

HYALUOL

— INJECTABLES —

SAFE DERMAL FILLERS

BASED ON CROSSLINKED HYALURONIC ACID
FOR CONTOUR CORRECTION AND COMPLEX VOLUMIZATION



Alexa Smooth/Medium/Volume
Fillers are GMP
(Good Manufacturing Practice),
the highest standard of production
of pharmaceutical products
and medical devices, certified



Alexa Smooth/Medium/Volume
Fillers are produced
in accordance with
ISO 9001, ISO 13485



Sterile production
conditions according to
ISO 14644 STANDARD

■ HIGH PRODUCTION TECHNOLOGIES



Streptococcus zoepidemicus bacteria produce HA

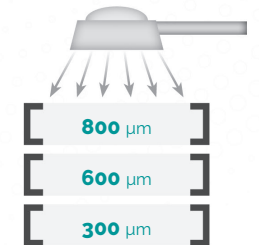
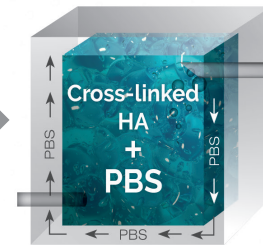
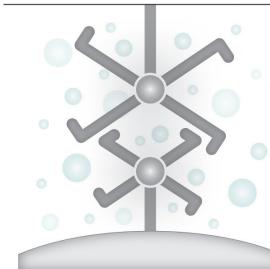
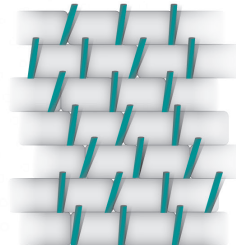
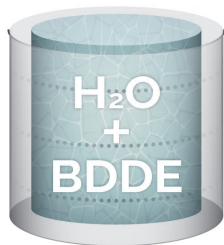
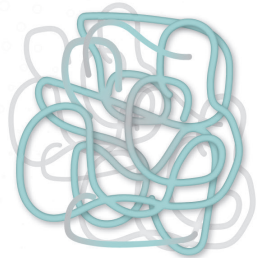
Crosslinking process

Formation of Crosslinking HA

Fragmentation of Crosslinked HA

Ultradialysis purification

Wet particle dispersion process



The native form of HA used in Alexa fillers has a biosynthetic origin with the highest degree of purification for maximum safety and predictable volumetric correction

Formation of processed HA form + H₂O + BDDE. Residual amount of **BDDE of Alexa is <1 p.p.m.**, which is two times safer than **FDA**¹ requirements and confirms its safety

99.99% of processed BDDE (butanediol diglycidyl ether) is nontoxic for skin. In this process, a stable transversed crosslinked HA formula maintains filler shape under the skin

Titanium niobium knives are used to grind filler mass. This type of knife helps prevent heavy metal particle entry into the gel to maximize filler purity

Alexa PBS filler is stabilized with a buffer system. This achieves the highest physiological stability of hydrogel with pH 7.4. Na⁺Cl⁻ and K⁺Cl⁻ ions in isotonic concentration provide minimal hygroscopicity, which reduces the risk of edema

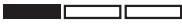



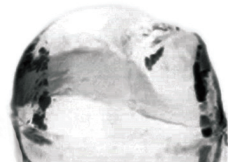

Wet scattering of hydrogel particles ensures particle size accuracy within each batch. Uniquely chosen particle fraction sizes for each product in the Alexa line improve successful fillers applications for different areas of skin at different depths

1. KOENRAAD DE BOULLE, MD, RICHARD GLOGAU, MD et al., A Review of the Metabolism of 1,4-Butanediol Diglycidyl Ether Crosslinked Hyaluronic Acid Dermal Fillers. 2013 by the American Society for Dermatologic Surgery, Inc. Published by Wiley Periodicals, Inc. ISSN: 1076-0512 Dermatol Surg 2013;1-9 DOI: 10.1111/dsu.12301.

