



INNOVATING FUTURE LIFE

ABOUT BIOCERAMED

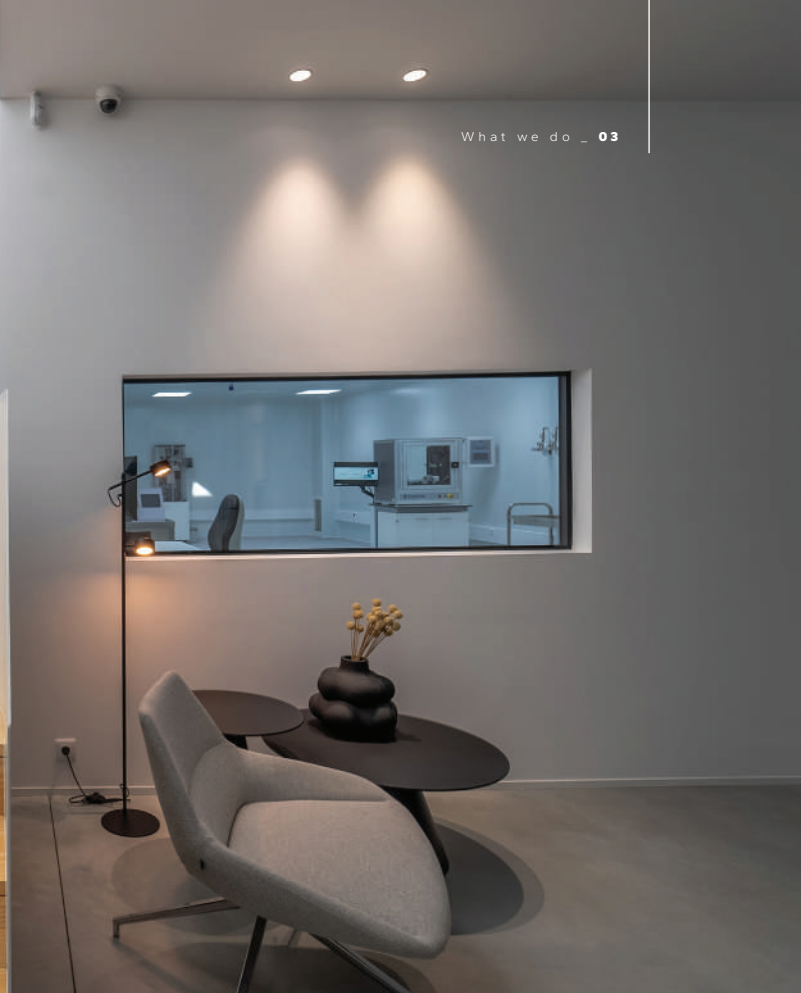
Bioceramed, a Hydrumedical company, is a leading European orthobiologic healthcare company, specializing in the design, manufacture, and sale of calcium phosphate substitutes for bone regeneration. With a strong focus on regenerative approaches, **Bioceramed's** portfolio also includes advanced solutions such as viscosupplementation, featuring hyaluronic acid injections, and Platelet-Rich Plasma (PRP) therapies.

Currently, **Bioceramed** products are sold in over 50 countries. The company is ISO 13485:2016 certified, ensuring that all production complies with European medical device directives and regulatory requirements.

Innovation is at the core of **Bioceramed's** strategy. Our R&D team, in collaboration with academic partners, develops solutions to enhance the performance of medical devices. **Bioceramed** has designed and developed innovative biomaterials for bone regeneration across various medical fields, including orthopedic, trauma, spine, dental, and craniofacial surgeries.

Bioceramed headquarters





ISO 7 clean rooms



Transparency in every step forward

WHAT WE DO

Bioceramed S.A. is a manufacturer specialized in bone substitute biomaterials used in Orthopedics, Spine, and Dental applications.

We are also an orthobiologic company with a comprehensive portfolio that includes PRP (Platelet-Rich Plasma) and viscosupplementation with Hyaluronic Acid.

