DUROLANE is a single-injection treatment to relieve the pain of osteoarthritis in specific knee and hip joints. 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 either a 1ml or 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.

DUROLANE is a single dose preparation and should only be injected once per treatment course.

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

• Based on the improvement from baseline, DUROLANE has shown to be longer lasting than methylprednisolone steroid in 26 weeks post single injection treatment (p<0.04).
• Patients that received two DUROLANE injections had a 38% reduction from baseline to week 26 and nearly 50% at 52 weeks.
• After second injections of DUROLANE no allergic reactions have been observed.

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

DUROLANE SJ (1ml): Symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, elbow, wrist, fingers, and toes.

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

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.

Full prescribing information can be found in product labeling, or at www.durolane.com.

Product Information

Product code:
• DUROLANE (3ml) 1082012

www.durolane.com
www.BioventusGlobal.com

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SMK-000680

The original single injection for osteoarthritis pain relief

Since 2001
Effective relief from osteoarthritis pain with one safe treatment

DUROLANE is a single-injection treatment to relieve the pain of osteoarthritis in specific knee and hip joints. 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.

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

References

**DUROLANE® advanced and unique NASHA® technology**

DUROLANE is a stabilised hyaluronic acid (HA), from a non-animal source, therapy for the intra-articular treatment of mild to moderate osteoarthritis in knee and hip joints.

DUROLANE uses advanced and unique NASHA technology which gives it a unique gel bead structure. The patented stabilization 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.

For antibody production.

**NASHA structure**

![Image](https://via.placeholder.com/150)

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

Entanglement of HA chains (natural cross-links)

BDDE (1, 4 butanediol diglycidyl ether) Linker

NASHA technology to increase residence time in the joint.

**Significant and sustained benefits for hip** and knee OA patients

- Antibody levels in DUROLANE treated animal blood significantly greater (p<0.001) than saline or DUROLANE.

- Antibody production in DUROLANE treated animal blood.

**Effectiveness in hips**

Significant (p<0.001) improvements at six months following injection under fluoroscopic control.

- Forty 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 six months.

- 71% were classified OMERACT-OARSI responders.

- Both DUROLANE injection and saline injection reduced pain in a bipartite synth.

**Long lasting by design**

DUROLANE uses unique and advanced NASHA technology to increase residence time in the joint.

Data from human and animal studies have shown that:

- **DUROLANE has a half-life of 4 weeks or 32 days in the joint in a single injection treatment regime**

- **DUROLANE has a longer half-life than unmodified hyaluronic acid (HA) and cross-linked Synvisc® (hylan G-F 20)**

**Effectiveness in comparison to corticosteroid**

A randomised, blinded trial comparing one HA injection to corticosteroid for knee osteoarthritis patients:

- The pain relief effect measures in WOMAC pain responder rate (patients %) of DUROLANE was shown to be non-inferior to methylprednisolone over 12 weeks.

- Based on the improvement from baseline, DUROLANE has shown to be longer lasting than methylprednisolone stored at 26 weeks post-single injection treatment (p<0.034).

**Pre-clinical evidence for the efficacy of DUROLANE**

DUROLANE prevented knee osteoarthritis progression in an animal model:

- DUROLANE injection protected joints from femoral cartilage erosion as well as tibial and femoral bone lesions (see graph).

- DUROLANE maintained the cartilage structure (Stance time) that was observed prior to the experiment, whereas animals treated with saline had worsening gait pattern, as observed by increasing stance time.

- Both DUROLANE injection and saline injection reduced pain in a bipartite synth., but the DUROLANE effect was more pronounced and prolonged than the saline injection.

- DUROLANE was compared to other HA preparations* and a saline control.

- The saline control was least effective at pain relief shown by the least amount of pressure applied to the knee joint after injection to induce a response.

- The pain relief DUROLANE provided was significantly better than unmodified sodium hyaluronate and Hylan G-F 20 at multiple time points (*p<0.01; **p<0.001).

- A single injection of DUROLANE provided pain relief out to 56 days in this animal knee pain model.

**DUROLANE provided superior pain relief, compared to Synvisc®, in an animal knee joint pain model**

Joint Tissue Pathology: Scores showing the protective effects of palifermin, hyaluronan (mg) or matrix metalloproteinase (MMP-1) proteinase. Significance was assessed using a Mann-Whitney test for the five standard deviation groups. Asterisks indicate statistically significant and dose specific effects of DUROLANE on murine OA pathology.

