

BIOXIS
PHARMACEUTICALS

#BIOXIS BEYOND
INNOVATION



Edito

Experiencing
**Premium
Technology**

—



«Our vision of widening research and technology to free us from the constraints of age opens up a unique space within the industry to build on strong capabilities, innovative solutions and safe, lasting results...»

FREDERIC BERTAINA - Bioxis CEO

In an exciting, ever-changing world, becoming a global leader in regenerative aesthetics may seem ambitious, especially given that we only began in 2010.

But, it's an ambition we believe in.

Our vision of widening research and technology to free us from the constraints of age opens up a unique space within the industry to build on strong capabilities, innovative solutions and safe, lasting results.

Over the last 7 years, we have been working on a unique portfolio that draws on public research programs by prestigious institutions such as CNRS, INSA and Lyon I University, as well as in-house insights shaped by new practitioner behaviors.

In 2018, BIOXIS Pharmaceuticals will launch its first medical device, CYTOSIAL. This premium range of dermal fillers is based on singular cross-linking technology that delivers easy-to-inject products with enhanced correction results and improved safety.

CYTOSIAL is the first step towards our aim of inventing the aesthetics of tomorrow.»

BIOXIS

PHARMACEUTICALS

**From research
partnership to
aesthetics pioneer.**

Born in 2010 from a cutting-edge research partnership, BIOXIS Pharmaceuticals is **driven by the desire to develop premium technology at the service of aesthetics, well-being and practitioners.** BIOXIS Pharmaceuticals **focuses on delivering technological innovations in beauty, anti-aging and regenerative medicine.**

Strengthened by a talented research and development team, the young company offers the same advantages as its more established counterparts - product security, production quality and standardized processes – to guarantee the highest standards.

For Bioxis, innovation has a dual objective: improving the experience for practitioners and providing high-quality results for patients. To achieve this, Bioxis has developed hyaluronic-acid based products offering some of the most qualitative results on the market.

Driven by an unwavering commitment to safety.

R&D processes are enabled by the latest pharmaceutical equipment including an ISO-7 cleanroom, industrial steam sterilization, pharmaceutical-standard water purity, and extensive final analysis of syringes before release.

The 130,000 syringes produced by Bioxis each year are subject to stringent standards to ensure a safer experience for practitioners and patients.

Bioxis has full control of all its manufacturing and development processes, directly in France, through ISO 13485 (Dir 93/42/CEE).

LABORATORY AND PRODUCTION MANUFACTORY BASED IN LYON, FRANCE

MANUFACTURING PROCESSES CERTIFIED IN EUROPE AND UNDER CFDA INSPECTION

THE HIGHEST EUROPEAN STANDARDS : ISO 13485 CERTIFICATION AND CE MARK BY BS

HIGHER LEVELS OF QUALITY CONTROL THAN RECOMMENDED BY THE INDUSTRY

During 2019, production will be scaled up with integrated processes compliant to CE, CFDA and US FDA.



Supported by **major organisations in the French Biotech Ecosystem**

ACADEMIC PARTNERS



INSTITUTIONAL PARTNERS



Inspired by a desire to Hatch innovative solutions.

At the cutting edge of aesthetic medicine,
**Bioxis is dedicated to improving results and
methods for practitioners and patients alike.**

The talented team of researchers and developers has spent years developing monophasic cross-linked HA products with some of the most qualitative results on the market. They are also committed to ambitious R&D projects to further disrupt regenerative medicine.

UNDER DEVELOPMENT

The first dermal filler in 20 years
to use a new matrix since
hyaluronic acid and collagen.

« Our research is based on innovative tissue engineering strategies. Using new natural polymers that stimulate the regenerative capacity of tissues guarantees lasting, qualitative results. »

CHITOSAN

A natural, highly biomimetic polysaccharide. Bioxis teams have successfully harnessed its capacity for bio-reabsorption and regeneration to create a lasting, yet re-absorbable implant for safer, longer-lasting results.

MTI-12[®]

Liquid-to-gel injectable monophasic tissular inductor. Drawing on the exceptional regenerative properties and high tolerance of chitosan, this device makes application smoother and safer to deliver improved natural results. Currently under clinical testing.

CYTOSIAL

The New Generation Hyaluronic Acid

CYTOSIAL® is **a range of new-generation monophasic hyaluronic acid dermal fillers**

that regenerate the skin to wipe away the signs of aging, with natural looking results.

