smith&nephew

DUROLANE®

Hyaluronic Acid Stabilised
Single Injection

The single injection hyaluronic acid treatment for OA of both the knee and hip

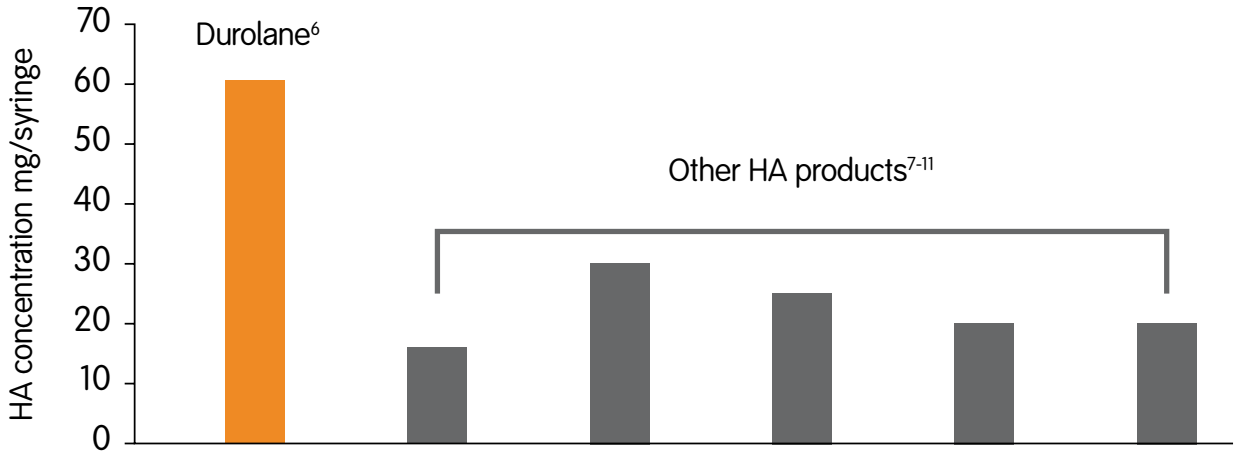
Not available in the USA

References:

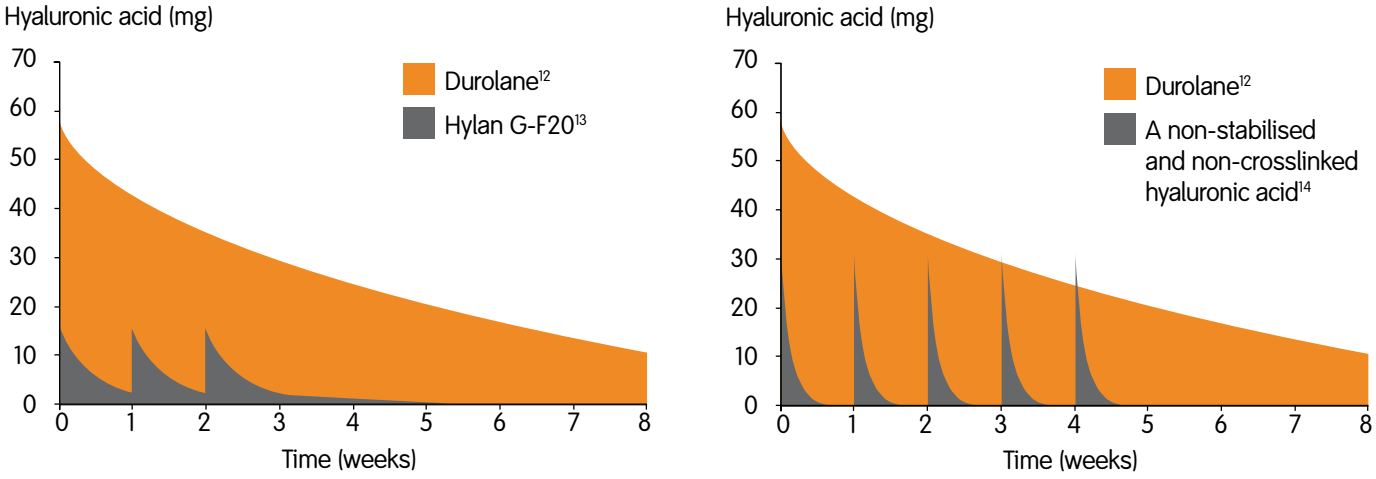
1 Bellamy N et al. Viscosupplementation for the treatment of osteoarthritis of the knee (Review). Cochrane Database of Systematic Reviews 2006, Issue 2.
2 Jordan KM et al. Ann Rheum Dis 2003; 62: 1145-1155 (EULAR).
3 American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis and Rheumatism 2000; 43: 1905-1915.
4 Bjordal JM et al. BMJ 2004; 327: 1317-1320.
5 Carruthers A et al. Dermatol Surg 2005; 31: 1591-1598.
6 Durolane® Instructions For Use.
7 Synvisc® Prescribing Information.
8 Orthovisc® Prescribing Information.
9 Supartz® Prescribing Information.
10 Hyalgan® Prescribing Information.
11 Ostenil® Prescribing Information.
12 Durolane® Data on File.
13 Synvisc® http://www.fda.gov/cdrh/pdf/p940015.pdf P940015. Synvisc® Hylan G-F 20 Filed: May 31, 1994 Conditions of Approval Issued: 5-2-95.
14 Brown TJ et al. Exp Physiol 1991; 76: 125-134.
15 Åkermark C et al. Clin Drug Invest 2002; 22: 157-166.
16 Altman R et al. Osteoarthritis Cart 2004; 12: 642-649.
17 Berg P and Olsson U. Clin Exp Rheumatol 2004; 22: 300-306.
18 Jackson DW et al. J Bone Joint Surg 2002; 84-A: 1522-1527.
19 Goldberg VM and Coutts RD. Clin Orthop 2004; 419: 130-137.

