


# Techniques for Administering Intra-articular Injections of Hyalgan® (sodium hyaluronate) for the Treatment of Osteoarthritis Knee Pain (working title)

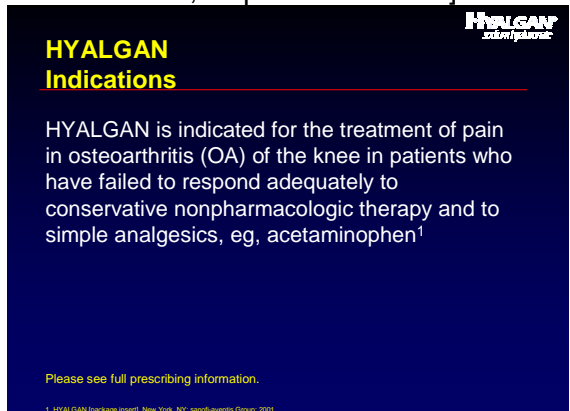
## Injection Technique DVD: Introduction

<p>[Taped action, recorded voice-over (v/o) and graphics combined throughout]</p>	
<p>[Drs. Axe and Stitik walk on screen to appear on camera full screen:]</p> <p>[Super, lower third:]  <b>Michael Axe, MD</b>          Clinical Professor          Department of Physical Therapy          University of Delaware</p> <p><b>Todd Stitik, MD</b>          Associate Professor          Physical Medicine and Rehabilitation          University of Medicine and Dentistry of New Jersey/New Jersey Medical School          Newark, NJ</p>	<p>I'm Dr. Michael Axe, sports orthopedist and Clinical Professor in the Department of Physical Therapy at the University of Delaware.</p> <p>And I'm Dr. Todd Stitik, Associate Professor of Physical Medicine and Rehabilitation at the University of Medicine and Dentistry of New Jersey, New Jersey Medical School.</p> <p>We're here to review with you injection techniques that we teach to our residents and fellows and recommend that you consider when administering HYALGAN (sodium hyaluronate) in your patients with osteoarthritis knee pain. We each have administered thousands of intra-articular injections into patients with osteoarthritis of the knee and have served as national educators at dozens of injection technique workshops held around the country. In this program, we'll be sharing our experience with you to help improve the reliability of the injections that you give in your patients to optimize their clinical benefit. But before we introduce these techniques, let's briefly review the basic pathophysiology of osteoarthritis, its clinical features, and current treatment approaches.</p>
<p>[Insert graphic showing joint changes in OA, w/ professional v/o]</p>  <p><b>Joint Changes Associated With Osteoarthritis (OA)</b></p> <ul style="list-style-type: none"> <li>• Imbalance of biosynthesis and degradation<sup>1</sup></li> <li>• Inflammation<sup>1</sup></li> <li>• Softening and loss of articular cartilage<sup>1</sup></li> <li>• Decrease in concentration and average molecular weight of HAs in synovial fluid<sup>2</sup></li> </ul> <p><small>1. Brandt KD. In: Harrison's Principles of Internal Medicine, 13th ed. New York, NY: McGraw-Hill, 1994:1692-1698. 2. Balazs EA, et al. J Rheumatol. 1993;20(suppl 39):3-9.</small></p> <p>[Slide 2, 2006 Promotional Slide Kit]</p>	<p>Osteoarthritis occurs when the cartilage surface deteriorates between bones within the joint. As the disease progresses, the cartilage loses its ability to protect the joint from the impact of movement. Several changes have been noted within the joint that appear to contribute to the development and progression of osteoarthritis. These include an imbalance between cartilage synthesis and degradation, an increase in proinflammatory activities, softening and loss of the articular cartilage, changes in joint stability, weakness and pain, and changes in the composition and quantity of hyaluronans, a key component of the cartilage and synovial fluid. [Slide 2, 2006 Promotional Slide Kit; Lewek, 2004; Mizner 2005]</p> <p>Brandt KD. Osteoarthritis. In: Isselbacher KJ, et al, eds. <i>Harrison's Principles of Internal Medicine</i>. 13th ed. New York, NY: McGraw-Hill; 1994:1692-1698.</p> <p>Balazs EA, et al. <i>J Rheumatol</i>. 1993;20(suppl 39):3-9.</p> <p>Lewek MD, Rudolph KS, Snyder-Mackler L. Control of frontal plane knee laxity during gait in patients with medial compartment</p>

