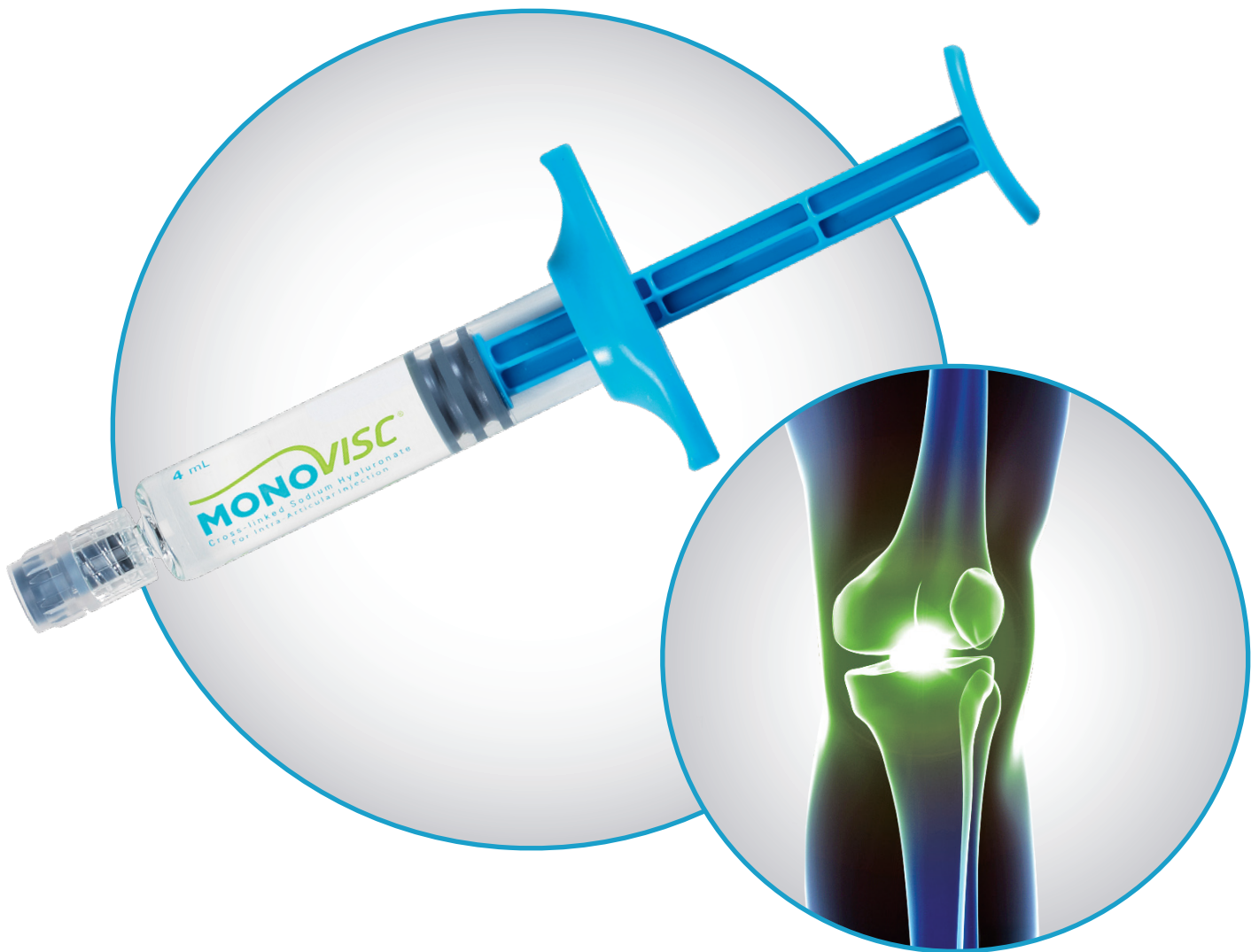


Monovisc™

Hyaluronic Acid Single Injection

Product Brochure



Long-lasting knee pain relief

The market-leading single injection viscosupplement utilised to treat joint pain caused by osteoarthritis.