Advantages of DUROLANE® single injection therapy

Delivers a high concentration of hyaluronic acid to the joint space[6]



Stabilised for prolonged joint residence time[12]



The elimination of hyaluronic acid from the joint space as a function of time for the DUROLANE® product and for products containing non-stabilised hyaluronic acid

Single injection

Relieves pain and improves joint mobility for at least three months[15,17]

May mean less injection-related discomfort and fewer hospital visits, encouraging patients to continue long-term treatment

May be more efficent use of healthcare resources

Non-animal source

Non-animal source has minimal risk of contamination with animal allergens or pathogens (eg viruses)

No reported reactions of painful and severe acute inflammatory reactions (pseudosepsis)[19] which have been known to occur with animal-based HA

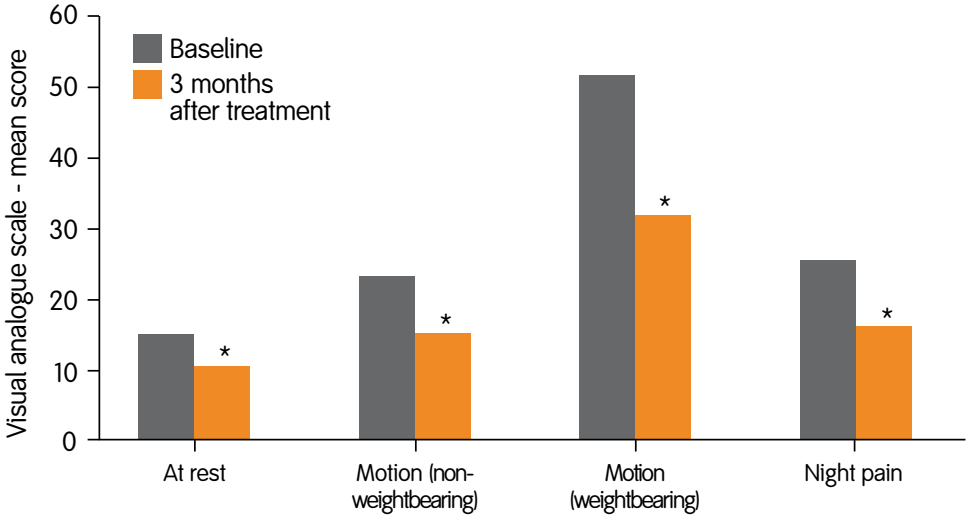
Proven efficacy in knees

Significant reductions in pain at 3 months vs. baseline[15]

Highly 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[15]

80% of these patients reported satisfaction with the treatment (very good/good/fair)[15]

Adverse events (5%) were generally transient and did not require medical interventions[15]



