Powerful and Long-lasting Pain Relief

A single-injection hyaluronic acid (HA) treatment that has proven:

- Greater reduction in knee pain vs. Synvisc-One® (hylan G-F 20)[1*]
- Longer-lasting knee pain relief vs. steroid[2]
- Clinically equivalent performance to five-injection HA therapy[3,4]

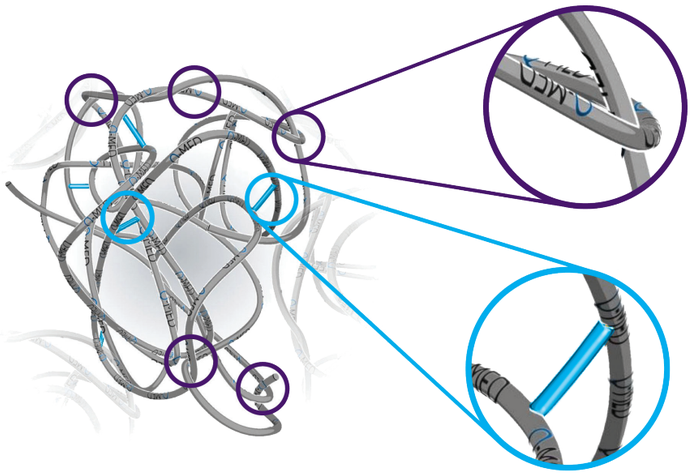
*Some patients were treated with a three-injection Synvisc® regimen. A three-injection Synvisc regimen is equivalent to one injection of Synvisc-One.

DUROLANE®

hyaluronic acid, stabilized single injection

DUROLANE was designed as a single-injection therapy with unique stabilizing technology[5]

DUROLANE is a high-molecular-weight, non-avian HA stabilized using a carefully controlled cross-linking process to increase residence time in the knee joint.[5-7]



Entanglement of HA chains
(natural cross-links)

Covalent bond
(<1% modification)

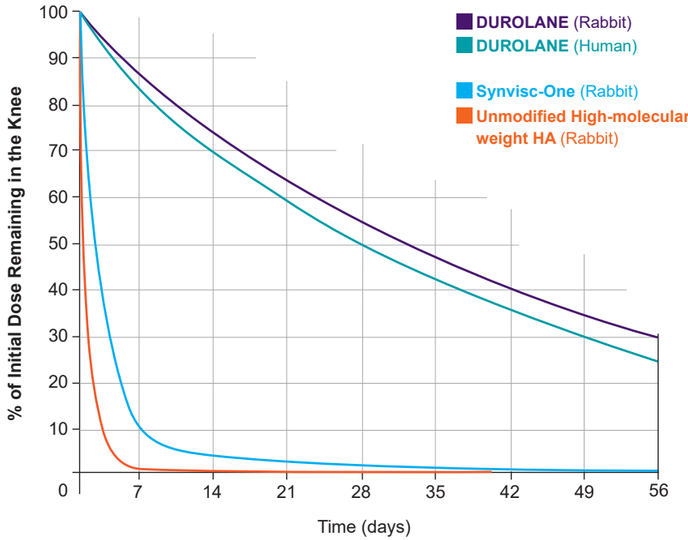
Long lasting by design

DUROLANE proved to have an increased residence time in the knee joint[5-9]

- A half-life of 4 weeks in the knee joint[6,7]
- The longest reported half-life of any HA[7-9]

DUROLANE is the only HA to have residence time measured in humans.

Terminal half-life of HA injected into the knee*

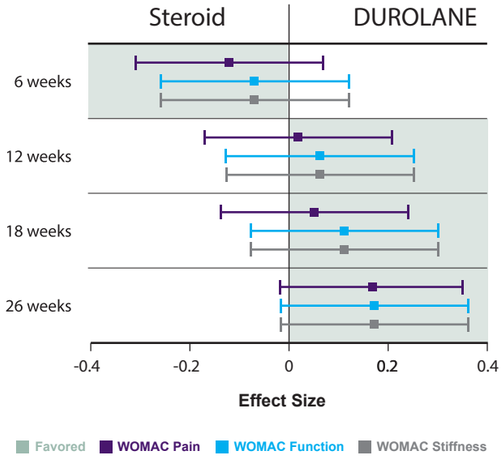


*Animal performance may not be predictive of performance in humans

Longer-lasting knee pain relief vs. steroid[2*]

In a Level-1 study,

- DUROLANE was proven to be noninferior to steroid at 6 weeks[†]
- Significant reduction in pain from baseline with DUROLANE vs. steroid at week 26
- DUROLANE is safe for repeated use



Effect-sizes for WOMAC domains with 95% CIs during the blinded phase of the study.