Monovisc™

Hyaluronic Acid Single Injection

Monovisc

is a single high dose viscosupplement injection approved for the treatment of OA in the knee joint¹

Lightly Cross-Linked

Monovisc is a sodium hyaluronate injection that is lightly cross-linked to increase residence time in the knee^{1,3}

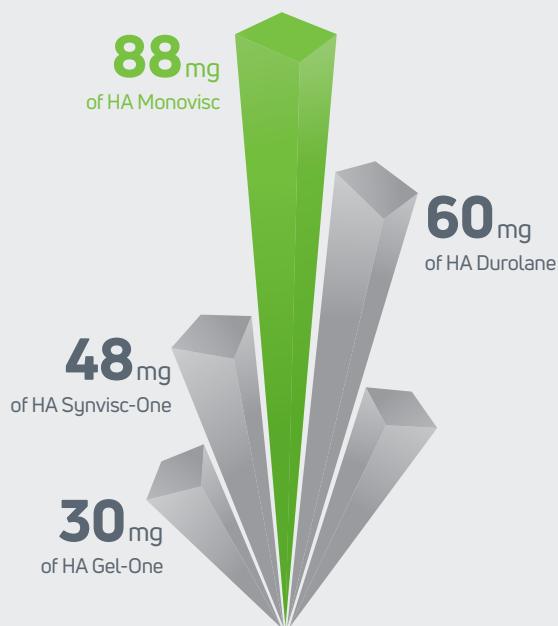
Non-Avian HA

Monovisc is manufactured from ultra pure, high molecular weight sodium hyaluronate produced by bacterial fermentation¹

#1 U.S. Viscosupplements

Monovisc is FDA approved and as a viscosupplement franchise, Monovisc & Orthovisc are the most prescribed in the United States⁴

Monovisc delivers a higher dose of HA²



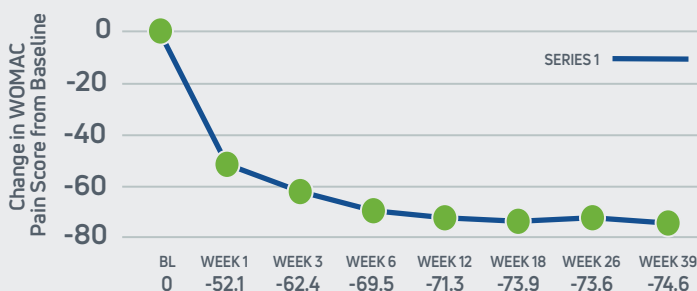
Extended pain relief

Up to 39 weeks of clinically proven efficacy with a single injection in the knee⁵



92.4% of patients whose knee joints were treated with Monovisc responded positively in the areas of pain, stiffness, and physical function at 39 weeks.

Percentage change in WOMAC Pain Score from Baseline at 39 weeks



*Monovisc 17-02: percentage change from baseline in WOMAC Pain Score

Monovisc is formulated to mimic the properties of endogenous HA^{6,7}

In human joints, endogenous HA is present in the cartilage extracellular matrix and synovial fluid and has several functions, including:

Mechanical effect

HA binds well to water, producing a viscous, jelly-like consistency that provides lubrication and acts as a shock absorber within the joint.

Analgesic effect

HA diminishes nerve impulses and the sensitivity of nociceptive nerve endings.⁸

Anti-inflammatory effect

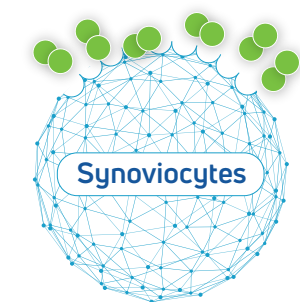
HA plays an important role in reducing joint inflammation and pain caused by injury or tissue degeneration.^{7,8}

Chondroprotective effect

HA has a biomechanical structure that protects cartilage when surrounding chondrocytes.⁷

Monovisc aims to improve the rheological properties of the synovial fluid, thereby promoting mechanical, analgesic, anti-inflammatory, and chondroprotective effects.^{1,9,10}

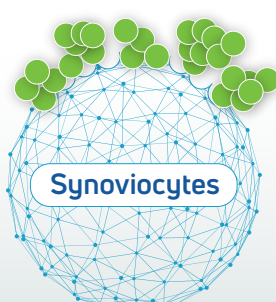
Optimal high molecular weight HA^{11,12}



