

A woman and a man are riding bicycles on a sandy beach. The woman is on the left, wearing a blue long-sleeved shirt and light-colored pants, riding a yellow bicycle. The man is on the right, wearing a striped sweater and blue jeans, riding a teal bicycle. They are both smiling and looking towards the right. The background shows a clear blue sky and the ocean horizon.

Fermathron[®] Viscosupplements

Fermathron | Fermathron Plus | Fermathron S



ZIMMER BIOMET
Your progress. Our promise.[®]

Natural Viscosupplementation



- **Natural, biocompatible material**
- **For the relief of pain and stiffness of the knee, hip, shoulder and ankle joints in patients with mild to moderate osteoarthritis resulting from degenerative and traumatic changes to the synovial joint**
- **Increasing mobility**
- **Ease of application**
- **By intra-articular injection**



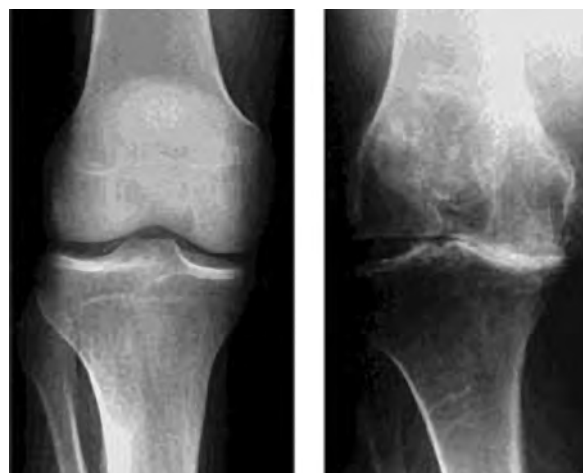
In healthy people synovial fluid is the lubricant of most joints such as the knee and the hip. One of the most important components of the synovial fluid is Hyaluronic Acid (HA) in the form of sodium hyaluronate. Hyaluronic Acid is a natural material found in the human synovial where it is synthesized in the synovial tissue and extruded into the synovial fluid where it accumulates on the cartilage and ligament surfaces. The presence of the viscoelastic Hyaluronic Acid in the joint provides protection, lubrication and mechanical stability to the collagen network. Hyaluronic Acid protects the articular cartilage cells from biomechanical wear and tear and shields the pain receptors from irritation.^{1-5,13}

Osteoarthritis

Osteoarthritis is a non-inflammatory progressive disorder affecting moveable joints, in particular weight-bearing joints such as the knee and hip.

Osteoarthritis causes alterations of the synovial fluid:

- Reduction of the viscoelasticity
- Decrease in Hyaluronic Acid concentration
- Decrease in the average molecular weight of the Hyaluronic Acid molecules
- Reduction in the interaction of Hyaluronic Acid molecules



Normal knee

Osteoarthritic knee

These changes result in disruption of the collagen network and sensitization of the pain receptors in the joint capsule.^{1,14,16}

Natural Supplementation


Supplementation of the natural synovial fluid with Fermathron Viscosupplement restores and augments the natural properties of the synovial compartment.¹⁶ Intra-articular injection with the natural, viscoelastic material Hyaluronic Acid has been shown in clinical studies^{15-20,22} to be an effective therapy for reducing pain and increasing mobility in this debilitating condition. Patients receiving Hyaluronic Acid injections have been shown to receive a total knee replacement later than those who haven't.²¹



Freedom to remain active



How does Fermathron work?

An anatomical illustration of a human knee joint, showing the femur (thigh bone) at the top, the tibia (shin bone) at the bottom, and the patella (kneecap) in the center. The joint is surrounded by ligaments and tendons. Overlaid on the joint are colorful, abstract molecular structures in shades of purple, green, and yellow, representing the hyaluronic acid supplement. The background is a light blue gradient.