- **DUROLANE was compared to other HA preparations** and a saline control.

- **The saline control was least effective at pain relief shown by the least amount of pressure applied to the knee joint after injection to induce a response.**

- **The pain relief DUROLANE provided was significantly better than unmodified sodium hyaluronate and Hylan G-F 20 at multiple time points (*p<0.01; **p<0.001).**

- A single injection of DUROLANE provided pain relief out to 56 days in this animal knee pain model.

**A history of safe use**

DUROLANE does not generate product specific antibodies

Mice were injected with different HA products under the skin in an air pouch. Then blood samples were obtained to test for antibody production.

- Antibody levels in DUROLANE treated animal blood were no different to controls.

- DUROLANE did not cause a systemic immune response.

- Antibody levels in Hylan G-F 20 treated animal’s blood were significantly greater (p=0.01) than saline or DUROLANE.

- Hylan G-F 20 stimulated a systemic immune response.

**DUROLANE® prevented knee osteoarthritis progression in an animal model**

- DUROLANE injection protected joints from femoral cartilage erosion as well as tibial and femoral bone lesions (see graph).

- DUROLANE maintained the cartilage structure (Stance time) that was observed prior to the experiment, whereas animals treated with saline had worsening gait pattern, as observed by increasing stance time.

- Both DUROLANE injection and saline injection reduced pain in a bipartite synth., but the DUROLANE effect was more pronounced and prolonged than the saline injection.

- DUROLANE was compared to other HA preparations* and a saline control.

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Mice were injected with different HA products under the skin in an air pouch. Then blood samples were obtained to test for antibody production.

- Antibody levels in DUROLANE treated animal blood were no different to controls.

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- Hylan G-F 20 stimulated a systemic immune response.
DUROLANE® advanced and unique NASHA® technology

DUROLANE is a stabilised hyaluronic acid (HA), from a non-animal source, therapy for the intra-articular treatment of mild to moderate osteoarthritis in knee and hip joints.

DUROLANE uses advanced and unique NASHA technology which gives it a unique gel bead structure. The patented* approach.

• NASHA structure
  - Stabilised HA: 1% stabilisation forms a flexible molecular network which resists physiological catabolism.
  - Optical density 405 unit
  - Significance (p<0.001) than saline or DUROLANE were no different to controls

Table 1: Anti-inflammatory effect of Hylan G-F 20 and DUROLANE in a murine OA model.

For intra-articular needle placement in knees with no effusion, an accuracy rate of 93% has been reported using a lateral midpatellar extended-leg injection approach.

A history of safe use

• Antibody levels in Hylan G-F 20 treated animal’s blood were significantly greater (p<0.001) than saline or DUROLANE were no different to controls

• Antibody binding to viscosupplements, as seen with increased optical density.

• Antibody binding to DUROLANE was observed as compared against extrapolated data for Synvisc® (hylan G-F 20) and low molecular weight HA vs. controls.

Pre-clinical evidence for the efficacy of DUROLANE

DUROLANE provided superior pain relief, compared to Synvisc®, in an animal knee joint pain model.

DUROLANE prevented knee osteoarthritis progression in an animal model.

DUROLANE® is a stabilised hyaluronic acid (HA) product. DUROLANE prevents knee osteoarthritis progression in an animal model. A randomised, blinded trial comparing one HA injection to corticosteroid in a single injection treatment regime (hylan G-F 20) showed a dramatic drop in mechanical thresholds from day 1, all hyaluronic acid compounds showed an effective response. These results were consistent with published findings and had a profound effect on nociceptive threshold.

A single injection of DUROLANE provided pain relief to 56 days in this animal knee pain model.

Significant and sustained benefits for hip and knee OA patients

Effectiveness in comparison to corticosteroid*

• A randomised, blinded trial comparing one HA injection to corticosteroid for knee osteoarthritis patients at 26 weeks post-single injection treatment (p=0.034).

Effectiveness in hips

• Forty 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 six months.

• 71% were classified OMARAT-GAPPS responders.

Long lasting by design

DUROLANE uses unique and advanced NASHA technology to increase residence time in the joint.

Data from human and animal studies have shown that:

• DUROLANE has a half-life of 4 weeks or 32 days in the joint in a single injection treatment regime.