MW $\leq$ 500,000

Low Binding Affinity

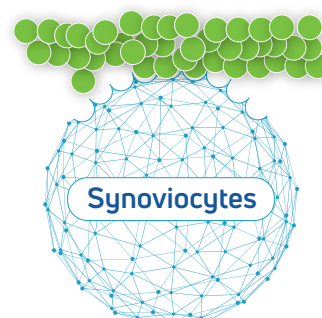
Limited stimulation of biosynthesis of HA



500,000 < MW < 4,000,000

Optimal Binding Affinity

Stimulation of biosynthesis of HA¹²



MW $\geq$ 4,000,000

Steric Hindrance

Limited stimulation of biosynthesis of HA

1,000,000 Da < 2,900,000 Da

MONOVISC

Clinically proven long lasting pain relief through 6 months^{13,14}

- Monovisc delivers a **65% improvement** in WOMAC pain at week 26 relative to baseline ($p = 0.0352$)^{*13}
- Monovisc delivers an **85% responder rate** in the OMERACT-OARSI Responder Index through 26 weeks^{*14}
- Monovisc patients experienced a clinically meaningful reduction in OA knee pain within 2 weeks of their injection^{**15}



*Study design: The referenced clinical study was a randomized, double-blind, saline-controlled, three-arm, multicenter clinical trial. A total of 368 patients with knee osteoarthritis (KL grades I-III) were treated (150 received MONOVISC).¹³

**Study design: The referenced clinical study was a randomized, double-blind, saline-controlled, multicenter clinical trial. A total of 369 patients with knee osteoarthritis (KL grades II-III) were treated (184 received MONOVISC).¹⁵

Indications

Monovisc is indicated as a viscoelastic supplement or a replacement for synovial fluid in human knee joints. Monovisc is well suited for the treatment of the symptoms of mild to moderate osteoarthritis of the human knee joints for patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics. In clinical studies, Monovisc has been proven to have a duration of effect of at least 6 months and a second injection 6 months after the first injection was shown to be safe.

1 Monovisc IFU **2** Instructions for use for Monovisc, Durolane, Synvisc-One, Gel-One, Ostenil Plus. **3** Clinical Efficacy and Safety of MONOVISC™: A lightly cross-linked highly concentrated hyaluronan specially formulated for single injection in osteoarthritis. White Paper Study conducted by Michael J. Daley, PhD. 2013 **4** Data on file, Anika Therapeutics, Inc. **5** 17-02 Data on File. **6** Vincent HK, Percival SS, Conrad BP, et al. Hyaluronic Acid (HA) Viscosupplementation on Synovial Fluid Inflammation in Knee Osteoarthritis: A Pilot Study. Open Orthop J. 2013 Sep 20;7:378-84. doi: 10.2174/1874325001307010378. PMID: 24093052; PMCID: PMC3788189. **7** Garantziotis S, Savani RC. Hyaluronan biology: a complex balancing act of structure, function, location and context. Matrix Biol. 2019 May;78-79:1-10. **8** Synovial Fluid Inflammation in Knee Osteoarthritis: A Pilot Study. Open Orthop J. 2013 Sep 20;7:378-84. doi: 10.2174/1874325001307010378. PMID: 24093052; PMCID: PMC3788189. **9** Brandt KD, Smith GN, Simon LS. Intra-articular injection of hyaluronan as treatment for knee osteoarthritis. Arthritis Rheum 2000;43:1192-1203. **10** de Rezende MU, de Campos GC. VISCOSUPPLEMENTATION. Rev Bras Ortop. 2015 Dec 6;47(2):160-4. **11** Smith MM, Ghosh P. The synthesis of hyaluronic acid by human synovial fibroblasts is influenced by the nature of the hyaluronate in the extracellular environment. Rheumatol Int. 1987; 7(3):113-22. **12** Ghosh P, Guidolin D. Potential mechanism of action of Intraarticular Hyaluronan Therapy in Osteoarthritis: Are the effects Molecular Weight Dependent?; Seminars in Arthritis and Rheumatism, Vol 32, No 1 (August), 2002: pp 10-37. **13** Hangody L, Szody R, Lukasik P, et al. Cartilage 2017 May; doi: 10.1177/1947603517703732. **14** CINGAL 13-01, a randomized, double-blind, placebo-controlled, active comparator Phase 3 study. **15** Petterson SC, Plancher KD. Knee Surg Sports Traumatol Arthrosc (2018). <https://doi.org/10.1007/s00167-018-5114-0>

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