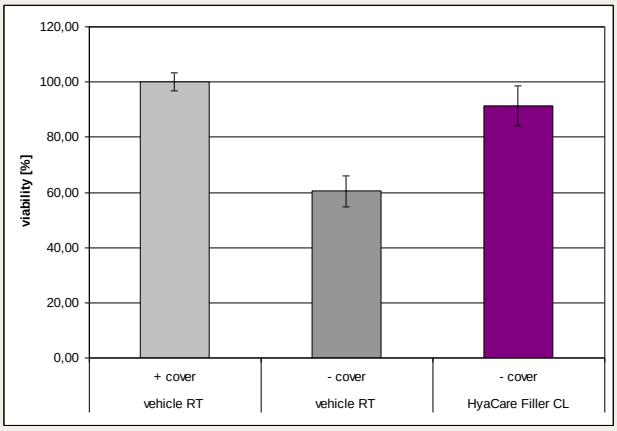

Fig. 3: Cell viability (MTT-assay) after drying of the skin models (n=3) after 8 h of cultivation.

The histology images (figure 4) show that drying of skin models has an effect on the structure of the whole epidermis. In a nutshell, Hematoxylin stains cell nuclei in blue whereas Eosin stains proteins in red. Image a) shows a less compact composition of the stratum corneum (SC) and a detachment of the SC from the underlying viable epidermis layer due to drying out of the skin models. In case of treatment with HyaCare® Filler CL prior to the drying step, this effect can not be seen (image b). The SC and the underlying layers of the epidermis look very tight and better structured. This goes in line with the higher cell viability compared to the vehicle

treatment that was observed in the MTT assay (figure 3).

a: vehicle **b**: HyaCare® Filler CL

Fig. 4: Histology images of Hematoxylin and Eosin stained SkinEthic skin models after 8 h under different cultivation conditions.

The results of this study show that HyaCare® Filler CL has superior water binding capacity, leading to superior moisturization properties and imparting long-term protection from drying out on re constructed epidermis models.

- ***Ex vivo* evaluation of HyaCare® Filler CL on skin**

The topical dermal filler properties of HyaCare® Filler CL can be demonstrated by applying fluorescently labelled material on pig skin. The labelling is achieved by adding Fluorescein to the Hyaluronic acid emulsion prior to cross-linking, hereafter the dye is covalently incorporated.

Labelled material was spread equally on *ex vivo* pig skin and the localization of the cross-linked Hyaluronic Acid spheres was inspected by fluorescent microscopy. It was observed that HyaCare® Filler CL particles accumulate in skin structures like fine lines and wrinkles.

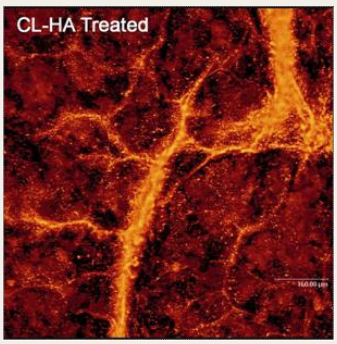

Fig. 5: Fluorescently labelled HyaCare® Filler CL on pig skin

This *ex vivo* result could be confirmed by *in vivo* measurement using PRIMOS Pico, a contactless method of measuring wrinkles.

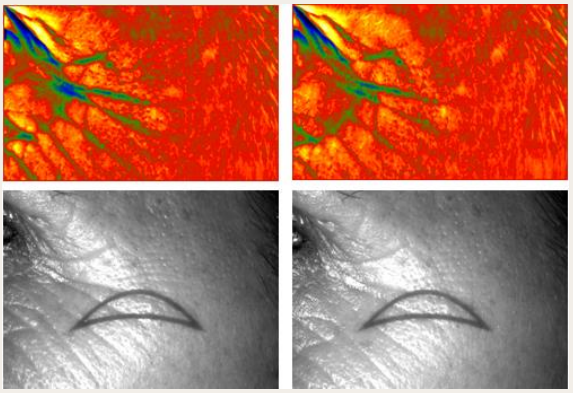

Fig. 6: PRIMOS Pico photos at start (left column) and 1 h after application (right column)

