smith&nephew

DUROLANE®

Hyaluronic Acid, Stabilised
Single Injection

The original single injection

DUROLANE®
The original single injection
since **2001**

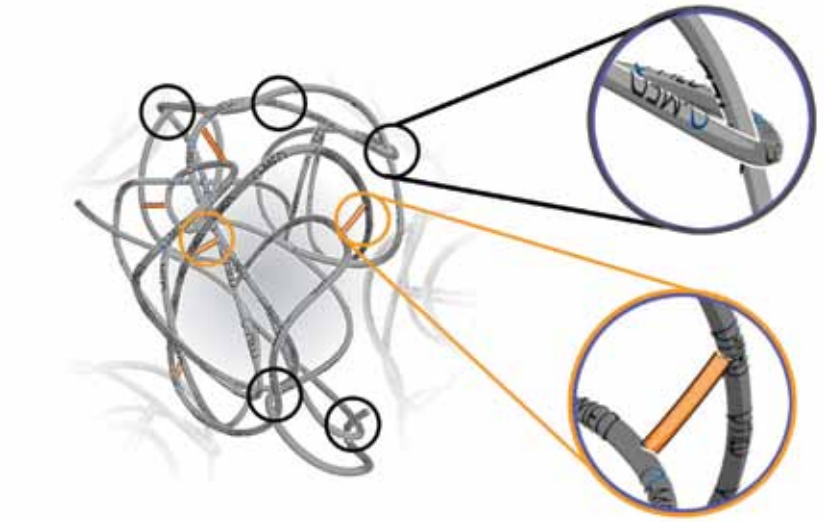
Not approved for sale in the USA

DUROLANE® is stabilised and different from other HA products

DUROLANE is a stabilised, hyaluronic acid (HA)-based, viscoelastic gel for the intra-articular treatment of mild to moderate osteoarthritis of the knee and hip.

DUROLANE uses patented NASHA™ technology which gives it a unique gel particle structure. The unique and patented stabilisation technique ensures that the naturally cross-linked and entangled HA network is kept in place by introducing a very limited number of synthetic cross-links, resulting in minimal modification.

NASHA™ structure



Stabilised HA: 1% stabilisation forms a flexible molecular network which resists physiological catabolism.[1]

1. Edsman K et al. The ability of DUROLANE to withstand degradation by free radicals. Poster presented at the 55th Annual Meeting of the Orthopaedic Research Society, February 22-25, 2009; Las Vegas, Nevada, USA.
2. Lindqvist U et al. Elimination of stabilised hyaluronan from the knee joint in healthy men. Clin Pharmacokinet 2002; 41: 603 13.
3. Larsen NE et al. Clearance kinetics of a single injection cross-linked hylan-based viscosupplement in a rabbit model. Osteoarth Cart 2007; 15(Suppl. C): C64.
4. Brown TJ et al. Turnover of hyaluronan in synovial joints: elimination of labelled hyaluronan from the knee joint of the rabbit. Exp Physiol 1991; 76: 125-134.
5. Wooley PH et al. Evaluation of the biocompatibility of Durolane using the murine air pouch model. Poster presented at the 55th Annual Meeting of the Orthopaedic Research Society, February 22-25, 2009; Las Vegas, Nevada, USA.
6. Harrison A et al. DUROLANE provides anti-nociceptive effects in a model of articular joint pain. Poster presented at the 2008 World Congress on Osteoarthritis, September 18-21, Rome, Italy.

Proven effectiveness in knees

Statistically significant reductions in pain at 3 months vs. baseline.[7]

- Significant ($p<0.001$) reductions in pain at 3 months versus baseline as measured by the visual analogue scale (VAS) for 103 patients who received DUROLANE single injection therapy.
- 80% of these patients reported satisfaction with the treatment (very good/good/fair).
- Adverse events (5%) were generally transient and did not require more than mild analgesics.

Significantly superior pain response compared to placebo at 6 weeks.[8]

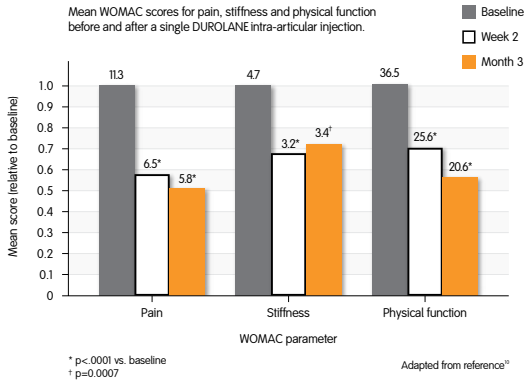
- Patients treated with DUROLANE for OA of the knee (n=216) were shown to have a significantly superior pain response compared to placebo at 6 weeks ($p=0.025$).
- The benefit was greater in patients (n=82) with OA restricted to the study knee.
- Treatment-related adverse events were similar in both placebo and DUROLANE treated patients.

