CORRECTION OF LOWER EYELID BY HYALURONIC ACID (HA) FILLER

INTERNATIONAL EXPERT CONSENSUS ON THE USE OF ABOBOTULINUM TOXIN A

RESTYLANE® SKINBOOSTERS™ FOR IMPROVEMENT OF THE SKIN QUALITY RESULTS OF A CONSENSUS MEETING
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BEST DERMAL FILLER

WINNER OF THE ANTI-AGEING & BEAUTY TROPHY 2017

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What we need is details and overview

Knowledge and skills are necessary to perform good clinical medicine. In aesthetic medicine, however, the details become very important to achieve satisfying results. In the present issue of COSMETIC MEDICINE INTERNATIONAL we focus on details in treatment with botulinum toxin A and filler injections. These are the most frequently used techniques in facial rejuvenation. Because they look so simple, guidelines and workshops are important to transfer the knowledge of experts in the hands of trained physicians. We all know that lay persons try to use these tools as well. This can end up in disastrous situations for the patients and undermine trust in aesthetic medicine in general.

In the present issue international experts in this field report about their experience and illustrate their techniques in detail for various aesthetic indications such as eyelid corrections, gummy smile or full face treatment to name just a few.

We proudly present the International Expert Consensus on the use of Abobotulinum Toxin A for facial rejuvenation and primary hyperhidrosis. Under the leadership of Professor Alessio Redaelli (Milan, Italy) experts from different medical specialties and from Russian Federation, United Kingdom, Italy, Germany, Israel, Belarus, and Ukraine developed these scientifically grounded recommendations for a safe and effective use of this particular botulinum toxin A.

A German expert panel under the leadership of Professor Martina Kerscher (Hamburg) prepared a consensus report on the use of skin boosters to stimulate skin rejuvenation without sculpturing for face, hands, décolletage and to improve skin hydration by these hyaluronic acid-based products.

The present and even more the future is combination treatment. Dr. Michael Weidmann (Augsburg, Germany) presents impressive results that have been obtained by a synergistic approach with minimal invasive procedures.

Last but not least the 2017 Filler Guide is presented by Douglas Grosse, who has done a tremendous work to collect all these data and details to gain a representative overview on the ever enlarging field of soft tissue filler products. Make your own choice!

With kind regards,

Prof. Dr. Uwe Wollina, Dresden
Therapy Focus

Martina Kerscher, Heike Buntrock, Martina Hund et al.
Restylane® Skinboosters™ for improvement of the skin quality
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Synergistic combination therapies are highlighted in 2017!

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Calendar
Correction of lower eyelid by hyaluronic acid (HA) filler, depending on anatomic features

Anna Reznik

**KEY WORDS:**
Periorbital ageing, facial rejuvenation, hyaluronic acid, fillers, danger zones.

**SUMMARY:**
Periorbital rejuvenation is important for facial aesthetics. According to the type of anatomical ageing-related changes different techniques of hyaluronic acid-based filler placement are presented for rejuvenation. In addition, the choice of filler product is crucial for optimal outcome. The knowledge of danger zones for filler placement increases safety for patients.

**INTRODUCTION**
Traditionally, a major method of a rejuvenation of the periorbital area is surgical blepharoplasty. But its frequently limited efficiency in the long-term prospect, and the increasing interest in low-invasive procedures create injection blepharoplasty as an important method of correction of a palpebromalar groove and tear trough, an injection camouflage of prominent orbital fat of a lower eyelid.

The delayed adverse effects of correction of the tear trough and injection camouflage of prominent orbital fat of a lower eyelid are important. They include the accumulation of hyaluronic acid (HA)-filler out of tear trough, enlargement of hernia of a lower eyelid, puffiness of a periorbital zone, short and insufficient effect of correction [4]. All this can develop several months after the procedure.

We would like to consider options of injection correction of a lower eyelid by means of HA-filler depending on anatomic features of the patient, and specifically expression of prominent orbital fat of a lower eyelid to decrease the possibility of emergence of these adverse effects [1, 5, 6]. We suggest our clinical classification of aging changes in lower eyelid area for convenience correction. We mark out 3 types of a zone of a lower eyelid (Fig. 1) [5, 6].

The first type is characterized by loss of volume in lower eyelid. This type is most common in young patients or patients after surgical blepharoplasty [2, 5]. In this case we recommend to place filler in the space limited from above (ranial) by bony orbital margin or septae, lower (caudal) – by ORL, deeply with periosteum and superficially by SMAS (Fig. 2) [1, 5, 6].

We use microboluses fan injections by sharp needle for precise injection of filler in this space (Fig. 2). Dangerous zones should be marked before an injection for the prevention of their trauma by a needle. They are: zone of angular vessels and a zone of an infraorbital neurovascular fascicle [3].

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After we mark space borders where we will enter filler. It is a projection of edge of an orbit and eyelid-cheek junction (ORL projection). We do a puncture of a skin 1–2 mm higher than eyelid-cheek junction, we enter a needle perpendicular to a surface of a skin and we move a needle till periosteum. Then we turn a needle almost parallel to periosteum and we enter all length under the SMAS [2]. We inject filler into space limited by...
Luminera Derm, offers you a complete line of injectable beauty solutions. All of them developed and manufactured in the highest standards for maximum safety and efficiency.
The second type of changes of a lower eyelid is prominent orbital fat of a lower eyelid in a medial part of an orbit and visualization of bony edge of an orbit in a lateral part of an orbit [1]. We also use the microboluses, retrograde fan injections by needle with preliminary marking of dangerous zones for correction of this type (Fig. 3) [3, 5].

Filler is injected under SMAS in lateral part of an orbit into the space limited by ORL (eyelid-cheek junction) and bony edge of orbit as well as in the first type. And in a medial part of an orbit filler is injected in a deep fatty tissue caudal to ORL and in projection of ORL fixation [1]. To avoid injection of filler in hernia we don’t inject filler cranial to ORL projections in a medial part of an orbit.

It is possible to use for correction of this type a blunt cannula with entry points: in a lateral part between a lateral canthus and eyelid-cheek junction, in a medial part in a buccal zone below eyelid-cheek junction.

The third type of changing in a zone of an upper eyelid is determined by visualization of hernias of a lower eyelid both in medial, and in a lateral part of an orbit [1]. This type is indication to surgical blepharoplasty usually. If there are contraindications to surgery, it might be corrected by HA-filler. Incomplete correction of the tear through and palpebromalar groove is preferable to the prevention of effect „pillow face” in this case.

It is possible to use both a needle, and a blunt cannula in correction of this type. Filler should be injected into deep fat compartments caudal to ORL projections (eyelid-cheek junction). We prefer the microboluses technique by needle (Fig. 4) [3, 5].

When correcting the lower eyelid, the right choice of filler is very important. Filler must have the necessary elasticity and plasticity to evenly fill the depression and prevent contouring. We use monophasic HA-filler of average degree of a reticulation – Filorga XHA-3 0.2–0.5 cc – on the side with good clinical effect from 10 to 18 months (Fig. 5).

We recommend to correct loss of volume of a buccal and malar zone as first procedure, and then correct zone of a lower eyelid for obtaining optimum effect in all cases [6].
In conclusion, it is important to underline that correction with HA-filler of lower eyelid has to be performed with consideration of anatomic features of every patient, especially existence and expression of prominent orbital fat of a lower eyelid for optimum results and decreasing risks of adverse events. It is necessary to use a filler with specific physicochemical properties. In our hands, HA-filler Filorga XHA-3 is optimal for the correction of this area.

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Literature:
2. Павленко ОЮ, Хрусталева ИЭ, Атаманов ВВ, Грищенко СВ, Стенько АГ (2014) Возможности филлеров в коррекции нежелательных явлений после блефаропластики и липофиллинга нижних век. Инъекционные методы в косметологии 3: 48-54.

Revised IDMP standards to improve description of medicinal products worldwide

A series of standards called IDMP (Identification of Medicinal Products) standards is under revision and will bring a host of benefits to patients and the healthcare community. Implementing these standards should simplify the exchange of information between stakeholders and enhance the interoperability of systems in the medical field.

IDMP standards and technical specifications, comprising ISO 11616, ISO 11615, ISO/DIS 11238, ISO/TS 20451, ISO/TS 20443 and ISO/TS 19844, support the activities of medicines agencies worldwide. These cover a variety of regulatory activities related to the development, registration and life-cycle management of medicinal products, as well as pharmacovigilance and risk management.

Christian Clay, Senior Consultant Healthcare for GS1 Global Office and Convenor of working group 6, Pharmacy and medicines business, of ISO technical committee IS0/tC 215, Health informatics, explains: “IDMP standards are essential for the world’s increasingly integrated healthcare. They provide the precise architecture for the computerization of information on medicinal products all around the world. When regulators adopt IDMP, their capacity to interoperate with each other makes for safer patient care; this is, for example, a huge benefit for adverse-event reporting and for documenting medication in patient records.”

“The revision has become necessary as a consequence of the development of IDMP implementation guides (which take the form of four CEN1) ISO technical specifications). The overall standard has not really changed but has gained in usability for implementers. By developing implementation guides, it has been possible to shift some detailed information from the standard itself to its corresponding implementation guide,” says Christian Hay.

“By publishing the ISO IDMP standards in 2012, the community has been able to understand a potential fundamental change in each respective data model – which are currently very diverse. Having learned from users’ reactions, the IDMP project leaders have initiated an ambitious standards development programme, which consists of working on implementation guides (namely, the four CEN ISO technical specifications). Now, one can expect the creation of educational material and a uniform implementation both on the part of the manufacturer and the regulator. In parallel, IDMP provides a basis for existing or new IT solutions, such as prescriptions, medication reports, medicinal product dictionaries for clinical use, and more,” he adds.

Using ISO IDMP within regulatory activities brings benefits to regulators, industry and, ultimately, patients. “The trend towards global standards continues to increase. I cannot imagine the world without IDMP, whose implementation programme is going to last several years. Without IDMP, the existing information fragmentation by country or region would cause increasing risks to patients globally – not only those who travel, but those who are faced with mobile health or because of the globalization of supply chains,” explains Christian Hay.

ISO IDMP standards were developed by ISO technical committee ISO/TC 215, Health informatics, whose secretariat is held by ANSI, ISO’s member for the USA. It is now available from your national ISO member or through the ISO Store.

For more information visit: www-iso.org
"Gingival (gummy) smile" – diagnostic value and treatment with botulinum neurotoxin

M.I. SOYKHER¹, O.R. ORLOVA¹, M.G. SOYKHER¹, L.R. MINGAZOVA¹, EM SOYHER²

KEY WORDS: Gummy smile, facial aesthetics, aetiology, treatment, botulinum toxin

SUMMARY: Smile is an important human facial expression of nonverbal communication. Smile aesthetics represent a target for minimal invasive procedures such as botulinum neurotoxin injections for improvement and correction. We present pathogenesis, diagnostic relevance and treatment options of so-called gingival or gummy smile. The aesthetic correction of gummy smile is a multidisciplinary task.

INTRODUCTION

Today, more and more people are striving to realize [4, 14] in their own life the motto: “everything in a human being should be perfect” [15]. Mostly, we pay a lot of attention to our appearance and special importance is attached to our face [5, 6]. Every unique human face has important personal significance for each of us. Smile and lips are the leading factors in the perception of face aesthetics. Many authors like Pererverzev (1978), Khoroshikina (1979), Persin (1988), Polma L (1996, 2010), Arsemima (1998), Ricketts (1981), Bishara (1985), Baccetti (2000), Servis (2001), and Ackerman (2004) made great contributions to the study of the issue of face aesthetics and its violations.

The motivation of patients for dental treatment in recent years is increasingly aimed at obtaining an aesthetic result. Analysis of the reasons why patients turn to dentists showed [7, 11], that 23.0 % of patients want to improve the aesthetic appearance of their teeth, 71.2 % orthodontic patients want to improve face and teeth aesthetics such as reconstruction of the teeth rows. During the last years, facial aesthetics is especially associated with the smile zone. The smile zone is a special structural, a functional and aesthetically significant area. It consists of different macro- (facial and labial) and micro- (gingival and tooth crowning) parameters [3].

The smile formation process divides into 4 stages:
1. stage – lips are closed
2. stage – lips are ajar (half-opened)
3. stage – natural smile (three quarters opened lips)
4. stage – broad smile.

Currently, smile analysis is the key to diagnosis and planning of rehabilitation of dental patients. A smile can destroy or emphasize the face harmony. Therefore, an attractive smile becomes an important indicator of successful dental rehabilitation. The clinical value of a harmonious balance is determined by the limits of the possible effect on soft tissues and the direction of orthopedic treatment, which allows to achieve the best aesthetic result.

What is “the perfect smile”? Are there any clear criteria for this concept? We can easily tell which smile is beautiful, but it is difficult for us to describe those characteristics, that creates it. Many investigations of the problem of aesthetic facial disorders of young patients indicates the presence of “gingival smile” in 10–15 % of cases.

Actually, smile aesthetics depends on: ratio parameters between teeth and gums, their compliance with the rules of structural beauty, the ratio between the teeth and lips parameters and their harmonious integration with the components of the face. Mimic muscles are the main component of a smile [32, 33]. Approximately 7 % of men and 14 % of women have excessive visualization of gums with a smile. Excessive gum visualization is a descriptive term rather than diagnosis that involves the mandatory conduct of a specific treatment.

Gummy smile (or gingival smile) – it’s a kind of structure of tissues of the oral cavity, wherein smile occurs during displacement of the upper lip exposing the gums. For the correct diagnosis doctor requires knowledge in the field of facial aesthetics. The main parameter of the estimation is the height of the face oval. The height of the middle part of the face should be equal to the height of the lower part with a relaxed state of mimic muscles. A „gummy smile“ may be a symptom of a disorder in structures of the facial skeleton and hyperactive facial muscles (Fig. 1).

Anatomical reference point of the middle part of the face is glabella – the most prominent point of the frontal bone between the superciliary arches and the lower point of the
nasal septum. The lower part is measured from the bottom point of the nasal septum to the lowest point of the soft tissues of the mandible, i.e. the lower edge of the chin.

It is necessary to measure the length of the upper lip after making assessment of the height of the face. In the state of relaxation of the facial muscles length from the bottom of the nasal septum up to the lower edge of the upper lip is 20–22 mm on average for young women (Fig. 2a) and 22–24 mm for young men. In this case for women, 3–4 mm maxillary central incisors are usually visualized (Fig. 2b), and 2 mm less for men. Over time, there is a trend to upper lip lengthening.

Short or hyperactive upper lip is one of the factors forming a “gummy smile”. Usually, with a broad smile, teeth crowns 10–11 mm long are completely visible. However, for patient with a hyperactive upper lip these parameters can be raised in 1.5 times (Fig. 3).

In addition, excessive lengthening of the teeth of the frontal group of the maxilla [20] leads to a displacement of the gingiva together with the underlying bone, and their lower position leads to the appearance of a „gummy smile“.

The reason of excessive visualization of the gum also might be an increase in the height of the mandible, which makes the lower part of the face longer relatively to the middle part [16, 18, 22]. According to Jiao Wei et al. (2015), one of the aetiological factors of the „gingival smile“ may be dysplasia of the nasal septum [21]. The most complicated case that require special attention – is a combination of several factors.

Smile is unique for each person. There are several classifications of smiles. According to the Rubin and Philips classification, there are three basic types of smile [12, 30, 31].

The first type is a commissural smile (“La Gioconda’s smile”) – occurs in 67 % of people. When smiling, the corners of the lips move laterally upwards by 7–22 mm. The corners of the lips (commissures) occupy a position above the upper lip and the lateral part of the lips forms an angle of 40° (more often 24–38°) to the horizon. Lips form two curved arcs, in the gleam of them only the upper teeth are visible, sometimes even wisdom teeth. Zygomaticus major and minor muscles are involved in the formation of this type of smile.

The second type of smile – „canine“ or „labial“ – is observed at 31 % of people. It is formed without a significant shift up the corners of the mouth. Upper lip rises upwards, exposing 6–8 upper teeth, lower teeth are closed with lower lip. The lower lip takes the form of an arch, the upper one has curves, in one of which the canines are exposed (this is the reason of the characteristic name). Muscles lifting the upper lip and the one lifting the upper lip and the wing of the nose are involved in the formation of this type of smile.

The third type – „full denture“ or „complex“ smile – found at 2 % of people. With a smile, both upper and lower teeth are exposed and the lips have the form of two practically parallel lines. The maximum number of antagonist muscles of middle and lower third of the face is involved in the formation of this type of smile. Therefore, the key characteristic of this smile – strong muscular tension and displacement of the lower lip down and backward [13].

Multifactor analysis [10] (2009) carried out by Polma allowed to reveal a syndrome, accompanying unaesthetic types of smiles, for which patients complain. A high type of smile („gummy“ smile) is common not only due to vertical enlargement of the upper jaw, or the increase in the height of the lower part of the face and the prevalence of the vertical type of growth, but also as a result of soft tissue anatomy. In 90 % of cases a straight or downward bending of the upper lip is noted. Large percentage of „gummy“ smiles (90 %) arises due
to anterior rotation of the upper jaw, and in 75% of cases it is accompanied by a retraction of incisors of the upper jaw.

There are five variations for exposing teeth and gums in a smile:

Type 1 – only the upper teeth;
Type 2 – upper teeth and more than 3 mm of gum;
Type 3 – only lower teeth;
Type 4 – upper and lower teeth;
Type 5 – neither upper nor lower teeth.

With aging, there is an elongation of the upper lip occurs with simultaneous reduction of the alveolar processes of the upper jaw and the maxillary bone in general. Against this background, the exposure of the gum with a smile is leveled. Mazzuco and Haxsel suggested an aesthetic-functional classification of “gingival smile” [23, 24] (Tab. 1).

Multifactorial analysis of the smile and its consistent design are the key stages of diagnosis and planning aesthetic correction. Diagnosis of smile aesthetics disorders should be conducted on an interdisciplinary basis, acknowledging the standards of harmonious smile, professionally installed for different age-sex and ethnic groups.

The plan for aesthetic correction of the “gummy smile” is developed after an accurate diagnosis and includes the use of both orthodontic correction and maxillofacial surgery, also the use of botulinum neuroprotein, for mimic muscle relaxation [21] (Fig. 4).

According to various authors injections of botulinum neuroprotein (or botulinum toxin) are necessary for patients with gingival smile for reduce hypermobility of the upper lip [8, 12, 25, 29]. The main target muscle is the one that lifts the upper lip (m. levator labii superioris) together with m. zygomaticus minor, m. zygomaticus major, m. depressor septi nasi, m. orbicularis oris [17, 28] (Fig. 5).

Injection of botulinum toxin into the muscle lifting the upper lip may be accompanied sometimes by ptosis of the upper lip and its excessive elongation, protrusion of the lower lip and its asymmetry [19, 32].

The mechanism of action of the botulinum neuroprotein is due to the progress of chemodenervation – direct peripheral influence on motor fibers (neuromuscular transmission), binding to the presynaptic terminal and blockade of transport protein, that takes from 1 to 3 days, so the effect of muscle relaxation begins to manifest a few days after the injection of botulinum toxin into the muscles [1]. The use botulinum toxin for the correction of muscle hypertonicity is based on the following positions [3]:

1. Botulinum toxin provides long lasting muscle relaxation, that allows to break the vicious circle of muscle tension and pain, and to eliminate nerve compression by the tense muscle, if the last exists.
2. Important advantages of treating with botulinum toxin are its local, predictable, dose-dependent effect and a low risk of systemic side effects.