Alexa filler line Smooth | Medium | Volume

To obtain excellent results



	Alexa Smooth 	Alexa Medium 	Alexa Volume 
HA CONCENTRATION	15 mg/ml	17,5 mg/ml	20 mg/ml
RESIDUAL QUANTITY OF BDDE*	<1 p.p.m	<1 p.p.m	<1 p.p.m
VOLUME IN A SYRINGE	1 ml	1 ml	1 ml
NEEDLES	1 * 30G	1 * 27G	2 * 27G
INDICATIONS	Fine wrinkles Improving skin quality	Lips, wrinkles of medium depth	Deep creases and wrinkles + areas of volume deficit
TECHNOLOGIES	Cannula	Needle, cannula	Needle, cannula
GEL TEXTURE			

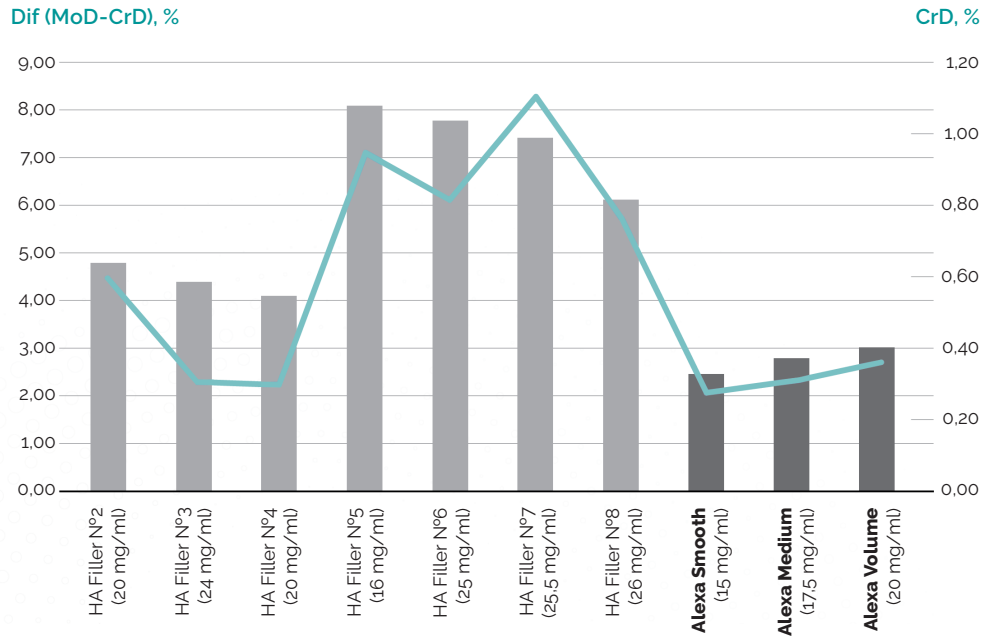
Why Alexa

Alexa filler line		
Residual BDDE is <1 p.p.m., which is half the FDA limit (0.0002 parts per million) Formation of reacted BDDE: 99.999%	Fully biodegradable	Low risk of side effects (fibrosis)
PBS buffer system (Phosphate + NaCl + KCl)	<ul style="list-style-type: none"> • 1:1 volumization • Quick tissue adaptation • The physiological stability of the hydrogel is within the range of pH 7.2-7.4 • Osmolarity of Alexa fillers is close to physiological values (=300 mOsmol/kg) 	<ul style="list-style-type: none"> • Predictable result • No edema syndrome (no delayed over-correction) • Short rehabilitation period • Less pain and unpleasant sensation upon injection • No inflammatory reaction at the injection site
HA manufactured by Shiseido (Japan)	<ul style="list-style-type: none"> • Longterm global experience in cosmetics manufacturing (since 1872) • Studies acknowledged by FDA and EDQM 	Guaranteed safety and efficacy of Alexa fillers
Optimal particle size of the fillers: Alexa Smooth — 300 µm, Alexa Medium — 600 µm, Alexa Volume — 800 µm	Uniquely selected particle fraction sizes for each filler	Corrects all esthetic facial problems at various skin depths according to product indication

* Institute Hyalual production technology has allowed to create a cross-linked filler with the lowest residual BDDE content, which is below FDA requirements (KOENRAAD DE BOULLE, MD, RICHARD GLOGAU, MD et al., A Review of the Metabolism of 1,4-Butanediol Diglycidyl)