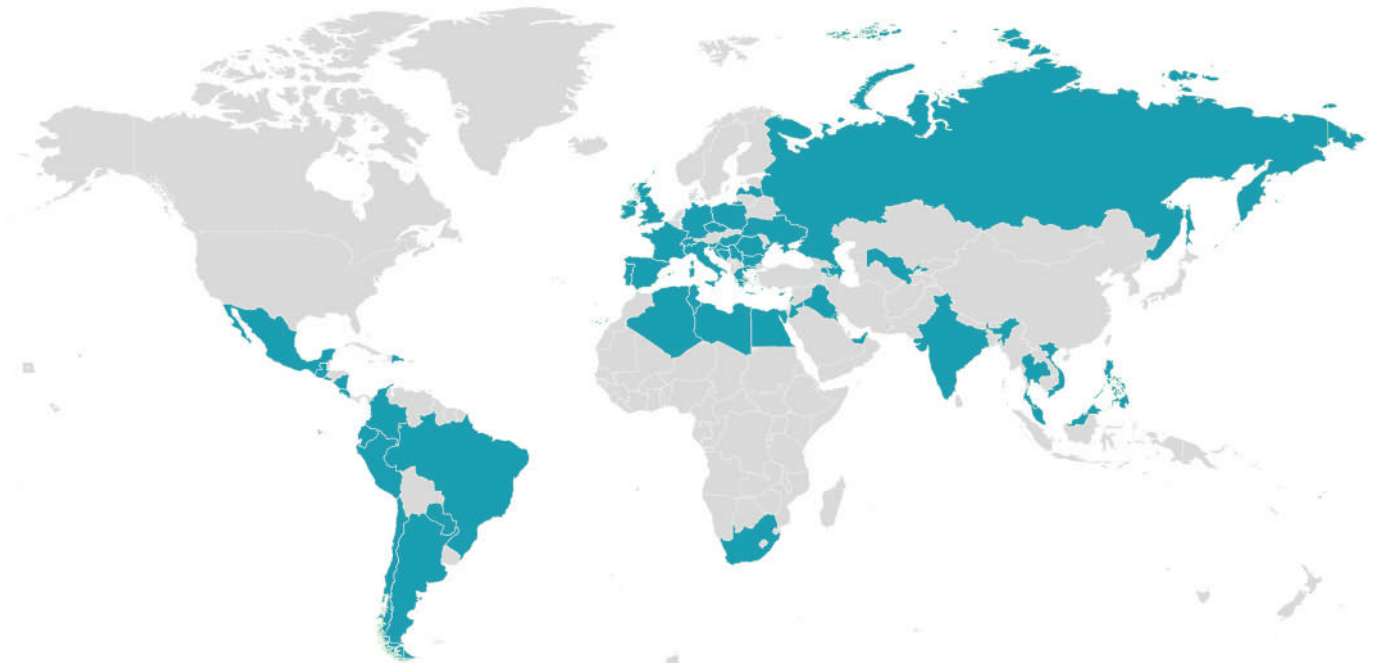
Our offerings encompass solid structures (granules, blocks, wedges), injectable bone substitutes, and Calcium Phosphate Cement.

Committed to advancing patient care, we continuously innovate to support tissue regeneration and improve clinical outcomes across various medical fields.



- +90 000
surgeries
- +50
countries
- +40
distributors

OUR GLOBAL IMPACT



COMPANY VALUES

IMPROVING QUALITY OF LIFE: We strive to enhance people's lives through innovative, high-tech medical devices based on scientific and clinical evidence. This commitment to well-being is the foundation of all our actions.

INNOVATION AND CONTINUOUS DEVELOPMENT: Innovation is at the heart of our work. We invest in new ideas and solutions that push the boundaries of medical technology, working in partnership with researchers, doctors, and research institutions, and supported by our own internal research and development department.

EXCELLENCE AND HIGH QUALITY STANDARDS: We maintain high quality standards in every stage of the development and production of our devices, ensuring each product is reliable, effective, and safe, grounded in proven clinical results.

TRANSPARENCY AND TRUST: The trust of our clients and partners is essential. We foster transparent, honest relationships, supported by concrete information and real results, with complete integrity in every interaction.

VALUING AND DEVELOPING OUR TEAM: We believe that the growth of our employees is crucial to the growth of the company. We invest in training and individual development plans, creating a safe, transparent workplace that fosters the potential of each person.

