Unpacking Hyaluronic Acid (HA)

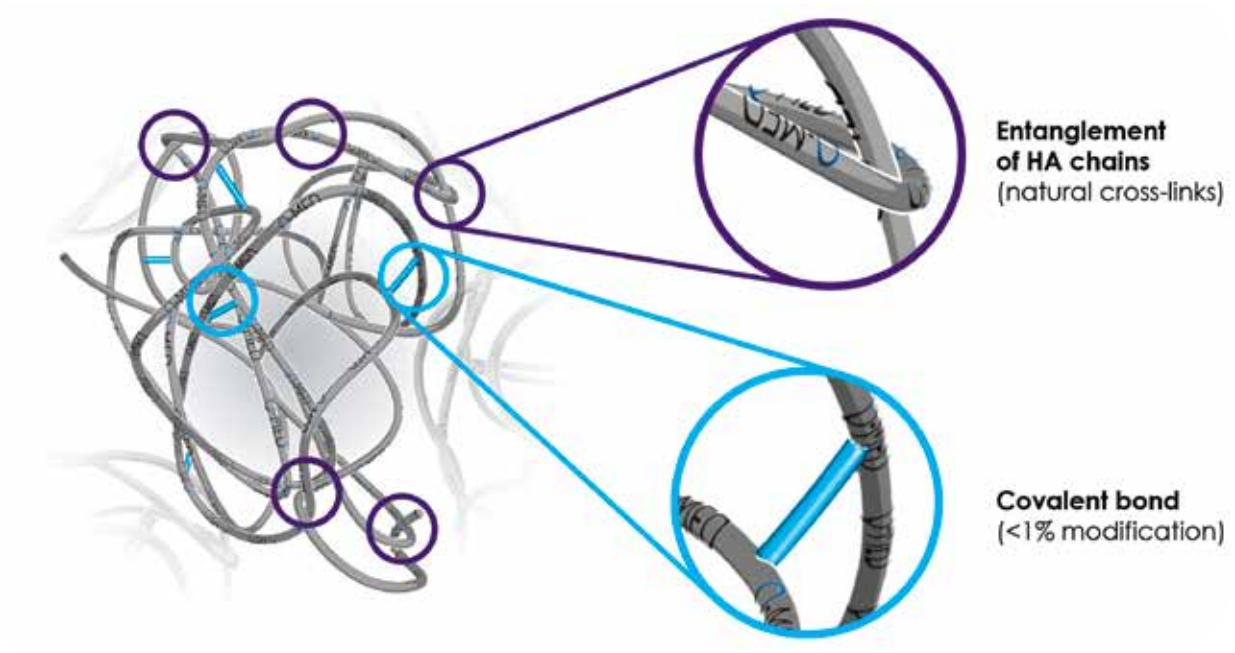
A review of Durolane High Molecular Weight HA and the clinical and cost-effectiveness evidence for treatment