*p<.001 vs. baseline

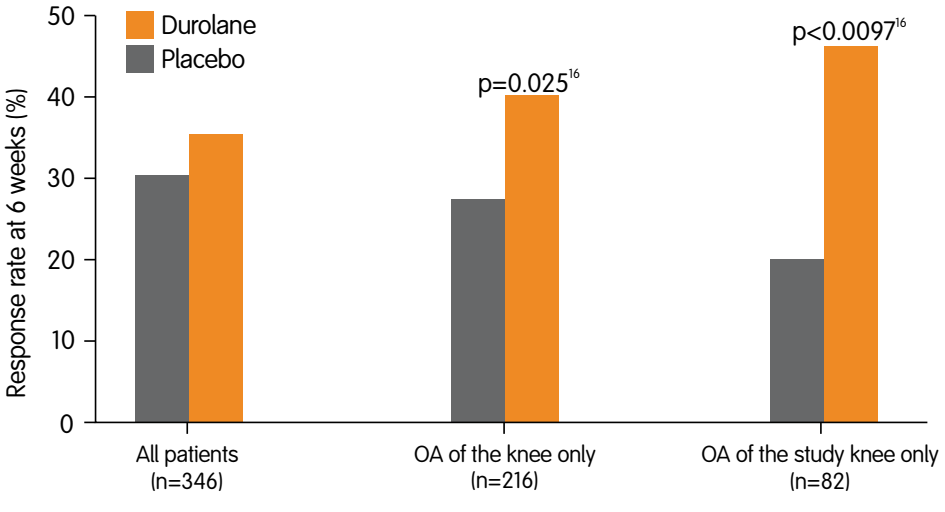
Adapted from reference[15]

Significantly superior than placebo[16]

DUROLANE therapy was significantly superior to placebo at week 6 (n=216)[16]

The benefit was greater in patients (n=82) with OA restricted to the study knee[16]

Treatment-related adverse events affected similar numbers of patients in both arms of the study[16]



Adapted from reference[15]

26-week double-blind, multicentre study, 346 patients were randomly allocated to receive DUROLANE® therapy (n=172) or placebo (n=174). A positive response to treatment was defined as a reduction in WOMAC pain score from baseline of at least 40% together with an aboslute decrease of at least five points.

Proven efficacy in hips

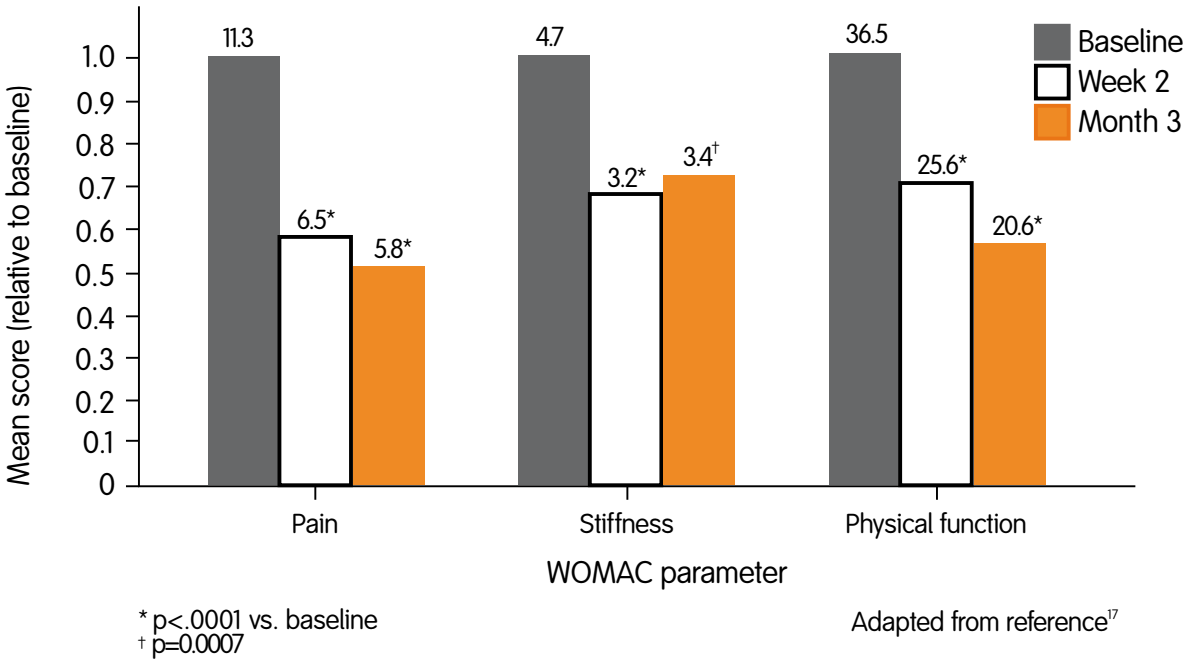
Reduction in pain and stiffness with improvement in physical function vs. baseline[17]