RESPECT AND EQUALITY: We promote an inclusive environment, where honesty, boldness, respect for differences, and equality in gender, race, and beliefs are fundamental. We value diverse perspectives and believe they enrich our ability to innovate.

SUSTAINABILITY AND SOCIAL RESPONSIBILITY: We are committed to minimizing environmental impact and maximizing positive community impact. Social responsibility is a priority, both through providing medical devices that improve health and quality of life and through active involvement in innovation ecosystems and partnerships with public and nonprofit research institutions.

Our team
↓





H Y A L U R O N I C A C I D

Healviscos One
Healviscos 2.2
Healviscos Mini
Healviscos Tendon
Healviscos Dental

HEALVISCO®

ENHANCED JOINT MOBILITY

Healvisco hyaluronic acid viscosupplementation is intended to augment the native synovial fluid, which may be deficient in both quantity and quality in individuals suffering from joint disorders such as osteoarthritis or following traumatic injuries.

OPTIMIZED PARAMETERS

Each **Healvisco** model possesses a meticulously chosen concentration, tailored for its specific application, and an optimal high molecular weight, capable of effectively binding to and clustering numerous CD44 receptors. This interaction induces an anti-catabolic response in joint cells.

PATIENTS BENEFITS

→ Reduced Pain:

- › Provides enduring alleviation from joint pain and discomfort.
- › Superior pain mitigation compared to corticosteroid interventions.

→ Improved Joint Function:

- › Augmented joint lubrication, thereby enhancing mobility and alleviating stiffness.



BIOLOGICAL RESPONSES

→ Anti-inflammatory Effect:

- › Impedes the activation of pivotal pro-inflammatory cascade factors such as COX-2 and iNOS in cartilage cells.
- › Reinstates collagen type II production amidst pro-inflammatory conditions.

→ Chondroprotective Effect:

- › Fosters a conducive milieu for chondrocyte proliferation and function.

→ Antinociceptive Effect:

- › Mitigates nerve impulse activity, exerting an antinociceptive influence.

→ Induction of Endogenous HA Production:

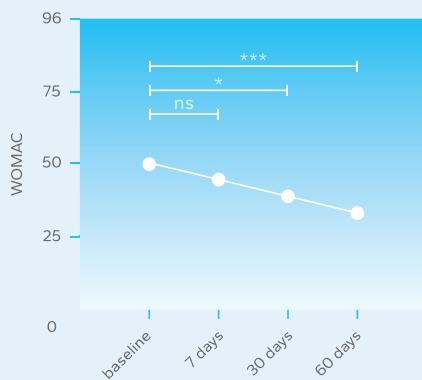
- › Intra-articular administration of Healvisco elicits an augmentation in endogenous HA synthesis.

HEALVISCO® ONE

- Sodium hyaluronate: 120mg in 4.8 ml
- Molecular weight: 1800-3200 kDa
- Viscosity: 350-650 PA-s
- The highest amount of HA in a single injection – 120mg

CLINICALLY CONFIRMED EFFECTIVENESS AFTER A SINGLE INJECTION

A single injection of Healvisco One has shown significantly reduced pain and stiffness, while also improving patient mobility, enhancing joint function and the overall physical condition of patients.



Functional status of OA patients treated with Healvisco® One
(*** - $p < 0.0001$, * - $p < 0.05$)





HEALVISCO® 2.2

- Sodium hyaluronate: 44 mg in 2 ml
- Molecular weight: 1200 - 1400 kDa
- Viscosity: 200-380 Pa·s

THE MOST VERSATILE HYALURONIC ACID

- Intra-articular injections can be administered at weekly intervals.
- Suitable for use in various joints, including the knee, elbow and shoulder.



MULTIPLE INJECTION THERAPY FOR OSTEOARTHRITIS RELIEF

- Improved joint mobility and pain relief during the recovery period, especially after arthroscopy, acting synergistically with rehabilitation.
- Administration is recommended as a triple intra-articular therapy. Clinical data show that three consecutive intra-articular injections of hyaluronic acid gel with suitable properties, such as Healvisco® 2.2, at seven-day intervals, are effective in improving osteoarthritis symptoms for at least six months.