<table>
<thead>
<tr>
<th>TABLE 1. CLASSIFICATION OF „GUMMY SMILE“.</th>
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<td><strong>Type of „gummy smile“</strong></td>
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<tr>
<td>Front type</td>
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The purpose of this research

Determination of the dose of botulinum toxin and the zones of injection (muscle-targets), for the correction of the „gummy smile”, considering the functional type of the smile.

MATERIALS AND METHODS

Criteria for selection were complaints about aesthetic dissatisfaction with a smile, exposure of the gum more than 3 mm. The research included 18 patients, men 22%, women 78%, the average age is 29.5 years.

Attention was drawn to the following clinical signs: facial expression, the condition of the mimic musculature with a smile, degree and nature of exposure of the gum. Gingival distance (GD) Is estimated as the distance between the area of the upper lip and the border of the cutting edge of the teeth. Depending on the type of „gummy smile”, all patients were divided into four groups (Table 2).

The examination included: analysis of data of anamnesis, Clinical examination (examination of the face, oral cavity, Functional tests of mimic muscles), photoanalysis (portrait and intraoral photos). Depending on the type of gingival smile all patients were classified into four groups (see Table 2).

All patients were injected by botulinum toxin, injection points were selected depending on the nature of muscular hyperactivity.

METHODOLOGY

In the apical area of the nasolabial fold 5–10 ED of Dysport® were injected symmetrically on both sides. It is possible to determine the injection point of the drug by placing the tip of the index finger on the edge of the pear-shaped hole direct under the nasal-maxillary suture (Fig. 6). Injection sites and dose of botulinum toxin were defined depending on the type of „gingival smile” (Table 3).

The result was evaluated after 7, 14, 28 days and six months by changing the gingival distance (GD) (Table 4).

| TABLE 2. CLASSIFICATION OF PATIENTS ACCORDING TO THE TYPE OF „GINGIVAL SMILE“. |
|-----------------|------------------|----------------|----------------|
| Group | Type of smile | Sex M/F | Gingival Distance (mm) M/F |
| I    | Frontal     | 1/3        | 22/20              |
| II   | Side        | /2         | /18.8              |
| III  | Mixed       | 3/7        | 21.5/19            |
| IV   | Asymmetrical | /2        | /18.5              |

| TABLE 3. DOSES OF BOTULINUM TOXIN (DYSPORT UNITS). |
|-----------------|------------------|---------------------|
| Group | Type of smile | Muscle | The dose of Dysport |
| I    | Frontal     | m. levator labii superioris | 5–10 units |
| II   | Side        | m. zygomaticus minor, m. zygomaticus major | 5–10 units |
| III  | Mixed       | m. levator labii superioris, m. zygomaticus minor, m. zygomaticus major | 5–10 units |
| IV   | Asymmetrical | m. levator labii superioris, m. zygomaticus minor, m. zygomaticus major only on one side | 5–10 units |
Analysis of clinical patient’s data demonstrated, that initial positive dynamics in the form of reduced gingival distance was noted on 7th day, and the maximum – on the 14th day after the injection. All the patients noted improvement of smile aesthetics. After 6 months, there was a return of muscular hyperactivity and a “gummy smile”, that required a repeat of injection. In subsequent injections, the doses of botulinum toxin depend on the result of the treatment. Therapy should be conducted very carefully, starting from the lowest dosage. The key to the success of the “gummy smile” correction is the careful selection of patients and use of minimally necessary dosages of botulinum toxin.

**RESULTS**

Since injections of the botulinum toxin are safe, reliable and reproducible [29], and the effect is reversible [26]. Botulinum therapy is an independent therapeutic effect for the temporary correction of gingival smiles, also it gives the ability to supply or postpone surgical interventions for a later period [27].

**CONCLUSION**

Since injections of the botulinum toxin are safe, reliable and reproducible [29], and the effect is reversible [26]. Botulinum therapy is an independent therapeutic effect for the temporary correction of gingival smiles, also it gives the ability to supply or postpone surgical interventions for a later period [27].

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**Literature:**

15. Chekhov. A.P. „Uncle Ivan“.
Scientists from the University of Würzburg have synthesized a complex sugar molecule which specifically binds to the tumor protein Galectin-1. This could help to recognize tumors at an early stage and to combat them in a targeted manner.

Galectins are a family of proteins that have become a promising source of cancer research in recent years. A representative thereof is galectin-1. It sits on the surface of all human cells; on tumor cells, however, it occurs in enormous quantities. This makes it an interesting target for diagnostics and therapy.

“Among other things, it is known that galectin-1 hides the tumor cells from the immune system,” explains Professor Jürgen Seibel of the Institute of Organic Chemistry at the Julius-Maximilians-Universität (JMU) Würzburg in Bavaria, Germany. Recent studies have shown that when Galectin-1 is blocked, the immune system can recognize the tumor and attack it with T cells.

Sugar molecule with docking station
No wonder, therefore, that galectin-1 has become a major focus of research. Seibel and his colleague Dr. Clemens Grimm is interested in a very specific section of this protein, the so-called carbohydrate recognition domain. They have now designed a complex sugar molecule that fits perfectly into this domain, as the scientists report in journal “ChemBioChem”.

“We have equipped the sugar molecule with a docking site, for example, to connect it with a fluorescent dye or an drug,” says Seibel. In addition, the scientists have described the binding of their molecule to galectin-1 with high-resolution X-ray structure analyzes.

“Our findings can serve the development of high-affinity ligands of the protein Galectin-1 and thus of new drugs,” said Clemens Grimm.

Quick test for Galectin-1 in progress
Now the JMU scientists are working on a rapid test for the detection of galectin-1. It is designed to enable early detection of tumors such as neuroblastoma. For the future, Seibel’s team would like to expand the sugar molecules into a kind of shuttle system that allows pharmaceutical agents to be transported directly to the tumors.

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International expert consensus on the use of AboBotulinum Toxin A (AboTA) for facial rejuvenation and primary hyperhidrosis

KEY WORDS: Abobotulinum toxin A, AboTA, Botulinum Toxin A, hyperhidrosis, rejuvenation, mimics, mimical muscles

SUMMARY:
Introduction: Recent developments in our understanding of facial ageing have led to a greater appreciation of the part played by dynamic wrinkles. Botulinum toxin is increasingly used to lessen hyperdynamic muscular activity and to rejuvenate the ageing face.

Materials and method: A group of international experts convened to consider the literature and, in the light of their own clinical experience, discuss the optimal uses of abobotulinum toxin A (abota) for myomodulation. To assist doctors, the international expert group here presents consensus guidelines for the use of AboTA in various clinical indications.

Discussion: To achieve optimal results, the clinician requires a detailed understanding of facial anatomy, correct dilution technique, injection procedure and aftercare.

Conclusions: AboTA may be used to rejuvenate the face and other areas. AboTA treatment is effective, safe, and relatively easy to perform and has high patient satisfaction. Duration of action is up to 5½ months.

INTRODUCTION

In modern society, beauty canon is increasingly identified with perfect symmetry and important characters. Women and men have a self-evaluation fee that is reprogrammed from time to time. Common distinctive requirements are oval face, skin compactness and uniformity, eye magnetism, and lips’ appeal. Time is inexorably affecting every single of these beauty factors by marking the skin with wrinkles [1, 2] that develop even in younger persons, from habitual or dynamic muscular hyperactivity, as consequence of emotions or other stimuli. The severity and physiological changes of our body redesign the features of facial compartments, launching a big challenge to self-acceptance.

The advent of modulators for dynamic wrinkles enhancement has expanded rapidly by lengthening the time before resorting to surgery for facial rejuvenation [3].
Although the law rules differently the use of botulinum toxin in each states of the world, the scientific community has universally recognized this product with a high security profile for the patient and after years of research identified parameters for a correct use even in those districts considered “off-label”.

One of the most used BtxA toxins is botulinum toxin A (AbotA). In Russia AbotA was approved in 1999 for neurological indications, in 2004 for aesthetic indications and in April 2009 FDA approved it also for therapeutic use. Very popular and largest used among neurologists and ophthalmologists, each area of the three-thirds of the face that present muscle hyperkinetic activity can benefit from this type of treatment, starting with glabella, forehead, periorbital and perioral regions, from masseter to platysma for aesthetic and functional purpose too. In some countries, mainly in Europe, AbotA is marketed under another trade name.

MATERIALS AND METHODS

In PubMed: Abobotulinumtoxin A. Abbreviation, AbotA

AbotA is not so widely used in aesthetic medicine as it is in neurology and so we have developed guidelines with the purpose of sharing knowledge, experience and expertise to help enhance the quality of service provided to patients by doctors using AbotA.

These guidelines for the use of AbotA are designed to help identify and/or specify:

- Characteristics and properties of AbotA
- Pre-treatment considerations
- Anatomical danger areas
- Technical considerations
- Post-treatment conclusions
- Aesthetic indications for “on label indications”
- Aesthetic indications for “off label indications” (according to the experience of the authors)
- Anticipated results

AbotA is present into the market in vial of 300 and 500 U. The chain of BTA joined with some non-toxic accessory proteins (NAPs) weighs 150 kDa. AbotA acts at the neuromuscular junction in the targeted muscle, thereby reducing muscular contraction. This lessens muscular strength and also lessens resting tone and so achieves temporary improvement in the appearance of dynamic lines.

The mechanism of action is simple. The exocytosis of acetylcholine into the synaptic gap is performed by a protein complex (SNARE) that allow the consequent activation of the muscle fiber [4]. Once injected, the toxin penetrates inside the cell for endocytosis, and in the presynaptic cytoplasm plays a proteolytic on the SNARE complex and then blocks the release of acetylcholine. By time, the nerve cell will synthesize and transport the SNARE complex’s proteins again to the presynaptic terminal. This is the reason why AbotA action can be considered reversible.

The authors conducted a search in Ovid MEDLINE, PubMed, Embase, and the Cochrane Library looking for “AbobotulinumtoxinA”, “facial rejuvenation” and „lines” and they carried out a systematic review of the more recent literature, specifically from January 2010 to October 2016 (Table 1).

By texts, contents and thanks to their long experience in the use of AbotA, they summarized the found data in specific guidelines to allow doctors to have a reference point for a good use of the product regarding immunological, safety and efficacy aspects. All patients, without distinction of sex or ethnicity, can be successfully treated with AbotA in on Label areas [5–8].

AbotA can also be used in other “off-label” areas affected by ageing such as neck and chest [9, 10, 28, 29] or for the treatment of masseter hypertrophy [11], as well as in other indications like hyperhidrosis [12].

Crow’s feet:

Many studies have been conducted to assess the influence of the number of injections in this area for the distribution of the same amount of units. It has emerged that treating one side with a single injection of 36 U in the middle of central lateral at the ocular cantus does not show statistically significant differences in terms of results compared to three injections of 12 U each distributed along the same area [13].

Glabellar lines:

Other studies have been conducted to evaluate the efficacy of two different injective schemes for the treatment of glabellar wrinkles [14]. Specifically, the procerus and the two corrugators were injected in 3 points with 10 U per point and the results were compared with the same partner to which two injective points (one on each side at 1 cm above the corrugator) of 10 U were added. The researchers pointed out that the two additional points with a larger number of units are irrelevant to the final result and that it didn’t improve efficacy.

Even the best dose in effect has been studied by comparing the results obtained by injecting respectively 20, 50 and 75 U into the glabellar area to improve the appearance of wrinkles. The most tolerated, effective and safe dose was judged at 50 U. The important factor is that all patients treated with AbotA showed high satisfaction for the type of results obtained, declaring an improvement in the quality of social life throughout the time that AbotA was active [15].

Safety:

The safety profile of AbotA used for facial rejuvenation is well established. Among thousands of patients treated no serious adverse events (AE) have been observed. All reported AEs were mild or moderate in severity and are usually caused by wrong technique [16–19, 30].

In addition to being well tolerated, the safety and efficacy of AbotA for glabellar wrinkles [4, 5], universal „on label” treatment, is confirmed by many researchers in international scientific literature.

Numerous studies have been also conducted to analyze the different results based on the dilution of AbotA. Each dilution
analyzed showed rapid and long-lasting efficacy, equal to injection pain [20].

Nowadays, after years of research, it is possible to compare the efficacy of different toxins in other areas of the face [21–31]. The efficacy and safety of AboTA injections is similar when used with a conversion factor of 1:2.5 – 1:3 compared with OnaTA or IncoTA [24].

DISCUSSION

This expert group included dermatologists, plastic and maxillofacial surgeons and aesthetic physicians. They gathered to discuss about recognized texts in literature found through online research and to share their own knowledge. Particular attention has been paid to the doses to be injected, to which specific points, with what dilutions, at which depth with emphasis on anatomical details, that are different for each individual.

The expert group reached a consensus on most issues with special recommendations for the use of AboTA in different anatomical areas.

The specialist’s advice to start with a set-up phases before treatment with AboTA that includes different points:

Pre treatment considerations
As in all branches of medicine:

- History, clinical examination and diagnosis are necessary steps before any treatment is considered.
- Absolute contraindications and relative contraindications should be excluded.
- Any bleeding tendency should be considered.
- Informed consent: Oral, and preferably written, informed consent is desirable.
- Medical Record: A medical record should be kept.
- Photography: Photography may be helpful.

Patients are treated in a reclining position, 30°. The skin of the patient is cleansed to remove residues, as make-up can result in post-operative complications [1, 12]. Particular attention and care is taken disinfecting the anatomical area to be treated.

Following a post-treatment protocol of skin care, according to some of the experts, produced better results and a decreased rehabilitation period after procedure.

For the treatment of very sensitive anatomical areas or in patients particularly sensitive to painful stimuli, topical anesthetic may be used.

Anatomical danger areas [18] (Anatomical study by Saban I.)
The anatomical details suggested by anatomical studies suggest the depth of injection and the exact injection site.

Glabellar area, 1st area of caution: Note that the procerus muscle runs from its deep bony origin on the nasal bones caudally to its insertion into the deep aspect of the skin in the glabellar area cephalically, superficial to and between the two frontalis muscles.

In the glabellar area, frontalis is always very superficial while the depressor muscles are deeper. For this reason, and to avoid the classical “Botox look”, it is important to inject deeply thereby only injecting the depressor muscles.

Crow’s feet inferior area, 2nd area of caution:
- The finger is placed just inferior to the caudal border of the zygomatic arch; the tip of the finger is blocked anteriorly by the body of the zygomatic bone (Fig. 1a)
- Just cephalic to the tip is located the bony origin of the zygomaticus major muscle [18]
- The zygomatic arch and bone have been drawn on the skin (Fig. 1b)
- The anterior border of the masseter m. is marked
- The orbicularis oculi (pars orbitalis) is represented, following the limits of the crow’s feet wrinkles
- The zygomaticus major muscle is drawn between its zygomatic bony insertion and the modiolus
- The depressor anguli oris (DAO) and depressor labii inferioris (DII) muscles are already marked (Fig. 1b)
- The zygomatic area is shown, after resection of 3 first layers (Fig. 1c):
  - 1st the skin
  - 2nd the malar subcutaneous fat pad
  - 3rd the orbicularis oculi layer
- The bony origins of zygomaticus major and minor muscles are exposed.

Fig. 1a–c: Crow’s feet inferior area, 2nd area of caution.
• The suborbicularis oculi fat (SOOF) (*) is the fat pad located in the prezygomatic space, which is just cephalic to the origins of these muscles.

Depressor anguli oris (DAO) and depressor labii inferioris (DLI): 3rd area of caution:
• DAO muscle is a triangle with its base on the mandible (origin), its anterior border running perpendicularly upwards to the oral commissure (insertion) and its posterior border running obliquely downwards and backwards from lateral to oral commissure (Fig. 2a).
• DLI is a rectangle whose infero-posterior part lies deep to DAO. It originates from the mandible and inserts into the lateral half of the lower lip.
• The blue square, 3 cm wide, represents the area of the dissection.
• The * represents the foramen of the trigeminal nerve 3rd branch (Fig. 2a).
• The DAO lies deep on the caudal border of the mandible where it originates and where it is covered by the subcutaneous fat; it becomes more superficial and inserts into the modiolus (Fig. 2b).
• The DLI and the orbicularis oris muscles have been resected (Fig. 2c).
• Note that the DLI caudal fibers are pass deep to the DAO as they run from their origin on the caudal border of the mandible. Its fibres are oblique cephalically and medially and pass deep to the OO muscle.
• The exit point of the mandibular sensory nerve (Fig. 2a): its foramen is located where DAO overlaps superficial to DLI.
• Lateral to DAO, the inferior labial artery is dissected. (**)

Masseter and risorius muscles: 4th area of caution.

The lateral fibres of risorius originates in the preparotid fascia. Very near, but more deeply lie the fibres of masseter muscle. To avoid asymmetries of the smile, it is important to inject masseter deeply.

Knowledge and understanding of these 4 areas of caution is very important in order to avoid complications and bad results.

Group discussion:
The optimum interval between treatments is 4 months or more. Subsequent treatments follow the same scheme or are adapted to the current situation.

It is the unanimous opinion of the international expert consensus group that to use AbotA the operator requires a degree in medicine and surgery. Specialization in dermatology or plastic surgery is an advantage. Training in aesthetic medicine through accredited courses is helpful. The treatment should be performed in a clinical setting.

CONCLUSIONS

Innumerable scientific clinical studies and countless years of injector experience have demonstrated the efficacy and safety of AbotA as well as its action in terms of onset and duration. Moreover, considering the annual cost of the treatment with AbotA instead of with other neuromodulators, it results lower [32].