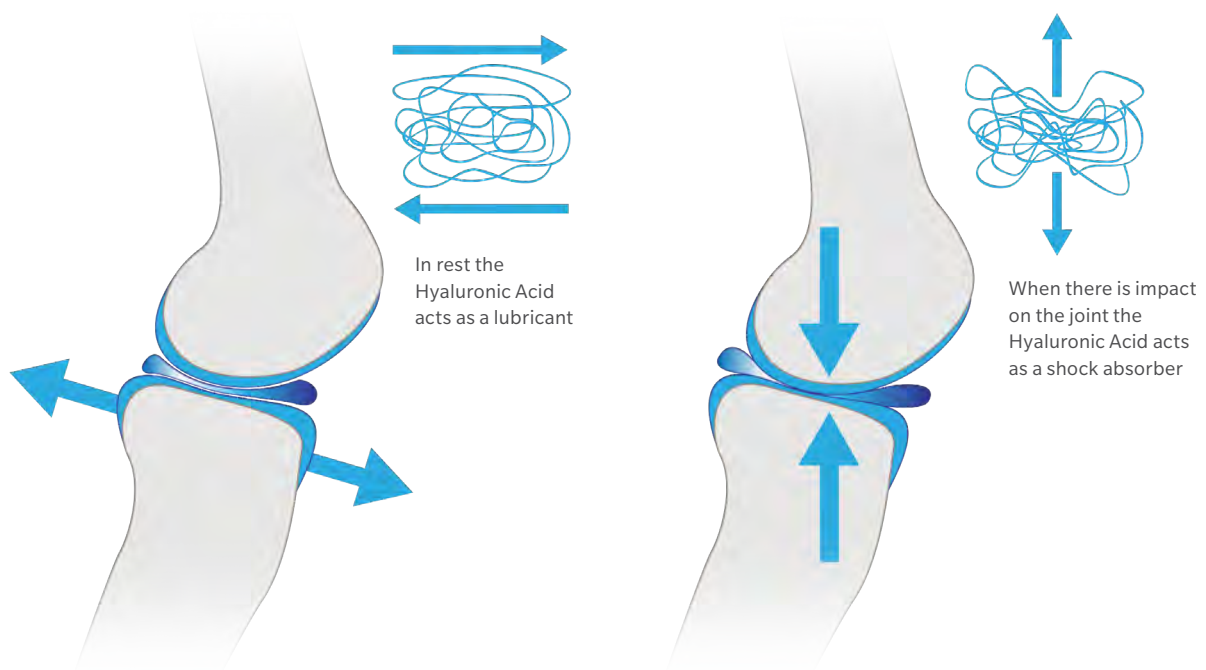
Fermathron Viscosupplement replaces degraded natural Hyaluronic Acid in patients with mild to moderate osteoarthritis that have painful or stiff joints.

Fermatron products are viscosupplements composed of ultra pure sodium hyaluronate indicated for the relief of pain and stiffness of the knee, hip, ankle and shoulder synovial joints by providing support and lubrication.

Mechanical properties

One of the essential properties of Hyaluronic Acid and Hyaluronic Acid solutions is its adaptive behavior to the needs of the joint. Hyaluronic Acid solutions can serve as effective lubricants when movements are slow and as shock absorbers when movements are fast.^{2,13}

This behavior is due to the fact that the molecule, which is highly folded at rest, begins to unfold as shear is applied. Under increased shear Hyaluronic Acid completely unfolds reaching a liquid state.^{1,2} Fermatron products consist of long-chain, highly folded molecules that exhibit the classical variation of viscosity and can supplement degraded natural Hyaluronic Acid.¹⁶



Biological Properties

Research has shown that Hyaluronic Acid solutions not only have mechanical properties but also influence the biological activities in the joint such as:

- Promotion of endogenous Hyaluronic Acid production⁶
- Interaction with pain receptors⁷⁻¹²
- Inhibition of pro-inflammatory mediator synthesis by joint cells⁷⁻¹²