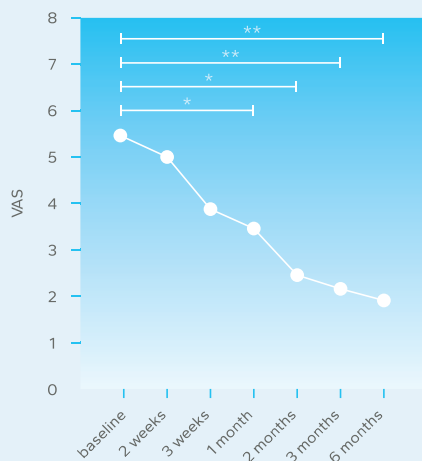
HEALVISCO® MINI

- Sodium hyaluronate: 16 mg in 1 ml
- Molecular weight: 1200-1400 kDA
- Viscosity: 60-100 Pa·s

Healvisco Mini® is indicated for the treatment of osteoarthritis and other degenerative conditions. Meticulously designed to ensure precision and efficacy, the product effectively aids in restoring mobility and relieving pain, providing lubrication and impact absorption in the treated joints.

METICULOUSLY DESIGNED TO ENSURE PRECISION, PARTICULARLY SUITABLE FOR SMALL JOINTS:

- Facet joint
- Metatarsophalangeal joint
- Carpometacarpal joint
- Temporomandibular joint
- Interphalangeal joint
- Ankle joint



Pain measured on VAS scale in OA patients treated with 3 injections of Healvisco® Mini
 (** - $p < 0.01$, * - $p < 0.05$)

EFFECTIVE PAIN REDUCTION AFTER ONE TO THREE INTRA-ARTICULAR INJECTIONS:

- A three intra-articular injections therapy regimen of Healvisco Mini has been clinically proven to alleviate osteoarthritis (OA) symptoms in the ankle joint for a duration of at least six months.

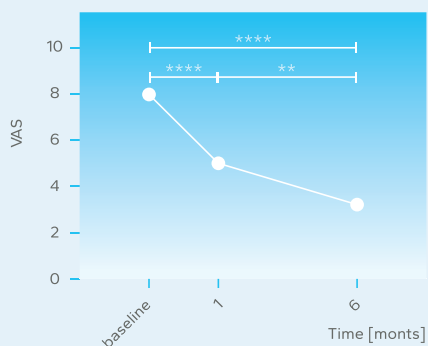
HEALVISCO® TENDON

- Sodium hyaluronate: 16 mg in 1 ml
- Sodium hyaluronate: 32 mg in 2 ml
- Molecular weight: 1400-1600 kDA
- Viscosity: 70-200 Pa·s

PRECISELY SELECTED OPTIMALLY HIGH MOLECULAR WEIGHT:

- Optimal long-chain hyaluronic acid ensures effective binding to CD44 receptors, promoting a robust cellular response with anti-catabolic effects that help prevent cartilage breakdown and may slow degenerative changes. This activation also inhibits pro-inflammatory cytokines, reducing inflammatory cell migration and activity, which contributes to decreased inflammation over time.

EFFECTIVE AND LONG-LASTING PAIN REDUCTION IN MULTIPLE INDICATIONS



Pain measured on VAS scale in patients with Patellar Tendinopathy treated with Healvisco® Tendon
 (**** - $p < 0.0001$, * - $p < 0.01$)



MECHANISM OF ACTION:

- Reduction of catabolic enzymes synthesis
- Inhibition of negative effects of oxidative stress
- Reduction of the inflammatory phase
- Inhibition of excessive cell proliferation

HEALVISCO® PRODUCT LINE FAQs

1. Why does HEALVISCO use a linear molecule design for hyaluronic acid (HA)?

The linear molecule design of native HA provides the same duration of clinical benefit as cross-linked HA but without the additional risk of side effects. The market trend is moving away from cross-linked HA, favoring the safer linear design.

2. What is the expiry period for HEALVISCO products?

All HEALVISCO HA products have an expiry period of 36 months from the production date.

3. How long does the effect of HEALVISCO 2.2 typically last?

The clinical effect of HEALVISCO 2.2 generally lasts around 7-8 months, though factors such as age, injury history, joint biomechanics, and obesity levels can influence the duration. Clinical data collection is ongoing to further confirm this duration.