CYTOSIAL MEDIUM

Is indicated for:

- Volume restoration and the filling of cutaneous depressions and wrinkles.
 - Facial reconstruction of volumes in the event of light-to-moderate lipodystrophies, i.e. due to HIV treatment.
- Cytosial Medium is indicated for the filling of moderate cutaneous depressions as perioral or commissural area.*

CYTOSIAL DEEP WRINKLES

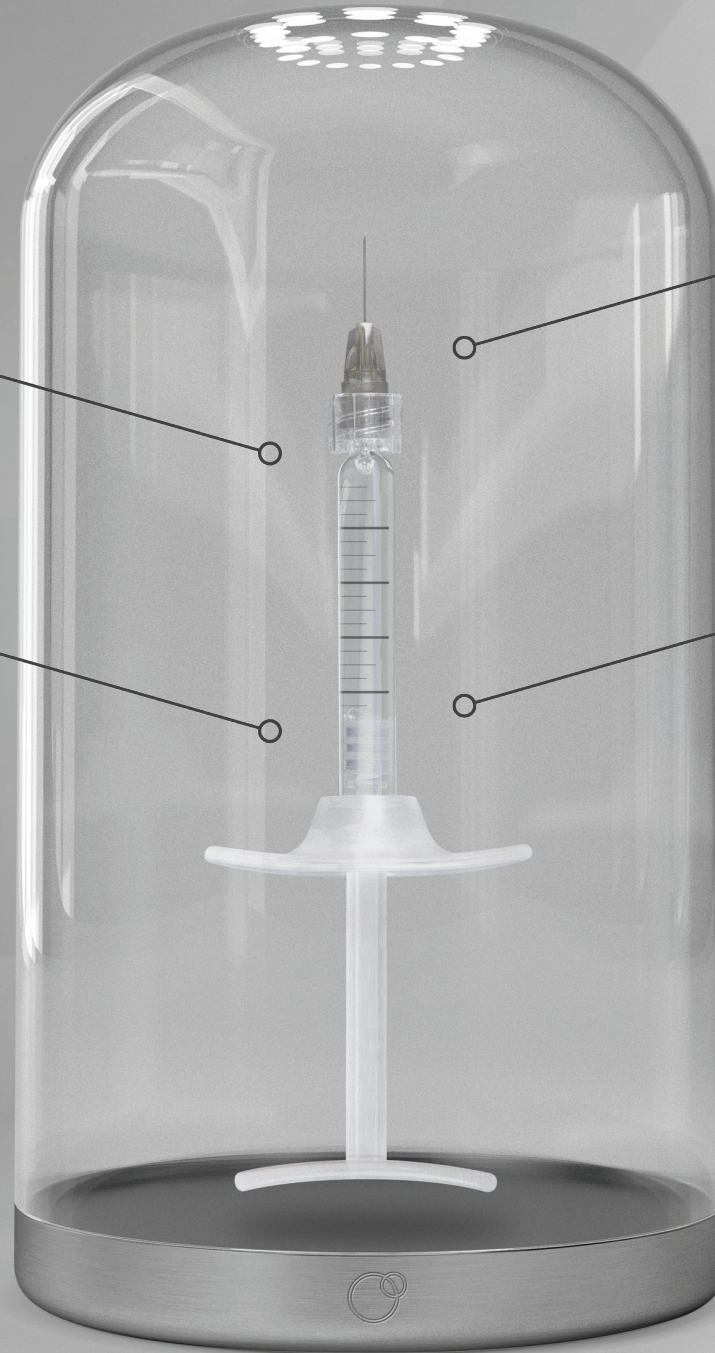
Is indicated for:

- Volume restoration and the filling of cutaneous depressions and wrinkles.
 - Facial reconstruction of volumes in the event of light-to-moderate lipodystrophies, i.e. due to HIV treatment.
- Cytosial Deep Wrinkles is indicated for the filling of deep facial wrinkles, such as nasolabial folds and marionette lines.*

CYTOSIAL VOLUME

Is indicated for:

- Volume restoration and the filling of cutaneous depressions and wrinkles.
 - Facial reconstruction of volumes in the event of light-to-moderate lipodystrophies, i.e. due to HIV treatment.
- Cytosial Volume is indicated for the augmentation of cheeks, cheekbones and facial contours, as well as the filling of very deep wrinkles.*



SAFE

*Fewer impurities.
Very low bioburden and residual BDDE rate.
High level of controls during manufacturing.*

EFFICIENT

*Enhanced rheological performance.
Easy-to-inject product.
1.1 mL of HA per syringe.*

LASTING

*Low shear rate.
Very good mechanical resistance.
and degradation ratio.*

QUALITATIVE

*CE mark by BSI.
Homogenous Final product.
Biofermentation HA origin.*



**MANUFACTURING PROCESSES
CE MARK CERTIFIED AND
UNDER CFDA INSPECTION**



**CERTIFICATION ISO 13485
AND CE MARK BY BSI, THE
HIGHEST EUROPEAN STANDARDS**

CYTOSIAL MEDIUM

Is indicated for :