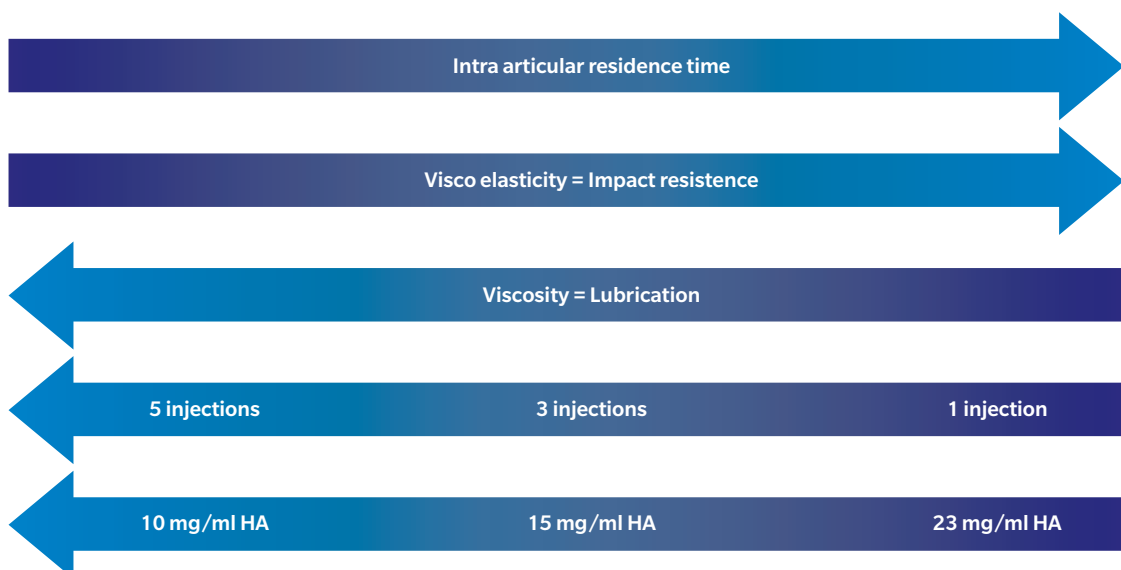
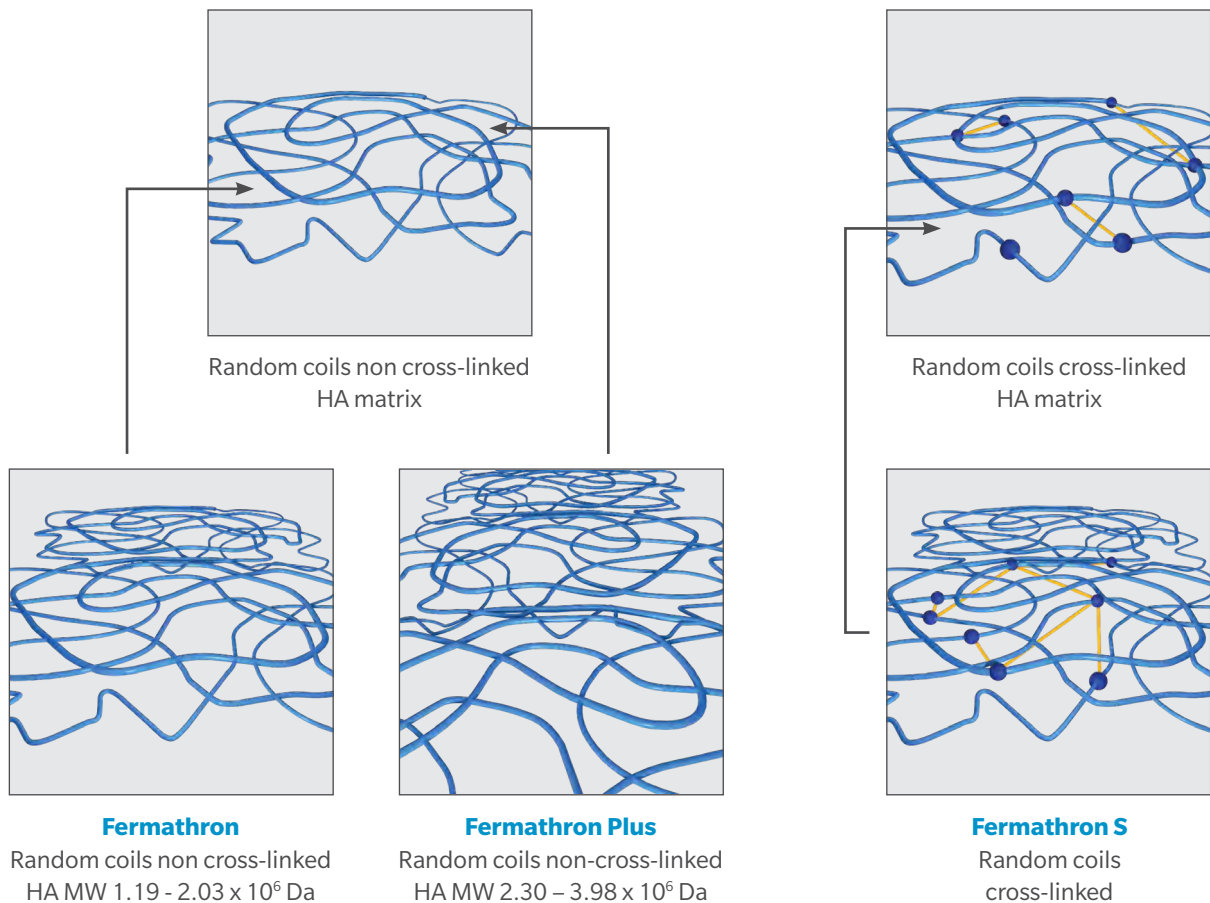