DUROLANE®
hyaluronic acid, stabilized single injection

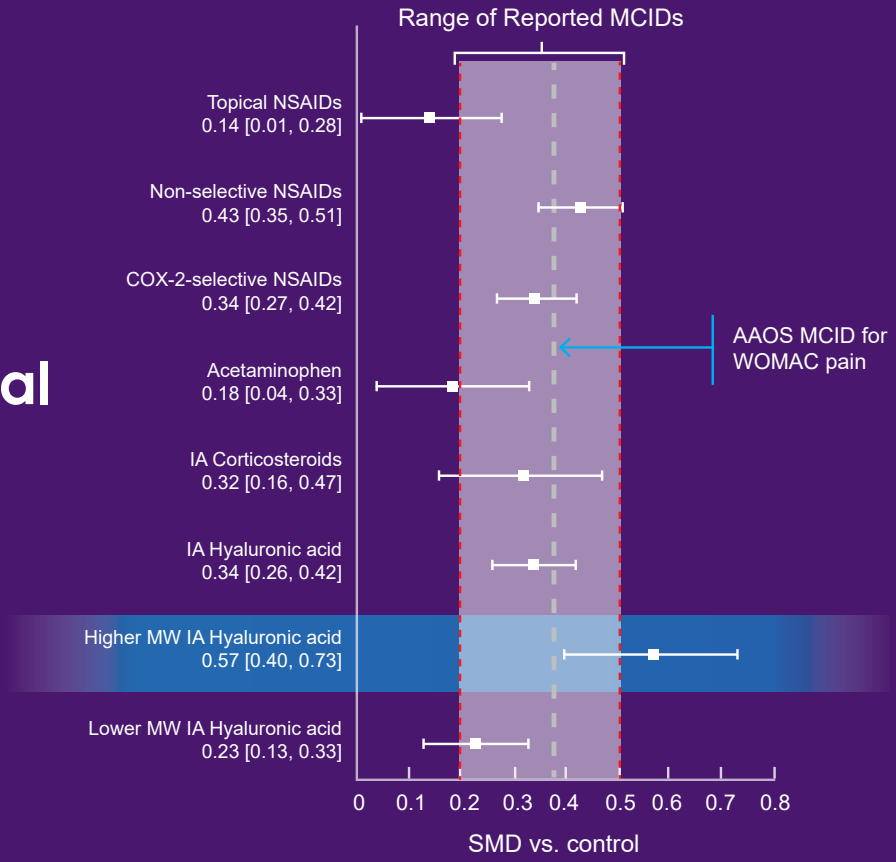
Not all Hyaluronic Acids are the same....

DUROLANE has the highest reported molecular weight of any HA – 10^{15}kDa[*5,6]

DUROLANE is a non-animal, stabilized HA that is cross-linked and entangled to create an HA with a long residence time.



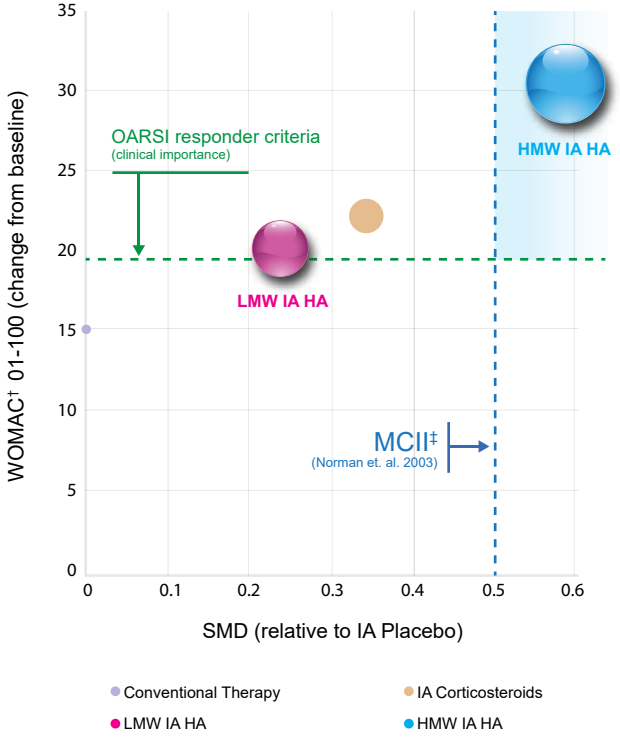
High molecular weight (HMW) HAs are superior to low molecular weight (LMW) HAs and other nonsurgical therapies for the management of osteoarthritis (OA)[1-4]



Comparison of treatment effect estimates for therapies under consideration from meta-analysis by Concoff A, et al, 2019.[4] The dashed grey line indicates the American Academy of Orthopaedic Surgeons (AAOS) minimal clinically important difference (MCID) for Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain (0.39), and the dashed red line indicates the range of other reported MCIDs in guidelines and studies (0.20 to 0.50). HMW HAs were the only therapy to consistently exceed the MCID regardless of how the threshold is defined. SMD = standardized mean difference.