	<p>knee osteoarthritis. Osteoarthritis Cartilage. 2004 Sep;12(9): 745-51.</p> <p>Mizner RL, Petterson SC, Stevens JE, Axe MJ, Snyder-Mackler L. Preoperative quadriceps strength predicts functional ability one year after total knee arthroplasty. J Rheumatol. 2005 Aug;32(8):1533-9.</p>
<p>[Insert graphic showing clinical features of OA, w/ professional v/o]</p> 	<p>Osteoarthritis is associated with a number of symptoms, predominantly pain, decreased joint mobility, stiffness, the formation of osteophytes, or bone spurs, and occasionally swelling. The ends of the bones may become enlarged and the joints may appear misshapen. Although any joint may be affected by osteoarthritis, the knee is one of the most common sites. [Slide 2, Community Outreach]</p> <p>National Institute of Arthritis and Musculoskeletal and Skin Diseases. Available at: <a href="http://www.niams.nih.gov/hi/topics/arthritis/oahandout.htm">http://www.niams.nih.gov/hi/topics/arthritis/oahandout.htm</a>. Accessed March 9, 2005.</p> <p>Arthritis Foundation. Available at: <a href="http://www.arthritis.org/conditions/DiseaseCenter/oa.asp">http://www.arthritis.org/conditions/DiseaseCenter/oa.asp</a>. Accessed March 9, 2005.</p>
<p>[Dr. Stitik on camera full screen:]</p> <p>[Insert text; reveal each bullet]</p> <ul style="list-style-type: none"> <li>• Nonpharmacologic therapies</li> <li>• Oral and topical analgesic and anti-inflammatory therapies</li> <li>• Intra-articular treatments</li> <li>• Surgery</li> </ul>	<p>Our primary goals when treating osteoarthritis of the knee are to control pain symptoms and improve or maintain joint function. Current treatment options fall into 4 major categories:</p> <ul style="list-style-type: none"> <li>• <b>Nonpharmacologic therapies</b>, such as physical therapy, exercise, weight loss, assistive devices, and bracing</li> <li>• <b>Oral and topical drug therapies</b>, which include a range of analgesic and anti-inflammatory agents</li> <li>• <b>Intra-articular treatments</b>, with injections of corticosteroids or hyaluronans, and, finally</li> <li>• <b>Surgery</b>, from arthroscopy and cartilage repair procedures to osteotomy and joint replacement</li> </ul> <p>[Slide 3, Community Outreach Slide Kit]</p> <p>American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Available at: <a href="http://www.rheumatology.org/publications/guidelines/oa-mgmt/oa-mgmt.asp?aud_mem">http://www.rheumatology.org/publications/guidelines/oa-mgmt/oa-mgmt.asp?aud_mem</a>. Accessed March 9, 2005.</p> <p>All of these approaches are safe and can be effective when used to treat osteoarthritis knee pain. A specific treatment approach is selected based on the patient's unique profile, including the severity and nature of the symptoms and surface cartilage damage, the degree of functional impairment, and the presence of other medical conditions. In this program, we'll be focusing on intra-articular treatment with the hyaluronan HYALGAN. Before we</p>