Alexa Smooth/Medium/Volume

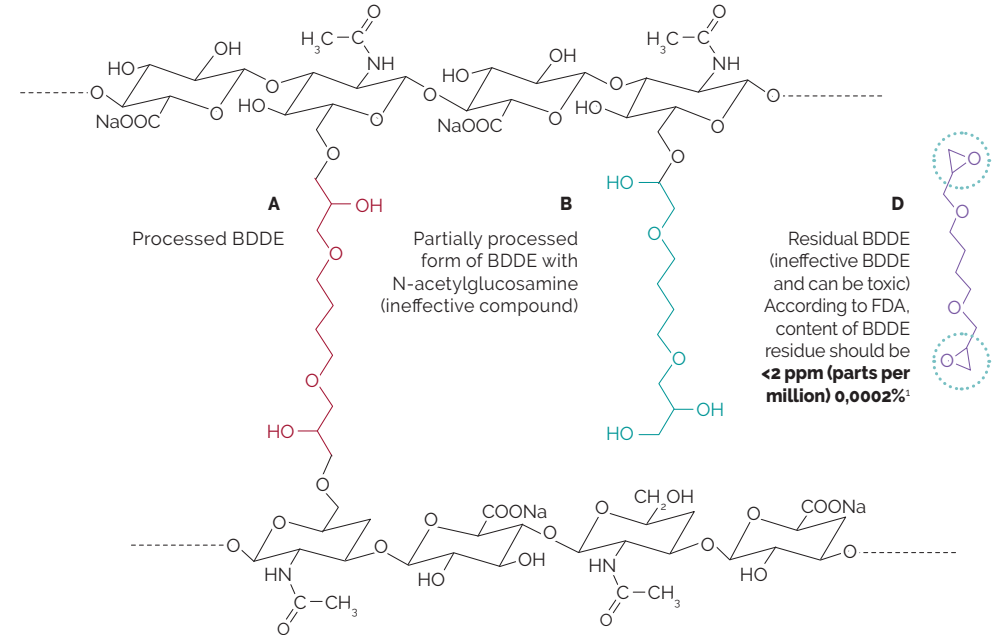
Alexa fillers do not cause an inflammatory response and they have a short recovery period with the least amount of residual BDDE



Most dermal HA fillers contain a high percentage (more than 0.4%) of partially processed BDDE with HA (pendant), which may cause longer rehabilitation period, soreness, and increased swelling²

Alexa Smooth/Medium/Volume

Alexa fillers contain the smallest residual amount of BDDE and provide a high safety profile



BDDE

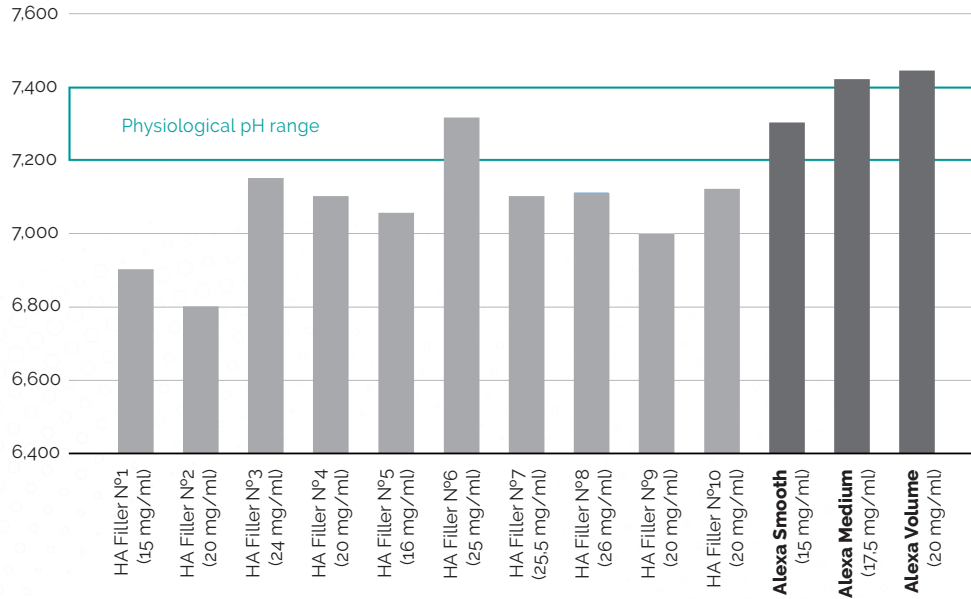
BDDE — (1,4-butanediol diglycidyl ether): The hydrolyzed (processed) form of BDDE is not toxic or mutagenic and can be used in a higher concentration than other dermal filler manufacturers. Partially-processed BDDE form or residual BDDE can be ineffective and have toxic effects. (J.X. Roca-Martinez)¹