- ***In vivo* evaluation of HyaCare® Filler CL**

For this study 16 volunteers were recruited. On the inner forearm of the panellists 4 test fields (4 cm^2) were marked. On these fields the two test formulations were applied. As test formulations O/W creams containing 0.1% HyaCare® and 2.5% HyaCare® Filler CL, respectively were used. Skin moisturization and the skin surface were evaluated before the application and 2 h after the application.

Before each measurement the panellists acclimatized for at least 15 min at 21 – 22 °C and 55% relative humidity.

Skin moisturization was measured using a Corneometer. For the evaluation of the skin surface a special camera (Visioscan VC 98, Courage & Khazaka) was used. This camera possesses a black/white video sensor and a ring-shaped UV light source. The picture taken with this camera is converted into a digital signal with 256 grey levels. Via the grey level distribution the software calculates a volume parameter which describes the volume which is necessary to fill the wrinkles. Skin surfaces with more wrinkles and wrinkles which are deeper will have a higher volume parameter.

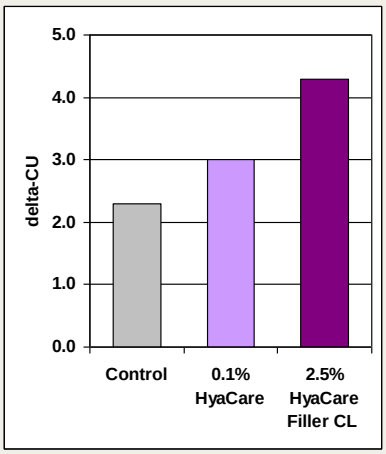

Fig. 7: Increase of Corneometer Units 2h after application

HyaCare® improved skin moisturization, but the results clearly show the superior moisturizing properties of HyaCare® Filler CL.

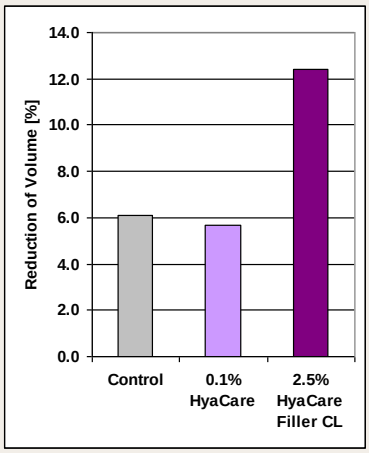

Fig. 8: Reduction of skin volume after the application of the test formulation

Two hours after application the formulation containing HyaCare® Filler CL led to a strong reduction of the skin volume. A reduction of the skin volume means that the number and depth of wrinkles was reduced. This observation can be explained by the accumulation of HyaCare® Filler CL particles in fine lines shown in Fig. 5.

- ***In vivo* evaluation "long" lasting wrinkle filling with HyaCare® Filler CL**

Beside the short term effect the "lasting" effect of wrinkle reduction with HyaCare® Filler CL was analyzed. The wrinkle reducing properties of HyaCare® Filler CL were examined depend on different concentration levels.

For this study 11 volunteers were recruited. In summary 18 test fields (5 cm^2) per formulation were analyzed. As test formulations O/W creams containing 1.0%, 2.0% and 5.0% HyaCare® Filler CL were applied on the inner forearm. Skin surface and roughness parameters were evaluated with the Visioscan VC 98 camera before the application, 1 h and 6 h after application.

Before each measurement the panelists acclimatized for at least 15 min at 21 – 22 °C and 45–50% relative humidity.