Effectiveness in comparison to corticosteroid [9]

- The pain relief effect of DUROLANE was shown to be non-inferior to methylprednisolone over 12 weeks.
- WOMAC pain scores were significantly improved in DUROLANE patients compared to control patients at 26 weeks.
- One subset (n = 27) of patients showed the benefits lasted for 9 months.

7. Akemark C, Berg P, Björkman A, Malm P. Non-animal stabilised hyaluronic acid in the treatment of osteoarthritis of the knee. A tolerability study. Clin Drug Invest 2002;22:157-66.
8. Altman RD, Akermark 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;12:642–649.
9. Leighton, R. and N. Arden. A randomized blinded trial comparing one HA injection to corticosteroid for knee osteoarthritis pain. Oral presentation #640 AAOS, 2010 New Orleans.

Proven effectiveness in hips

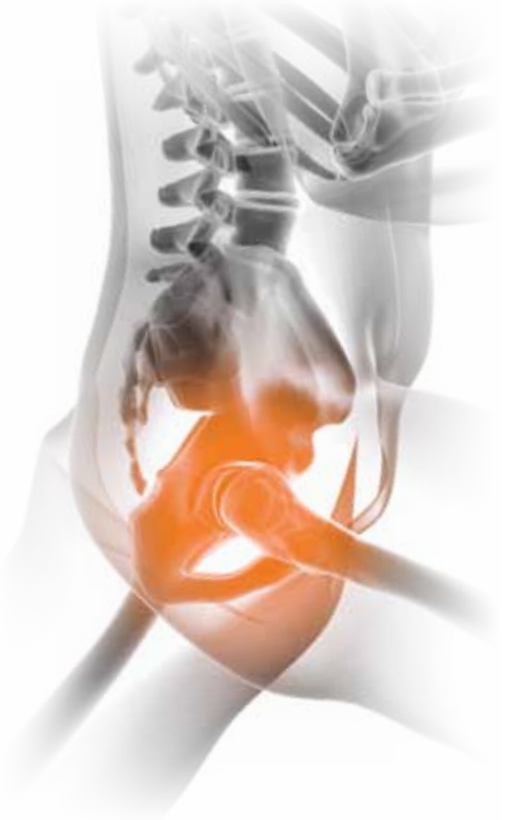


Reduction in pain and stiffness with improvement in physical function vs. baseline at three months.[10]

- The overall response rate was 54%.
- The proportion of patients rating their global status as 'good or very good' increased from 0% at baseline to 46% at 3 months.
- DUROLANE was well-tolerated with no serious adverse events.

Significant improvements at six months following injection under fluoroscopic control: [11]

- Fourty patients with hip OA were treated with a single intra-articular injection of DUROLANE.
- Walking Pain, Patient Global Assessment, WOMAC A & B decreased significantly between baseline and 6 months.
- 71% were classified OMERACT-OARSI responders.

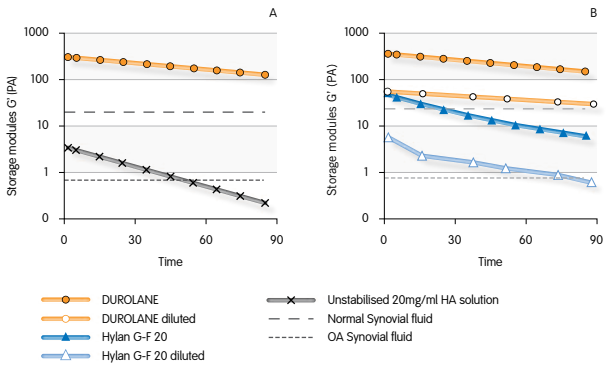


10. Berg P. and Olsson U. Intra-articular injection of non-animal stabilised hyaluronic acid (NASHA) for osteoarthritis of the hip: A pilot study. Clin Exp Rheumatol 2004;22:300-6.
11. Conrozier, T. et al. Safety, efficacy and predictive factors of efficacy of a single intra-articular injection of non-animal-stabilized-hyaluronic-acid in the hip joint: results of a standardized follow-up of patients treated for hip osteoarthritis in daily practice. Arch Orthop Trauma Surg (2009) 129:843–848.