*The filling of moderate cutaneous
depressions as perioral
or commissural area*

HA concentration : 25 mg/ml

Volume : 1.1ml

Needle size : 27 G^{1/2} or 30 G

Injection : Mid and Upper dermis, lips

Ejection force : 10 - 25 N

BDDE rate : 1.15%

BDDE residual rate : ≤ 2 ppm



PERIORAL WRINKLES

LIP VOLUME AND CONTOURS



CYTOSIAL MEDIUM

CYTOSIAL DEEP WRINKLES

Correct deep lines :

*Deep wrinkles
Deep nasolabial fold
Deep marionette fold*

HA concentration : 25 mg/ml

Volume : 1.1ml

Needle size : 27 G^{1/2}

Injection : *Deep and mid dermis*

Ejection force : 10 - 25 N

BDDE rate : 1.50%

BDDE residual rate : ≤ 2 ppm

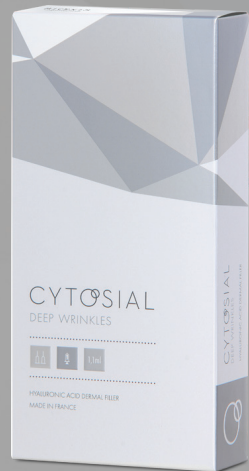


GLABELLA WRINKLES

CROW'S FEET

NASOLABIAL FOLDS

MARIONETTE LINES



CYTOSIAL DEEP WRINKLES

CYTOSIAL VOLUME

Restore facial volume :

*Cheeks and cheekbones
Chin
Facial volume loss*

HA concentration : 25 mg/ml

Volume : 1.1ml

Needle size : 27 G^{1/2}

Injection : Deep and mid dermis

Ejection force : 10 - 25 N

BDDE rate : 2.15%

BDDE residual rate : ≤ 2 ppm



CHEEKS

TEMPLES

CHIN

OVAL FACE

NECK REMODELING



CYTOSIAL VOLUME

Plunge into the heart of **Velvet Technology**®

HA-Tech is based on the unique, patented savoir-faire BIOXIS developed to help aesthetic practitioners cater to the evolving the needs of their patients.

HOMOGENEOUS

Optimized linearization process
Thin layer crosslinking
Product similar to extracellular matrix

RHEOLOGICAL PERFORMANCE

Constant force injection
Less BDDE for the same rheological properties

NATURAL RESULTS

Low shear rate destructureation
Slow degradation by hyaluronidase

SAFETY & TOLERANCE

Continuous dialysis process
to eliminate all residues
Better conserve HA chains



« The CYTOSIAL® range was imagined around one main concept, homogeneity. Based on this simple idea, Velvet Technology was designed to create the most regular hyaluronic acid network possible without any structural failures or crosslinking anomalies. Thanks to this original approach, Velvet Technology guarantees adapted indication-specific rheological performance, while maximizing patient comfort. »

ALEXANDRE GUERRY - Scientific Research Manager

SHARE IN A SINGULAR VISION OF HA CROSSLINKING

SMOOTH, HOMOGENEOUS GEL TO ENSURE EASY APPLICATION, **MINIMUM SIDE EFFECTS AND REGULAR DEGRADATION**

1

MIXING AND DISSOLUTION

Linearization for better homogeneity.

2

THIN LAYER CROSSLINKING

Boost rheological performance.

3

LOW SHEAR RATE DESTRUCTURATION

Preserve quality product until injection.

4

CONTINUOUS DIALYSIS

Enhance safety and tolerance.

Velvet Technology® Homogeneous

Optimized linearization process

Thin layer crosslinking

Product similar to extracellular matrix

Velvet Technology®

Rheological performance

Constant force ejection

Excellent ejection force stability

RHEOLOGICAL PROPERTIES COMPARISON

At BIOXIS, we compared the rheological properties of competitor products (Allergan, Galderma and Merz...) with the Cytosial range in terms of Ejection force (EF), stability of Ejection force (sEf), Viscosity (η) and Elasticity ($Tan\delta$).⁽¹⁾

MAIN EJECTION FORCE DEFECT

Generally admissible ejection force does not exceed 25N-30N. Ejection force is in function of the injection system (syringe, needle) and the formulation (rheological parameters). Both can modulate the value of ejection force. The ejection force gives access indirectly to the structure of the matrix (presence of particles, bloc, bubble and other defect). Three main anomalies can be observed:

Punctual anomaly : *Caused by punctual particles, small blocs, fibers, impurities (punctual increase of EF), or bubbles (punctual decrease of EF)*