"Amalgamation of LMW and HMW may have blurred the benefits of intraarticular HA (IAHA) in the past, leading to negative recommendations."[1]

- Meta-analyses have demonstrated that HMW HAs (≥3,000 kDa) are superior to LMW (<3,000 kDA) HAs on both pain and function outcomes[1-3]
- HMW HAs are the only HA formulation to consistently exceed the minimum clinically important improvement (MCII) threshold set by clinical practice guidelines such as the AAOS recommendations on osteoarthritis management[1,4]



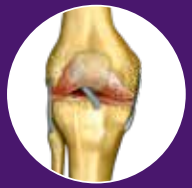
Cluster graph showing absolute efficacy (change from baseline on WOMAC 0–100 scale) plotted against relative efficacy (compared to IA Placebo) taken from a network meta-analysis by Hummer CD, et al, 2020.[1] HMW HAs were the only therapy to exceed the minimally clinically important improvement (MCII) threshold.

Not all Hyaluronic Acids are the same

The DUROLANE® Difference

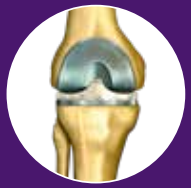
Product	Source	Modification Process	Cross-linking Agent	Average Molecular Weight (kDA)	Half-life	Injection Regimen	Concentration
DUROLANE[1]	**Bacterial Fermentation**	**Mild Stabilisation <1%**	**BDDE Linker***	**>100 billion 3D gel particles**	**28 Days**	**1**	**60 mg/3 mL**
Synvisc-One®[2] (hylan G-F 20)	Rooster Combs	Highly Cross-linked; 20%	Formaldehyde and Divinyl Sulfone	6000 + Gel	8-10 Days	1	48 mg/6 mL
Monovisc®[3]	Bacterial Fermentation	Lightly Cross-linked	Proprietary Cross-linker	1950	Unknown	1	88 mg/4 mL (Nominal Amount)
Synvisc®[4] (hylan G-F 20)	Rooster Combs	Highly Cross-linked; 20%	Formaldehyde and Divinyl Sulfone	6000 + Gel	8-10 Days	3	16 mg/2 mL
Euflexxa®[5]	Bacterial Fermentation	Nil	Nil	3000	Unknown	3	20 mg/2 mL
Orthovisc®[6]	Bacterial Fermentation	Nil	Nil	1950	Unknown	3	30 mg/2 mL

PROVEN CLINICAL AND COST-EFFECTIVENESS



The typical follow-up period of RCT studies evaluating intraarticular injectables for OA is **3-6 months**[7,8]

Most patients live with OA for **many years** prior to total joint replacement[9,10]

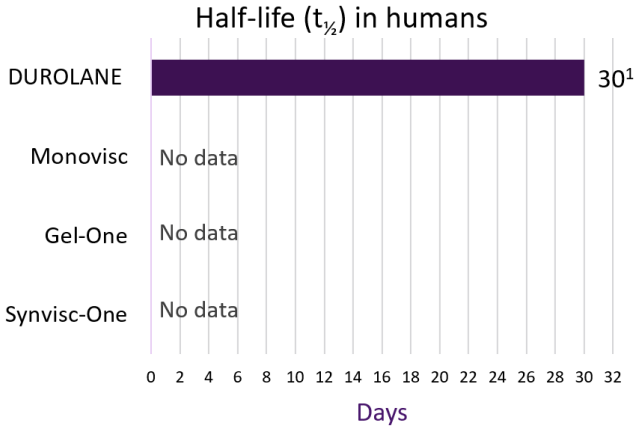


In a 6-year cohort study with 623 patients, pain relief from DUROLANE injections was sustained for an average **466.8 days (15.3 months)** post initial treatment[11]