At three months post-treatment, the overall response rate was 55%[17]

The proportion of patients rating their global status as 'good or very good' increased from 0% at baseline to 46% at month three[17]

DUROLANE® was well tolerated with no serious adverse events reported over the three months of follow-up[17]

Mean WOMAC scores for pain, stiffness and physical function before and after a single DUROLANE® intra-articular injection



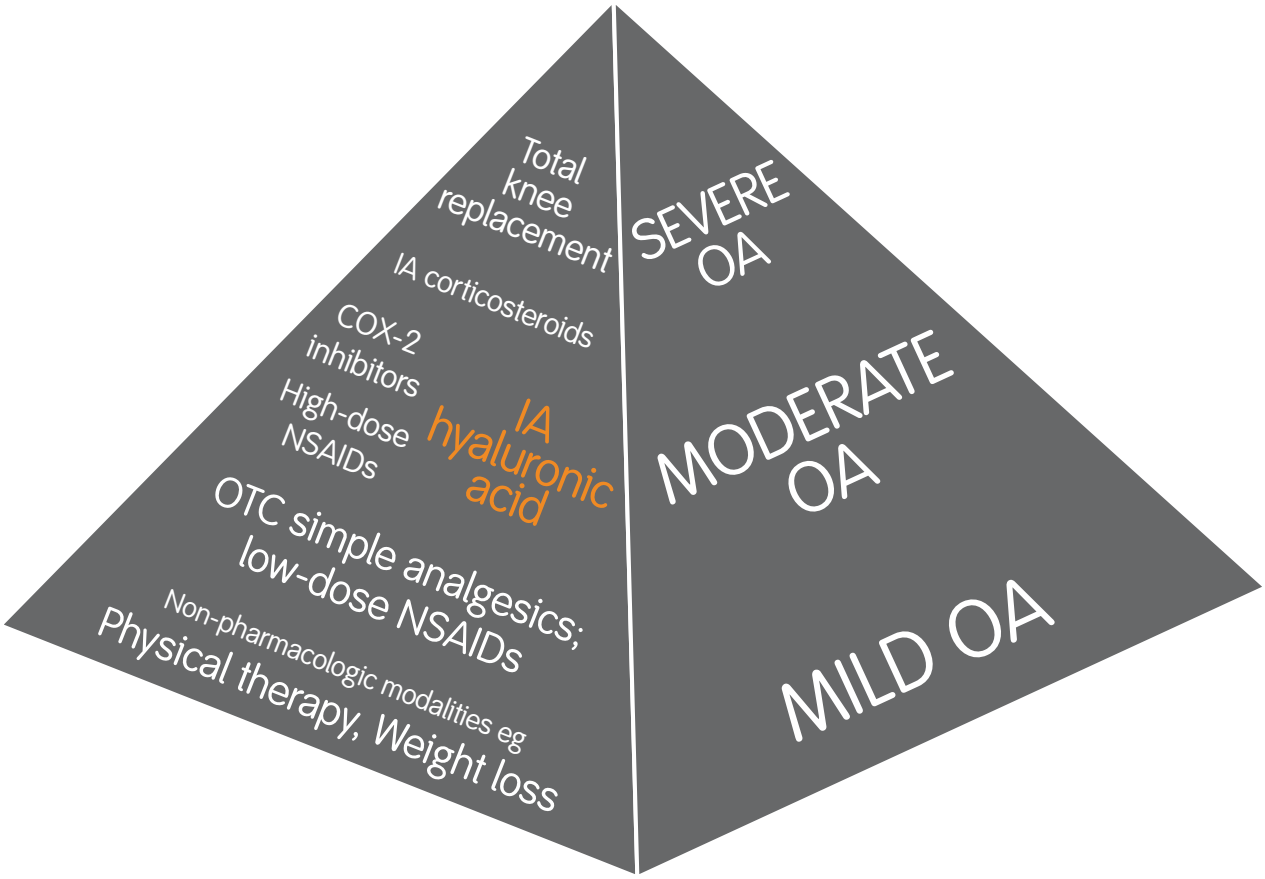
* p<.0001 vs. baseline
† p=0.0007

Adapted from reference[17]