Low frequency anomaly : *due to of large and dense bloc (slow increase then decrease of EF more than 100 μ l)*

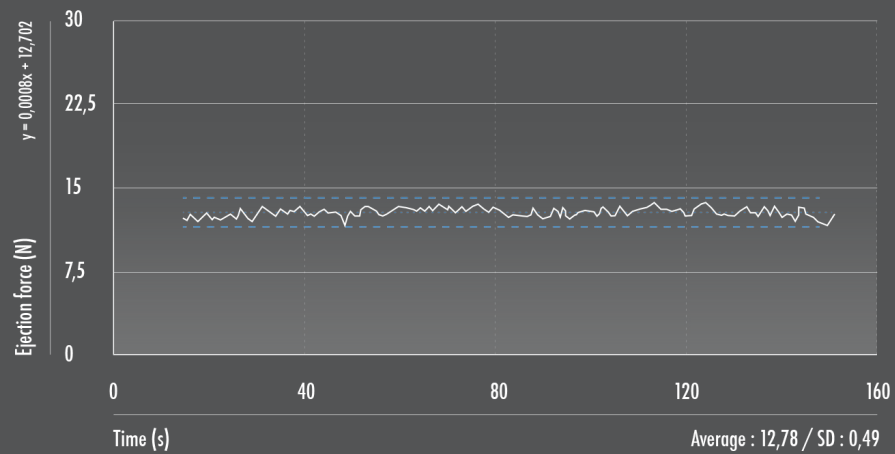
High frequency anomaly : *Caused by numerous particles, granular texture, numerous aggregate (quick variations of ejection forces)*

⁽¹⁾ Rheological properties of competitive ranges : ejection force, viscosity and elasticity of 4 products of the market (Allergan, Bioxis, Galderma and Mertz) ; IMCAS 2018, commented poster, in process

CYTOSIAL DEEP WRINKLES

The Cytosial range is characterized by a very stable injection force without any significant variation. This means the gel is homogenous and does not contain any over or under crosslinked areas, particles or bubbles. Given the high rheological properties of the Cytosial range, the ejection force is low.

EJECTION FORCE CYTOSIAL DEEP (27G)



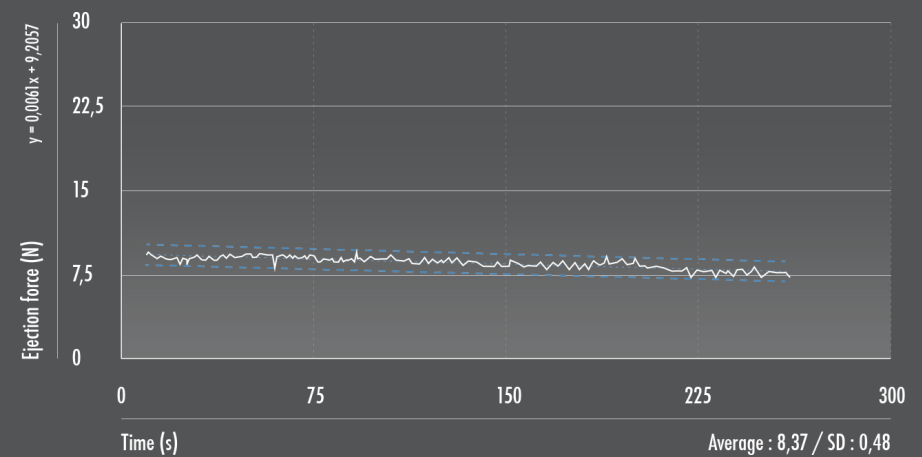
ELASTICITY (Tan delta): 0.18

VISCOSITY (Pa.s): 2900

PRODUCT 1

This first competitor's brand provides a stable ejection force, mainly thanks to the syringe design. However, anomalies can be detected and amplified by the large amplitude of syringe. Moreover, high amplitude syringes can cause discomfort to practioners with smaller hands.

EJECTION FORCE PRODUCT 1 (27G)