The science of the single injection

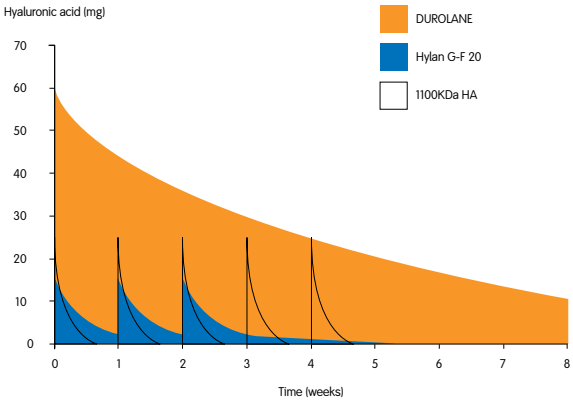
DUROLANE® is resistant to dilution and degradation,[1] giving DUROLANE a longer residence time in the synovial joint compared to other stabilised and unstabilised HA products.[2-4]

Resistance to degradation [1]



Storage modulus at 1Hz during degradation by hydroxyl radicals.
A) DUROLANE and 20mg/ml unstabilised HA solution.
B) DUROLANE and Hylan G-F 20 diluted and undiluted.
(Diluted = 1:1, product: 20mg/ml HA solution)

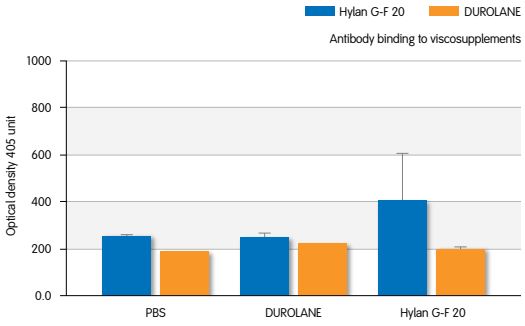
Residence time [2-4]



Graph based on elimination of hyaluronic acid from the joint space of human[2] and rabbits[3,4] as a function of time for DUROLANE; based on a single injection of 20mg/ml in a 3ml volume (i.e. 60mg total dose); compared against extrapolated data for the residence time of Hylan G-F 20[3]; calculated based on projected clearance of 3 weekly injection of 16mg of Hylan G-F 20 in a rabbit model.[3]

DUROLANE does not generate significant product specific antibodies[5] and shows superior anti-nociceptive properties in comparative pre-clinical studies.[6]

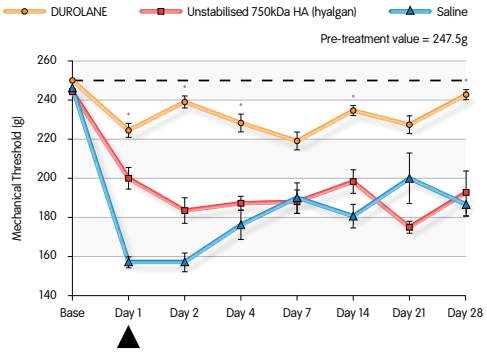
Safety [5]



The findings suggest that DUROLANE is not antigenic to an excessive level in this murine model.

- Significantly less antibody reactivity or lymphocyte response were observed in the DUROLANE group compared to Hylan GF-20.

Pain relief [6]



DUROLANE provided significant anti-nociceptive effects compared to the saline control and unstabilised HA, both in terms of force required to initiate a pain response and static motor behaviour at days 1, 2, 4, 14 and 28 in mice.

Effective relief from OA knee and hip pain with one safe treatment[7-10]

DUROLANE® is a single injection treatment to relieve the pain of knee or hip osteoarthritis. It is based upon a safe and proven technology of stabilised hyaluronic acid, NASHA™. Hyaluronic acid (HA) is a naturally occurring molecule that provides the lubrication and cushioning in a normal joint.

DUROLANE is a sterile, transparent viscoelastic gel supplied in a 3ml glass syringe with a luer-lok fitting, packed in a blister pack.

DUROLANE contains 20mg/ml of stabilised, non-animal hyaluronic acid (NASHA) in buffered physiological sodium chloride solution pH7.

The contents of the syringe are sterile.

DUROLANE is a single dose preparation and should only be injected once per treatment course. The recommended dose is 3ml (one syringe) per knee or hip joint.

DUROLANE is indicated for the symptomatic treatment of mild to moderate knee or hip osteoarthritis.

PRODUCT CODE:
3ml : 1081 - 110

For details of your local distributor and full prescribing information, visit our website.

www.durolane.com

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