31 patients with OA of the hip (according to ACR criteria, WOMAC pain score of at least 7 in one hip and significant hip pain for the majority of days prior to the study) received a single DUROLANE® injection. A positive response to treatment was defined as a reduction in WOMAC pain score from baseline of at least 40%, together with an absolute decrease of at least five points.[17]

When to use DUROLANE® injection therapy

ACR and EULAR recommendations for OA knee management[2,3]



Derived from references 2 and 3

Long -term use of NSAIDs, including COX-2 inhibitors not supported[4]

Bjordal JM et al reported their conclusions form a systematic review and meta -analysis of 23 randomised, placebo-controlled trials in a 2004 BMJ article[4]

> *"NSAIDs can reduce sort term pain in osteoarthritis of the knee slightly better than placebo, but the current analysis does not support long term use of NSAIDs for this condition"[4]*

> *"As use of oral NSAIDs may incur serious adverse effects, they can only be recommended for limited use in osteoarthritis of the knee"[4]*

How to use DUROLANE® injection therapy

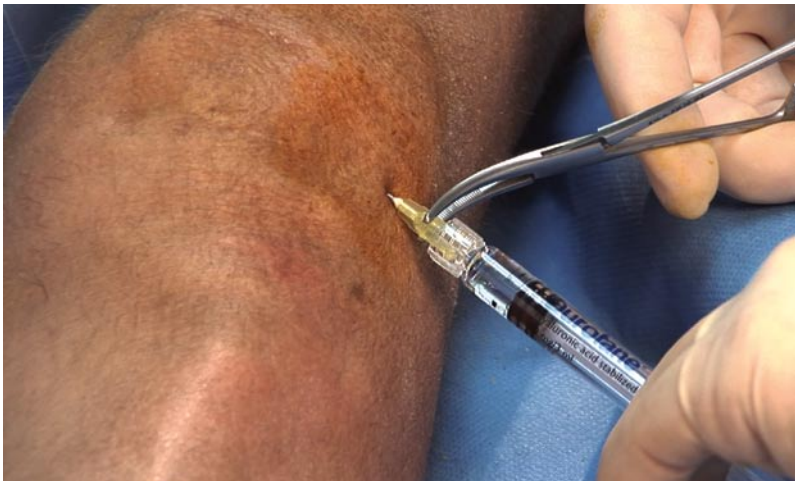
Clinicians using a lateral midpatellar extended-leg injection technique reported the most accurate (93%) approach for intra-articular needle placement in a knee with no effusion[3]

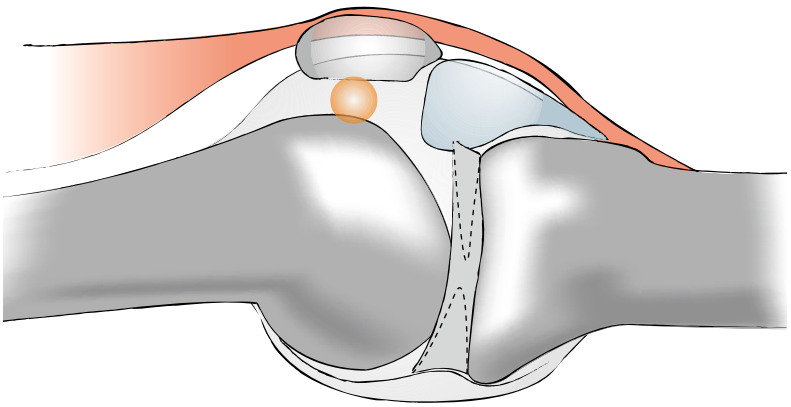
Rates of accuracy of intra-articular injections

Portal	Total no. of injections	Placement of needle (no. of injections) Extra-articular	Intra-articular	Accuracy Rate
Anterolateral	80	23	57	71%
Antermedial	80	20	60	75%
Lateral midpatellar	**80**	**6**	**74**	**93%**

From: Jackson DW et al. J Bone Joint Surg 2002; 84-A: 1522-1527

Injection into the lateral midpatellar portal





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