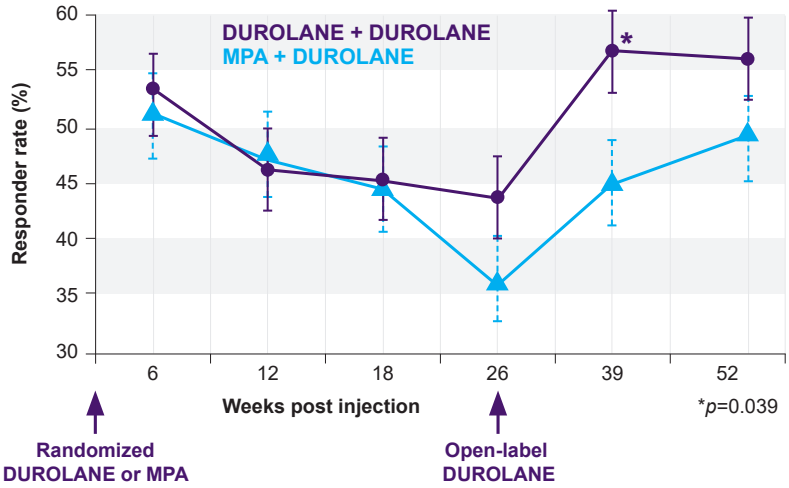
DUROLANE®

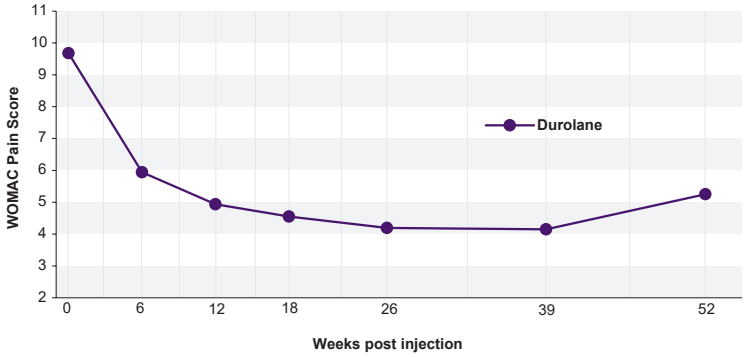
hyaluronic acid, stabilized single injection

Powerful & Lasting Pain Relief[1-8]



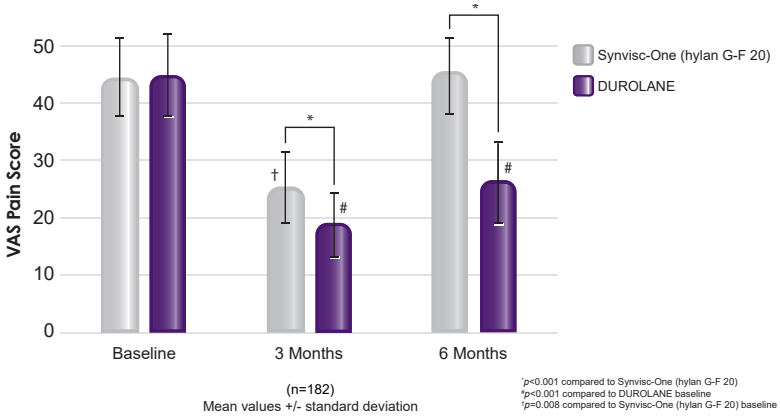
More powerful, lasting pain relief versus methylprednisolone acetate (MPA)[1]

- **DUROLANE** is as effective as MPA at 6 weeks in improving WOMAC pain score
- **DUROLANE** demonstrates enhanced pain relief with the second injection
- **DUROLANE** can be given following a steroid injection



DUROLANE – Long-lasting pain relief up to 12 months[1]

- 31 of 221 patients from the DUROLANE group chose not to receive a 2nd injection at 26 weeks
- Patients maintained relief from baseline pain over a 12-month period
- Responder rate was 50% at 1 year



More powerful, lasting pain relief versus Synvisc-One®[3]

- **DUROLANE** showed a significantly greater reduction in VAS scores at 3 and 6 months
- At 6 months, only **DUROLANE** showed a significant reduction versus baseline in VAS scores ($p<0.001$)