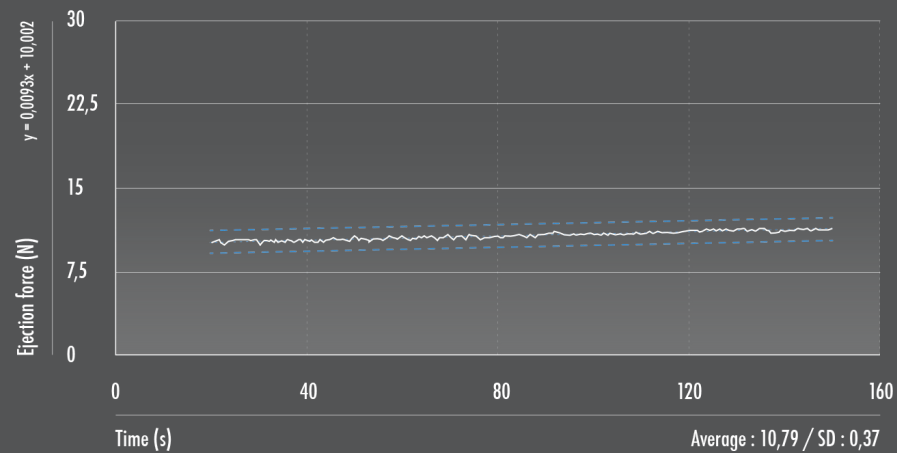
ELASTICITY (Tan delta): 0.21

VISCOSITY (Pa.s): 2465

PRODUCT 2

This HA gel is a biphasic product and therefore displays low viscosity and low elasticity. Particle migration within the skin can be associated with the rheofluidifying behavior observed in viscosity.

EJECTION FORCE PRODUCT 2 (29G)



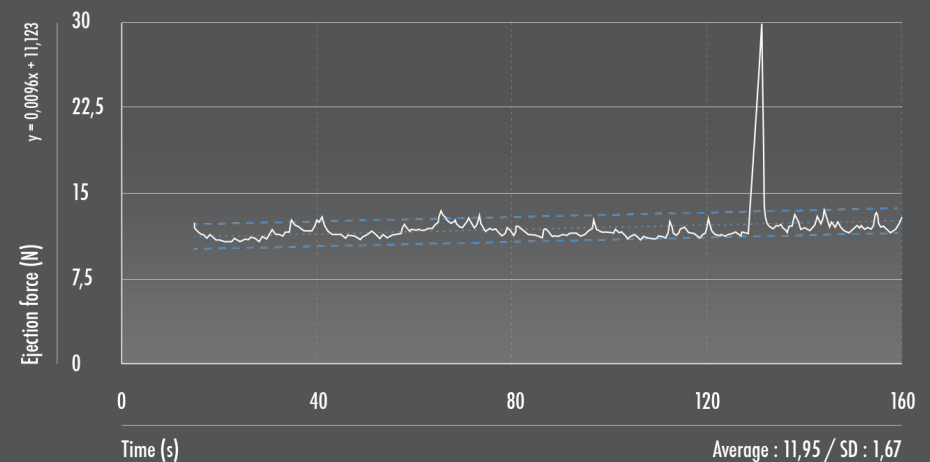
ELASTICITY (Tan delta): 0.32

VISCOSITY (Pa.s): 1646

PRODUCT 3

With regards to the ejection force, the rheological properties are very low. The heterogeneity of the gel artificially increases the ejection force. 228 Pa.s is representative of a solution with a low quantity of crosslinking areas. This observation also applies to the elasticity. Due to the unexpected results, the test was carried out on two different batches of this competing product Balance with the same properties observed on both occasions.

EJECTION FORCE PRODUCT 3 (27G)



ELASTICITY (Tan delta): 0.73

VISCOSITY (Pa.s): 228

Velvet Technology®

Natural Results

Low shear rate destructureation

Slow degradation by hyaluronidase

Very good mechanical resistance

**Dermal fillers based on crosslinked hyaluronic acid
with BDDE exhibit 3 main forms of degradation in vivo:**

Mechanical degradation
Free radical degradation
Enzymatic degradation

Resistance to mechanical stress

The G' value indicates the deformation energy contained in the matter during deformation. When the stress or pressure is removed, this energy is available to restore the matter to its original shape, fully or partly reversing the deformation.(1)

The G' plays a major role for the efficacy of crosslinked HA dermal filler. This parameter is determined by the HA concentration, the molecular weight of the HA and the share of non-crosslinked HA in the end product. The high elastic modulus have a better filling effect and a longer retention time in soft tissue. In addition, the high value of G' means that less product is required to achieve the same effect as with less elastic dermal fillers.(1,2)

Higher gel concentration produces more molecular estrangement and in so doing increases the modulus of the formulation. Gels with higher G' are better at resisting dynamic forces occurring during facial muscle movement and thus may provide better support and lift, as well as longer duration. Gels with low G' are probably better suited to areas with static and superficial wrinkles, where resistance to deformation is not critical (3,4)

Resistance to free radical degradation (Oxidative stress)

Glycosidic bonds are very weak against oxidative stress. Resistance to free radical degradation is directly linked to the number of glycosidic linkages and therefore also HA.(5)