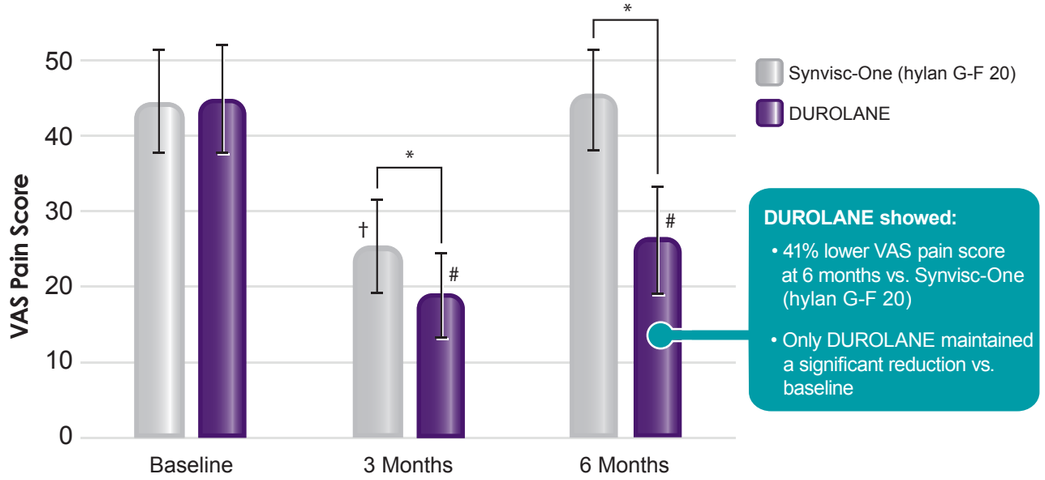
*Methylprednisolone acetate (MPA)

[†]The primary outcome was the WOMAC pain responder rate, defined as at least 40% relative improvement and 5-point absolute improvement from baseline values at 12 weeks.

DUROLANE is a single-injection HA designed to deliver powerful, long-lasting knee osteoarthritis (OA) pain relief.[1-5]

Greater reduction in knee pain vs. Synvisc-One (hylan G-F 20)[1]

In a Level-1 study, reduction in Visual Analog Scale (VAS) pain scores at 3 and 6 months was significantly greater for DUROLANE compared to Synvisc-One (hylan G-F 20) (p<0.001).[1]



DUROLANE showed:

- 41% lower VAS pain score at 6 months vs. Synvisc-One (hylan G-F 20)
- Only DUROLANE maintained a significant reduction vs. baseline

Some patients were treated with a three-injection Synvisc regimen. A three-injection Synvisc regimen is equivalent to one injection of Synvisc-One.

(n=182)
Mean values +/- standard deviation

*p<0.001 compared to Synvisc-One (hylan G-F 20)
#p<0.001 compared to DUROLANE baseline
†p=0.008 compared to Synvisc-One (hylan G-F 20) baseline

Unlike Synvisc-One

- DUROLANE does not include components of an avian source[4,11]
- DUROLANE was designed as a single-injection therapy[4,5]

Comparison chart[4,11]	DUROLANE	Synvisc-One
Injection Volume	3.0 mL	6.0 mL
Concentration	2.0% HA	0.8% HA
HA per Dose	60 mg	48 mg
HA Source	Biofermentation-derived	Avian-based

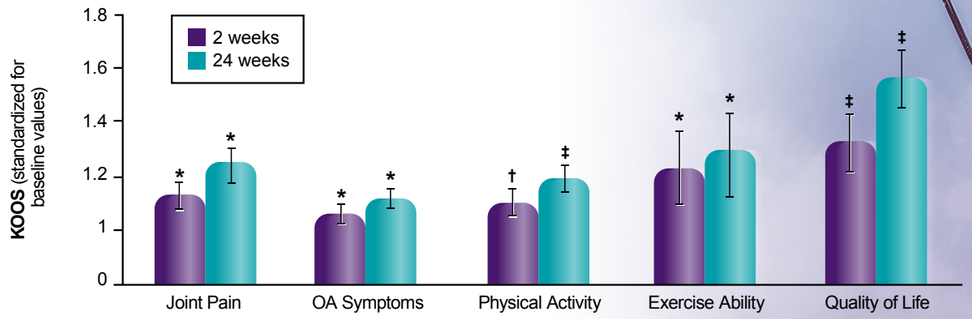
DUROLANE is the only single-injection HA proven to be clinically equivalent to a five-injection therapy[3,4]

- In a Level-1 study, one injection of DUROLANE produced noninferior pain reduction at 6 months to five injections of the comparator HA
  - 79% of patients experienced improved pain control for up to 26 weeks[3]

Choose convenience without compromise and get powerful results

DUROLANE significantly improved Quality of Life

A single injection of DUROLANE significantly improved all KOOS (Knee and Osteoarthritis Outcome Score) parameters in as early as 2 weeks and continued for up to 24 weeks.[12]



* $p<0.05$ vs baseline
† $p<0.01$ vs baseline
‡ $p<0.001$ vs baseline

(n=50)
Mean values +/- standard error of the mean

Available worldwide since 2001, with a low post-market adverse event rate

A History of Safe Use

Strong clinical evidence. More clinical studies than any other single-injection HA knee therapy.