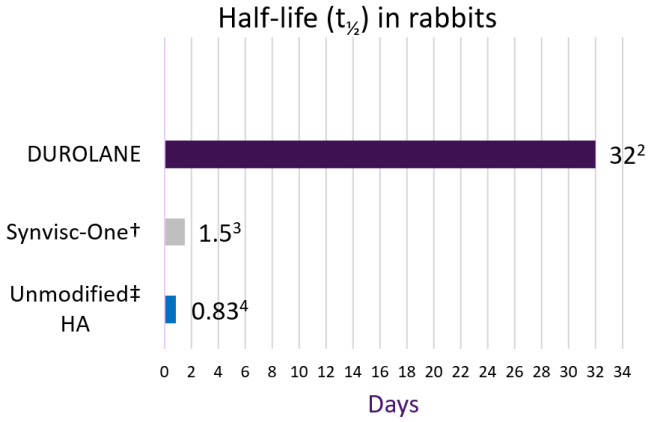
Repeat IAHA injections are associated with **delay to time to total joint replacement**[12-15]

Choose DUROLANE for:
Half-Life of 30 days

Only single-injection HA with half-life data in humans

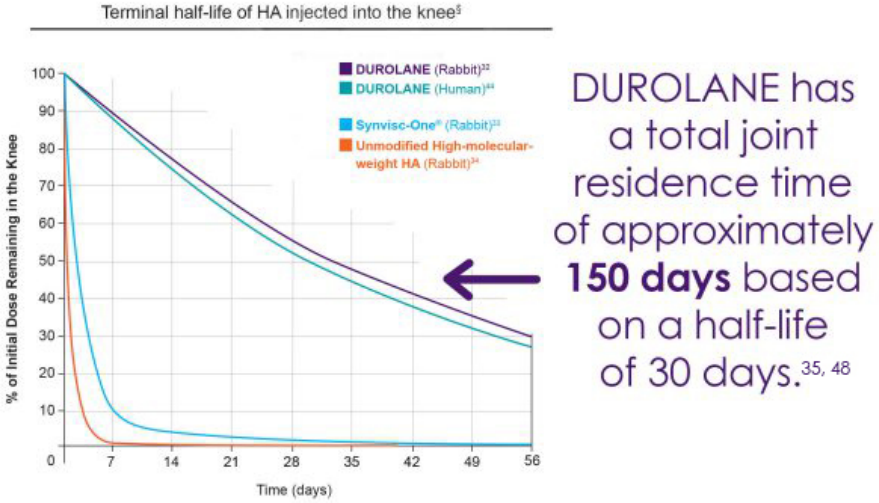


Longer half-life in rabbit knee than other HA products



‡Dose was 0.3 mL of a 20-mg/mL product.
†Hylan G-F 20, 0.3 mL; half-life of 1.5 days corresponds to hylan A fluid (90% w/v of total product).
*Non-cross-linked, 1 mg/0.1 mL/kg.