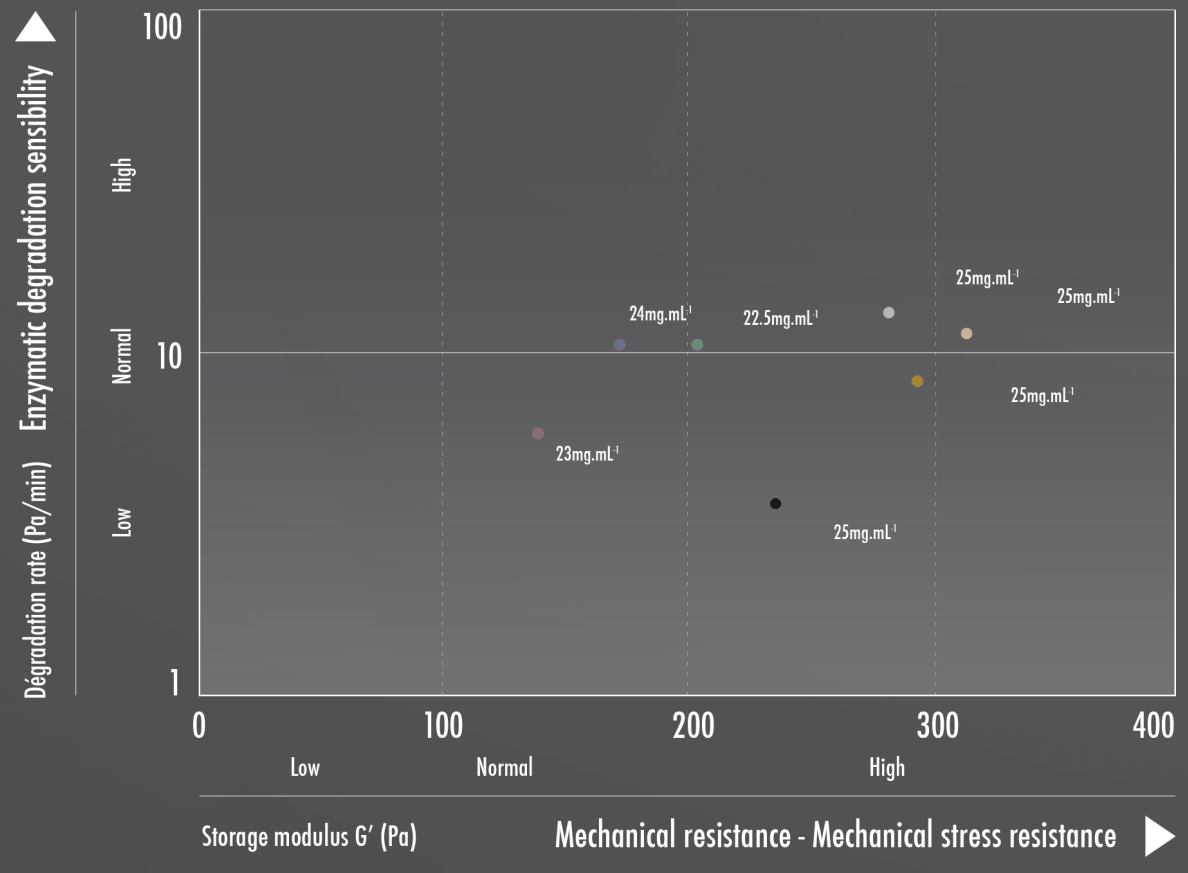
Resistance to enzymatic degradation

Degradation behavior of dermal fillers were very heterogeneous in function of the references. Cytosial products have a balanced position, which is a good compromise between initial mechanical properties and degradation rate.

CYTOSIAL Range has a very good resistance to enzymatic and mechanical degradation : a promise of a long lasting effect.

(1) Bingöl, A. F.; Dogan, A. *Magazin für ästhetische Chirurgie* 2012, 2, 6-12. *Physical Properties of Hyaluronic Acid Fillers and Their Relevance for Clinical Performance*
 (2) Edsman, K.; Nord, L. I.; Öhrlund, Å.; Lärkner, H.; Kenne, A. H. *Dermatologic Surgery* 2012, 38, 1170-1179. *Gel Properties of Hyaluronic Acid Dermal Fillers*
 (3) Kablik, J.; Monheit, G. D.; Yu, L.; Chang, G.; Gershkovich, J. *Dermatologic Surgery* 2009, 35, 302-312. *Comparative Physical Properties of Hyaluronic Acid Dermal Fillers*
 (4) Pierre, S.; Liew, S.; Bernardin, A. *Dermatologic Surgery* 2015, 41, S120-S126. *Basics of Dermal Filler Rheology*
 (5) Boule, K.; Glogau, R.; Kono, T.; Nathan, M.; Tezel, A.; Roca-Martinez, J. X.; Paliwal, S.; Stroumpoulis, D. *Dermatologic Surgery* 2013, 39, 1758-1766. *A Review of the Metabolism of 1, 4-Butanediol Diglycidyl Ether-Crosslinked Hyaluronic Acid Dermal Fillers*