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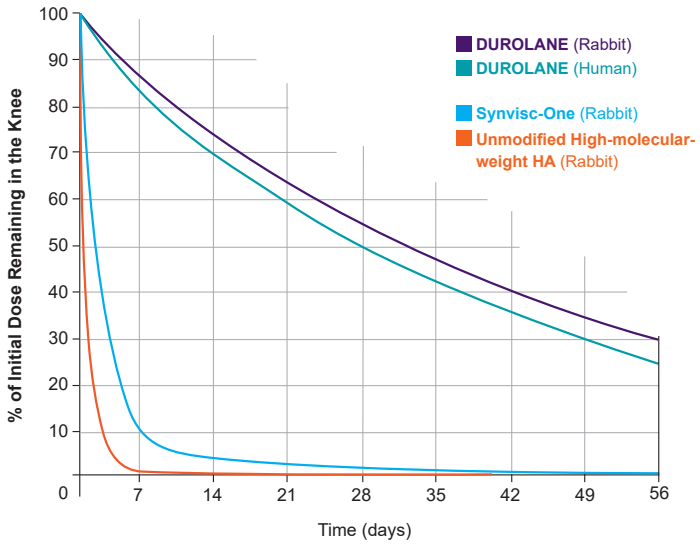
Powerful & Lasting Pain Relief[1-8]

DUROLANE proved to have an increased residence time in the knee joint[9-13]

DUROLANE was designed as a single injection treatment[9]

- **DUROLANE** has longer residence time than unstabilized HA[10-13]
- **DUROLANE** has a half-life in humans of 28 days
  - *Synvisc-One half-life: 1-8 days*

Terminal half-life of HA injected into the knee



References: 1. 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. **2.** Arden NK, Åkermark C, Andersson M, Todman MG, Altman RD. A randomized saline-controlled trial of NASHA hyaluronic acid for knee osteoarthritis. *Curr Med Res Opin*. 2014;30(2):279-86. **3.** 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. **4.** Romero Jurado M, Enrique Fidalgo A, Rodríguez Villar V, Mar Medina J, Soler López B. Factors related with the time to surgery in waiting-list patients for knee prostheses. *Reumatol Clin*. 2013;9(3):148-55. **5.** Conrozier T, Couris CM, Mathieu P, et al. Safety, efficacy and predictive factors of efficacy of a single intra-articular injection of non-animal-stabilized-hyaluronic-acid in the hip joint: results of a standardized follow-up of patients treated for hip osteoarthritis in daily practice. *Arch Orthop Trauma Surg*. 2009;129(6):843-8. **6.** Krocker D, Matziolis G, Tuischer J, et al. Reduction of arthrosis associated knee pain through a single intra-articular injection of synthetic hyaluronic acid. *Z Rheumatol*. 2006;65(4):327-31. **7.** Altman RD, Åkermark C, Beaulieu AD, Schnitzer T. Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2004;12(8):642-9. **8.** Berg P, Olsson U. Intra-articular injection of non-animal stabilised hyaluronic acid (NASHA) for osteoarthritis of the hip: a pilot study. *Clin Exp Rheumatol*. 2004;22(3):300-6. **9.** 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. **10.** 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. **11.** Edsman K, Hjelm R, Lärkner H, et al. Intraarticular duration of Durolane™ after single injection into the rabbit knee. *Cartilage*. 2011;2(4):384-8. **12.** Larsen NE, Dursema HD, Pollak CT, Skrabut EM. Clearance kinetics of a hylanbased viscosupplement after intra-articular and intravenous administration in animal models. *J Biomed Mater Res B Appl Biomater*. 2012;100 (2):457-62. **13.** 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.

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Summary of Indications for Use:
DUROLANE (3 mL): Symptomatic treatment of mild to moderate knee or hip osteoarthritis.

There are no known contraindications.

You should not use DUROLANE if you have infections or skin disease at the injection site. DUROLANE has not been tested in pregnant or lactating women, or children. Risks can include transient pain, swelling and/or stiffness at the injection site.

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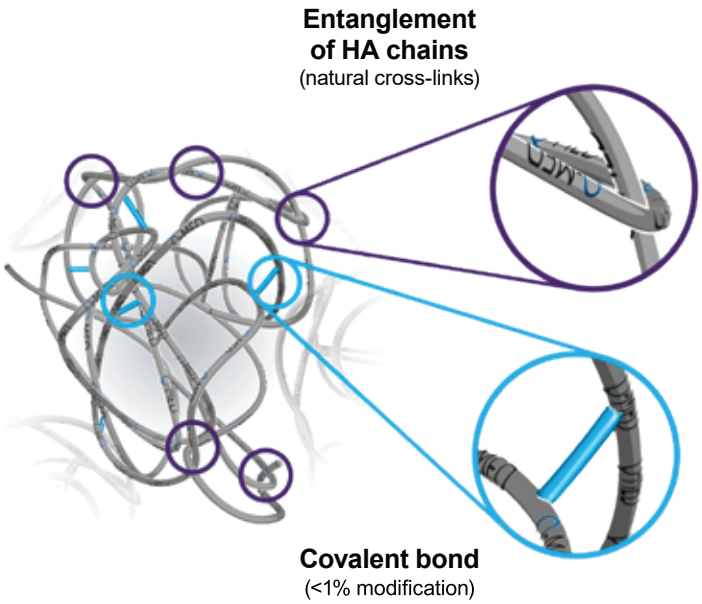
The DUROLANE Difference