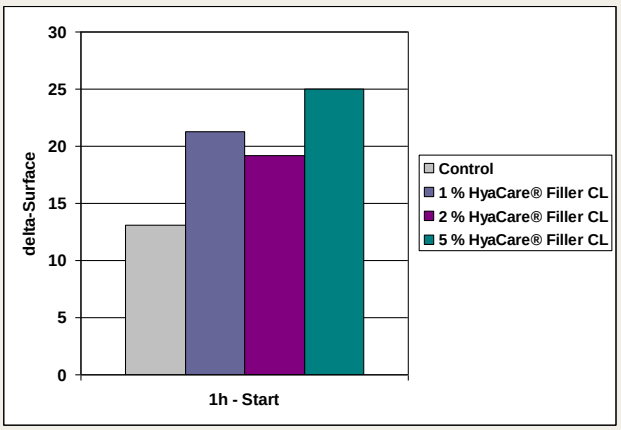

Fig. 9: Improvement of skin surface 1 h after application

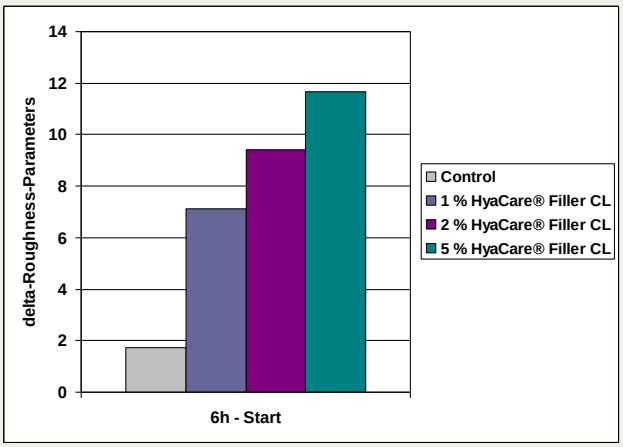

Fig. 10: Improvement of skin roughness (R1–R5) 6 h after application

A significant improvement of skin surface and therefore, a wrinkle reduction after 1 h can already be achieved with 1% HyaCare® Filler CL. This positive effect on skin roughness (reduction of wrinkle depth) lasts for at least 6 h.

To further demonstrate the observed effects an O/W cream containing 5% HyaCare® Filler CL was applied on the face. The following pictures show furrows before and after the application (Figures 11, 12).

Fig. 11: Application of an O/W cream containing 5% HyaCare® Filler CL (left side before application, right side 15 minutes after application)

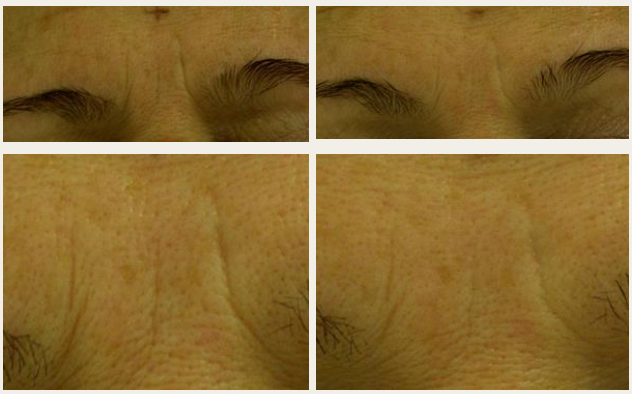

Fig. 12: Application of an O/W cream containing 5% HyaCare® Filler CL (left side before application, right side one hour after application)

HyaCare® Filler CL possesses strong moisturizing properties due to the strong water absorbing properties of the cross-linked Hyaluronic Acid. Therefore, it is able to act as topical dermal filler, quickly reducing the appearance of wrinkles after application. This makes it especially suitable for day creams, eye creams or color formulations, like make-up, foundation and lip sticks, claiming an immediate wrinkle reducing effect.

Preparation

- **Preparation of an O/W-Emulsion (Cream or Lotion):**

Normally HyaCare® Filler CL should be added to the oil phase of the emulsion. Then the emulsion is prepared as usual.