The guidelines here presented by the international expert consensus group are based on our current knowledge. The guidelines reflect data obtained from reference scientific literature. Subsequent studies may lead to amendments or changes to these recommendations and/or to these conclusions of this document. Compliance with the guidelines guarantees neither treatment satisfaction nor a risk-free procedure. The data should always be analyzed and interpreted carefully, with proper critical analysis. All AbotA procedures should depend on the clinical assessment. The clinical experience and the clinical judgement of the doctor performing the treatment is much more important than any guidelines can ever be. The use of AbotA raises ethical, cultural and legal considerations both for medical users and for manufacturers.
### SUMMARY OF THE RECOMMENDATIONS OF THE INTERNATIONAL EXPERT CONSENSUS – ALL AREAS

Recommendations of the AbotA international expert consensus group concerning the preparation and use of AbotA

#### Technical considerations

| **Reconstitution** | With a needle, take the necessary 9% sterile, preservative-free saline solution. After inserting the needle into the AbotA vial, vacuum will aspirate the solution automatically while you need to manually inject the remaining volume. If you do not notice the suction, do not use the vial. It is then advisable to rotate the vial to allow mixing of the toxin in the solution. The resulting solution will be clear and colorless. |
| **Dilution** | Each 125 unit vial has to be reconstituted with either 0.63 mL or 2.5 mL as regards 500 U vial or 1.5 mL as regards 300 U vial. The concentration of the resulting solution will be 20 Speywood units per 0.1 mL. It is possible to dilute more or less, based on the area to be injected and on the physician’s experience and preference. |
| **Storage** | To store AbotA after reconstitution refrigeration is needed at 2–8°C, away from light. It is forbidden to use it after the expiry date stated on the vial. In spite of company’s recommendations, once the toxin has been reconstituted and in case it is not consumed within 24 hours, the experts’ experience indicates that the drug maintains its efficacy and safety for at least one week. |
| **Product injection** | After drawing up AbotA in a sterile syringe, all possible eventual air bubbles have to be eliminated. |
| **Product placement for on label areas** | Depending on the area physician want to treat, based on patient’s desire, a dynamic patient study is performed while moving the specific muscles, palpating the strength points and mapped its with a demographic pencil |
| **Product amount** | See summary of consensus recommendations for all areas below. Adjust dose to individual’s need to achieve natural or “frozen” look, based on the muscle mass and doctor-patient preference. |
| **Conversion rate** | When calculating doses, it is not recommended to use conversion factors of activity units of the toxin in different preparations. Should be based on clinical recommendations for specific preparation BTX. After the evaluation of clinical data regarding the clinical and safety issues of AbotA, the experts advice is to use a conversion ratio AbotA:Ona::2.5:1.0 or even lower in order to achieve equipotancy with Ona. |

#### Pre-treatment considerations

| **Position technique** | The patient may sit, recline or lie down. |
| **Injection technique** | After having taken pictures and/or an animated video and disinfecting the skin, the experts suggest marking the injection points during animation. To inject AbotA the experts suggest using a 0.5–0.3 mL insulin syringe with a bonded 8 mm 30 g needle. The needle is advanced through the skin into the underlying muscle. The depth of injections may be subcutaneous or intramuscular, according to the depth of the muscle and other anatomical details. |
| **Onset of action** | Some experts choose to insert the needle directly during muscular contraction and inject the muscle relaxed. |
| **Dose duration** | Median time for initial onset of action is 2–4 days, with full effect apparent by 8–10 days. Median duration of effect assessed by experts was 120-180 days for single treatments and up to 4–6 months for repeated treatments. Cases with more than 6 months duration were reported. |
## Post-treatment Considerations

<table>
<thead>
<tr>
<th>Touch up</th>
<th>A touch up session to perfectly refine the dose of toxin in some points, and/or to evaluate the response, is suggested at 10 days, especially for patients treated for the first time or by novice injectors. It is recommended touch up treatments are performed no later than one month after the initial treatment.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunogenity</td>
<td>In the experts’ experience, the non-responder rate (possibly probably due to the development of neutralizing antibodies) is less than 0.1%. [25]</td>
</tr>
<tr>
<td>In combination with other techniques</td>
<td>Very often to counteract the aging process doctors suggest an integrated protocol that includes AbotA with other injectable drugs such as hyaluronic acid or biorevitalizing products rather than with energy based devices (laser, radiofrequency, ultrasounds, ...) to try avoid surgery. [26] For example nasal improvement can be also achieved with AbotA and fillers with very good outcome [27, 31]. The expert committee is confident that if AbotA and HA fillers are used to treat different areas, this can be done on the same day with no increase in risk. Some of the experts believe that injecting the same area on the same day with both AbotA and HA may slightly increase the risk of product diffusion which might perhaps increase the risk of vascular compromise but, despite this, they still continue to do this.</td>
</tr>
</tbody>
</table>
| Post-treatment | After treatment, some of the experts advise that the patient should:  
• remain upright  
• not bend excessively  
• perform active facial expressions within 2 hours of the procedure  
• avoid alcoholic drink  
• avoid to wear make-up on the injection sites to avoid pigmentation  
• Do not massage the area to avoid diffusion of the injected fluid nearby  
• avoid sunbath and saunas  
• avoid strong gym activity  
• avoid other treatments on the face the same day. |
| Age and maximum dosage | The experts do not consider that youth or age affect AbotA safety and efficacy. The experts suggest that 500–600 AbotA units might be a sensible upper limit for a single treatment session. |

## Disclosures:
- Landau M, Atamanov V, Gubanova E are trainers and speakers for Galderma Company  
- Kobaladze N, Diaspro A, Zhabeova S, Gavashely L are trainers for Aptos Company  
- Sanches E is medical adviser of the company Oftaderm  
- Orlova O is trainer and speaker for Allergan, Martinex, Microgen and Merz Aesthetics Companies  
- Reznik A is speaker and trainer for the Institute Hyalual Company  
- Sharova A is trainer and speaker for Innovation and LG company  
- Goltsova E is trainer and speaker for the Merz Aesthetics Companies  
- Redaelli A, Zhumatova G are trainers and speakers for Filorga company  
- Rowland Payne C is a key opinion leader for Venn and an occasional speaker for Ipsen & Sesderma.  
- Battistello M is trainer and speaker for General Project, Wavemed, Attiva, Venus Concept Companies

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Recommendations of the AboTA international expert consensus group concerning specific anatomical areas.

<table>
<thead>
<tr>
<th>Aesthetic indications</th>
<th>Fig. 3: Injection points</th>
<th>Area of use and pattern of injections</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>On Label</strong></td>
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<tr>
<td>In some countries, AboTA is licensed for use in these areas.</td>
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<tr>
<td><strong>Frontal area:</strong></td>
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<tr>
<td>m. frontalis</td>
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<td><strong>Glabella:</strong></td>
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<tr>
<td>m. corrugator</td>
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<tr>
<td>m. procerus</td>
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<tr>
<td>m. depressor supercilii</td>
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<tr>
<td><strong>Crow’s feet:</strong></td>
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<td></td>
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<tr>
<td>m. orbicularis oculi</td>
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<td></td>
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<tr>
<td><strong>Nasal root:</strong></td>
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<td></td>
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<tr>
<td>m. levator labii superioris alienae nasi</td>
<td></td>
<td></td>
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<tr>
<td>nasalis pars transversa</td>
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<tr>
<td><strong>Lateral eyebrow lift:</strong></td>
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<tr>
<td>m. orbicularis oculi pars orbitalis</td>
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<tr>
<td>m. frontalis</td>
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<tr>
<td><strong>Wrinkles of the nose:</strong></td>
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<tr>
<td>m. nasalis pars transversa</td>
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<tr>
<td><strong>Bar code wrinkles:</strong></td>
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<tr>
<td>m. orbicularis oris</td>
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<td><strong>Chin:</strong></td>
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<tr>
<td>m. mentalis</td>
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<tr>
<td><strong>“Bunny lines”:</strong></td>
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<tr>
<td>m. levator labii superioris alienae nasi</td>
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<tr>
<td><strong>Tip of the nose:</strong></td>
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<tr>
<td>m. depressor septi nasi</td>
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<tr>
<td><strong>“Marionette lines”:</strong></td>
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<tr>
<td>m. depressor anguli oris</td>
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<tr>
<td><strong>Quadralized face and/or bruxism:</strong></td>
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<tr>
<td>m. masseter</td>
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</tbody>
</table>

**Fig. 4a:** AboTA is not licensed for use in these areas

**Fig. 4b**

**Fig. 4c**
<table>
<thead>
<tr>
<th>Injection site</th>
<th>Injection technique</th>
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<tbody>
<tr>
<td>Forehead and Glabella</td>
<td>Superficial intramuscular injections with perpendicular orientation.</td>
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<tr>
<td></td>
<td>Intradermal injections (suggested by some authors) can be also done with more uniform</td>
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<tr>
<td></td>
<td>muscle diffusion and reduction of asymmetries</td>
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<tr>
<td>Frontalis</td>
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<td>2–8</td>
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<td></td>
<td>Maximum 100</td>
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<td>Inferior to the hairline. At 3</td>
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<td>cm superior to the supraorbital</td>
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<td>edge</td>
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<td>Lateral Corrugators</td>
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<td>2–4</td>
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<td>Medial Corrugator</td>
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<td>5–10</td>
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<tr>
<td>Depressor supercilii</td>
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<td>2</td>
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<tr>
<td>Procerus</td>
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<td>5–16</td>
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<tr>
<td>Crow’s feet</td>
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<tr>
<td>2–10</td>
<td>The distance between lateral orbital margin and injection points is 1 cm and the</td>
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<tr>
<td></td>
<td>needle is directed laterally</td>
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<tr>
<td>Nose (bunny lines)</td>
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<tr>
<td>2–8</td>
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<tr>
<td>Injection site</td>
<td>Dose per injection point (Speywood Units)</td>
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<td>----------------------------------------</td>
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<tr>
<td>Lateral eyebrow lift</td>
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<td>Nose tip</td>
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<td>Nasal flares</td>
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<tr>
<td>Perioral region</td>
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</tbody>
</table>

References:

<table>
<thead>
<tr>
<th>Injection Site</th>
<th>Injection Technique</th>
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<tbody>
<tr>
<td><strong>Depressor anguli oris</strong></td>
<td></td>
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<tr>
<td><strong>5</strong></td>
<td>1 per side</td>
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<tr>
<td><strong>5</strong></td>
<td>1 cm lateral and below the modiolus</td>
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<td></td>
<td>Superficial intramuscular injections.</td>
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<td><strong>Chin</strong></td>
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<tr>
<td><strong>5–20</strong></td>
<td>1–2</td>
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<tr>
<td><strong>5–20</strong></td>
<td>1 point in the middle or 2 points close to the middle at the bony jawline.</td>
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<tr>
<td></td>
<td>Deep intramuscular injections with perpendicular orientation.</td>
</tr>
<tr>
<td><strong>Masseter hypertrophy</strong></td>
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<tr>
<td><strong>10–15</strong></td>
<td>3–5 per side</td>
</tr>
<tr>
<td><strong>40–100</strong></td>
<td>In the lower part of the muscle</td>
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<tr>
<td></td>
<td>Deep intramuscular injections when the patient relaxes the muscle after clenching. Intramuscular injection.</td>
</tr>
<tr>
<td><strong>Platysmal bands</strong></td>
<td></td>
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<tr>
<td><strong>2–5</strong></td>
<td>2–5 points for each band</td>
</tr>
<tr>
<td><strong>Maximum dose 50 per side</strong></td>
<td></td>
</tr>
<tr>
<td>From the jaw line inject one point every 2 cm until the middle part of the bands. Number of points depends on the number and length of the bands but should not exceed the total maximum dose.</td>
<td>Deep intramuscular injections into the bands in a perpendicular direction.</td>
</tr>
<tr>
<td><strong>Décolleté</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Some authors continue to use it, others do not find it efficacious.</td>
</tr>
<tr>
<td><strong>1–2</strong></td>
<td>“Meso-AbotA” technique</td>
</tr>
<tr>
<td></td>
<td>Max 40 U diluted in 1 ml: up to 0.8 ml 0.8 % NaCl solution +/- 0.2 ml carbocaine</td>
</tr>
<tr>
<td></td>
<td>V-shape zone</td>
</tr>
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<td></td>
<td>Superficial intradermal injections at 1 cm intervals in order to cover the whole area.</td>
</tr>
<tr>
<td><strong>Axillary, plantar and palmar primary hyperhidrosis</strong></td>
<td>For horizontal lines of the neck same quantity per point at 1 cm intervals in order to cover the whole area.</td>
</tr>
<tr>
<td><strong>2</strong></td>
<td>The number of injections depends on the Minor test and on the size of the affected area</td>
</tr>
<tr>
<td>2 to 4 U for point. 1 point for each cm²</td>
<td>2–5</td>
</tr>
<tr>
<td></td>
<td>Multiple intradermal injections, “meso-AbotA” technique, is strongly suggested in order to avoid diffusion into deeper muscles</td>
</tr>
</tbody>
</table>
32. Ravi Jandhyala

Onabotulinum toxin A against migraine

Chronic migraine patients suffer at least 15 days a month from headache that has at least half of migraine symptoms such as sensitivity to light or noise, nausea and worsening with physical activity. If this disease does not respond to conventional acute or prophylaxis therapies, migraine headaches are referred to as resistant to therapy. The aim of a study by Bratbak and colleagues (2017) was to investigate the safety of Botox treatments for therapy-resistant chronic migraine, which was carried out mainly in Trondheim, Norway, in cooperation with the Mayo Clinic, USA. Botox (OnabotulinumtoxinA) was injected into the sphenopalatine ganglion, a bundle of nerves with pathways to the tear glands and mucous membranes in the nose and palate. The success of the treatment was assessed according to the number and type of adverse reactions as well as the frequency of headache days before and after treatment. 10 patients with therapy-resistant chronic migraine were observed for one month and subsequently received a botox injection. After 12 weeks, the effects of the treatment were examined. All patients suffered adverse effects as a result of the treatment, but none of them were classified as serious. Typically, unpleasant sensations in the face and jaw area were reported. The number of headache days in month 2 after treatment was significantly reduced compared to the pre-treatment month: 8 out of 10 patients suffered from less than 50% of previous headache days.

The results of the Botox injection in this small study therefore appeared promising in terms of both treatment safety and long-term efficacy. Randomized, placebo-controlled studies are therefore appropriate to clarify Botox’s potential contribution to the treatment of chronic migraine, which has been resistant to therapy up to now.

Reference:

Source:
idw-online
Dysport®. Full-face approach for correction of mimic lines

**KEYWORDS:**
Dysport, full-face correction, botulinum toxin type A

**SUMMARY:**
This article describes a method of full-face correction in patients with moderate and severe wrinkles of the face.

**CASE REPORT**

A 54-year-old patient had severe horizontal wrinkles in the frontal area, vertical wrinkles in the glabellar area and crow’s feet. In addition, there were also changes in the lower third of the face in the form of activity of m. mentalis, m. DAO, m. platysma. Furthermore, the patient had low tails of the eyebrows.

Patient had a porous and thick skin with a severe form of cuperose. Subcutaneous fat was expressed moderately. Muscles did, however, not have excessive hypertonicity.

**Treatment regimen:**
Dysport 500 U was dissolved with 1.25 ml of saline. M. frontalis – 7 points. In each point – 8 U. Injections were made at the top of the muscles, superficially, by V drawing. M. procerus – 8 U. M. corrugator – 8 U and 4 U on each side. M. depressor supercili – 2 U on each side. Lateral side of MoO.

5 points in staggered order in two lines (1 – stepping from the edge of the orbit by 1 cm and the second by 0.2–0.3 cm from the first). At each point of the first line – 8 U. At each point of the second line – 4 U. Lower eyelid – 2 points to the pupillary line of 2 U. For correction of the tail of the eyebrows – 2 points of 4 U. The first point at the intersection of the line drawn from the alae of the nose along the lateral edge to the intersection with the eyebrow. The second was at the intersection of the line drawn from the alae of the nose along the edge of the iris to the eyebrow.

The spine of the nose was injected to decompensate wrinkles. Used for 4 U in each part of m. nasalis pars transversa.

For correction of m. mentalis, at the central point – 10 U of Dysport. To determine the point for correction, M. DAO – step back 2 cm from the commissure laterally and 3 cm perpendicular down. A dose of Dysport 4 U allowed to correct the lowered corners of the mouth. Align the oval allows injection in M. platysma at 1 cm above the edge of the lower jaw. Three points are used – 4 U of Dysport on each side.

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**Literature:**
Restylane® Skinboosters™ for the improvement of the skin quality

Results of a consensus meeting

MARTINA KERSCHER, HEIKE BUNTROCK, MARTINA HUND, ANNA MOkosch, ALEXANDRA OGlVIE, SHIRIN SAMIMI-FARD, MAJA WAIBEL

For every woman, beauty plays a significant role in their lives beyond the age 40. With a good constitution and an active lifestyle, women on average feel ten years younger than they are and they want to look as young as they feel. More than half of women define attractiveness through a firm, wrinkle-free skin [7, 18]. Study results from Fink et al. document that a smooth skin texture, therefore fine, tight, full skin without wrinkles, as well as a healthy skin tone with a special glow significantly influences perceived attractiveness. As a result, female attractiveness is assessed higher if the skin shows less blemishes [4, 12, 13]. In our society, youthfulness and beauty are positively attributed and also determine interactions and positioning in the social as well as the professional environment [2, 6, 10, 14, 17]. Therefore, the need for attractiveness is quite understandable. But with increasing age, the quality of the skin changes. Histological studies, for example, show a reduction and incorrect cross-linkage of the elastin fibers and a decreasing hyaluronic acid (HA) synthesis with reduced water binding (50% reduced HA concentration in 60-year-old women) [21]. The reduced number and activity of fibroblasts additionally lead to a reduced collagen synthesis and a decrease of dermal collagen I and III. Visible signs of the intrinsic aging process include dehydration, loss of tissue tightness and elasticity, wrinkle formation as well as a thinning of the skin and can be superimposed by extrinsic skin aging (especially UV-induced photo aging).

Minimally invasive aesthetic treatments intended to delay the skin's aging process are increasing in demand. Today, patients want an out-patient aesthetic treatment with little side effects and a long-term outcome, leading to effective but also natural results with minimal recovery time. Accordingly, the substitution of HA by means of intradermal injections is an established anti-ageing measure, with proven, evidence-based efficacy and safety.

In principle, injectable HA products can be classified into two groups with different therapeutic goals. Whereas HA fillers are used for targeted wrinkle augmentation and volume substitution, skin boosters are injected superficially for the revitalization of the skin. They improve the signs of skin aging through stimulation of the extracellular matrix (ECM) [5, 22, 26]. The biological significance of HA for the skin as well as its excellent physiological properties, especially its high water-binding capacity, determine injectable HA based skinboosters for improvement of skin quality. Although native HA is ubiquitous in the human body, the largest amount is located in the skin. With 7-8 g of HA, the skin contains approximately 50-56% of the total body content. HA is a significant stabilizing component of the ECM, can bind large amounts of water and is essential for hydration homeostasis. Apart from its significance as a structural substance, HA is also an important functional tissue component, because extracellular substance transport (diffusion of electrolytes, nutrients and decomposition products in the tissue) as well as the activity of the immune system are associated with the hydration status of the ECM. In addition to this, HA is pivotal for cellular processes such as proliferation, differentiation and migration. Amongst other processes, it stimulates fibroblast proliferation and activity with an increased biosynthesis of collagen and other components of the ECM. Apart from regenerative tasks such as improved wound healing under HA, it also has cell protecting properties against external noxious substances. In current studies, it is being discussed whether HA itself fulfills the function of a radical catcher for the deactivation of ROS or whether a reaction with free radicals attacks and leads to it's destruction [11, 28].

The efficacy and safety of the widely applicable Restylane® Skinboosters™ are excellently proven on the basis of current data. According to these findings, they ensure an improvement of skin quality without significant volume changes. The skin is hydrated [8, 15, 27], its elasticity increased [8, 15, 16, 20, 23, 27], the skin surface smoothened [8, 16, 20, 27] and fine lines and wrinkles are reduced [16]. Restylane® Skinboosters™ are injected subcutaneously and have a clinically proven effect duration of up to 12 months [16]. The long lasting and significant effect is due to the use of non-animal stabilized hyaluronic acid (NASHA), especially in direct comparison with non-stabilized hyaluronic acid. This was proven by a number of studies including Coruthers et al. (2014) as well as Williams et al. (2009) [5, 27]. The substitution leads to a stimulation of fibroblast proliferation and activity with new synthesis of collagen, elastin and other extracellular components such as HA, leading to more skin elasticity, skin tension and moisture.
The positive study results are supported by high patient satisfaction. According to blinded live-rating, skin quality improved in more than 80% of the patients. 85% assessed the therapeutic success positively and stated that they would repeat the treatment. Furthermore, patients as well as blinded evaluators indicated significant aesthetic improvements on the basis of the Global Aesthetic Improvement Scale (GAIS).