4. Does the 4.8 ml volume of HEALVISCO ONE cause discomfort after injection?

The 4.8 ml volume is specifically designed to ensure effective single-dose treatment and is well-tolerated by the knee joint. There have been no reported complaints regarding discomfort due to this volume.

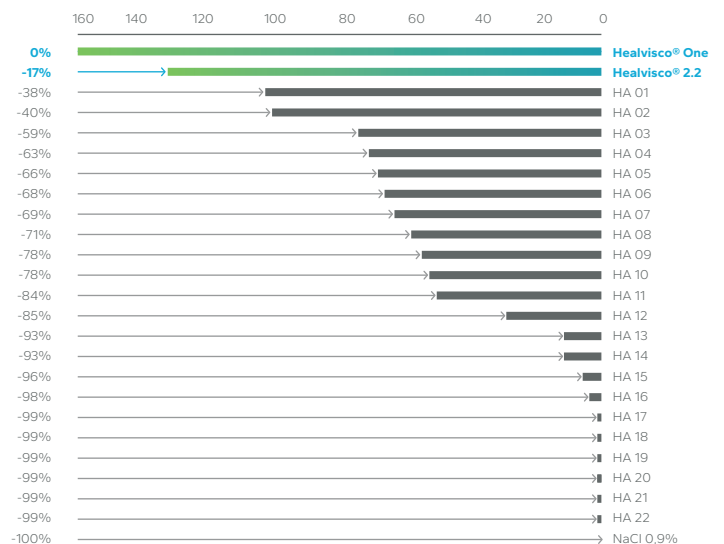
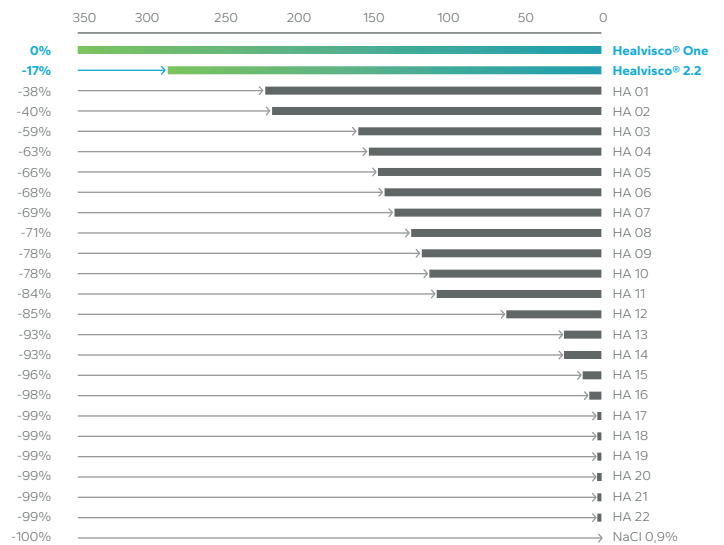
5. What factors might diminish the effectiveness of HA therapy?

To optimize HA therapy, it's recommended to avoid combining it with steroids, especially in the same injection. Steroid treatments should be stopped at least 14 days prior to HA injection. Factors like past trauma (e.g., meniscus tears), the stage of osteoarthritis (OA), and lifestyle factors (such as regular physical activity guided by a physiotherapist) can also impact therapy effectiveness.

6. What shear rate is used to measure the viscosity of HEALVISCO?

The viscosity (Pa·s) of HEALVISCO products is measured across shear rates ranging from 0.001 to 100 Pa·s.

Elasticity measured under conditions analogous to running activity (2.5 Hz). G' module [Pa*s] H01 to H22 - commercial Hyaluronic Acids available (data on file Bioceramed) ↓



↑ Viscosity measured under conditions analogous to walking activity (0.5 Hz). G' module [Pa*s] H01 to H22 - commercial Hyaluronic Acids available (data on file Bioceramed)

7. How does HEALVISCO compare to competitors like Durolane and Synvisc One in terms of viscosity?

• HEALVISCO's viscosity values are tailored specifically to its indications, rather than competing on higher viscosity or molecular weight. Excessively high molecular weight (MW) in cross-linked HA products is not ideal for CD44 receptor signaling, as it may lead to less elasticity and increased brittleness. HEALVISCO's optimal viscosity and molecular weight are designed for effective, durable results in OA treatment.