¹ Internal data 2017. Comparison was made with available officially registered dermal HA fillers with certificate of conformity. Analysis was carried out by LC/MS Q-TOF method. Reference method: <https://www.sciencedirect.com/science/article/pii/S01444861712008405>, <https://doi.org/10.1016/j.carbpol.2012.08.066>.
² Reference values do not exist. Alexa smooth/medium/volume is developed to minimize inefficient use of butanediol diglycidyl ether

¹ KOENRAAD DE BOULLE, MD, RICHARD GLOGAU, MD et al... A Review of the Metabolism of 1,4-Butanediol Diglycidyl Ether Crosslinked Hyaluronic Acid Dermal Fillers. 2013 by the American Society for Dermatologic Surgery, Inc. Published by Wiley Periodicals, Inc. ISSN: 1076-0512 Dermatol Surg 2013;1-9 DOI: 10.1111/dsu.12301.

LABORATORY CONFIRMATION OF QUALITY¹

Alexa Smooth | Medium | Volume fillers have a physiological pH of 7.2 to 7.4, which confirms its safety



¹ Hyaluronic fillers with CE Mark were used in laboratory analysis

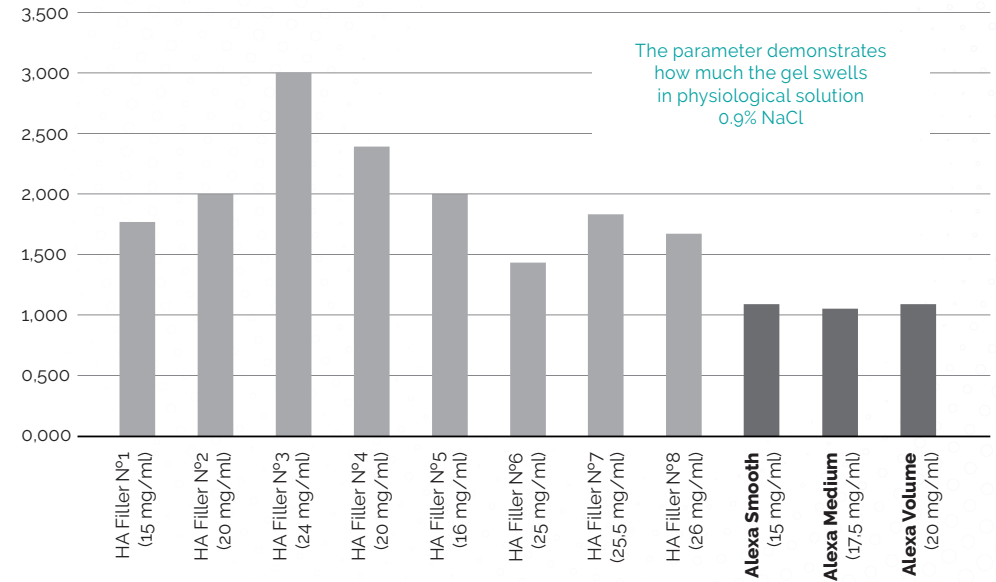
pH

pH indicates filler's overall physiology in relation to tissues

¹ Internal data 2017, pH determination was carried out by Ph method. Eur 2.2.3.

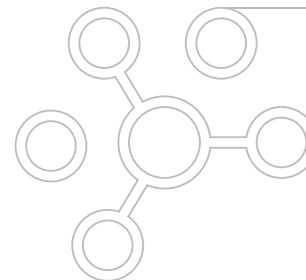
LABORATORY CONFIRMATION OF QUALITY¹

Alexa Smooth/Medium/Volume shows liquid cumulation in relation to injected gel with 1:1 ratio, that confirms net volumizing effect without accumulation of excess fluid



The parameter demonstrates how much the gel swells in physiological solution 0.9% NaCl