For the standardization of therapy protocols, a consensus meeting with six experts from the field of aesthetic dermatology took place (committee members see Appendix). The objective of the scientific expert committee was the compilation of an updated guideline for the application of Restylane® Skinboosters™. Current evidence-based studies and the expertise of the committee members were included in the new standardized treatment protocols for the various indications, which through clear recommendations (e.g. injection depth, application intervals) are intended to guide novices as well as experienced users towards Restylane® Skinboosters™ and provide support for the application in everyday practice. For the indication-appropriate application, the treatment protocols define the respective treatment area, the target group and indications, the protocol selection and injection amount, technique, points and volumes for every indication.

### PRODUCT SELECTION

The target group for Restylane® Skinboosters™ are patients who want an improved skin structure. In the past, the choice for the correct Restylane® Skinboosters™ has been individually made for every patient based on the Glagau Scale (classification of skin aging in skin types I-IV). However, since this classification method is very complex, the Glagau Scale is now being replaced by a simpler system. This updated classification is supposed to help even novices to easily arrive at the correct product selection for their patients. It will also help experienced practitioners improve day-to-day efficiency.

First, the skin in the treatment area should be defined. The new classification differentiates between more mature, thicker, partially light-damaged skin with more covering tissue (Type A skin, e.g. cheeks) and younger, thinner, more sensitive skin with less covering tissue (Type B skin, e.g. neck). For Type A skin, the use of Restylane® Skinboosters™ Vital is suitable with strong tissue coverage and low lifting capacity. For Type B skin, the practitioner can select Restylane® Skinboosters™ Vital Light with low tissue coverage and very low lifting capacity (Table 1). Special challenges could be posed by thick photo-aged skin, mature and thin or sensitive skin, although even younger skin can be associated with less tissue coverage in certain areas. Here, the success of the treatment is closely associated with the expertise of the practitioner, whose patient-individual choices are decisive for treatment results. For example, with an optimal treatment, skin aging symptoms (e.g. dehydration, loss of tissue tightness and elasticity, wrinkle formation, atrophy and photo aging) as well as deep acne scars can be reduced and skin quality can thereby be visibly improved. With UV-damaged skin, a more conservative application of Restylane® Skinboosters™ should be considered. The stronger the UV-damage, the more difficult it is to activate the fibroblasts. In this

### Table 1: Product recommendations.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Vital</th>
<th>Vital Light</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg/ml stabilized hyaluronic acid with or without 0.3 % lidocaine</td>
<td>12 mg/ml stabilized hyaluronic acid with or without 0.3 % lidocaine</td>
<td></td>
</tr>
<tr>
<td>Lifting capacity</td>
<td>Low</td>
<td>Very low</td>
</tr>
<tr>
<td>Technology</td>
<td>NASHA™</td>
<td>NASHA™</td>
</tr>
<tr>
<td>Skin quality</td>
<td>Aged or thicker skin</td>
<td>Younger or thin or sensitive skin</td>
</tr>
<tr>
<td>Treatment areas</td>
<td>Face, neck, hands, décolletage, upper arms</td>
<td>Face, neck, hands, décolletage, upper arms</td>
</tr>
<tr>
<td>Tissue coverage</td>
<td>Strong</td>
<td>Weak</td>
</tr>
<tr>
<td>Injection depth</td>
<td>Subcutaneous</td>
<td>Subcutaneous</td>
</tr>
</tbody>
</table>

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**Figure 1: Revised treatment protocol for Restylane® Skinboosters™.**
case, combination treatments or alternative treatments are preferred. Especially with UV-damaged skin, exclusive therapy with laser has been regarded as helpful. However, prior to laser treatment with a fractioned ablative Co2-laser, Angelis and tretti recommend the injection of stabilized hyaluronic acid [1]. The Restylane® Skinboosters™ stimulate the fibroblasts, which should then respond better to the thermal stimulation of the laser.

**Restylane® Skinboosters™ Injection**

On recommendation of the experts and based on the current state of research, the injection of Restylane® Skinboosters™ should generally be performed superficially in the subcutaneous tissue. It is important not to equate Skinboosters treatment with mesotherapy. Whereas with mesotherapy non-stabilised hyaluronic acid and diverse other substances are injected into various skin layers, the efficacy and safety of the Restylane® Skinboosters™, which exclusively contain non-animal stabilised HA, is clinically proven [19, 20, 23, 24, 27] and must be performed in the area of the deep dermis and subcutis.

Unwanted effects and results – apart from local injection-related reactions such as short-term erythemas or hematomas – usually occur due to incorrect treatment, for example by injecting the Skinboosters too superficially. If Skinboosters are applied too superficially and the skin is too thin, there is a risk for nodules/papules formation and an accumulation of the injected material. This undesirable effect can be prevented with injections into the correct skin layer. Nevertheless, if it occurs the committee recommends the application of the enzyme hyaluronidase. Another safety issue besides the defined injection depth is the selection of a suitable cannula. Depending on the expertise of the practitioner the injection can be performed with blunt cannulas or with sharp needles. Blunt cannulas are principally associated with lower side-effects and are therefore usually preferred by the patients. Blunt ending cannulas (Pix’L23G - 50 mm to 25G - 40 mm) have been clinically proven to reduce injection-related reactions [3, 9]. With less penetration points and a reduced risk of hematoma formation, patient comfort is increased. Furthermore, the lateral outlet of the cannula ensures a more even distribution of the Skinboosters and the treatment is experienced as being less painful. Through the optional SmartClick™ System, application safety can additionally be increased: for each 10 µl injected, a click is triggered, enabling the practitioner to completely focus on the injection and attend to the patient while the product is evenly delivered.

For an indication-conforming application, the injection amount, technique,
points and volumes are recommended in the treatment protocols for the respective treatment area (tables 2-5, figure 2).

**APPLICATION INTERVALS**

So far, the treatment regimen for Restylane® Skinboosters™ recommends three build-up treatments at an interval of four weeks and two repeated treatments after six months respectively. As Restylane® Skinboosters™ are medicinal products, deviations can be made from the described treatment scheme in clinical practice if safety is ensured.

Results from current studies and the experience of the experts suggest a reorientation in the recommendation on application intervals. The expert committee agreed that two applications lead to very good results and a current investigation from Kerscher et al. substantiates this [19]. The new treatment protocol (figure 1) recommends two, optionally three initial treatments at an interval of respectively four weeks. In everyday practice however, patient-individual decisions are recommendable: for patients who wish for less treatments, longer intervals can be planned between the appointments. Although a few days after the first treatment an increasing amount of water is bound in the patient's skin and a visible effect is achieved, only repetitive treatment can stimulate the fibroblasts and instigate a collagen biosynthesis. For high patient satisfaction and a long-term relationship to the treating physician patient education is paramount, especially regarding the expectations towards the delayed occurring effect. Furthermore, the revised treatment protocol is based on current research on the effect duration of the Restylane® Skinboosters™: for Restylane® Skinboosters Vital [24] a duration of the aesthetic effect of nine months was substantiated, for Restylane Skinbooster Vital even up to 12 months [16]. Subsequent to the two to three initial treatments, two repeated treatments are only recommended after respectively 9-12 months (figure 1).

Figure 2: CONSENSUS – Restylane® Skinboosters™ Volume per Indication.

<table>
<thead>
<tr>
<th>Indication perioral (smoker's lines)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition perioral area</strong></td>
</tr>
<tr>
<td>Distal border:</td>
</tr>
<tr>
<td>A few cm around the border of the vermilion around the vertically running smoker’s lines</td>
</tr>
<tr>
<td><strong>Target group</strong></td>
</tr>
<tr>
<td>Younger patients (preventive treatment) as well as patients with loss of elasticity</td>
</tr>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Wrinkles and perioral loss of elasticity</td>
</tr>
<tr>
<td><strong>Product selection</strong></td>
</tr>
<tr>
<td>Vital Light or Vital (see below CAVE)</td>
</tr>
<tr>
<td><strong>Injection volume</strong></td>
</tr>
<tr>
<td>(complete treated area per session)</td>
</tr>
<tr>
<td>0.25–0.5 ml</td>
</tr>
<tr>
<td><strong>Injection technique</strong></td>
</tr>
<tr>
<td>Blunt; sharp</td>
</tr>
<tr>
<td><strong>Injection points and volumes</strong></td>
</tr>
<tr>
<td>See figure &quot;Indication cheek&quot;</td>
</tr>
<tr>
<td><strong>CAVE:</strong> Use of Vital possible, if the region above the lip is sunken in (use marginal injection volume)</td>
</tr>
</tbody>
</table>

Table 3: CONSENSUS – Indication perioral (smoker’s lines).
**TREATMENT PROTOCOLS FOR FACE, DÉCOLLETAGE AND HANDS**

**CONSENSUS – FACE**

**Indication cheek/indication periorbital (crow’s feet):**
The indication cheek includes the upper and the lower cheek area. The indication periorbital (crow’s feet) is allocated to the treatment area „upper cheek“ (table 2).

**Indication perioral (smoker’s wrinkles):** (table 3)

**CONSENSUS – Indication Décolletage** (table 4)

**CONSENSUS – Indication hands** (table 5)

The indications forehead, temples and neck are expert indications for Restylane® Skinboosters™ treatment. Therefore no recommendations are given in this consensus.

**SUMMARY**

Restylane® Skinboosters™ are outstandingly suitable for deep hydration of the skin, and their effect is long-term and safe. Natural treatment results fulfill the needs of the patients and increase the patient-practitioner relation. In the new guidelines on the optimal application of Restylane® Skinboosters™ Vital Light and Vital the indications, application intervals, injection technique and compliance are addressed in detail. Furthermore, illustrated application recommendations (e.g. injection amount, technique, points and volumes) for different target groups and treatment areas such as face, décolleté and hands will provide the practitioner security in handling Restylane® Skinboosters™.

**Literature**


### INDICATION HANDS

| Definition hand area | Distal border: only dorsum of the hand (no fingers)  
Proximal border: wrist |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Target group</td>
<td>Mostly patients above 30 years; seldom younger (25–30 years)</td>
</tr>
<tr>
<td>Indications</td>
<td>Younger patients (Approx. ≥ 30 years): prophylaxis; dry skin, hands with clearly visible sinews (thin hypodermic tissue, bulging veins and sinews)</td>
</tr>
<tr>
<td>Product selection</td>
<td>Vital or Vital Light for dry, thin skin</td>
</tr>
<tr>
<td>Injection volume</td>
<td>0.5 ml (for 3 treatments) (see CAVE below)</td>
</tr>
</tbody>
</table>
| Injection technique  | Depending on expertise  
choice: blunt; 2. choice: sharp (bolus technique) |

### Injection points and volumes

**Blunt – possibility no. 1:**  
Four points: between the finger joints, Retrograde injection  
1. Injection of multiple, small boli  
or  
2. Injection of few, larger boli (0.1–0.2 ml, see figure) followed by distribution of depots (massage)

**Blunt – possibility no. 2:**  
• One point: dorsum, proximal  
• Retrograde injection  
• 1. Injection of multiple, small boli  
or  
• 2. Injection of few, larger boli (0.1–0.2 ml, see figure) followed by distribution of depots (massage)

**Sharp: (bolus technique):**  
• Four points: between the finger joints – Retrograde injection  
• 1. Injection of multiple, small boli (0.1–0.2 ml, see figure)  
or  
• 2. Injection of few, bigger boli followed by distribution of depots (0.1–0.2 ml, see figure) followed by distribution of depots in direction of the arrows (massage)

### CAVE: Small depots to avoid nodules.

**Table 5: Consensus – Indication hands.**

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**THE COMMITTEE MEMBERS**

**Dr. med. Maja Waibel, Berlin** – After working at the Benjamin Franklin clinic in Berlin, Dr. Waibel established herself in her own practice in Berlin as an expert for aesthetic dermatology, laser medicine and melanoma prevention.

**Dr. med. Martina Hund, Berlin** – Dr. Hund is specialist for dermatology and venerology in her own practice in Berlin. She is co-author of several dermatology reference books and has long-term experience working at the skin tumour centre of the Charité Berlin.

**Dr. med. Alexandra Ogilvie, Munich** – As a senior physician of the skin clinic at the University clinic Erlangen, Dr. Ogilvie was involved in various scientific advisory boards. She is a specialist for dermatology and allergology and works in her own practice in Munich.

**Shirin Samimi-Fard, Gladbeck** – Shirin Samimi-Fard is a specialist for dermatology and venerology, allergology and has a diploma in esthetic laser medicine. She is the head of the Derma Loft.

**Prof. Dr. med. Martina Kerscher, Hamburg** – Prof. Kerscher heads the cosmetic science workgroup at the University Hamburg. She is a specialist for dermatology and venerology and expert for skin physiology; skin ageing and minimal invasive cosmetic procedures.

**Dr. med. Anna Mokosch, Düsseldorf** – Dr. Mokosch is a specialist for dermatology and venerology in Düsseldorf. She is also a lecturer at the academy for cosmetic medicine in Düsseldorf.

CAVE: The presented treatment scheme has proven (itself) to be evidence based, very effective and safe in most patients. There are, however, individual deviations of volume, frequency and injection time intervals, but their effectiveness is not scientifically proven.

Acknowledgements: The consensus meeting was supported by Galderma Laboratorium GmbH (Düsseldorf, Germany).
Skin revival with hyaluronic acid

Hyaluronic acid based dermal fillers

Labial angle - before
Labial angle - after 14 days

Scars treatment - before
Scars treatment - after 14 days

Reduced pain sensitivity in treatment with BTX, fillers and surgery

Body contouring
Skin tightening
Skin cooling

Studies show that Cryo 6 Derma significantly reduces the pain associated with facial treatments.
Synergistic Combination Therapies are Highlighted in 2017!

MICHAEL J. WEIDMANN, MD

Listening to lectures on the International Congresses and visiting the booths of different producers I was really disappointed about the progress in single therapy advantages. Maybe I am wrong, but there is really nothing which I would call a „hot topic“ in 2017 ... except ... the discussion about synergies we are able to produce by combining different therapy options. The discussion about this topic still is on a low level, the speakers presented single cases with – sometimes – good results, studies are difficult to manage and therefore few, cooperation amongst colleagues with different therapy options seems necessary.

Steffen Giesse, one of our Network speakers, and I have published a first proposal to create a system of good and even bad synergies we can produce based on publications for single combinations and our own experiences with the combinations we use until now [1]. But this systematization could only be a first step in a right direction, not more.

In my opinion the synergistic view on the patient becomes more and more necessary, and some combinations I use today produce amazing results. Inside the Academy we have the opportunity to invite volunteers to many different training sessions like injection-lipolysis, fillers, botulinum toxin (BTX), threads, needling, lasers, mesotherapy or PRP. Therefore we have the chance which sometimes is rare in the doctor’s office to discuss together the progress of each single therapy step and to propose further treatments to the volunteer who does not have to look at the economic frame conditions during a training session. In other words, we are free to optimize the results step by step, and we are free to discuss bad results as well.

We are working on this project since 2014 which we call Compositional Aesthetics, and we are able to present some interim results which we can recommend as synergistic optimization.

BODY CONTOURING

The body contouring market is divided at the moment into 4 groups: group one uses the cryo devices, group two uses injectables for fat pad reduction like PC/DC for injection lipolysis (IL), group three treats with „soft“ lasers like the SculpSure® system from Cynosure, and group 4 is still offering surgical procedures like invasive lasers and liposuction with its different technologies (ultrasound assisted, tumescent, ...).

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1 Medical Director Globalhealth Academy for Aesthetic Medicine
The use of PC/DC injectables to correct the results of surgical procedures has been used since a decade nearly, and it really was helpful for surgeons as the need to correct occurring dents by a second liposuction has not longer been a necessity. 2014 a half side comparison study of I. Tausch and I. Kruglikov has been published using on one side the single therapy with PC/DC, and on the other side a combination of PC/DC and Dual Frequency Ultrasound (LDM) with an increase of volume reduction of about 65% [2].

In 2016 a workgroup with the cryo specialist Matthias Sandhofer from Linz, Austria and the PC/DC specialist Joerg Faulhaber from Schwaebsich-Gmuend, Germany has combined Cryolipolysis together with IL in a single treatment session on 22 patients. Their results were overwhelming and we really can state a synergistic increase of fat reducing effects [3]. We still have to rise the number of treatments to present a standardized protocol for such a combination, but the first results are more than promising (Fig. 1 a+b, 2 a+b).

**FACE COMPOSITION**

During the last decades the number of treatment options for the face has been tremendously snowballed, especially on the minimal invasive level. Analyzing (reading) the anatomic structures of the face to know what aging has caused to the skin and the fat compartments is not longer a luxury but belongs to the standards of today’s high quality treatments, and the patients want it more and more. But do we really know already, which combinations in which sequence – following or parallel – should be chosen to arrive at the horizon of a better efficacy? It seems we are not at the end but still at the beginning.

Nevertheless we already have experiences, and some combinations we already can recommend to our colleagues as there are:

- **IL and Fillers** for the jowls, the submandibular shadow line (chin-line) correction and the nasolabial fold (Fig. 3 a+b and 4 a+b)
- **PRP and Needling** for the treatment of acne scars (Fig. 5 a+b)
- **BTX** (Mastic) and **IL** for the correction of moonfaced contours (Fig. 6 a–d)
- **IL, Fillers, BTX, MesoLift** (Fig. 7 a+b)
- **IL, Fillers, BTX** and **Threads** for more or less declined facial structures (Figure 8a+b)
- **Mesotherapy** and **PRP** for the treatment of hair loss

1+1 = 3 = SYNERGY

There are surely more combinations which raise the efficacy scale like Lasers and PRP, Lasers and Threads, HiFu Ultrasound and Fillers, Radiofrequency and Mesotherapy, but a lot of work still has to be done to find optimal combinations which have a high potential for synergies and therefore create results better than the addition of the single therapies.
The conclusion of three years of experience with combinations is simply that this will be the next bigger step to optimize treatment results, more than any new single therapy will bring us.

Non disclosure. No conflict of interest.

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**Literature:**

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**New EU regulation tightens market surveillance of medical devices**

Researchers at the University of Witten/Herdecke present detailed figures on medical device monitoring for the first time. They see potential for improvement in the use of product-specific data from clinical practice.

Medical technology manufacturers are legally obliged to continue to systematically monitor the safety of their products even after market introduction - but how the industry actually fulfils this obligation has been largely unknown to date. Prof. Dr. Sabine Bohnet-Joščko and Dr. Claus Zippel from the University of Witten/Herdecke have now published data on the use of appropriate monitoring instruments by medical device companies operating in Germany for the first time.

Overall, manufacturers are relatively broadly positioned in this area,“ sums up Dr. Claus Zippel, the results of the nationwide expert survey. Safety-relevant product information is particularly frequently obtained through company-internal sources of knowledge as well as literature screening, monitoring and reporting systems, customer contact and market analyses. In the industry, on the other hand, there is room for improvement in the use of data on the use of products in patient care, for example by means of clinical medical device studies or registers.

The higher the risk class, the higher the level of market observation due to the large differences within the industry, researchers have analysed the results by company size and risk group. Another result of the Witten scientists is that the higher the risk class of the manufactured products, the more intensively the manufacturers use the instruments for market observation on average. This makes sense - after all, more risky products such as artificial hip and knee joints, cardiac pacemakers or implantable defibrillators are subject to stricter legal requirements to ensure product safety and performance than those from the group with the lowest risk, such as surgical textiles or dressing materials.

The data provide detailed insights into how knowledge about the use of the products is gained in practice. Companies can use our results to compare their quality and risk management methods with the industry average,” said Zippel. The results were determined by a nationwide survey of quality management experts from the medical technology sector.