• DUROLANE has a longer half-life than unaltered hyaluronic acid (HA) and cross-linked Synvisc® (hylan G-F 20).**

*NOTE: Clinical dosage of Hylan G-F 20 is 20mg/ml. Mice and rats are single injections.
DUROLANE® advanced and unique NASHA® technology

DUROLANE is a stabilised hyaluronic acid (HA), from a non-animal source, for the intra-articular treatment of mild to moderate osteoarthritis in knee and hip joints.

DUROLANE uses advanced and unique NASHA technology which gives it a unique gel bead structure. The 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
Entanglement of HA-chains (natural cross-links)

BDDE (1, 4 butanediol diglycidyl ether) Linker
Stabilised HA: 1% stabilisation forms a flexible molecular network which resists physiological catabolism.\n
Mice were injected with different HA products under the skin in an air pouch. Then blood samples were obtained to test antibody production.

• Antibody levels in Hylan G-F 20 treated animal's blood were significantly higher (p<0.05) than saline or DUROLANE injection to induce a response.

**Patent available in certain countries**

A history of safe use

For intra-articular needle placement in knees with no effusion, an accuracy rate of 93% has been reported using a lateral midpatellar extended-leg injection approach.\n
A significant and sustained benefits for hip and knee OA patients

DUROLANE was compared to other HA preparations* and a saline control: the pain relief DUROLANE provided was significantly better than unmodified sodium hyaluronate and Hylan G-F 20 at multiple time points (* p<0.05; ** p<0.01) than saline.

• The saline control was least effective at pain relief shown by the least amount of pressure applied to the knee joint after injection to induce a response.

• The pain relief DUROLANE provided was significantly better than unmodified sodium hyaluronate and Hylan G-F 20 at multiple time points (* p<0.05; ** p<0.01)

• DUROLANE injection was associated with slight and transient pain compared to saline injection.

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Pre-clinical evidence for the efficacy of DUROLANE

DUROLANE prevented knee osteoarthritis progression in an animal model

In an OA model:

• DUROLANE injection protected joints from femoral cartilage erosion as well as tibial and femoral tissue loss (see graph).

• DUROLANE maintained the gait pattern (Stance time) to that observed prior to the experiment, whereas animals treated with saline had worsening gait pattern, as observed by increasing stance time.

• Both DUROLANE injection and saline injection reduced pain in alldynia score, but the DUROLANE effect was more pronounced and prolonged than the saline injection.

For intra-articular needle placement in knees with no effusion, an accuracy rate of 93% has been reported using a lateral midpatellar extended-leg injection approach.\n
A significant and sustained benefits for hip and knee OA patients

Critical aspects of urine were assessed following an injection of pain inducing agents by examining wastes applied to the animal knee joint. after a single injection of NASHA (DUROLANE, Hylan G-F 20, Synvisc, Synvisc-One, and Hyalgan) in an OA rabbit model. Although all marketed products showed a dramatic drop in mechanical thresholds from day 1, all hyaluronan compounds showed anti-inflammatory properties. These were most pronounced for Hyalgan and Hylan G-F 20, which were applied at a higher dose, and were particularly evident for Hyalgan.

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Effective relief from osteoarthritis pain with one safe treatment

DUROLANE is a single-injection treatment to relieve the pain of osteoarthritis in specific knee and hip joints. 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.

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DUROLANE is a single dose preparation and should only be injected once per treatment course.

DUROLANE is a single-injection treatment to relieve the pain of osteoarthritis in specific knee and hip joints.

DUROLANE is indicated* for the symptomatic treatment of mild to moderate osteoarthritis.

DUROLANE (3ml): Symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, elbow, wrist, fingers, and toes.

DUROLANE SJ (1ml): Symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, elbow, wrist, fingers, and toes.

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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Full prescribing information can be found in product labeling, or at www.durolane.com.

Product Information

Product code:  
DUROLANE (3ml) 1082012

* Summary of Indications for Use

DUROLANE (3ml): Symptomatic treatment of mild to moderate knee or hip osteoarthritis.

DUROLANE SJ (1ml): Symptomatic treatment associated with mild to moderate osteoarthritis pain in the ankle, elbow, wrist, fingers, and toes.

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

**There are no known contraindications.**

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

Full prescribing information can be found in product labeling, or at www.durolane.com.

References

13. Krocker D1, Matziolis G, Tuischer J, et al. Reduction of arthrosis associated knee pain following knee arthroscopy assessed using WOMAC pain score at 26 weeks, prior to the second injection and nearly 50% at 52 weeks. Since 2001*

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The original single injection for osteoarthritis pain relief

Since 2001*