	<p>review the recommended injection techniques for administering HYALGAN, let's take a look at how hyaluronans may work and why they are used for the treatment of osteoarthritis knee pain.</p>
<p>[Insert graphic showing possible causes of joint pain in OA, with professional v/o]</p>  <p>[Slide 5, 2005 Promotional Slide Kit]</p>	<p>Joint pain in osteoarthritis may have one or more causes, including increased intraosseous pressure from vascular congestion of the subchondral bone, osteophytes, synovitis or other inflammation, capsular fibrosis, joint contracture, joint laxity, or muscle spasm. Because the exact causes of osteoarthritis symptoms are not yet well understood, it is not surprising that we also do not yet know precisely how treatments work that alleviate these symptoms.</p> <p>Hyaluronan is a viscous and elastic substance found in the synovial fluid of articular joints and is an integral component of the cartilage extracellular matrix. In the healthy knee, hyaluronans provide cushioning and lubrication for the joint, helping maintain normal joint function and protecting the joint against injury. Research suggests that in the knee affected by osteoarthritis, hyaluronans are present in reduced weight and concentration. The synovial fluid may then become thinner and may lose its ability to protect the joint against physical damage. Evidence of the protective role of endogenous hyaluronans in joints led to the development of hyaluronan products that are injected into the knee to supplement depleted hyaluronans and relieve pain.</p> <p>[Slide 2, 2006 Promotional Slide Kit; Slides 2 and 4, Community Outreach Slide Kit]</p> <p>Brandt KD. Osteoarthritis. In: Isselbacher KJ, et al, eds. <i>Harrison's Principles of Internal Medicine</i>. 13th ed. New York, NY: McGraw-Hill; 1994:1692-1698.</p> <p>Hammesfahr JFR, Knopf AB, Stitik T. <i>Am J Orthop</i>. 2003;32:277-283.</p> <p>Arthritis Foundation. Available at: <a href="http://www.arthritis.org/AFStore/StartRead.asp?idProduct=3328">http://www.arthritis.org/AFStore/StartRead.asp?idProduct=3328</a>. Accessed January 13, 2005.</p> <p>Altman RD. <i>Curr Rheum Reports</i>. 2003;5:7-14.</p> <p>Balazs EA, et al. <i>J Rheumatol</i>. 1993;20(suppl 39):3-9.</p>
<p>[Insert graphic showing rationale for use of hyaluronans, with professional v/o]</p>	<p>Support for the earlier adoption of intra-articular hyaluronans in your treatment algorithm for osteoarthritis knee pain is provided by many levels of evidence. First, hyaluronans have been proven safe and effective in numerous randomized clinical trials when compared with saline injection controls, and in a recent Cochrane Collaboration meta-analysis. Hyaluronan therapy is a recommended treatment option of the American College of Rheumatology and</p>



<p>[Slide 5, 2006 Promotional Slide Kit]</p>	<p>Patients receiving HYALGAN had a decrease in mean pain severity from 54 millimeters at baseline to 17.9 millimeters at the study's end.          [Slide 5, 2006 Promotional Slide Kit]</p> <p>Altman RD, Moskowitz R, and the Hyalgan Study Group. <i>J Rheumatol.</i> 1998;25:2203-2212.</p>
<p>[Drs. Axe on camera full screen:]</p>	<p>Clinical trial evidence and clinical practice experience tell us that HYALGAN is a safe and effective treatment in patients with osteoarthritic knee pain. To achieve the full therapeutic benefits of HYALGAN, you need to inject the product directly into the intra-articular space of the knee. Delivery of HYALGAN into the soft tissue may not only compromise its effectiveness but also may increase the risk of adverse reaction, such as local pain. In the slide review and live demonstrations available in this program, we will review the injection techniques that we recommend you consider when administering HYALGAN in your patients with osteoarthritis knee pain, to improve the reliability of your injection delivery. We hope that these techniques, which are based on this product's FDA-approved labeling and our own clinical experience, will help enhance the quality of care you provide for your patients and may improve outcomes when receiving HYALGAN.</p>
<p>[Insert graphics showing fair balance slides for HYALGAN, w/ professional v/o]</p> 	<p>HYALGAN is indicated for the treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative nonpharmacologic therapy and to simple analgesics, such as acetaminophen.</p> <p>HYALGAN [package insert], 2001.</p>

## HYALGAN Important Safety Information

**HYALGAN**  
sodium hyaluronate

- HYALGAN is contraindicated in patients with known hypersensitivity to hyaluronate preparations. Intra-articular injections are contraindicated in cases of past and present infections or skin diseases in the area of the injection site<sup>1</sup>
- The effectiveness of a single treatment cycle of less than 3 injections has not been established<sup>1</sup>
- In the US clinical trial of 495 patients, the only adverse event showing statistical significance vs placebo was injection-site pain<sup>1</sup>

Please see full prescribing information.

<sup>1</sup> HYALGAN [package insert], New York, NY: sanofi-aventis Group, 2001.

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HYALGAN [package insert], 2001.

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- Other adverse events included gastrointestinal complaints, headache, local ecchymosis and rash, local joint pain and swelling, and local pruritus. However, the incidence of these events was similar in the HYALGAN and placebo groups<sup>1</sup>
- In other clinical studies, the frequency and severity of adverse events occurring during repeat treatment cycles did not increase over that reported for a single treatment cycle<sup>1</sup>
- Anaphylactoid and allergic reactions have been reported with this product. In the 2 events reported as anaphylactoid reactions, HYALGAN treatment was discontinued and both had favorable outcomes. Three cases of allergic reactions were reported in which the patients were discontinued from HYALGAN treatment and the incidents resolved

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If you have any questions about the use of HYALGAN, please see the full prescribing information for the product.

HYALGAN [package insert], 2001.