**Source:**
idw-online
In our dermatology practice we use increasingly cross-linked fillers in men, such as Z Fill deep for regenerative augmentation. On behalf of a 47 year old man, the approach and the pleasing results after three months are exemplified.

A 47 year old man without preceding diseases introduced himself in our practice for aesthetic treatment of his facial wrinkles. After a thorough anamnesis and questioning to his personal attitude and desires, augmentation of the nasolabial folds was performed (Fig. 1).

For such treatments we use the Z Fill series of the company Zimmer MedizinSysteme (Neu-Ulm, Germany). Modern fillers, such as Z Fill contour and Z Fill deep with their cross-linked HA for regenerative augmentation, are ideal materials with long durability.

Hyaluronic acids initiate on the one hand biologic processes for tissue regeneration and on the other hand have a high moisture-binding capacity. This treatment enables a more fresh appearance, without being noticeable and it is also well suited for male patients, to treat deep and distinct folds. That is why we decided in this case, to use the newly developed compound Z Fill deep. The cross-linked monophasic HA shows very good filling and volumizing effects, as well as an excellent tissue integration. In addition, this HA is easily implanted and easy to mold.

Z Fill deep was injected employing the Tower Technique according to Gerhard Sattler, into both nasolabial folds and subsequently molded. The volumina amounted to 1 ml on each side.

Although the lifting effect, directly after implantation of Z Fill deep, was not so much pronounced, a very nice result with great volume effect was visible after the 3 month control examination (Fig. 2). One can see nicely, that besides the tissue regeneration, a distinct moisture binding capacity contributed to the treatment results.

In a further treatment, one could augment the cheek region with Z Fill deep. This sequence one could have treated before augmentation of the nasolabial folds, but was not desired by the patient at that point. More and more male patients turn to aesthetic dermatology and the average age will decline.

We also observe a trend to low-level invasive treatments. Here, the different HA products of the Z Fill series are an excellent instrument to fulfill patient demands in the field of wrinkle reduction. The Z Fill series of Zimmer MedizinSysteme offers for each treatment area the appropriate product with the respective properties.

Z Fill is – considering our experience – an excellent filler for volume and lifting, with which lost volumina can be replaced by a remarkable lifting effect and receding contours can be tighten, resulting in a fine aesthetic result.

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Algeness a new polysaccharide based filler

INTERVIEW WITH RICHARD F. BURTT, EXECUTIVE CHAIRMAN OF ADVANCED AESTHETIC TECHNOLOGIES INC. CONCERNING ALGENESS® A NEW BIOMATERIAL CONSISTING OF A PURIFIED AGAROSE GEL (POLYSACCHARIDE), DERIVED FROM A SPHISTICATED AND PATENT PENDING MANUFACTURING PROCESS.

KM: Richard Burtt, your company developed and brought to market a new polysaccharide based filler under the name Algeness®. What is the story behind the filler?

RB: An all-natural alternative to Hyaluronic acid fillers has been the dream of many clinicians, including our Leonard Miller, MD, a noted plastic surgeon in the US. As a result of his research of published papers and aesthetic contacts, Dr. Miller discovered the wealth of data and information on agarose gels derived from red algae. Armed with this knowledge and data, he identified the manufacturer of this filler composed of highly purified agarose in an all natural formulation. We then formed Advanced Aesthetic Technologies, Inc. to acquire this technology in late 2014 and launched Algeness® to a limited test market in 2015. Based on the success of the test market in the UK, Italy and Colombia, we are now scaling up our distribution to bring Algeness® to the entire European Union, eastern Europe, Middle East, and Asia.

KM: What is the difference to other fillers on the market and how is the feedback from practitioners and patients?

RB: Algeness® is distinguished by its ability to instantly volumize soft tissue for a more defined natural look with a technique we call, “Master Your Results™”. Additionally, unlike all HA fillers, Algeness® is full biodegradable and biocompatible. In our “Master Your Results” program, we instruct practitioners in the art of the technique to maximize the unique properties of Algeness® for consistent excellent outcomes that are achieved immediately with little to no migration over time. All unique capabilities.

KM: In which countries is Algeness available and in which countries will it be available soon?

RB: By the end of June of this year, Algeness® will be available throughout the European Union and Eastern Europe. Then subject to registration time Middle East and Asia countries will come online.

KM: Are there any evidence based data available?

RB: Yes. We have a data package of pre-clinical studies conducted by Wake Forest Research Institute in the US, 3 post-market comparative clinical studies of over 150 subjects, and 3 comparative studies in process. Our intent is to make these data available to all including published papers as they come available.

KM: How are the results?

RB: We are delighted with the results in all studies completed to-date. These data have shown Algeness® to be safe, efficacious, nominal to no adverse effects, and offering excellent persistence and low migration.

KM: Which indications is Algeness® approved for?

RB: Algeness® holds a CE Mark certification for implantation in soft facial tissue.

KM: Can we expect an extension of the Algeness range?

RB: Our intent is to offer a full range of dermal products for all facial applications and other soft tissue anatomical areas that can benefit from this all natural biomaterial.

Dear Mr. Burtt, we thank you for this interview.
Dear readers,

The number of fillers, especially those based on hyaluronic acid, has risen sharply in recent years. This is due to the trend towards non-invasive procedures and the increasing ageing population, as well as to the meanwhile high acceptance of such interventions in the population.

In 2011, sales of botulinum toxin and fillers in Europe amounted to € 544 million and in 2016 to around € 830 million. The estimated annual growth rate is approximately 9.5% per annum.

The idea to publish a Filler Guide came from the book „Illustrated Guide to Aesthetic Botulinum toxin Injections“ by KVM Publications, which contains a Filler overview. Publisher Dr. Bernard Kolster gave us permission to build on their table. Many thanks for that at this point. We have been able to extend the table with some products and we would like to thank the companies who supported us with this project.

We do not claim to be complete with regard to the data listed. For current and further information, please refer to the websites of the manufacturers listed in the back of this issue. Further information on indications and contraindications can be found in the product descriptions of the preparations, which are to be regarded as a primary source in any case.

We hope we have provided you with a good source of information and hope you enjoy studying the list.

Kind regards

Douglas Grosse
## Fillers for Superficial Augmentation

<table>
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<tr>
<th>Product name</th>
<th>Company</th>
<th>Indications</th>
<th>Application depth</th>
<th>Material i.e. hyaluronic acid concentration and crosslinkage</th>
<th>Needle and/or cannula size</th>
<th>Special material properties</th>
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<tbody>
<tr>
<td><strong>BELOTERO® Soft</strong></td>
<td>Merz Aesthetics</td>
<td>Correction of superficial wrinkles</td>
<td>Upper dermis</td>
<td>20 mg/ml dynamically multi-cross-linked HA (CPM®-Technology)</td>
<td>Needle: 30 G 1/2</td>
<td>Poly densified, cohesive gel, very good tissue integration, low water retention. Estimated duration: 6–9 months. Very well tolerated, available with lidocaine</td>
</tr>
<tr>
<td><strong>HYABELL® Lips + Lidocaine</strong></td>
<td>Adoderm GmbH</td>
<td>Lip contouring, lip augmentation</td>
<td>Lip muscle</td>
<td>12 mg/ml crosslinked hyaluronic acid plus 0.3 % lidocaine</td>
<td>Needle: 27 G</td>
<td>Exceptionally soft injection; intermediate value of 10 N at G’ and G” with 0.1 Hz is lower than 35 Pa; for excellent properties in shaping and distribution of the filler; for natural and elegant appearance of lip volume, low water uptake</td>
</tr>
<tr>
<td><strong>Hyal®-ACP</strong></td>
<td>Merz Aesthetics</td>
<td>Improvement of skin resilience and elasticity</td>
<td>Intra dermal</td>
<td>ACP (Auto-Cross-linked Polymer) = auto-crosslinked HA</td>
<td>Needle: 30 G 1/2</td>
<td>Stabil without adding adjuvants, long lasting bio stimulation. Documented proliferation of fibroblasts and keratinocytes</td>
</tr>
<tr>
<td><strong>Hydryalix Gentle</strong></td>
<td>Luminera Derm Ltd.</td>
<td>The product is indicated for superficial lines, fine to moderate wrinkles and minor skin damages. The product can be used on wrinkles, lines and creases around the mouth.</td>
<td>Superficial and mid dermis</td>
<td>20 mg/ml HA, cross-linked (Bdde &lt; 2 ppm). Presentation of 1.25 ml in each syringe. Two syringes in a box.</td>
<td>Needle: 27 G or 30 G, thin-wall</td>
<td>In our Hybrid MoBi™ technology, the gel is monophase, fully homogeneous, smooth and easy to inject. The particle nature of the gel gives the ability to mold the injected material to the desired shape in the tissue and gives the product its firmness. All the products are available with lidocaine as well.</td>
</tr>
<tr>
<td><strong>Juvéderm® ULTRA 2</strong></td>
<td>Allergan Inc.</td>
<td>Correction of fine lines and wrinkles</td>
<td>Mid dermis</td>
<td>24 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>Needle: 30 G 1/2</td>
<td>Smooth gel, well tolerated, long lasting, with lidocaine (0.3 %)</td>
</tr>
<tr>
<td><strong>Juvéderm® VOLBELLA</strong></td>
<td>Allergan Inc.</td>
<td>Fine lines, ideal for treatment of the tear trough</td>
<td>Superficial</td>
<td>15 mg/ml crosslinked HA (VYCROSS-Technology™)</td>
<td>Needle: 30 G 1/2</td>
<td>Good duration, good dispersion (reason: low cohesion), with lidocaine (0.3 %)</td>
</tr>
<tr>
<td><strong>Juvéderm® HYDRATE</strong></td>
<td>Allergan Inc.</td>
<td>Improvement of skin moisture and elasticity</td>
<td>Upper dermis</td>
<td>13.5 mg/ml crosslinked HA with 0.9 % mannitol</td>
<td>Needle: 30 G 1/6, 32 G</td>
<td>Good water absorption, low durability</td>
</tr>
<tr>
<td><strong>Juvéderm® VOLITE – Skin Juvénizer</strong></td>
<td>Allergan Inc.</td>
<td>Improvement of skin moisture and elasticity</td>
<td>Intra dermal</td>
<td>12.5 mg/ml slightly crosslinked with VYCROSS-Technology™</td>
<td>Needle: 32 G 1/2</td>
<td>E-Brid™-Technology; easily injectable, well tolerated, slight lifting capability, with lidocaine (0.3 %)</td>
</tr>
<tr>
<td><strong>Restylane® Fynesse</strong></td>
<td>Galderma</td>
<td>Superficial wrinkles (especially perioral and periorbital)</td>
<td>Superficial dermis</td>
<td>20 mg/ml HA, gel with low crosslinkage and calibration grade (Balance Technology)</td>
<td>Needle: 30 G 1/2</td>
<td>Very soft gel with moderate lifting capacity</td>
</tr>
<tr>
<td><strong>PERFECTHA® Finelines</strong></td>
<td>Sinclair Pharma</td>
<td>Superficial facial lines and skin depressions, periorbital lines, perioral lines</td>
<td>Superficial dermis</td>
<td>20 mg/g hyaluronic acid, cross linking agent BDDC (&gt; 1 % )</td>
<td>Needle: 30 G * 1/2&quot;</td>
<td>E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting</td>
</tr>
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<tr>
<td>PERFECTHA® Complement</td>
<td>Sinclair Pharma</td>
<td>Superficial facial lines and skin depressions, forehead fine lines</td>
<td>Superficial dermis</td>
<td>20 mg/g hyaluronic acid, cross linking agent BDDE (&lt; 1 % )</td>
<td>Needle: 30 G * 1/2</td>
<td>E-Brind™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting</td>
</tr>
<tr>
<td>STYLAGE® S</td>
<td>Laboratoires VIVACY</td>
<td>Correction of first wrinkles and for filling of small and mid-deep wrinkles</td>
<td>Upper to middle dermis</td>
<td>16 mg IPN cross-linked HA with added antioxidant mannitol</td>
<td>Needles: 4 x 30 G 1/2</td>
<td>IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas. Also available with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>TEOSYAL® “Redensity [I]“</td>
<td>TEOXANE</td>
<td>Beauty booster for redensification and hydration of the skin as well as prevention of the signs of ageing (face, neck and decolleté)</td>
<td>Intradermal (superficial to mid dermis)</td>
<td>15 mg/g non-cross-linked HA combined with 8 amino acids, 3 antioxidants, zink, copper and vitamin B6 (patented “nutrients supplemented buffer”)</td>
<td>Needle: 30 G 1/2</td>
<td>Well tolerated, with lidocaine</td>
</tr>
<tr>
<td>TEOSYAL® RHA 1</td>
<td>TEOXANE</td>
<td>Fine and superficial dynamic wrinkles and folds, perioral wrinkles</td>
<td>Mid dermis</td>
<td>A mixture of 15 mg/g cross-linked and non-cross linked HA (RHA®-technology), BDDE crosslinker only 1.9 %</td>
<td>Needle: 30 G 1/2</td>
<td>Especially for dynamic regions (face, neck, decolleté), with lidocaine Estimated duration 9–12 months</td>
</tr>
<tr>
<td>Z Fill contour²</td>
<td>Zimmer Medizin-Systeme</td>
<td>Forehead wrinkles, globella, nasolabial folds, marionette lines and mentolabial folds, lip contour and lip volume</td>
<td>Superficial til mid dermis</td>
<td>23 mg/ml crosslinked HA with BDDE</td>
<td>Needle: 27 G 1/2</td>
<td>Estimated duration: 6–9 months</td>
</tr>
<tr>
<td>Z Fill refresh²</td>
<td>Zimmer Medizin-Systeme</td>
<td>Mesotherapy of the face, neck, decolleté, dorsum orh the hands and upper arm</td>
<td>Upper dermis</td>
<td>18 mg/ml non-cross-linked HA</td>
<td>Needles: 30 G 1/2</td>
<td>This with the additional active ingredient glycerin enriched HA produces a long-lasting increase of skin moisture. Estimated duration: 3–4 months</td>
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**FILLERS FOR MEDIUM DEEP AUGMENTATION**

<table>
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<tr>
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<th>Indications</th>
<th>Application depth</th>
<th>Material i.e. hyaluronic acid concentration and crosslinkage</th>
<th>Needle and/or cannula size</th>
<th>Special material properties</th>
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<tbody>
<tr>
<td>ALGENESS® HL 1.5 %</td>
<td>Advanced Aesthetic Technologies</td>
<td>Marionette lines, fine wrinkles, lip augmentation and contouring, oral commissures, oro-mandibular wrinkles</td>
<td>Immediately subcutaneous</td>
<td>1.5 % Agarose (low density), 98.5 % sterile saline solution</td>
<td>Needle: 30 G</td>
<td>100 % Natural and biodegradable injectable implant, ALGENESS® is composed of an Agarose gel, totally biocompatible to the human body and does not containing cross-linked synthetic chemicals (BDDE) associated with Hyaluronic Acid (HA) fillers. Durability: 4–8 months and longer</td>
</tr>
<tr>
<td>Product name</td>
<td>Company</td>
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<tr>
<td>BELOTERO® Balance</td>
<td>Merz Aesthetics</td>
<td>Mid-deep wrinkles, lip augmentation and lip contour</td>
<td>Mid dermis</td>
<td>22.5 mg/ml dnowled-mically multi-cross-linked HA (CPM®-Technology)</td>
<td>Needle: 27 G 1/2, 30 G 1/2</td>
<td>Medium viscose poly-densified cohesive gel. Very good tissue integration, almost no water retention. Estimated duration: 12 months. Very well tolerated, available with lidocaine</td>
</tr>
<tr>
<td>Luminera Derm Ltd.</td>
<td>Designed to restore facial volume and correct facial deficiencies by promoting the generation of natural endogenous collagen. Based on a composite matrix of cross-linked Hyaluronic Acid embedding Calcium Hydroxypatite microspheres, Luminera provides a strong volumizing, lifting effect.</td>
<td>Deep dermal and sub-dermal layers</td>
<td>Calcium Hydroxyapatite (55.7 %) microspheres of a diameter of 25–65 microns in a cross-linked HA gel</td>
<td>20 mg/ml</td>
<td>Needle: 25 G or 27 G, thin wall</td>
<td>Collagen stimulation increases due to the combination of both active ingredients. Calcium Hydroxypatite stimulates new natural collagen production, while Hyaluronic Acid forms a supporting extracellular matrix, which modulates fibroblasts proliferation. The presence of Hyaluronic Acid elevates skin hydration and moisture. Susceptible to Hydroxidase, physiologically osmolarity level. Available with lidocaine as well.</td>
</tr>
<tr>
<td>Adoderm GmbH</td>
<td>Correction of medium wrinkles. Lip volume and lip correction.</td>
<td>Medium to deep dermis</td>
<td>16 mg/ml cross-linked hyaluronic acid plus 0.3 % lidocaine</td>
<td>Needle: 27 G</td>
<td>Exceptionally soft injection; and G’ with 1 Hz is lower than 70 Pa, for excellent properties in shaping and distribution, for stronger volume in the lips</td>
<td></td>
</tr>
<tr>
<td>Luminera Derm Ltd.</td>
<td>The product is indicated for the correction of deep facial wrinkles and folds such as nasolabial folds and marionette lines.</td>
<td>Deep dermis</td>
<td>20 mg/ml HA, cross-linked (BBDE: &lt; 2 ppm). Presentation of 1.25 ml in each syringe. Two syringes in a box.</td>
<td>Needle: 27 G or 27 G, thin-wall</td>
<td>In our Hybrid MoBi™ technology, the gel is monophasic, fully homogenous, smooth and easy to inject. The particle nature of the gel gives the ability to mold the injected material to the desired shape in the tissue and gives the product its firmness. All the products are available with lidocaine as well.</td>
<td></td>
</tr>
<tr>
<td>Luminera Derm Ltd.</td>
<td>The product is indicated for volume augmentation and facial shape restoration. The product can be used on severe wrinkles.</td>
<td>deep dermis or subcutaneously</td>
<td>20 mg/ml HA, cross-linked (BBDE: &lt; 2 ppm). Presentation of 1.25 ml in each syringe. Three syringes in a box.</td>
<td>Needle: 25 G or 27 G, thin-wall</td>
<td>In our Hybrid MoBi™ technology, the gel is monophasic, fully homogenous, smooth and easy to inject. The particle nature of the gel gives the ability to mold the injected material to the desired shape in the tissue and gives the product its firmness. All the products are available with lidocaine as well.</td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>Mid and deep wrinkles, lip contour and lip volume</td>
<td>medium/ deep dermis</td>
<td>*</td>
<td>Needle: 25 G or 27 G, thin</td>
<td>Smooth gel, duration nasolabial 12 months, with lidocaine (0.3 %)</td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>Deep wrinkles, volume creation in lips and cheeks</td>
<td>Deep dermis</td>
<td>24 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>Needle: 27 G 1/2</td>
<td>Smooth gel, long duration with lidocaine (0.3 %)</td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>Mid and deep wrinkles, lip contour and lip volume</td>
<td>medium/ deep dermis</td>
<td>24 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>Needle: 30 G 1/2</td>
<td>Smooth gel, long duration with lidocaine (0.3 %)</td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>Fine lines, ideal for treatment of the tear trough</td>
<td>mid-dermis</td>
<td>15 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>Needle: 30 G 1/2</td>
<td>Good duration, good dispersion (reason: low cohesion), with lidocaine (0.3 %)</td>
<td></td>
</tr>
<tr>
<td>Allergan Inc.</td>
<td>Mid and deep wrinkles</td>
<td>Deep dermis (Recommendation: not intro dermal)</td>
<td>17.5 mg/ml cross-linked HA (VYCROSS-Technology™)</td>
<td>Needle: 30 G 1/2</td>
<td>Good duration, good dispersion, excellent tissue integration and collagen neogenesis, with lidocaine (0.3 %)</td>
<td></td>
</tr>
<tr>
<td>Sinclair Pharma</td>
<td>Medium facial lines and skin depressions, globellar lines, lip contour</td>
<td>Mid-dermis</td>
<td>20 mg/g hyaluronic acid, cross linking agent BBDE (&lt; 1 %)</td>
<td>Needle: 30 G * 1/2*</td>
<td>E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting</td>
<td></td>
</tr>
</tbody>
</table>