In some cases HyaCare® Filler CL might disturb the build up of the liquid crystalline structure of the O/W-emulsion. In these cases, it is recommended to add it during the cooling process at temperatures below 40 °C.

If high concentrations of HyaCare® Filler CL are used (4 – 5%), it increases the viscosity of the O/W emulsion. In this case, the viscosity can be adjusted by decreasing the concentration of consistency enhancers like fatty alcohols (TEGO® Alkanol 16, 1618 or 18) and glyceryl stearate (TEGIN® M Pellets).

- **Preparation of a W/O-Emulsion (Cream or Lotion):**

The W/O emulsion is prepared as usual. At the end of the production HyaCare® Filler CL is added.

Recommended usage concentration

0.5 – 5% of HyaCare® Filler CL

Patent position

The production and cosmetic use of HyaCare® Filler CL is subject of patent application WO2009077399 (crosslinked hyaluronic acid in emulsion).
To the best of our knowledge no third party patent right exists that prevents customers from using HyaCare® Filler CL in cosmetic formulations.

Applications

- Anti-wrinkle eye care products
- Anti-aging facial serum
- Special care for expression lines
- Skin plumping face care
- Facial sun care
- Intense moisturizing skin care
- Wrinkle reducing foundations

Packaging

5 kg package

Hazardous goods classification

Information concerning

- classification and labelling according to regulations for transport and for dangerous substances
- protective measures for storage and handling
- measures in case of accidents and fires
- toxicity and ecological effects

is given in our material safety data sheets.

Guideline formulations

Wrinkle Smoothing Eye Cream MAC 672/1/1	
Phase A	
TEGO® Care 450 (Polyglyceryl-3 Methylglucose Distearate)	3.0%
TEGIN® M Pellets (Glyceryl Stearate)	2.0%
TEGO® Alkanol 18 (Stearyl Alcohol)	2.0%
TEGOSOFT® CT (Caprylic/Capric Triglyceride)	7.5%
TEGOSOFT® DC (Decyl Cocoate)	9.5%
Avocado Oil	2.0%
Tocopheryl Acetate	0.5%
HyaCare® Filler CL	3.0%
Phase B	
Glycerin	3.0%
Water	67.5%
Phase C	
Lactic Acid (10%)	q.s.
Phase Z	
Preservative, Perfume	q.s.

Preparation:

1. Heat phase A and B to approx. 80 °C.
2. Add phase A to B while stirring.[1)]
3. Homogenize.
4. Cool down to 30 °C. Add phase C and Z below 40 °C.

[1)] Important: If phase A has to be charged into the vessel first, add phase B **without stirring**.

Dermal Filler Cream MAC 672/3/1	
Phase A	
Axol® C62 Pellets (Glyceryl Stearate Citrate)	1.5%
TEGIN® M Pellets (Glyceryl Stearate)	3.0%
TEGO® Alkanol 18 (Stearyl Alcohol)	2.0%
Stearic Acid	1.0%
TEGOSOFT® CT (Carpylic/Capric Triglyceride)	8.5%
TEGOSOFT® M (Isopropyl Myristate)	7.0%
TEGOSOFT® CR (Cetyl Ricinoleate)	2.0%
HyaCare® Filler CL	3.0%
Phase B	
Glycerin	3.0%
Water	68.0%
Phase C	
TEGO® Carbomer 134 (Carbomer)	0.2%
TEGOSOFT® CT (Caprylic/Capric Triglyceride)	0.8%
Phase D	
Sodium Hydroxide (10% in water)	q.s.
Phase Z	
Preservative, Perfume	q.s.

Preparation:

1. Heat phase A and B to approx. 80 °C.
2. Add phase A to B with stirring.[1)]
3. Homogenize.
4. Cool down to 60 °C and add phase C.
5. Homogenize again for a short time.
6. Cool down to 30 °C. Add phase D and Z below 40 °C.