It's not just what we make...

It's what we make possible™



Fermathron family



Choice of three variations

The Fermathron family consists of three variations. The key difference of the products is the concentration of hyaluronic acid and its specific viscoelastic properties. In Fermathron S the long spiral molecules of Hyaluronic Acid are interconnected so that a three dimensional network is created. By cross-linking the strands as opposed to only having free Hyaluronic Acid strands, Fermathron S viscosupplement achieves a pain and stiffness relief in knee and hip joints with only one injection as opposed up to 3 or 5 required with Fermathron or Fermathron Plus products.

Fermathron is indicated for the relief of pain and stiffness of the knee, hip, shoulder and ankle joints. Fermathron Plus is indicated for the relief of pain and stiffness in the knee, hip and ankle. Fermathron S is indicated for the relief of pain and stiffness of the knee or hip joint.

	Molecular weight of sodium Hyaluronate	Amount of HA per injection	Volume per injection	Concentration of Sodium Hyaluronate in weight/volume	Dosage**
Fermathron	1.19-2.03 million Dalton	20 mg	2.0 ml	1.0 %	5 injections*
Fermathron Plus	2.30-3.98 million Dalton	30 mg	2.0 ml	1.5 %	3 injections*
Fermathron S	Cross-linked	69 mg	3.0 ml	2.3 %	1 injection

*Up to three or five weekly injections is recommended for the knee joint. The dosage regimen should be adapted by the Healthcare Professional for injection into the synovial space of the hip, ankle and shoulder joints.

**It is recommended that injections in the hip, ankle and shoulder joints are performed using ultrasound or fluoroscopic guidance.

Product	Description	Art. No.
Fermathron	Sodium Hyaluronate 20 mg / 2.0 ml	236380-INT
Fermathron Plus	Sodium Hyaluronate 30 mg / 2.0 ml	236381-INT
Fermathron S	Sodium Hyaluronate 69 mg / 3.0 ml	236382-INT

Packed in a pre-filled glass syringe within a blister and an outer carton. Fermathron and Fermathron plus are sterilised using aseptic processing techniques. Fermathron S is sterilised using steam. The final product in the carton is terminally sterilized using ethylene oxide ensuring that the outer surface of the syringe is sterile.