**Product name**: BELOTERO® Balance, Luminera Derm Ltd., HYABEL® Basic + Lidocaine, Hydralix Deep, Hydralix Volume, Juvéderm® ULTRA 3, Juvéderm® ULTRA 4, Juvéderm® ULTRA SMILE, Juvéderm® VOLUME, PERFECTHA® Derm

**Company**: Merz Aesthetics, Luminera Derm Ltd., Adoderm GmbH, Allergan, Allergan Inc., Sinclair Pharma
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<tr>
<td><strong>PRINCESS® FILLER</strong></td>
<td>Croma Pharma</td>
<td>Correction of superficial and moderate deep facial wrinkles as well as perioral wrinkles, lip contours and increase of lip volume</td>
<td>Middle to deep dermis</td>
<td>2.3 % HA (23 mg/ml), also available with 0.3 % lidocaine</td>
<td>Needle: 2 x 27 G Terumo 1/2&quot; thin walled</td>
<td>Princess® Filler is a sterile, viscoelastic, completely clear, colourless, isotine, homogenised gel implant</td>
</tr>
<tr>
<td><strong>Restylane® Refyne</strong></td>
<td>Galderma</td>
<td>Mid-deep wrinkles (especially nasolabial folds and &amp; marionette lines, tear trough, cheek and lid folds)</td>
<td>Mid dermis</td>
<td>20 mg/ml HA, gel with moderate crosslinkage and low calibration grade (Balance Technology)</td>
<td>Needle: 30 G 1/2 (UTWN)</td>
<td>Soft gel with moderate lifting capacity, available with lidocaine</td>
</tr>
<tr>
<td><strong>Restylane® Kyss</strong></td>
<td>Galderma</td>
<td>Lip volume, Lip contour</td>
<td>Lip vermilion, submucosa</td>
<td>20 mg/ml HA, gel with moderate crosslinkage and low calibration grade (Balance Technology)</td>
<td>Needle: 30 G 1/2</td>
<td>Moderate soft gel with moderate lifting capacity, available with lidocaine</td>
</tr>
<tr>
<td><strong>Restylane®</strong></td>
<td>Galderma</td>
<td>Mid-deep wrinkles (especially nasolabial folds, marionette lines, oral commissures)</td>
<td>Mid dermis</td>
<td>20 mg/ml stabilized HA (NASHA Technology)</td>
<td>Needle: 29 G 1/2, Canula: 27 G Pal™, 28 G Pal+</td>
<td>Firm gel with moderate lifting capacity, available with lidocaine</td>
</tr>
<tr>
<td><strong>Restylane® Lyft</strong></td>
<td>Galderma</td>
<td>Deep wrinkles, light to moderate facial contouring (especially zygomatic bone, chin, mandibular contour)</td>
<td>Deep dermis or superficial subcutis</td>
<td>20 mg/ml stabilized HA (NASHA Technology)</td>
<td>Needle: 29 G 1/2, Canula: 23–25 G Pal™, 25 G Pal+</td>
<td>Firm gel with high lifting capacity, available with lidocaine</td>
</tr>
<tr>
<td><strong>STYLAGE® M</strong></td>
<td>Laboratoires Vivacy</td>
<td>Correction of mid to deep wrinkles in the Nasolabial region and the cheek and chin region as well as the forehead</td>
<td>Mid to deep dermis</td>
<td>20 mg/µl IPN crosslinked HA with antioxidant mannitol</td>
<td>Needles: 4 x 30 G 1/2&quot;</td>
<td>IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas. Also available with lidocaine (0.3 %)</td>
</tr>
<tr>
<td><strong>TEOSYAL® RHA 2</strong></td>
<td>TEOXANE</td>
<td>Moderate dynamic wrinkles, also universally for all indications, except tear trough</td>
<td>Mid-moist dermis</td>
<td>23 mg/g crosslinked HA (RHA® Technology), BDDE crosslinker only 3.1 %</td>
<td>Needle: 30 G 1/2</td>
<td>Especially for dynamic regions (forehead, glabella), with lidocaine. Estimated duration: 9–18 months</td>
</tr>
<tr>
<td><strong>TEOSYAL® Global Action</strong></td>
<td>TEOXANE</td>
<td>Moderate wrinkles, also universally for all indications, except tear trough</td>
<td>Mid-moist dermis</td>
<td>25 mg/g crosslinked HA</td>
<td>Needle: 30 G 1/2</td>
<td>Moderate viscous gel, also available with lidocaine. Estimated duration up to 9 months</td>
</tr>
<tr>
<td><strong>VARIODERM Lips &amp; Medium</strong></td>
<td>Adoderm GmbH</td>
<td>Lip contours, lip volume, moderate facial wrinkles</td>
<td>Medium to deep dermis</td>
<td>16 mg/ml crosslinked hyaluronic acid plus 0.3 % lidocaine</td>
<td>Needle: 27 G</td>
<td>Without lidocaine, exceptionally soft injection: intermediate value of 9 N at G' and G&quot; lower than 50 Po at 0.1 Hz. For moderate volume in the lips.</td>
</tr>
<tr>
<td><strong>VARIODERM Basic</strong></td>
<td>Adoderm GmbH</td>
<td>Medium facial folds in all areas, lip contouring</td>
<td>Medium to deep dermis</td>
<td>12 mg/ml crosslinked hyaluronic acid. Approximate duration in the skin: 6–12 months</td>
<td>Needle: 27 G</td>
<td>Without lidocaine, exceptionally soft injection: intermediate value of 9 N at G' more than 250 Po at 0.1 Hz. For a higher volume with less injection quantity.</td>
</tr>
<tr>
<td>Product name</td>
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<tr>
<td>Z Fill contour²</td>
<td>Zimmer Medizin-Systeme</td>
<td>Forehead wrinkles, global, nasolabial folds, marionette lines and mentalobial folds, lip contour and lip volume</td>
<td>Superficial to mid dermis</td>
<td>23 mg/ml crosslinked HA with BBDDE</td>
<td>Needle: 27 G 1/2</td>
<td>Estimated duration: 6–9 months</td>
</tr>
<tr>
<td>Z Fill deep²</td>
<td>Zimmer Medizin-Systeme</td>
<td>Cheeks, nasolabial folds, marionette lines and mentalobial folds. Improvement of facial contours and for volume expansion</td>
<td>Mid and deep dermis</td>
<td>23 mg/ml highly crosslinked HA with BBDDE</td>
<td>Needle: 27 G 1/2</td>
<td>Thanks to the excellent visco-elastic properties, the gel can be injected with ease through a thin needle with utmost precision. Estimated duration: 8–12 months</td>
</tr>
<tr>
<td><strong>FILLERS FOR DEEP AUGMENTATION</strong></td>
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<tr>
<td>Product name</td>
<td>Company</td>
<td>Indications</td>
<td>Application depth</td>
<td>Material i.e. hyaluronic acid concentration and crosslinkage</td>
<td>Needle and/or cannula size</td>
<td>Special material properties</td>
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<tr>
<td><strong>ALGENESS® VL 2.5 %</strong></td>
<td>Advanced Aesthetic Technolo-gies</td>
<td>Medium-deep volumizing wrinkles, furrows and folds Cheeks, jawline and chin Nasolabial folds Malar and Submalar Non-surgical rhinoplasty</td>
<td>Subcutaneous</td>
<td>2.5 % Agarose (High density) 0.5 % non crosslinked HA 97 % sterile saline</td>
<td>Needle: 27 G</td>
<td>100 % Natural and biodegradable injectable implant; Algeness® is composed of an Agarose gel, totally biocompatible to the human body. Instant volume: &quot;What you see, is what you get&quot;. Algeness® does not containing crosslinked synthetic chemicals (BBDDE) associated with Hyaluronic Acid (HA) fillers. Durability: 8–12 months and longer</td>
</tr>
<tr>
<td><strong>ALGENESS® DF 3.5 %</strong></td>
<td>Advanced Aesthetic Technolo-gies</td>
<td>Deep volumetric filling Cheeks, jawline and chin Nasolabial folds Malar-zygomatic arch Submalar Non-surgical nose rhinoplasty</td>
<td>Deep soft tissue supra-perio-steal</td>
<td>3.5 % Agarose (High density) 0.4 % non crosslinked HA 96.1 % sterile saline</td>
<td>Needle: 27 G</td>
<td>100 % Natural and biodegradable injectable implant; Algeness® is composed of an Agarose gel, totally biocompatible to the human body. Instant volume: &quot;What you see, is what you get&quot;. Algeness® does not containing crosslinked synthetic chemicals (BBDDE) associated with Hyaluronic Acid (HA) fillers. Durability: 8–12 months and longer</td>
</tr>
<tr>
<td><strong>BELOTERO® Intense</strong></td>
<td>Merz Aesthetics</td>
<td>Deep wrinkles, volume creation, contour compensation</td>
<td>Mid and deep dermis</td>
<td>25.5 mg/ml dynamically multi-crosslinked HA (CPM®-Technology)</td>
<td>Needle: 27 G 1/2</td>
<td>Highly viscous gel, well tolerated, available with lidocaine</td>
</tr>
<tr>
<td><strong>Crystalys</strong></td>
<td>Luminera Derm Ltd.</td>
<td>designed to restore facial volume and natural contours by promoting generation and deposition of natural collagen, the body’s physiological soft tissue filler.</td>
<td>Deep dermis</td>
<td>Calcium Hydroxyapatite (55.7%) microspheres of a diameter of 25–45 microns</td>
<td>Needle: 25 G or 27 G thin-wall</td>
<td>The calcium hydroxyapatite microspheres form a scaffold supportive of fibroblast ingrowth, which, in turn, produces and deposits new collagen, a natural volumizing agent in facial regions. Calcium hydroxyapatite degradation is synchronous with neo-collagen deposition at the injection site, providing a lasting, natural, full and youthful look. Available with lidocaine as well.</td>
</tr>
<tr>
<td>Product name</td>
<td>Company</td>
<td>Indications</td>
<td>Application depth</td>
<td>Material i.e. hyaluronic acid concentration and crosslinkage</td>
<td>Needle and/or cannula size</td>
<td>Special material properties</td>
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<tr>
<td>HAmonyCA</td>
<td>Luminero Derm Ltd.</td>
<td>Designed to restore facial volume and correct facial deficiencies by promoting the generation of natural endogenous collagen. Based on a composite matrix of cross-linked Hyaluronic Acid embedding Calcium Hydroxyapatite microspheres, HAmonyCA provides a strong volumizing, lifting effect.</td>
<td>Deep dermal and sub-dermal layers</td>
<td>Calcium Hydroxyapatite (55.7 %) microspheres of a diameter of 25–45 microns in a cross-linked HA gel 20 mg/ml</td>
<td>Needle: 25 G or 27 G, thin wall</td>
<td>Collagen stimulation increases due to the combination of both active ingredients. Calcium Hydroxyapatite stimulates new natural collagen production, while Hyaluronic Acid forms a supporting extracellular matrix, which modulates fibroblasts proliferation. The presence of Hyaluronic Acid elevates skin hydration and moisture. Susceptible to Hydrolysis, physiological osmolarity level. Available with lidocaine as well.</td>
</tr>
<tr>
<td>HYABELL® Deep + Lidocaine</td>
<td>Adoderm GmbH</td>
<td>Correction of deep folds</td>
<td>Deep dermis</td>
<td>20 mg/ml cross-linked hyaluronic acid plus 0.3 % lidocaine.</td>
<td>Needle: 27 G</td>
<td>Exceptionally soft injection: 12 N at G with more than 300 Pa at 0.1 Hz. For a strong volume effect with medium aged patients.</td>
</tr>
<tr>
<td>Hydryalix Deep</td>
<td>Luminero Derm Ltd.</td>
<td>Correction of deep facial folds, such as nasolabial and marionette folds</td>
<td>Lower dermis</td>
<td>20 mg/ml HA, cross-linked (BDDE &lt; 2 ppm). Presentation of 1.25 ml in each syringe.</td>
<td>Needle: 25 G or 27 G, thin</td>
<td>In our Hybrid MoBi™ technology, the gel is monophasic, fully homogenous, smooth and easy to inject. The particle nature of the gel gives the ability to mold the injected material to the desired shape in the tissue and gives the product its firmness. Also available with lidocaine.</td>
</tr>
<tr>
<td>Juvéderm® ULTRA 4</td>
<td>Allergan Inc.</td>
<td>Deep wrinkles, volume creation in lips and cheeks</td>
<td>Deep dermis</td>
<td>24 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>Needle: 27 G 1/2</td>
<td>Smooth gel, long duration with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>Juvéderm® VOLUMA</td>
<td>Allergan Inc.</td>
<td>Volume creation in the mid-face</td>
<td>Upper periosteal</td>
<td>20 mg/ml cross-linked HA (VYCRoSS-Technology™)</td>
<td>Needle: 27 G 1/2</td>
<td>Very long efficacy up to 24 months, excellent tissue integration and collagen neogenesis with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>Juvéderm® VOLIFT</td>
<td>Allergan Inc.</td>
<td>Mid and deep wrinkles</td>
<td>Deep dermis (Recommendation: not intra dermal)</td>
<td>17.5 mg/ml cross-linked HA (VYCRoSS-Technology™)</td>
<td>Needle: 30 G 1/2</td>
<td>Good duration, good dispersion, excellent tissue integration and collagen neogenesis, with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>PERFECTHA® Deep</td>
<td>Sinclair Pharma</td>
<td>Deep facial lines and skin depressions, lip volume, nose correction, nasolabial folds, marionette lines, oral commissures, cheekbones and chin moderate augmentation</td>
<td>Deep dermis</td>
<td>20 mg/g hyaluronic acid, cross linking agent BDDE (&lt; 1 %)</td>
<td>Needle: 27 G * 1/2”</td>
<td>E-Brìd™ Technology: safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting</td>
</tr>
<tr>
<td>PRINCESS® VOLUME</td>
<td>Croma Pharma</td>
<td>Correction of deep wrinkles and folds as well as sunken-in facial areas, facial contouring and volume expansion</td>
<td>Deep dermis</td>
<td>2.3 % HA (23 mg/ml), also available with 0.3 % lidocaine</td>
<td>Needle: 27 G Terumo 1/2”, thin walled</td>
<td>Also applicable for reconstructive treatments, i.e. lipotrophy of the face, debilitating scars and morphologic asymmetry</td>
</tr>
<tr>
<td>Radiesse*</td>
<td>Merz Aesthetics</td>
<td>Deep folds, volume creation and contour definition, collagen stimulation</td>
<td>Subdermal, sub cutaneous, supra periostal</td>
<td>Filler on Basis 70 % gel-matrix, 30 % microspheres, 25-45 µm</td>
<td>Needle: 27 G 1 1/4, 28 G 3/4, 25 G 1</td>
<td>Low water retention, skin tightening</td>
</tr>
<tr>
<td>Product name</td>
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<tr>
<td>Restylane® Defyne</td>
<td>Galderma</td>
<td>Deep wrinkles, light to moderate facial contouring (especially zygomatic bone, chin, mandibular contour)</td>
<td>Deep dermis or superficial subcutis</td>
<td>20 mg/ml HA, gel with very high crosslinkage and high calibration grade (Balance Technology)</td>
<td>Needle: 27 G 1/2 (UTWN)</td>
<td>Moderate firm gel with high lifting capacity, available with lidocaine</td>
</tr>
<tr>
<td>Restylane® Lyft</td>
<td>Galderma</td>
<td>Deep wrinkles, light to moderate facial contouring (especially zygomatic bone, chin, mandibular contour)</td>
<td>Deep dermis or superficial subcutis</td>
<td>20 mg/ml stabilized HA (NASHA Technology)</td>
<td>Needle: 29 G 1/2; Cannula: 23–25 G Pxl™, 25 G Pxl+</td>
<td>Firm gel with high lifting capacity, available with lidocaine</td>
</tr>
<tr>
<td>STYLAGE® L</td>
<td>Laboratoires VIVACY</td>
<td>Correction of very deep and pronounced wrinkles in the entire region of the face</td>
<td>Lower dermis</td>
<td>24 mg IPN crosslinked HA with antioxidant mannitol</td>
<td>Needles: 4 x 27 G 1/2</td>
<td>IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas. Also available with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>TEOSYAL® Deep Lines</td>
<td>TEOXANE</td>
<td>Deep wrinkles and folds</td>
<td>Deep dermis</td>
<td>25 mg/g crosslinked HA</td>
<td>Needle: 27 G 1/2</td>
<td>Moderate viscous gel, also available with lidocaine. Estimated duration: 9 months</td>
</tr>
<tr>
<td>TEOSYAL® RHA 3</td>
<td>TEOXANE</td>
<td>Deep dynamic wrinkles</td>
<td>Deep dermis</td>
<td>23 mg/g crosslinked HA (RHA®-Technology), Bdde crosslinker only 3.6 %</td>
<td>Needle: 27 G 1/2</td>
<td>Especially for dynamic regions (nasolabial folds, marionette lines), with lidocaine Estimated duration: 12–20 months</td>
</tr>
<tr>
<td>TEOSYAL® Ultimate</td>
<td>TEOXANE</td>
<td>Volume recovery for wide areas (oval of the face, cheeks, temples)</td>
<td>Subcutaneous and preperiosteum</td>
<td>22 mg/g crosslinked HA</td>
<td>Needle: 27 G 1/2</td>
<td>Moderate viscous volumizer, with good material distribution, also available with lidocaine Estimated duration: up to 18 months</td>
</tr>
<tr>
<td>VARIODERM Plus</td>
<td>Adoderm GmbH</td>
<td>Strongly defined facial folds. Moderate Volumising.</td>
<td>Deep dermis</td>
<td>18 mg/ml crosslinked hyaluronic acid. Approximate duration in the skin: 12-14 months.</td>
<td>Needle: 27 G</td>
<td>Exceptionally soft injection. 12 N at G’ over = 600 Pa at 0.3Hz to give great volume effect over 12–14 months.</td>
</tr>
<tr>
<td>Z Fill deep^2</td>
<td>Zimmer Medizin-Systeme</td>
<td>Cheeks, nasolabial folds, marionette lines and mentalabial folds. Improvement of facial contours and for volume expansion</td>
<td>Mid and deep dermis</td>
<td>23 mg/ml highly crosslinked HA with Bdde</td>
<td>Needle: 27 G 1/2</td>
<td>Thanks to the excellent visco-elastic properties, the gel can be injected with ease through a thin needle with utmost precision. Estimated duration: 8–12 months</td>
</tr>
</tbody>
</table>
### Fillers for Maximum Deep Augmentation