¹ Hyaluronic fillers with CE Mark were used in laboratory analysis

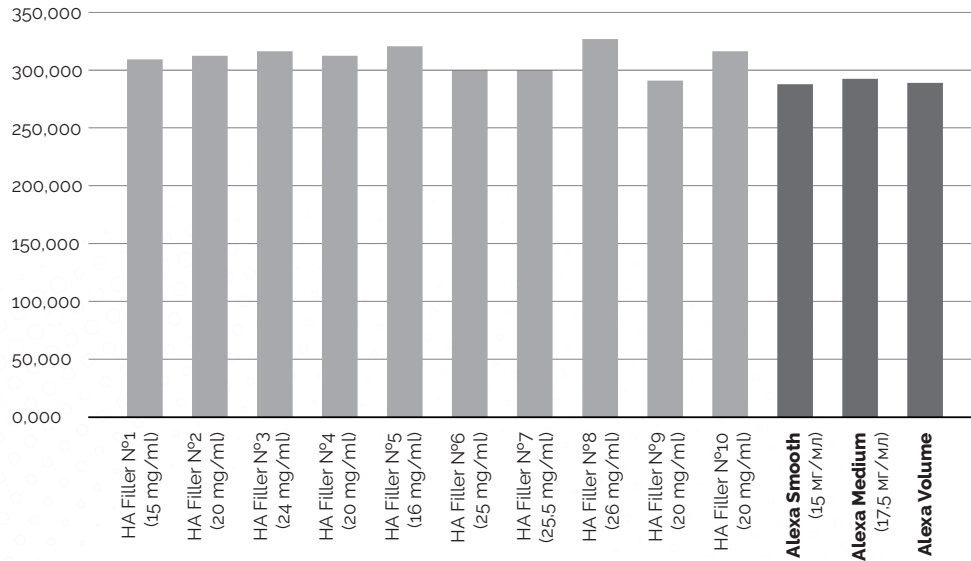


Most of the comparison fillers achieve volume due to HA molecule hygroscopicity. After several weeks, the volumetric effect becomes less pronounced due to a decreased binding effect of crosslinked HA and water in the intercellular matrix

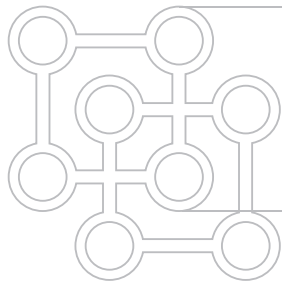
¹ Internal data 2017, pH determination was carried out by Ph method. Eur 2.2.3.

LABORATORY CONFIRMATION OF QUALITY¹

Alexa Smooth | Medium | Volume | osmolality is close to physiological values



¹ Hyaluronic fillers with CE Mark were used in laboratory analysis



Osmolality is the reading of salt and active substance concentration within a solution. The parameter is related to the swelling factor and pH. The physiological norm of an isotonic solution is 300 mOsmol per kg. The higher the indication, the higher the risk of swelling after volumetric correction

¹ Internal data 2017. pH determination was carried out by Ph method. Eur 2.2.3.

COMPARISON OF HA AND MODIFIED FORM CONTENTS IN DERMAL FILLERS¹

Alexa fillers containing more than 90% pure hyaluronic acid and the minimum fraction of inefficient BDDE

COMPARED FILLERS	Modification degree			Native HA, %
	Dif (MoD-CrD), %	CrD, %	MoD, %	
HA Filler N°1 (15 mg/ml)	4,84	0,72	0,72	92,15
HA Filler N°2 (20 mg/ml)	4,73	0,59	0,59	92,56
HA Filler N°3 (24 mg/ml)	4,31	0,31	0,31	94,18
HA Filler N°4 (20 mg/ml)	4,07	0,30	0,30	95,00
HA Filler N°5 (16 mg/ml)	8,04	0,94	0,94	89,72
HA Filler N°6 (25 mg/ml)	7,75	0,81	0,81	88,48
HA Filler N°7 (25,5 mg/ml)	7,37	1,09	1,09	87,94
HA Filler N°8 (26 mg/ml)	6,09	0,76	0,76	89,77
Alexa Smooth	2,44	0,28	0,28	94,51
Alexa Medium	2,78	0,31	0,31	93,68
Alexa Volume	3,01	0,36	0,36	92,53

¹ Hyaluronic fillers with CE Mark were used in laboratory analysis

- ***Dif (MoD-CrD), %** – residue of ineffective cross-linking, which can cause adverse reactions after administration to skin
- **CrD, %** – effectively cross-linked HA with BDDE that ensures volumetric correction result
- **MoD, %** – total volume of modified HA (CrD + partially processed HA)
- **Native HA, %** – native fraction of HA in a prefilled syringe

¹ Internal data 2017. Comparison was made with available officially registered dermal HA fillers with certificate of conformity. Analysis was carried out by LC/MS-Q-TOF method. Reference method: <https://www.sciencedirect.com/science/article/pii/S0144861712008405> <https://doi.org/10.1016/j.carbpol.2012.08.066>.