[1)] Important: If phase A has to be charged into the vessel first, add phase B **without stirring.**

Dual-Action Wrinkle Serum MK 3/10-25	
Phase A	
ABIL® EM 90 (Cetyl PEG/PPG-10/1 Dimethicone)	1.5%
ABIL® EM 97 S (Bis-PEG/PPG-14/14 Dimethicone; Dimethicone)	1.0%
Cyclopentasiloxane	12.0%
TEGOSOFT® DEC (Diethylhexyl Carbonate)	3.0%
HyaCare® Filler CL	2.5%
Tocopherol	0.5%
Zinc Stearate	0.5%
Phase B	
Water	69.7%
Glycerin	4.0%
Butylene Glycol	4.0%
Sodium Chloride	0.8%
TEGO® Pep 4-17 (Tetrapeptide-21; Glycerin; Butylene Glycol; Aqua)	0.5%
Phase Z	
Preservative, Perfume	q.s.

Preparation:

1. Heat phase A to approx. 80 °C.
2. Add phase B (80 °C or room temperature) slowly while stirring.
3. Homogenize for a short time.
4. Cool with gentle stirring below 30 °C and homogenize again.

Anti-Aging Foundation DCA-5787-200	
Phase A	
ABIL® EM 180 (Cetyl PEG/PPG-10/1 Dimethicone)	3.00%
TEGOSOFT® APM (PPG3-Myristyl Ether)	5.00%
TEGOSOFT® TN (C12-15 Alkyl Benzoate)	5.00%
TEGOSOFT® DEC (Diethylhexyl Carbonate)	10.00%
Phytosphingosine	0.05%
Talc	1.60%
Titanium Dioxide (BTD-11S2, Kobo)	5.00%
Iron Oxide	1.90%
Phase B	
Water	59.55%
HyaCare® 50 (Hydrolized Hyaluronic Acid)	0.10%
TEGO® Pep 4-17 (Tetrapeptide-21; Glycerin; Butylene Glycol; Aqua)	3.00%
Propylene Glycol	2.00%
Sodium Chloride	0.80%
Phase C	
HyaCare® Filler CL	3.00%
Phase Z	
Preservative, Perfume	q.s.

Preparation:

1. Mix the ingredients of phase A and ensure the proper dispersion of the pigments.
2. Mix the ingredients of phase B.
3. Add phase B slowly to phase A while stirring.
4. Homogenize.
5. Add phase C and stir until it is homogenous.

Caring Lip Balm CC004-0007	
Phase A	
HyaCare® Filler CL (Aqua; Ethylhexyl Stearate; Sodium Hyaluronate Crosspolymer; Polyglyceryl-4 Diisostearate/Polyhydroxystearate/Sebacat e; Sodium Isostearate)	5.00%
ISOLAN® GPS (Polyglyceryl-4 Diisostearate/ Polyhydroxystearate/Sebacat e)	0.5%
Phase B	
TEGOSOFT® G 20 (Octyldodecanol)	22.60%
TEGOSOFT® CT (Caprylic/Capric Triglyceride)	18.00%
TEGOSOFT® SH (Stearyl Heptanoate)	7.70%
TEGOSOFT® MM (Myristyl Myristate)	4.40%
TEGO® Alkanol 1618 (Cetearyl Alcohol)	2.20%
Microcrystalline Wax	21.50%
Ricinus Communis (Castor) Seed Oil	10.40%
Copernicia Cerifera (Carnauba) Wax	1.30%
Butyrospermum Parkii (Shea) Butter	1.00%
Simmondsia Chinensis (Jojoba) Seed Oil	1.00%
Beeswax	0.55%
Ethylhexyl Methoxycinnamate	3.30%
Butyl Methoxydibenzoylmethane	0.55%

Preparation:

1. Heat phase B to 85 °C.
2. Add phase A into Phase B at 85 °C.
3. Mould the mixture at 85 °C.
4. Cool down the mould to -15 °C after moulding and stay for 15-35 minutes.
5. Demould and pack.

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