<table>
<thead>
<tr>
<th>Product name</th>
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<th>Material i.e. hyaluronic acid concentration and crosslinkage</th>
<th>Needle and/or cannula size</th>
<th>Special material properties</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALGENESS® DF 3.5 %</strong></td>
<td>Advanced Aesthetic Technologies</td>
<td>Deep volumetric filling</td>
<td>Deep soft tissue super-periosteal</td>
<td>3.5 % Agarose (High density) 0.4 % non cross-linked HA 96.1 % sterile saline</td>
<td>Needle: 27 G</td>
<td>100 % Natural and biodegradable injectable implant. Algeness® is composed of an Agarose gel, totally biocompatible to the human body. Instant volume: „What you see, is what you get”. Algeness® does not containing cross-linked synthetic chemicals (BBDC) associated with Hyaluronic Acid (HA) fillers. Durability: 18-12 months and longer</td>
</tr>
<tr>
<td><strong>BELOTERO® Volume</strong></td>
<td>Cheeks, jawline and chin</td>
<td>Volume creation</td>
<td>Deep dermal, subcutaneous, supra periostal</td>
<td>26 mg/ml dynamically multi-crosslinked HA (CPM™-Technology)</td>
<td>Needle: 30 G 1/2, 27 G 1/2, Cannula: 27 G 37 mm</td>
<td>Poly-densified, ductile gel. Moderieren. In comparison to other volumizers, well moldable. Estimated duration: up to 18 months. Very well tolerated. Available with lidocaine</td>
</tr>
<tr>
<td><strong>CRYSTALYS®</strong></td>
<td>Luminera Derm Ltd.</td>
<td>designed to restore facial volume and natural contours by promoting generation and deposition of natural collagen, the body’s physiological soft tissue filler.</td>
<td>Deep dermis</td>
<td>Calcium Hydroxyapatite (55.7%) microspheres of a diameter of 25-45 microns</td>
<td>Needle: 25 G or 27 G thin-wall</td>
<td>The calcium hydroxyapatite microspheres form a scaffold supportive of fibroblast ingrowth, which, in turn, produces and deposits new collagen, a natural volumizing agent in facial regions. Calcium hydroxyapatite degradation is synchronous with neo-collagen deposition at the injection site, providing a lasting, natural, full and youthful look. Available with lidocaine as well.</td>
</tr>
<tr>
<td><strong>ELLANSÉ® S</strong></td>
<td>Sinclair Pharma</td>
<td>For the lasting correction of wrinkles and facial aging. Treatment areas: forehead, temple, brow area, nose shaping, malar augmentation, cheek, nasolabial folds, oral commissures, marionette lines, prejowl sulcus, mental crease, chin definition and jaw line</td>
<td>Subcutaneous layer, supra periostal</td>
<td>70 % Carboxymethylcellulose (CMC), 30 % Polyacrylactone (PCL)</td>
<td>Needle: 27 G 3/4&quot;</td>
<td>STAT Technology™ – Sustained performance, Tunable longevity and Total bioresorbability. Collagen stimulator with instant correction and subsequent volume creation through neocollagenesis; estimated duration of 1 year</td>
</tr>
<tr>
<td><strong>ELLANSÉ® M</strong></td>
<td>Sinclair Pharma</td>
<td>For the lasting correction of wrinkles and facial aging. Treatment areas: forehead, temple, brow area, nose shaping, malar augmentation, cheek, nasolabial folds, oral commissures, marionette lines, prejowl sulcus, mental crease, chin definition and jaw line</td>
<td>Subcutaneous layer, supra periostal</td>
<td>70 % Carboxymethylcellulose (CMC), 30 % Polyacrylactone (PCL)</td>
<td>Needle: 27 G 3/4&quot;</td>
<td>STAT Technology™ – Sustained performance, Tunable longevity and Total bioresorbability. Collagen stimulator with instant correction and subsequent volume creation through neocollagenesis; estimated duration of 2 years</td>
</tr>
<tr>
<td><strong>ELLANSÉ® L</strong></td>
<td>Sinclair Pharma</td>
<td>For the lasting correction of wrinkles and facial aging. Treatment areas: forehead, temple, brow area, nose shaping, malar augmentation, cheek, nasolabial folds, oral commissures, marionette lines, prejowl sulcus, mental crease, chin definition and jaw line</td>
<td>Subcutaneous layer, supra periostal</td>
<td>70 % Carboxymethylcellulose (CMC), 30 % Polyacrylactone (PCL)</td>
<td>Needle: 27 G 3/4&quot;</td>
<td>STAT Technology™ – Sustained performance, Tunable longevity and Total bioresorbability. Collagen stimulator with instant correction and subsequent volume creation through neocollagenesis; estimated duration of 3 years</td>
</tr>
<tr>
<td><strong>ELLANSÉ® E</strong></td>
<td>Sinclair Pharma</td>
<td>For the lasting correction of wrinkles and facial aging. Treatment areas: forehead, temple, brow area, nose shaping, malar augmentation, cheek, nasolabial folds, oral commissures, marionette lines, prejowl sulcus, mental crease, chin definition and jaw line</td>
<td>Subcutaneous layer, supra periostal</td>
<td>70 % Carboxymethylcellulose (CMC), 30 % Polyacrylactone (PCL)</td>
<td>Needle: 27 G 3/4&quot;</td>
<td>STAT Technology™ – Sustained performance, Tunable longevity and Total bioresorbability. Collagen stimulator with instant correction and subsequent volume creation through neocollagenesis; estimated duration of 4 years</td>
</tr>
<tr>
<td>Product name</td>
<td>Company</td>
<td>Indications</td>
<td>Application depth</td>
<td>Material i.e.</td>
<td>Needle and/or cannula size</td>
<td>Special material properties</td>
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<tr>
<td>HAmonyCA</td>
<td>Luminera Derm Ltd.</td>
<td>Designed to restore facial volume and correct facial deficiencies by promoting the generation of natural endogenous collagen. Based on a composite matrix of cross-linked Hyaluronic Acid embedding Calcium Hydroxyapatite microspheres, HAmonyCA provides a strong volumizing, lifting effect.</td>
<td>Deep dermal and sub-dermal layers</td>
<td>Calcium Hydroxyapatite (55.7%) microspheres of a diameter of 25–45 microns in a cross-linked HA gel 20 mg/ml</td>
<td>Needle: 25 G or 27 G, thin wall</td>
<td>Collagen stimulation increases due to the combination of both active ingredients. Calcium Hydroxyapatite stimulates new natural collagen production, while Hyaluronic Acid forms a supporting extracellular matrix, which modulates fibroblasts proliferation. The presence of Hydroxyapatite elevates skin hydration and moisture. Susceptible to Hyaluronic acid, physiological osmolarity level. Available with lidocaine as well.</td>
</tr>
<tr>
<td>HYABELL® Ultra + Lidocaine</td>
<td>Adoderm GmbH</td>
<td>Volumising and correction of deep folds</td>
<td>Subcutaneous</td>
<td>24 mg/ml cross-linked hyaluronic acid plus 0.3 % lidocaine.</td>
<td>Needle: 27 G</td>
<td>Exceptionally soft injection: 19N at G’ more than 700 Po. To achieve an excellent volume effect and lifting features of the skin.</td>
</tr>
<tr>
<td>Hydryalix Ultra Deep</td>
<td>Luminera Derm Ltd.</td>
<td>The product is indicated for the correction of deep facial wrinkles and folds such as nasolabial folds and for facial contours remodeling.</td>
<td>Deep dermal, subcutaneous and/or at the pre-periosteal area</td>
<td>20 mg/ml HA, cross-linked (BDDE +2 ppm). Presentation of 1.25 ml in each syringe. Two syringes in a box.</td>
<td>Needle: 25 G or 27 G, thin-wall</td>
<td>In our Hybrid MoBi™ technology, the gel is monophasic, fully homogenous, smooth and easy to inject. The particle nature of the gel gives the ability to mold the injected material to the desired shape in the tissue and gives the product its firmness. All the products are available with lidocaine as well.</td>
</tr>
<tr>
<td>PERFECTHA® SubSkin</td>
<td>Sinclair Pharma</td>
<td>Volume creation, facial contours, malar areas, chin and cheeks, nose bridge, hands</td>
<td>Subcutaneous or supraperiostal</td>
<td>20 mg/g hyaluronic acid, cross link agent BDDE (+ 1 % )</td>
<td>Needle: 21 G x 50 mm needle + 21 G x 50 mm cannula</td>
<td>E-Bríd™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting</td>
</tr>
<tr>
<td>Radiesse®</td>
<td>Merz Aesthetics</td>
<td>Deep folds, volume creation and contour definition, collagen stimulation</td>
<td>Subdermal, sub cutaneous, supra periostal</td>
<td>Filler on Basis 70 % gel-matrix, 30 % microspheres, 25–45 µm</td>
<td>Needle: 27 G 1/2, 28 G 3/4, 25 G 1</td>
<td>Low water retention, skin tightening</td>
</tr>
<tr>
<td>Juvéderm® ULTRA 4</td>
<td>Allergan Inc.</td>
<td>Deep wrinkles, volume creation in lips and cheeks</td>
<td>Deep dermis</td>
<td>24 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>Needle: 27 G 1/2</td>
<td>Smooth gel, long duration with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>Juvéderm® VOLUMA</td>
<td>Allergan Inc.</td>
<td>Volume creation in the mid-face</td>
<td>upper periosteal</td>
<td>20 mg/ml cross-linked HA (VYCRoSS-Technology™)</td>
<td>Needle: 27 G 1/2</td>
<td>Very long efficacy up to 24 months, excellent tissue integration and collagen neogenesis with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>Juvéderm® VOLIFT</td>
<td>Allergan Inc.</td>
<td>Mid and deep wrinkles</td>
<td>Deep dermis (Recommendation: not intra dermal)</td>
<td>15 mg/ml crosslinked HA (VYCRoSS-Technology™)</td>
<td>Needle: 30 G 1/2</td>
<td>Good duration, good dispersion, excellent tissue integration and collagen neogenesis, with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>Restylane® Volyme</td>
<td>Galderma</td>
<td>Volume creation (especially in the temporal and zygomatic bone region, mandibular contour)</td>
<td>Subcutaneous to supra periostal</td>
<td>20 mg/mlHA with high crosslinkage and high calibration grade (Balance Technology)</td>
<td>Needle: 27 G L1/2 (UTWN)</td>
<td>Moderate soft gel with very high lifting capacity, available with lidocaine</td>
</tr>
<tr>
<td>Restylane® SubQ</td>
<td>Galderma</td>
<td>Volume creation and strong facial contouring (chin on cheeks)</td>
<td>Subcutaneous to supra periostal</td>
<td>20 mg/ml stabilized HA (NASA Technology)</td>
<td>Needle: 21 G; Cannula: 21 G Piu™</td>
<td>Strong lifting effect, available with lidocaine</td>
</tr>
<tr>
<td>SCULPTRA®</td>
<td>Sinclair Pharma</td>
<td>Volume creation of caved areas, especially for correction of skin depressions such as lines wrinkles and scars</td>
<td>Subcutaneous, supra periostal</td>
<td>150 mg Poly-L-lactic acid (PLLA), 90 mg sodium carboxymethyl cellulose, 1275 mg proline free monomalt</td>
<td>Needle: 26 G</td>
<td>Collagen stimulator with duration of up to 2 years</td>
</tr>
<tr>
<td>Product name</td>
<td>Company</td>
<td>Indications</td>
<td>Application depth</td>
<td>Material i.e., hyaluronic acid concentration and crosslinkage</td>
<td>Needle and/or cannula size</td>
<td>Special material properties</td>
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<tr>
<td><strong>STYLAGE® XL</strong></td>
<td>Laboratoires VIVACY</td>
<td>For volumetric lifting, volume extension of the cheek bones, treatment of facial contours and for treatment of fallen-in temples</td>
<td>Lower dermis till subcutaneous</td>
<td>26 mg IPN cross-linked HA with antioxidant mannitol</td>
<td>Needle: 2 x 27 G 1/2&quot;, 2 x 23 G 11/4&quot;</td>
<td>IPN crosslinked HA with double 3D-matrix and antioxidant for reduction of possible swelling and hematomas. Also available with lidocaine (0.3 %)</td>
</tr>
<tr>
<td><strong>STYLAGE® XXL</strong></td>
<td>Laboratoires VIVACY</td>
<td>For volumetric lifting of large and very large volume defects as well as lipoatrophy</td>
<td>Subcutaneous</td>
<td>21 mg IPN cross-linked HA with antioxidant mannitol, also available with lidocaine (0.3 %)</td>
<td>Needle: 2 x 21 G 1 1/2&quot;, 1 x 21 G / 50 blunt canula, pricker</td>
<td>Highly cohesive and viscous for treatment of lipoatrophy and for volumetry</td>
</tr>
<tr>
<td><strong>TEOSYAL® Ultimate</strong></td>
<td>TEOXANE</td>
<td>Volume recovery for wide areas (oval of the face, cheeks, temples)</td>
<td>Subcutaneous (superficial fat compartments)</td>
<td>22 mg/g crosslinked HA</td>
<td>Needle: 27 G 1/2</td>
<td>Moderate viscous gel, volumizer with good material distribution, also available with lidocaine. Estimated duration: up to 18 months</td>
</tr>
<tr>
<td><strong>TEOSYAL® RHA 4</strong></td>
<td>TEOXANE</td>
<td>Volume in extended dynamic areas + cheeks + contours of the face</td>
<td>Subcutaneous and periosteum</td>
<td>23 mg/g crosslinked HA (RHA®-Technology), BDDE crosslinker only 4 %</td>
<td>Needle: 27 G 1/2</td>
<td>Especially for volume creation in larger dynamic regions (cheeks, facial contouring), with lidocaine. Estimated duration: 12–22 months</td>
</tr>
<tr>
<td><strong>TEOSYAL® Ultra Deep</strong></td>
<td>TEOXANE</td>
<td>Volume in targeted areas + cheekbones + chin</td>
<td>Subcutaneous (pre-periosteal)</td>
<td>25 mg/g crosslinked HA</td>
<td>Needle: 25 G 1</td>
<td>Firm gel with extra-long duration and excellent lifting effect, also available with lidocaine. Estimated duration: 9–20 months</td>
</tr>
<tr>
<td><strong>VARIODERM Subdermal</strong></td>
<td>Adoderm GmbH</td>
<td>For optimum volumising at very deep folds. Ideal for Dorsum, facial contouring and male patients.</td>
<td>Subdermal</td>
<td>27 mg/ml cross-linked hyaluronic acid. Approximate duration in the skin 14–18 months.</td>
<td>Needle: 27 G</td>
<td>Exceptionally soft injection: 19 N of G’more than 2000 Pa. Longest duration volume effect with all fillers, more than 14 months with less injected product compared. Ideal when high volume is needed, male patients and facial contouring.</td>
</tr>
</tbody>
</table>
## SPECIAL INDICATION: SKINSURFACE, MESOTHERAPY AND SKINBOOSTERS

<table>
<thead>
<tr>
<th>Product name</th>
<th>Company</th>
<th>Indications</th>
<th>Application depth</th>
<th>Material i.e. hyaluronic acid concentration and crosslinkage</th>
<th>Needle and/or cannula size</th>
<th>Special material properties</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BELOTERO® Soft</strong></td>
<td>Merz Aesthetics</td>
<td>Correction of superficial wrinkles</td>
<td>Upper dermis</td>
<td>20 mg/ml dynamically multi-crosslinked HA (CPM®-Technology)</td>
<td>Needle: 30 G 1/2</td>
<td>Poly densefied, cohesive gel, very good tissue integration, low water retention. Estimated duration: 6–9 months. Very well tolerated, available with lidocaine</td>
</tr>
<tr>
<td><strong>DESIRIAL®</strong></td>
<td>Laboratoires VIVACY</td>
<td>For intradermal injection in the genital area and for treatment of vaginal dryness and other symptoms of vulvo-vaginal atrophy</td>
<td>Depending on indication</td>
<td>IPN crosslinked HA</td>
<td>Needle: 2 x 30 G 1/2 2 x 27 G 1/2&quot;</td>
<td>Desirial is the first worldwide HA product licensed for intradermal injection in the genital area and for treatment of vaginal dryness and other symptoms of vulvo-vaginal atrophy (CE)</td>
</tr>
<tr>
<td><strong>Hyal®-ACP</strong></td>
<td>Merz Aesthetics</td>
<td>Improvement of skin resilience and elasticity</td>
<td>Intra dermal</td>
<td>ACP (Auto-Cross-linked Polymer) = auto-crosslinked HA</td>
<td>Needle: 30 G 1/2</td>
<td>Stabil without adding adjuvants, long lasting bio stimulation. Documented proliferation of fibroblasts and keratinocytes</td>
</tr>
<tr>
<td><strong>Hydryal</strong></td>
<td>Luminera Derm Ltd.</td>
<td>Designed to enhance skin hydration and restore skin vitality, improve skin elasticity and achieve a natural glowing look. According to the HA percentage-epidermal to mid-dermis*</td>
<td>Non-cross linked hyaluronic acid in different concentrations: 20, 30 or 40 mg/ml hyaluronic acid. Contains mannitol. Presentation of 1.25 ml in each syringe. Three syringes in a box.</td>
<td>Needle: 27 G thin-wall or 30 G thin-wall</td>
<td>Hydryal contains high concentration of hyaluronic acid that allows significant rehydration and revitalization. *According to the HA percentage: Hydryal 2 %-dermal epidermal junction and the superficial dermis Hydryal 3 %-superficial and mid-dermis Hydryal 4 %-mid-dermis</td>
<td></td>
</tr>
<tr>
<td><strong>Juvéderm® HYDRATE</strong></td>
<td>Allergan Inc.</td>
<td>Improvement of skin moisture and elasticity</td>
<td>Upper dermis</td>
<td>13.5 mg/ml non-crosslinked HA with 0.9 % mannitol</td>
<td>Needle: 30 G 1/6, 32 G</td>
<td>Good water binding capability, short duration</td>
</tr>
<tr>
<td><strong>Princess® RICH</strong></td>
<td>Croma Pharma</td>
<td>Enhancement of tonus and elasticity of the skin</td>
<td>Superficial dermis</td>
<td>2.3 % HA (18 mg/ml), 2 % glycerol (20 g/ml) non-crosslinked</td>
<td>Needle: 2 x 30 G 1/2, thin walled</td>
<td>Viscelastic solution that replaces age-related loss of HA and enhances tonus and elasticity of the skin, and fills up fine wrinkles such as crow’s feet, laugh lines or smoker’s lines around the mouth</td>
</tr>
<tr>
<td><strong>Restylane® Skinbooster™ Vital</strong></td>
<td>Galderma</td>
<td>Improvement of skin moisture, skin texture and skin elasticity, especially for mature and actinic skin</td>
<td>Subcutaneous</td>
<td>20 mg/ml stabilized HA (NASHA Technology)</td>
<td>29 G TWIN Smart Click System, 30 G Pixl™ or Injector</td>
<td>Strong water retention capability, well tolerated</td>
</tr>
<tr>
<td><strong>Restylane® Skinbooster™ Vital Light</strong></td>
<td>Galderma</td>
<td>Improvement of skin moisture, skin texture and skin elasticity, especially younger and thin, sensitive skin</td>
<td>Subcutaneous</td>
<td>12 mg/ml stabilized HA (NASHA Technology)</td>
<td>29 G TWIN Smart Click System, 30 G Pixl™ or Injector</td>
<td>Strong water retention capability, well tolerated</td>
</tr>
<tr>
<td><strong>STYLAGE® Hydro</strong></td>
<td>Laboratoires VIVACY</td>
<td>For mesotherapeutic treatments and restoration of skin moisture and improvement elasticity and firmness of the tissue</td>
<td>Superficial dermis</td>
<td>14.0 mg non-crosslinked HA</td>
<td>Needle: 2 x 30 G 1/8&quot;</td>
<td>Very long molecule chains (ca. 1.0 MDalton) for long durability</td>
</tr>
<tr>
<td><strong>STYLAGE® HYDROMAX</strong></td>
<td>Laboratoires VIVACY</td>
<td>For mesotherapy and intense hydration of the skin. Longlasting (4–6 Months)</td>
<td>Mid dermis</td>
<td>12.5 mg lightly crosslinked HA with antioxidant sorbitol</td>
<td>Needle: 2 x 30 G 1/8&quot;</td>
<td>Very long molecule chains (ca. 1.0 MDalton) for long durability</td>
</tr>
<tr>
<td><strong>TEOSYAL® Meso</strong></td>
<td>TEOXANE</td>
<td>Hydration of the face, neck and décolleté</td>
<td>Epidermal and ntradermal</td>
<td>15 mg/g non-crosslinked HA</td>
<td>Needle: 30 G 1/2</td>
<td>Soft gel with recommended treatment protocol</td>
</tr>
</tbody>
</table>
## Special Indication: Lips