Unique NASHA® Technology

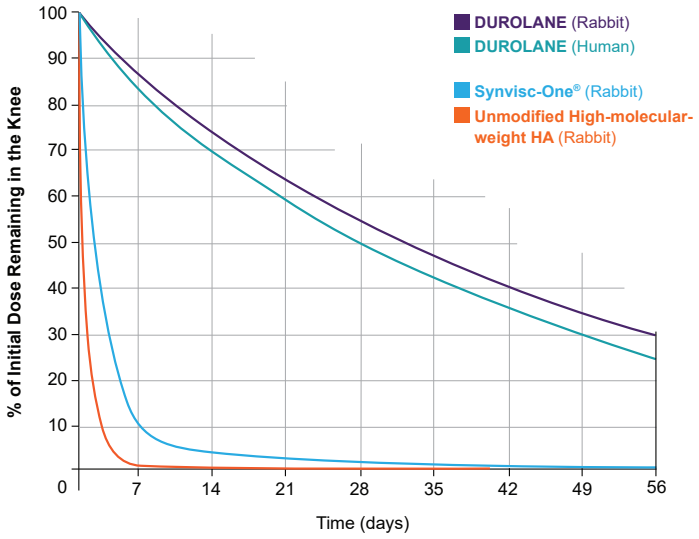
- DUROLANE was designed as a single injection, non-avian hyaluronic acid (HA) therapy[1]
- Stabilized by a carefully controlled cross-linking process that creates an entanglement of HA chains linked with covalent bonds[1-3]
- Unique manufacturing process with <1% modification, joins the molecules to one another, forming a 3D gel



Longest reported half-life of any HA[2-5]

- DUROLANE is designed to resist degradation and prolong knee joint residence time[1-4]
- Reported half-life of 4 weeks or 32 days in the knee[2,3]
- The only HA to have published residence time measured in humans

Terminal half-life of HA injected into the knee



DUROLANE's half-life is more than 3 times longer than other tested HA products

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The DUROLANE Difference

Why DUROLANE is Different

- Unique formulation in a single injection treatment[1]
- Uses NASHA technology to increase residence time in the joint[1-3]
- Has the longest half-life of any HA, with 4 weeks or 32 days in the knee joint[2,3]
- The only HA to have residence time measured in humans

	DUROLANE[6]	SYNVISC-ONE[7]	GEL-ONE®[8]	MONOVISC®[9]
HA Source	Bacterial (cross-linked)	Avian (cross-linked)	Avian (cross-linked)	Bacterial (cross-linked)
Half-life	Up to 4 weeks or 32 days in the knee[4,5]	1.5-8.8 days	Unknown	Unknown
Molecular Weight (daltons)	10^{13} M (>1 billion)*	6 M	n/a	1.0 – 2.9 M
Total Volume (per syringe)	3.0 mL	6.0 mL	3.0 mL	4.0 mL
HA Concentration	2.0% HA	0.8% HA	1% HA	2.2% HA
Active Ingredient (per treatment)	60 mg	48 mg	30 mg	88 mg
Repeat Injection	Yes	Yes	Yes	Yes

Summary of Indications 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.

*Based on theoretical calculations.

References: 1. 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. **2.** 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. **3.** Lindqvist U, Tolmachev V, Kairemo K, Åström G, Jonsson E, Lundqvist H. Elimination of stabilised hyaluronan from the knee joint in healthy men. *Clin Pharmacokinet*. 2002;41(8):603-13. **4.** Yamaguchi T, Toyoshima H, Namiki O, et al. Biological fate of sodium hyaluronate (SPH). (1) Studies on distribution, metabolism and excretion of ^{14}C-SPH in rabbits after intraarticular administration. *Pharmacometris*. 1984;28(2):375-387. **5.** 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. **6.** DUROLANE [package insert]. Durham, NC: Bioventus LLC; 2017. **7.** Synvisc-One [package insert]. Ridgefield, NJ: Genzyme Biosurgery; 2014. **8.** Gel-One [package insert]. Warsaw, IN: Zimmer; 2011. **9.** Monovisc [package insert]. Bedford, MA: Anika Therapeutics, Inc.; 2013.

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