Literature

1. Balazs EA, Denlinger JL. Viscosupplementation: a new concept in the treatment of osteoarthritis. *J Rheumatol Suppl.* 1993 Aug;39:3-9.
2. Balazs EA. Viscosupplementation for treatment of osteoarthritis: from initial discovery to current status and results. *Srg.Technol Int* 2004;12 p. 278-89
3. Fam H, Bryant JY, Kontopoulou m. Rheological properties of synovial fluids *Biorheology* 2007; 44 p. 59-74
4. Milas m, Rinaudo M, Characterisation and properties of hyaluronic acid (Hyaluronic Acid). In Dimitru S editor. *Polysaccharides: structural diversity and functional versatility*, New York; Marcel Dekker; 2004. P 535-49
5. Conrozier T. et al. Differences in the osteoarthritic synovial fluid composition and rheology between patients with and without flare: a pilot study. *Clin Exp Rheumatol* 2012;30 p.729-34
6. Bagga H. et al. Long term effects of intra-articular Hyaluronic Acid on synovial fluid in osteoarthritis of the knee. *J Rheumatol* 2006; 33 p. 946-50
7. Greenberg DD, et al. Biochemical effects of two different hyaluronic acid products in co-culture model of osteoarthritis. *Osteoarthr Cartil* 1993; 1 p. 97-103
8. Wang CT. et al. High Molecular weight hyaluronic acid down regulates the gene expression of osteoarthritis associated cytokines and enzymes in fibroblast like synoviocytes from patients with early osteoarthritis. *Osteoarthr Cartil* 2006;14 p. 1237-47
9. Li J, Gorski DJ, Anemaet W. et al. Hyaluronic Acid injection of murine osteoarthritis prevent TGFβ1-induced synovial neovascularization and fibrosis and maintains articular cartilage integrity by CD44-dependent mechanism. *Arthr Res Ther* 2012;14:R151
10. Waddell DD et al. Hyaluronan suppresses IL-1β induced metalloproteinase activity from synovial tissue. *Clin Orthop Relat Res* 2007;465 p. 241-8
11. Yasuda T. Hyaluronic Acid inhibits prostaglandins E2 production via CD44 in U937 human macrophages *Tohoku J Exp Med* 2010;220 p. 229-35
12. Boettger MK, Kummel D, Harrison A, Schaible HG. Evaluation of long-term antinociceptive properties of stabilized hyaluronic acid preparation (NASHA) in an animal model of repetitive joint pain. *Arthritis Res Ther.* 2011;13(4):R110.
13. Henrotin Et al 2015, Consensus statement on viscosupplementation with Hyaluronic acid on the management of osteoarthritis, *Seminars in Arthritis and Rheumatism*
14. M. G. Lequesne, C. Mery, M. Samson, P. Gerard: Indexes of severity for osteoarthritis of the hip and knee. *Scandinavian Journal of Rheumatology* 1987; Suppl. 65: 85-89.
15. C. McDonald, S. Hantel, M. Strohmeier: A randomised controlled study to compare the performance and safety of two sources of sodium hyaluronate given as a viscosupplement by intra-articular injection to patients with osteoarthritis of the knee. *Journal of Clinical Research* 2000; 3: 41-50.
16. Internal file: Clinical Evaluation Report – Fermathron ONE, version 2, March 2015, Hyaltech.
17. Conrozier T, Vignon E. Is there evidence to support the inclusion of viscosupplementation in the treatment paradigm for patients with hip osteoarthritis? *Clin Exp Rheumatol.* 2005 Sep-Oct;23(5):711-6
18. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Viscosupplementation for the treatment of osteoarthritis of the knee. *Cochrane Database Syst Rev.* 2006 Apr 19;(2):CD005321
19. van den Bekerom MP, Lamme B, Sermon A, Mulier M. What is the evidence for viscosupplementation in the treatment of patients with hip osteoarthritis? Systematic review of the literature. *Arch Orthop Trauma Surg.* 2008 Aug;128(8):815-23
20. Reid MC. Viscosupplementation for osteoarthritis: a primer for primary care physicians. *Adv Ther.* 2013 Nov;30(11): 967-86
21. Altman R, et al., Association between Hyaluronic Acid injections and Time-to-Total knee replacement surgery. *J Knee Surg*, 2015: DOI <http://dx.doi.org/10.1055/s-0035-1568992>. ISSN 1538-8506
22. Clementi D, et al., Efficacy of a single intra-articular injection of ultra-high molecular weight hyaluronic acid for hip osteoarthritis: a randomized controlled study, *European Journal of Orthopaedic Surgery & Traumatology*, Published Online November 2017 <https://doi.org/10.1007/s00590-017-2083-9>

This publication and all content, artwork, photographs, names, logos and marks contained in it are protected by copyright, trademarks and other intellectual property rights owned by or licensed to Zimmer Biomet or its affiliates unless otherwise indicated, and must not be redistributed, duplicated or disclosed, in whole or in part, without the express written consent of Zimmer Biomet.

This material is intended for health care professionals. Distribution to any other recipient is prohibited. Check for country product clearances and reference product specific instructions for use. For complete product information, including indications, contraindications, warnings, precautions, and potential adverse effects, see the package insert or contact your local Zimmer Biomet representative.

Not for distribution in France. Not intended for surgeons practicing medicine in France.

Fermathron® is a trademark of Hyaltech Ltd.

©2018 Zimmer Biomet



Responsible Manufacturer
Hyaltech Ltd.
Starlaw Business Park
Livingston EH54 8SF
United Kingdom

Distributor
Biomet GSCC B.V.
Toermalijnring 600
3316 LC Dordrecht
The Netherlands