<table>
<thead>
<tr>
<th>Product name</th>
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<th>Material i.e. hyaluronic acid concentration and crosslinkage</th>
<th>Needle and/or cannula size</th>
<th>Special material properties</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TEOSYAL® “Redensity [I]”</strong></td>
<td>TEOXANE</td>
<td>Beauty booster for redensification and hydration of the skin as well as prevention of the signs of ageing (face, neck and decolleté)</td>
<td>Epidermal and intra dermal</td>
<td>15 mg/g non-cross-linked HA combined with 8 amino acids, 3 antioxidants, zink, copper and vitamin B6 (patented “nutrients supplemented buffer”)</td>
<td>Needle: 30 G 1/2</td>
<td>Well tolerated, with lidocaine</td>
</tr>
<tr>
<td><strong>VARIODERM Mesolift</strong></td>
<td>Adoderm GmbH</td>
<td>Skinbooster, superficial folds, face, neck, decolleté, back of hand</td>
<td>Superficial dermis</td>
<td>12.8 mg/ml not-cross-linked hyaluronic acid, approximate duration in the skin 3 months.</td>
<td>Needle: 30 G</td>
<td>Not-cross-linked HA for hydrating skin</td>
</tr>
<tr>
<td><strong>Z Fill refresh</strong></td>
<td>Zimmer Medizin-Systeme</td>
<td>Mesotherapy of the face, neck, decolleté, dorsum of the hands and upper arm</td>
<td>Upper dermis</td>
<td>18 mg/ml non-crosslinked HA. Stabilizer: Glycerin</td>
<td>Needle: 30 G 1/2</td>
<td>This with the additional active ingredient glycerin enriched HA produces a long-lasting increase of skin moisture. Estimated duration: 3–4 months</td>
</tr>
</tbody>
</table>

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**Special Indication:** Lips

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>ALGENESS® HL 1.5 %</strong></td>
<td>Advanced Aesthetic Technologies</td>
<td>Marionette lines, fine wrinkles, lip augmentation and contouring, oral commissures, oro-mandibular wrinkles</td>
<td>Immediately subcutaneous</td>
<td>1.5 % Agarose (low density), 98.5 % sterile saline solution</td>
<td>Needle: 30 G</td>
<td>100 % Natural and biodegradable injectable implant, Algeness® is composed of an Agarose gel, totally biocompatible to the human body and does not containing cross-linked synthetic chemicals (BBDE) associated with Hyaluronic Acid (HA) fillers. Durability: 4–8 months and longer</td>
</tr>
<tr>
<td><strong>BELOTERO® Balance</strong></td>
<td>Merz Aesthetics</td>
<td>Mid-deep wrinkles, lip augmentation and lip contour</td>
<td>Mid dermis</td>
<td>22.5 mg/ml dynamically multi-crosslinked HA (CPM®-Technology)</td>
<td>Needle: 27 G 1/2, 30 G 1/2</td>
<td>Medium viscose poly-densified cohesive gel. Very good tissue integration, almost no water retention. Estimated duration: 12 months. Very well tolerated, available with lidocaine</td>
</tr>
<tr>
<td><strong>BELOTERO® Intense</strong></td>
<td>Merz Aesthetics</td>
<td>Deep wrinkles, volume creation, contour compensation</td>
<td>Mid and deep dermis</td>
<td>25.5 mg/ml dynamically multi-crosslinked HA (CPM®-Technology)</td>
<td>Needle: 27 G 1/2</td>
<td>Highly viscose gel, well tolerated, available with lidocaine</td>
</tr>
<tr>
<td><strong>Hydryalix Lips</strong></td>
<td>Luminera Derm Ltd.</td>
<td>The product is indicated for lips contour and volume.</td>
<td>Mid and deep dermis</td>
<td>20 mg/ml HA, cross-linked (BBDE ≤2 ppm). Presentation of 1.25 ml in each syringe. Two syringes in a box.</td>
<td>Needle: 27 G or 30 G, thin-wall</td>
<td>In our Hybrid MoBi™ technology, the gel is monophasic, fully homogenous, smooth and easy to inject. The particle nature of the gel gives the ability to mold the injected material to the desired shape in the tissue and gives the product its firmness. All the products are available with lidocaine as well.</td>
</tr>
<tr>
<td>Product name</td>
<td>Company</td>
<td>Indications</td>
<td>Application depth</td>
<td>Material i.e. hyaluronic acid and crosslinkage</td>
<td>Needle and/or cannula size</td>
<td>Special material properties</td>
</tr>
<tr>
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</tr>
<tr>
<td>Juvéderm® Ultra 3</td>
<td>Allergan Inc.</td>
<td>Mid and deep wrinkles, lip contour and lip volume</td>
<td>lips mucosa</td>
<td>24 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>27 G 1/2</td>
<td>Smooth gel, duration nasolabial 12 months, with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>Juvéderm® Ultra 4</td>
<td>Allergan Inc.</td>
<td>Deep wrinkles, volume creation in lips and cheeks</td>
<td>lips mucosa</td>
<td>24 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>27 G 1/2</td>
<td>Smooth gel, long duration with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>Juvéderm® Ultra SMILE</td>
<td>Allergan Inc.</td>
<td>Mid and deep wrinkles, lip contour and lip volume</td>
<td>lips mucosa</td>
<td>24 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>30 G 1/2</td>
<td>Smooth gel, long duration with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>Juvéderm® VOLBELLA</td>
<td>Allergan Inc.</td>
<td>Fine lines, ideal for treatment of the tear trough</td>
<td>lips mucosa</td>
<td>15 mg/ml crosslinked HA (HYLACROSS-Technology™)</td>
<td>30 G 1/2</td>
<td>Good duration, good dispersion (reason: low cohesion), with lidocaine (0.3 %)</td>
</tr>
<tr>
<td>PERFECTHA® Derm</td>
<td>Sinclair Pharma</td>
<td>Medium facial lines and skin depressions, glabellar lines, lip contour</td>
<td>Mid-dermis</td>
<td>20 mg/g hyaluronic acid, cross linking agent BDDE (&lt; 1 %)</td>
<td>30 G 1/2 * 1/2”</td>
<td>E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting</td>
</tr>
<tr>
<td>PERFECTHA® Deep</td>
<td>Sinclair Pharma</td>
<td>Deep facial lines and skin depressions, lip volume, nose correction, nasolabial folds, marionette lines, oral commissures, cheekbones and chin moderate augmentation</td>
<td>Deep dermis</td>
<td>20 mg/g hyaluronic acid, cross linking agent BDDE (&lt; 1 %)</td>
<td>27 G * 1/2”</td>
<td>E-Brid™-Technology; safe, well tolerated, easy to inject, high lifting and volumizing capacity, long lasting</td>
</tr>
<tr>
<td>PRINCESS® FILLER</td>
<td>Croma Pharma</td>
<td>Correction of superficial and moderate deep facial wrinkles as well as personal wrinkles, lip contours and increase of lip volume</td>
<td>Middle to deep dermis</td>
<td>2.3 % HA (23 mg/ml), also available with 0.3 % lidocaine</td>
<td>2 x 27 G Terumo 1/2”, thin walled</td>
<td>Princess® Filler is a sterile, viscoelastic, completely clear, colourless, isotone, homogenised gel implant</td>
</tr>
<tr>
<td>Restylane® Kysse</td>
<td>Galderma</td>
<td>Lip volume, Lip contour</td>
<td>Lip vermilion, submucosa</td>
<td>20 mg/ml HA, gel with moderate crosslinkage and low calibration grade (Balance technology)</td>
<td>30 G 1/2</td>
<td>Moderate soft gel with moderate lifting capacity, available with lidocaine</td>
</tr>
<tr>
<td>STYLAGE® LIPS</td>
<td>Laboratoires Vivacy</td>
<td>Lip volume, correction of disproportional upper and lower lips, definition and/or correction of lip contour, filling of fine lines above the upper lip, restoration of lip moisture</td>
<td>Lip mucosa</td>
<td>18.5 mg IPN crosslinked HA with added antioxidants mannitol, also available with lidocaine (0.3 %)</td>
<td>2 x 30 G 1/2”</td>
<td>Estimated duration: ca. 12 months</td>
</tr>
<tr>
<td>TEOSYAL® Kiss</td>
<td>TEOXANE</td>
<td>Harmonization of lip volume, lip contour and hydration of the lips</td>
<td>Labial mucosa</td>
<td>25 mg/g crosslinked HA</td>
<td>27 G 1/2</td>
<td>Moderate viscous gel, Estimated duration: up to 9 months</td>
</tr>
<tr>
<td>TEOSYAL® RHA 2</td>
<td>TEOXANE</td>
<td>Moderate dynamic wrinkles, also universally for all indications, except tear trough</td>
<td>Mid-dermis</td>
<td>23 mg/g crosslinked HA (RHA*-Technology), BDDE crosslinker only 3.1 %</td>
<td>30 G 1/2</td>
<td>Especially for dynamic regions (forehead, glabella), with lidocaine. Estimated duration: 9–18 months</td>
</tr>
<tr>
<td>TEOSYAL® RHA 3</td>
<td>TEOXANE</td>
<td>Deep dynamic wrinkles</td>
<td>Deep dermis</td>
<td>23 mg/g crosslinked HA (RHA*-Technology), BDDE crosslinker only 3.6 %</td>
<td>27 G 1/2</td>
<td>Especially for dynamic regions (nasolabial folds, marionette lines), with lidocaine. Estimated duration: 12–20 months</td>
</tr>
<tr>
<td>Z Fill contour²</td>
<td>Zimmer Medizin-Systeme</td>
<td>forehead wrinkles, glabella, nasolabial folds, marionette lines and mentolabial folds, lip contour and lip volume</td>
<td>Superficial to mid dermis</td>
<td>23 mg/ml crosslinked HA with BDDE</td>
<td>27 G 1/2</td>
<td>Estimated duration: 6–9 months</td>
</tr>
</tbody>
</table>
## Special Indication: Under Eye/Tear Trough

<table>
<thead>
<tr>
<th>Product name</th>
<th>Company</th>
<th>Indications</th>
<th>Application depth</th>
<th>Material i.e. hyaluronic acid concentration and crosslinkage</th>
<th>Needle and/or cannula size</th>
<th>Special material properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEOSYAL® “Redensity [II]”</td>
<td>TEOXANE</td>
<td>Tear trough and eye circle</td>
<td>Pre-periostal, deep sub-orbicular</td>
<td>Semi-crosslinked HA 15 mg/g; A mix of crosslinked and non-crosslinked HA (added with patented “nutrients supplemented buffer”)</td>
<td>Needle: 30 G 1/2</td>
<td>Especially developed for the eye region, low water retention. Estimated duration: 9–12 months, with lidocaine</td>
</tr>
</tbody>
</table>

## Special Indication: Vaginal Rejuvenation

<table>
<thead>
<tr>
<th>Product name</th>
<th>Company</th>
<th>Indications</th>
<th>Application depth</th>
<th>Material i.e. hyaluronic acid concentration and crosslinkage</th>
<th>Needle and/or cannula size</th>
<th>Special material properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESIRIAL®</td>
<td>Laboratoires VIVACY</td>
<td>For intradermal injection in the vaginal area and for treatment of vaginal dryness and other symptoms of vulvo-vaginal atrophy</td>
<td>Depending on indication</td>
<td>19 mg IPN crosslinked HA</td>
<td>Needle: 2 x 30 G 1/2, 2 x 27 G 1/2</td>
<td>Desirial is the first worldwide HA product licensed for intradermal injection in the genital area and for treatment of vaginal dryness and other symptoms of vulvo-vaginal atrophy (CE)</td>
</tr>
<tr>
<td>DESIRIAL® PLUS</td>
<td>Laboratoires VIVACY</td>
<td>Certified for vaginal surgical, volumetric treatments (i.e. clitoris and g-spot injections, labial modelling)</td>
<td>Depending on indication</td>
<td>21 mg IPN crosslinked HA</td>
<td>Needle: 2 x 30 G 1/2, 1 x 18 G 80 blunt cannula</td>
<td>Polydensified, plastic gel. Compared to other volumizers, well modable</td>
</tr>
</tbody>
</table>
In addition to cosmetic use, filler materials are frequently employed for reconstruction of contour defects. Scars and tissue defects after accidents, surgery and irradiation are also ideal indications for injectables. The ideal filler should be easy to inject, easy to form, and should have a long lasting effect. Synthetic fillers such as calcium hydroxyapatite (CaHA), provide initial volume replacement but have an additional biostimulatory effect to supplement facial volumization and lifting.

HArmonyCa is one of the few resorbable fillers on the market that immediately replenishes lost volume while at the same time stimulating the production of the skin’s natural collagen for long-lasting results. HArmonyCa is a unique product because it provides both replacement volume and collagen biostimulation as a primary mechanism of action. In addition, it is biodegradable and reabsorbed naturally by the host’s metabolic processes.

HArmonyCa is based on a composite matrix of cross-linked hyaluronic acid embedding calcium hydroxyapatite microspheres, thus providing a strong volumizing, lifting effect. The synergy of two in one HArmonyCa combines hydroxyapatite and hyaluronic acid dermal fillers in one syringe.

Calcium hydroxyapatite is added during the cross-linking process, generating a stable, inseparable gel. Due to both calcium hydroxyapatite and hyaluronic acid properties, HArmonyCa provides a synergistic effect with long lasting results. Due to the combination of both active ingredients, collagen stimulation is higher than the use of each ingredient alone. Calcium hydroxyapatite stimulates new natural collagen production, while hyaluronic acid forms a supporting extracellular matrix, modulating proliferation of the fibroblasts.

The presence of hyaluronic acid elevates skin hydration and moisture, while also embedding the calcium hydroxyapatite, which can prevent microspheres aggregation and dispersion, keeping the microspheres within their desired location.

**ADDITIONAL ADVANTAGES**

HArmonyCa is susceptible to hyaluronidase. The hyaluronic acid gel component can be completely dissolved thus breaking the composite matrix infrastructure, which is 70% of the compound’s volume. Compared to other fillers, there are reduced side effects, such as burning sensation, edema and erythema thanks to the unique qualities and low level of osmolarity.

**MORPHOLOGY**

The hyaluronic acid is of non-animal origin, biocompatible and biodegradable, consisting of 55.7% CaHA microspheres (diameter of 25–45µm), that are strongly embedded within high-quality cross linked Hyaluronic Acid (BDDE <2ppm) as well as a phosphate buffer. The microsphere size and smoothness enable easy extrusion and reduced friction flow from the syringe into the treated site.

The microsphere diameter minimizes risk of particle migration and phagocytosis, which, in addition to the microspheres' integration within a net of cross-linked Hyaluronic Acid, ensures a smooth appearance.

Sea water osmolarity is ~1000 mOsM/kg, and the osmolarity of CaHA dermal fillers reaches ~2000 mOsM/kg, a trait that generates a strong burning sensation. In comparison, HArmonyCa osmolarity is ~300 mOsM/kg, similar to that of physiological saline at ~250 mOsM/kg, this allows us to minimize pain and side effects.

HArmonyCa is produced in a manufacturing facility operating under strict ISO9001 & ISO13485 conditions and is provided in a 1.25ml prefilled graduated syringe, it is also available with lidocaine. It is a patent pending promising product and is considered to be the new generation of dermal fillers.

Besides the immediate filling effect, HArmonyCa has the exceptional capability to trigger the creation of collagen fibres. These fibres not only lead to a filling effect, as with usual fillers, but also lead to lifting effect over a very long period.

**Further Information:**

Luminera Derm LTD
1 Bat Sheva St., Lod, Israel
info@luminera.com
www.luminera.com
**TEOSYAL® RHA 4* receives the Anti-Aging & Beauty Trophy as „BEST DERMAL FILLER“**

We are delighted to receive this award and would like to thank our excellent research and development department in Geneva,” said Carolin Marx, Managing Director of TEOXANE LABORATORIES Germany.

TEOSYAL® RHA4* from TEOXANE is a highly cross-linked hyaluronic acid of the next generation, which for the first time supports the skin and tissue in every movement and thus preserves vitality and elasticity. Behind this is the realization that not only static features, but also the dynamics of a face contribute significantly to its attractiveness and uniqueness. TEOSYAL® RHA4 is specially designed for volume build-up in certain regions such as the chin, zygomatic bone, temples or jawline. The results are natural and immediately visible. Once injected by the doctor, the hyaluron gel smoothes wrinkles from the inside, supports the tissue and restores the skin’s elasticity. The face gets a new elasticity and at the same time preserves its liveliness and natural radiance. Another plus point: the product is not perceptible and palpable, but becomes one with the dermal structure.

TEOXANE has developed four products for different facial areas and indications with its TEOSYAL®RHA line. The fillers are particularly suitable for dynamic areas such as the mouth region, cheeks, nasolabial folds, forehead, crow’s feet, but also for the neck and décolleté. The line comprises four differently cross-linked products: RHA1 for superficial and fine wrinkles, RHA2 for moderate wrinkles and the mouth region, RHA3 for deep wrinkles and RHA4 for volume in extended areas.

TEOXANE Laboratories, based in Geneva, specializes in the development and manufacture of hyaluronic acid-based products for aesthetic medicine and is now one of the market leaders in this field/innovative products for wrinkle treatment.

**Further Information:**
For further Information:  
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Am Lohmühlbach 17  
85356 Freising  
www.teoxane.com

*TEOSYAL RHA® 4 is a medical device (class III) with CE certification (CE0086) according to this regulation.

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**SAVE THE DATE!**

**3RD ESCAD SPRING COURSE**

**Saturday May 5th 2018, Budva - Montenegro**  
We will meet again after the end of the EADV Spring Symposium in Budva

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18. January, 2018, Atlanta GA –USA

For further information:
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Phone: +1 (435) 901 2544
srussell@sesprs.org
www.sesprs.org

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For further information:
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11.–15. April 2018, Dallas, TX – USA

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THE AESTHETIC MEETING 2018

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