Choose DUROLANE for:
Joint Residence Time of 150 days

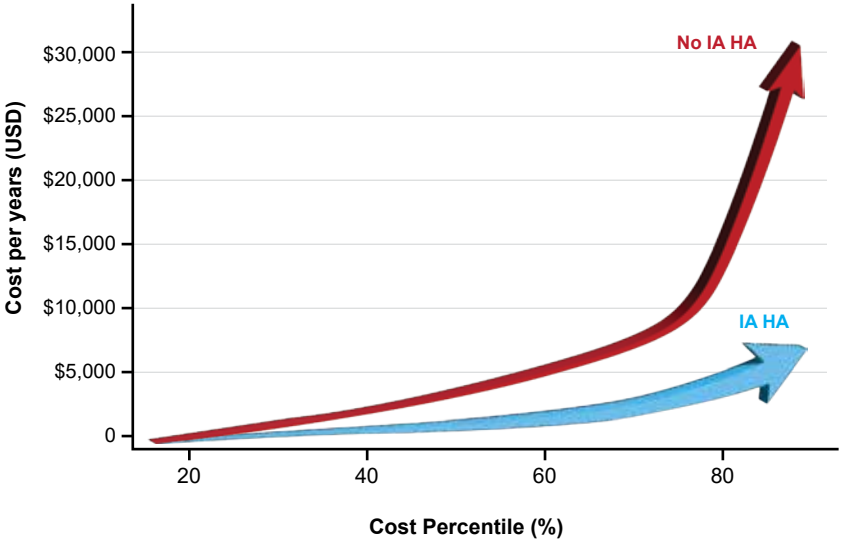


DUROLANE has a total joint residence time of approximately **150 days** based on a half-life of 30 days.[35, 48]

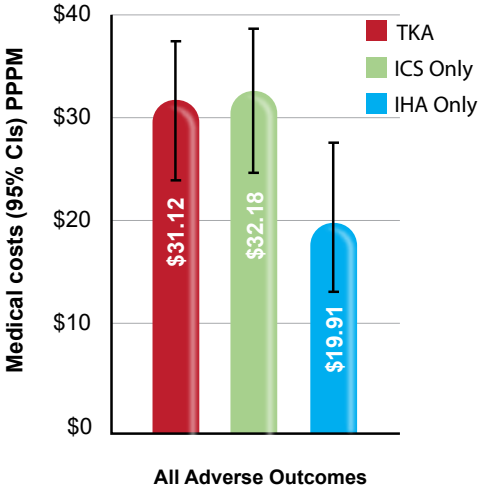
- **Total joint residence time of approx. 150 days based on a half-life of 30 days**
- **A half-life of 30 days (approximately 4 weeks) in the knee joint in a single-injection treatment regimen**
- **The longest reported half-life of any HA**

Choose DUROLANE for:

- Reductions in opioid and analgesic use[16-18]
- Improved quality of life and overall cost effectiveness vs standard of care[13,18-20]
- Reduced adverse outcome-related costs[18]



Knee OA-related costs per year by cost percentile among patients that required total knee arthroplasty (TKA) based on if patients received IAHA prior to arthroplasty or not[13]



Medical costs (95% CI) per patient per month (PPPM) for adverse outcomes during the 4-year observation period among patients that received either TKA only, intraarticular corticosteroid (ICS) only, or IAHA only[18]

Choose DUROLANE for:
Powerful and Lasting Pain Relief

- No risk of adverse reaction (NO Rooster Derivatives)
- Long lasting up to 15 months
- More powerful lasting pain relief versus MPA*
- More powerful pain relief versus Synvisc-One
- Unique formulation in a single injection treatment
- Uses NASHA® technology to:

  Increase residence time in the joint

  Impart unique viscoelastic properties compared to other hyaluronic acid (HA)

Choose DUROLANE for:
Numbers that speak for themselves

20+
years clinical use

2 +
million patients treated

30
days reported half life

12
Level I Clinical Studies

13
Level II Clinical Studies

DUROLANE®

hyaluronic acid, stabilized single injection

Visit **DUROLANE.com** to learn more.

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Summary of Indications for Use: DUROLANE (3 mL): Argentina, Australia,¶ Brazil, Chile, Colombia, EU,¶ India, Jordan, New Zealand,¶ Russia, Switzerland,¶ Turkey,¶ United Arab Emirates: Symptomatic treatment of mild to moderate knee or hip osteoarthritis. In addition, DUROLANE has been approved in Australia, EU and New Zealand for the symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, shoulder, elbow, wrist, fingers, and toes.

Mexico: Symptomatic treatment of mild to moderate knee osteoarthritis.

Taiwan: Treatment of pain in OA of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics,e.g., acetaminophen.

Canada¶: Symptomatic treatment of mild to moderate knee or hip osteoarthritis and symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, fingers and toes

¶DUROLANE is also indicated for pain following joint arthroscopy in the presence of osteoarthritis within 3 months of the procedure.

Full prescribing information can be found in product labeling, or at **DUROLANE.com**

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Innovations For Active Healing