DEGRADATION TEST COMPARING 7 HA PRODUCTS OF THE FRENCH MARKET



● **CYTOSIAL VOLUME**
● **CYTOSIAL DEEP WRINKLES**
● **ART FILLER UNIVERSAL**
● **PRINCESS**
● **TEOSIAL DEEP LINES**
● **JUVEDERM ULTRA 3**
● **STYLAGE M**

ART FILLER UNIVERSAL is a registered trademark of FILORGA - PRINCESS is a registered trademark of CROMA PHARMA
 JUVEDERM ULTRA 3 is a registered trademark of ALLERGAN - TEOSIAL DEEP LINES is a registered trademark of TEOXANE
 STYLAGE M is a registered trademark of VIVACY

Velvet Technology®

Safety & Tolerance

Continuous dialysis

Patented pH controlled process to eliminate all residues

Better conservation of HA chains

« BIOXIS Pharmaceuticals fully masters each production step from receiving the components to launching the finished product. The exacting standards applied during production are essential in ensuring patient safety and obtaining products that respect international requirements. »

Caroline ROSSET - Regulatory Affairs and Quality Manager

Welcome to a world of Privilege

With CYTOSIAL[®], BIOXIS[®] Pharmaceuticals
wants to provide the leading service
offering in realm of aesthetic innovation.

**YOU ARE NOT JUST BUYING A PRODUCT,
BUT ALSO A SERVICE OFFERING INCLUDING:**

CORE SERVICE

*Good products with high-quality
aftersales and warranty service*

AN EFFECTIVE CUSTOMER SERVICE

*Sales department, quality and
medical affairs and marketing
informations are at your disposal.*

PREMIUM SERVICE FOR PREMIUM CUSTOMERS

*Trainings, congress invitations,
participation in studies,
exclusive events & more*

ONE DRIVING GOAL

*Increase the satisfaction of BIOXIS
customers with Privilege Club.*

Deliver
dual-action
aesthetic
regeneration :
**Correct
& Restore.**

*« CYTOSIAL enables BIOXIS
to obtain natural, lasting
results to correct the signs
of aging. The patented
production method generates
a product that is easy
to inject, and therefore less
painful for patients and
easier for practitioners
to apply precisely. »*

ROMAIN HEMERY - VP Innovation & Medical



CYTOSIAL MEDIUM

Is indicated for :

The filling of moderate cutaneous depressions as perioral or commissural area

HA concentration : 25 mg/ml

Volume : 1.1ml

Needle size : 27 G^{1/2} or 30 G

Injection : Mid and Upper dermis, lips

Ejection force : 10 - 25 N

BDDE rate : 1.15%

BDDE residual rate : ≤ 2 ppm

CYTOSIAL MEDIUM is indicated for:

-Volume restoration and the filling of cutaneous depressions and wrinkles.
-Facial reconstruction of volumes in the event of light-to-moderate lipodystrophies, i.e. due to HIV treatment. Cytosial Medium is indicated for the filling of moderate cutaneous depressions as perioral or commissural area.



CYTOSIAL DEEP WRINKLES

Correct deep lines :

*Deep wrinkles
Deep nasolabial fold
Deep marionette fold*

HA concentration : 25 mg/ml

Volume : 1.1ml

Needle size : 27 G^{1/2}

Injection : Deep and mid dermis

Ejection force : 10 - 25 N

BDDE rate : 1.50%

BDDE residual rate : ≤ 2 ppm

CYTOSIAL DEEP WRINKLES is indicated for:

-Volume restoration and the filling of cutaneous depressions and wrinkles.
-Facial reconstruction of volumes in the event of light-to-moderate lipodystrophies, i.e. due to HIV treatment. Cytosial Deep Wrinkles is indicated for the filling of deep facial wrinkles, such as nasolabial folds and marionette lines.



CYTOSIAL VOLUME

Restore facial volume :

*Cheeks and cheekbones
Chin
Facial volume loss*

HA concentration : 25 mg/ml

Volume : 1.1ml

Needle size : 27 G^{1/2}

Injection : Deep dermis or subcutaneous

Ejection force : 10 - 25 N

BDDE rate : 2.15%

BDDE residual rate : ≤ 2 ppm

CYTOSIAL VOLUME is indicated for:

-Volume restoration and the filling of cutaneous depressions and wrinkles.
-Facial reconstruction of volumes in the event of light-to-moderate lipodystrophies, i.e. due to HIV treatment. Cytosial Volume is indicated for the augmentation of cheeks, cheekbones and facial contours, as well as the filling of very deep wrinkles.