8. How is the molecular weight of HEALVISCO's HA optimized?

• HEALVISCO products have high molecular weight HA, optimized to act as an anti-catabolic agent via CD44 receptors, helping reduce inflammation. Molecular weight can vary based on authorship and publication, but HEALVISCO maintains an ideal balance for clinical efficacy without compromising product flexibility.

9. How does HEALVISCO tailor its physicochemical properties for different applications?

• Each HEALVISCO product has a unique combination of hyaluronate concentration and molecular weight to achieve the optimal viscosity for its specific clinical application. This tailored approach ensures that products used in larger joints like the knee have different characteristics than those intended for peritendinous or smaller joint injections.

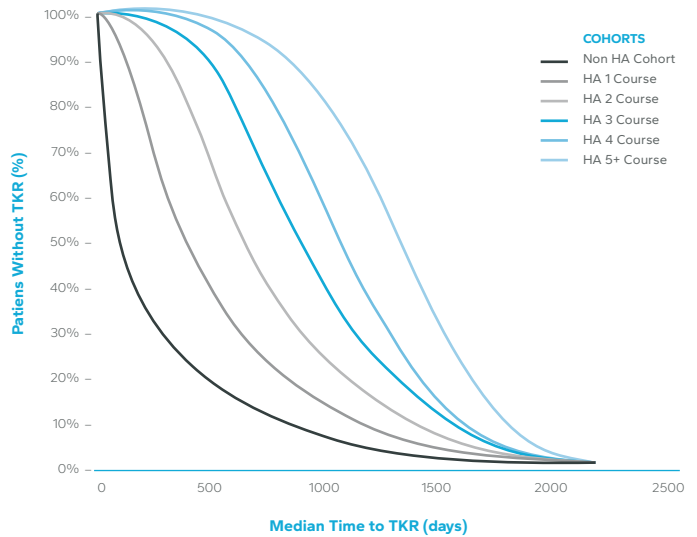
10. What are the details for HEALVISCO Tendon, including shots per pack, duration, and recommended injection frequency?

• HEALVISCO Tendon comes as a single-shot package. Clinical effects may last up to 12 months. For best results, a treatment of two injections with a 7-day interval is recommended.

11. What is the therapeutical approach for HEALVISCO Mini?

• The therapeutic approach for HEALVISCO Mini involves 1 to 3 intra-articular injections in small joints, with clinically proven efficacy in reducing pain.

Time-to-TKR as a function of number of courses of HA injection. [2]



This meta-analysis of 54 clinical trials with 7,545 participants compared intra-articular hyaluronic acid (IAHA) to placebo for knee osteoarthritis pain. IAHA showed effective pain reduction starting at week 4, peaking at week 8, and lasting up to 24 weeks, outperforming common analgesics like paracetamol and NSAIDs, thus supporting its use as a treatment option for knee OA.[1]

1. Bannuru RR, Natov NS, Dasi UR, Schmid CH, McAlindon TE. Therapeutic trajectory following intra-articular hyaluronic acid injection in knee osteoarthritis--meta-analysis. *Osteoarthritis Cartilage*. 2011 Jun;19(6):611-9.

This study of 182,022 knee osteoarthritis patients found that hyaluronic acid (HA) injections delayed total knee replacement (TKR) in a dose-dependent manner. Half of the patients without HA received TKR within 114 days of diagnosis, while those with HA treatment delayed TKR to an average of 484 days. Patients receiving multiple HA treatments postponed TKR significantly longer, with five or more courses extending the delay by 3.6 years. [2]

2. Altman R, Lim S, Steen RG, Dasa V. Hyaluronic Acid Injections Are Associated with Delay of Total Knee Replacement Surgery in Patients with Knee Osteoarthritis: Evidence from a Large U.S. Health Claims Database. *PLoS One*. 2015 Dec 22;10(12):e0145776. doi: 10.1371/journal.pone.0145776. Erratum in: *PLoS One*. 2016 Jan 29;11(1):e0148591. doi: 10.1371/journal.pone.0148591. PMID: 26694145; PMCID: PMC4687851.



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