During the pivotal trial:[4]

- No serious adverse events were considered related to DUROLANE treatment[4]
- The most common adverse events were arthralgia (8.6%), injection site pain (2.3%), and joint swelling (1.7%)[4]

DUROLANE is safe for repeated courses of therapy. Repeated use of DUROLANE does not increase the incidence of adverse events.[2,4]

Significant Reduction in Analgesic Use[12]

Mean Values	Weeks 1 - 2	Weeks 3 - 24
Analgesic	0.77 g/wk	0.33 g/wk
p-value	—	*p*=0.004

DUROLANE patients experienced a significant reduction in analgesic use.

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Summary of Indication for Use: DUROLANE is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacological therapy or simple analgesics, e.g. acetaminophen.

Do not inject DUROLANE in patients with knee joint infections, skin diseases, or other infections in the area of the injection site. Do not administer to patients with known hypersensitivity or allergy to sodium hyaluronate preparations. Risks can include transient pain or swelling at the injection site.

DUROLANE has not been tested in pregnant or lactating women, or children. Full prescribing information can be found in product labeling, at www.DUROLANE.com, or by contacting Bioventus Customer Service at 1-800-836-4080.

References: 1. McGrath AF, McGrath AM, Jessop ZM, et al. A comparison of intra-articular hyaluronic acid competitors in the treatment of mild to moderate knee osteoarthritis. *J Arthritis*. 2013;2(1):108. doi:10.4172/2167-7921.1000108. **2.** Leighton R, Åkermark C, Therrien R, et. al. NASHA hyaluronic acid vs methylprednisolone for knee osteoarthritis: a prospective, multi-centre, randomized, non-inferiority trial. *Osteoarthritis Cartilage*. 2014;22(1):17-25. **3.** Zhang H, Zhang K, Zhang X, et al. Comparison of two hyaluronic acid formulations for safety and efficacy (CHASE) study in knee osteoarthritis: a multicenter, randomized, double-blind, 26-week non-inferiority trial comparing Durolane to Artz. *Arthritis Res Ther*. 2015;17:51. doi: 10.1186/s13075-015-0557-x. **4.** DUROLANE [package insert]. Durham, NC: Bioventus LLC; 2017. **5.** Ågerup B, Berg P, Åkermark C. Non-animal stabilized hyaluronic acid: a new formulation for the treatment of osteoarthritis. *BioDrugs*. 2005;19(1):23-30. **6.** Edsman K, Hjelm R, Lärkner H, et al. Intra-articular duration of Durolane™ after single injection into the rabbit knee. *Cartilage*. 2011;2(4):384-8. **7.** Lindqvist U, Tolmachev V, Kairemo K, Aström G, Jonsson E, Lundqvist H. Elimination of stabilised hyaluronan from the knee joint in healthy men. *Clin Pharmacokinet*. 2002;41(8):603-13. **8.** Sakamoto T, Mizuno S, Miyazaki K, et al. Biological fate of sodium hyaluronate (SPH) (1) studies on distribution, metabolism and excretion of ^{14}C-SPH in rabbits after intra-articular administration. *Pharmacometris*. 1984;28(2):375-387. **9.** Larsen NE, Dursema HD, Pollak CT, Skrabut EM. Clearance kinetics of a hylan-based viscosupplement after intra-articular and intravenous administration in animal models. *J Biomed Mater Res B Appl Biomater*. 2012;100(2):457-62. **10.** McAlindon TE, LaValley MP, Harvey WF, et al. Effect of intra-articular triamcinolone vs saline on knee cartilage volume and pain in patients with knee osteoarthritis: a randomized clinical trial. *JAMA*. 2017:317(19):1967-75. **11.** Synvisc-One (hylan G-F 20) [package insert]. Ridgeway, NJ: Genzyme Biosurgery; 2014. **12.** Krocker D, Matziolis G, Tuischer J, et al. Reduction of arthrosis associated knee pain through a single intraarticular injection of synthetic hyaluronic acid. *Rheumatol*. 2006;65(4):327-31.

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