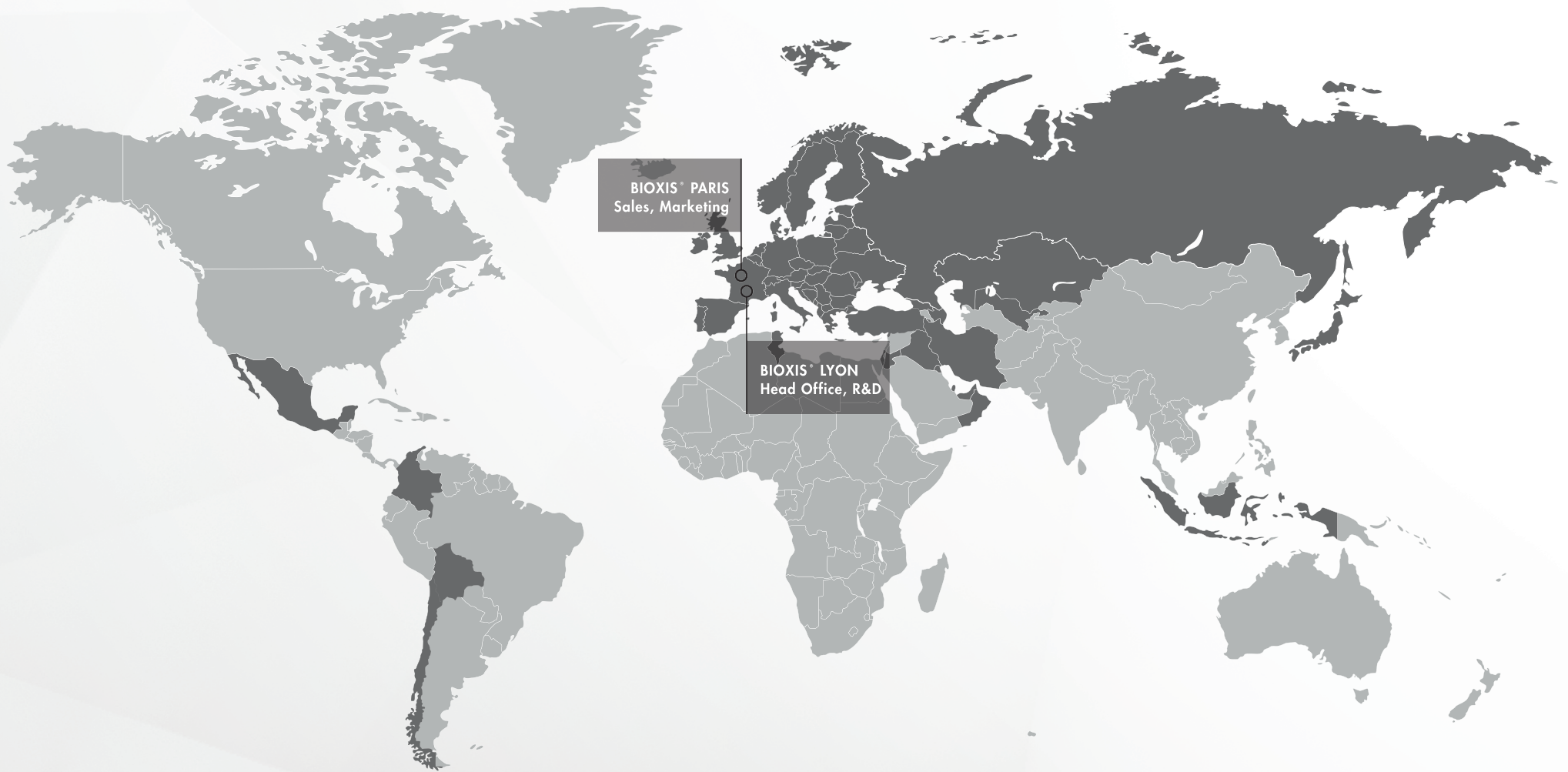
**DO YOU WANT TO KNOW WHAT
BIOXIS PHARMACEUTICALS CAN OFFER YOU?
CONTACT OUR SALES MANAGER
TO FIND THE MOST ADAPTED SOLUTION.**

info@estheticmed.ch

**« BIOXIS provides a complete
range of products adapted to
the needs of practitioners, as
well as a high level of service
to make their lives easier.
Agile and responsive, BIOXIS
is always available to listen
and support its clients. »**

J.M LAROCHE - VP Sales

CYTOSIAL® is available:



BIOXIS

PHARMACEUTICALS

BIOXIS PHARMACEUTICALS

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69007 Lyon, France

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contact@bioxis.com

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