Alexa Smooth

Filler for raising superficial wrinkles and improving skin quality

Science

Minimal risk of edema. Formulated with an isotonic concentration of Na⁺Cl⁻ and K⁺Cl⁻ ions for easy product distribution after injection

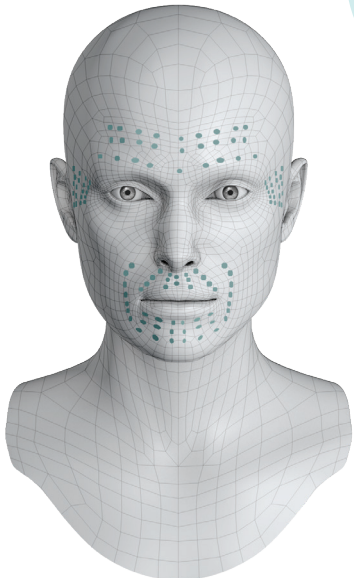
Maximum particle size = 300 µm
15 mg/ml

Results

Effective filling of superficial wrinkles:

- forehead and eyebrows
- temporal zone
- tear trough
- neck and hands

Eliminates purse-string wrinkles



Natalia, 34 years
Area treated: nasolabial folds
Product used: Alexa Smooth



Anna, 46 years
Area treated: vertical lip lines
Product used: Alexa Smooth

Results may vary. Unretouched photos were taken before treatment and 7 days after

Alexa Medium

Filler for correcting medium-depth wrinkles and lip augmentation

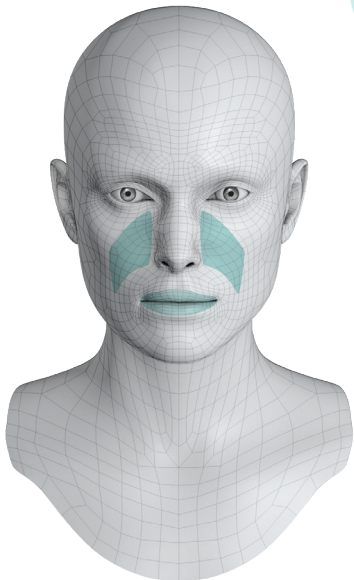
Science

Minimal risk of swelling at injection site: fluid cumulation/administered drug volume ratio is 1:1

Maximum particle size - 600 µm
17.5 mg/ml

Results

- Corrects tear trough and nasolabial folds
- Fills and contours lips
- Reduces snogged lips ("Kissed Lips" effect)



Lyudmila, 33 years
Area treated: smile lines
Product used: Alexa Medium



Yana, 32 years
Area treated: lips
Product used: Alexa Medium

Results may vary. Unretouched photos were taken before treatment and 7 days after

Alexa Volume

Filler for deep wrinkles and volumetric correction of facial contours

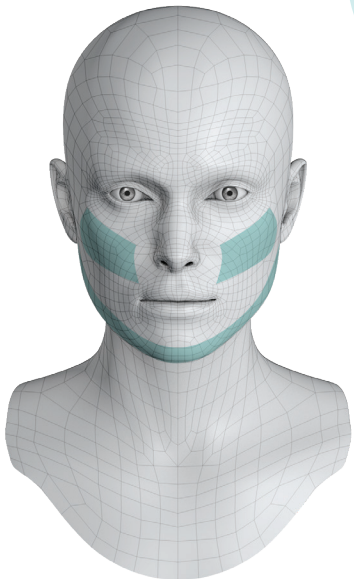
Science

Titanium-niobium knives grind filler mass for maximum purity of filler. This helps prevent heavy metal particles from entering the gel

Maximum particle size = 800 µm
20 mg/ml

Results

- Corrects facial volume and contours
- Fills deep wrinkles
- Chin remodeling



Elena, 45 years

Areas treated: cheekbones, jaw line, lips, philtrum ridge, chin
Products used: Alexa Medium, Alexa Volume



Irina, 34 years

Areas treated: cheekbones, tear trough, nasolabial folds, lips, chin
Products used: Alexa Medium, Alexa Volume

Results may vary. Unretouched photos were taken before treatment and 7 days after

HYALUAL

— INJECTABLES —

Information for medical and pharmaceutical professionals.

For distribution at medical seminars, conferences. You can find complete product information and possible side effects in the instruction for medical use.

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