

Can Orthovisc® help *Replace What's Missing™* in your osteoarthritic knee?

Is Orthovisc® right for you? Answer these questions, then discuss them with your doctor. Together, you'll determine if you're a candidate for this FDA-approved non-drug therapy, which can relieve your knee pain—and get you back to doing what you enjoy.

1. Have you tried over-the-counter (OTC) pain medications such as acetaminophen (Tylenol®) or non-steroidal anti-inflammatory drugs (Advil® or Motrin®), but found that they don't relieve your pain?		2. Have you ever used, then stopped taking, prescription strength NSAIDs or COX-2 inhibitors such as Celebrex® because they're no longer effective or cause unpleasant side effects?		3. Are you at a point where you simply tolerate knee pain because everything you've tried (ice packs, heating pads, exercise, weight loss, corticosteroid injections, OTC and prescription medications) is less effective than previously?		4. Do you find that you're cutting back on or simply not participating in daily activities you once enjoyed due to your osteoarthritic knee pain?		5. Has your doctor suggested the option of total knee replacement surgery, but you're not ready for such a procedure?	
Yes	No	Yes	No	Yes	No	Yes	No	Yes	No

www.orthovisc.com

ORTHOVISC®
HIGH MOLECULAR WEIGHT HYALURONAN



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Anika Therapeutics, Inc. Bedford, MA 01730 USA

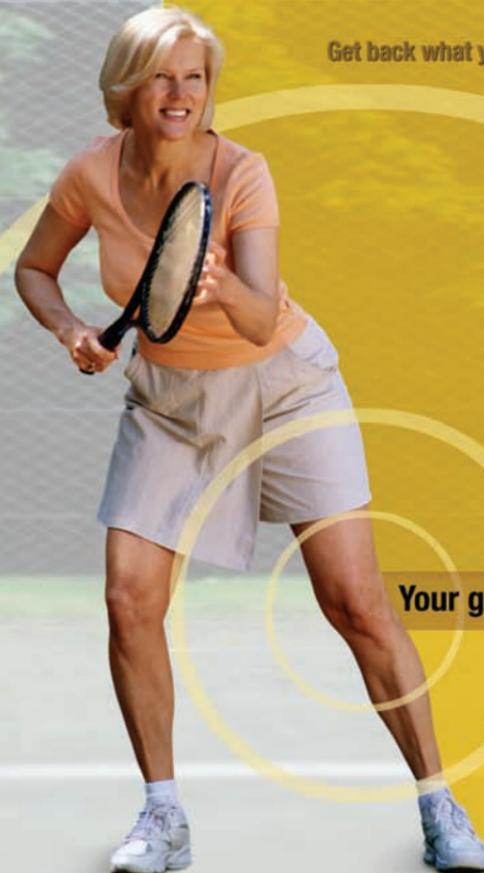
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For more information, call your DePuy Mitek representative at 1-800-382-4682 or visit us at www.orthovisc.com. DePuy Mitek, Inc., 325 Paramount Drive, Raynham, MA 02767

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Get back what you've been missing... with

ORTHOVISC®



Your guide to understanding the knee pain of osteoarthritis

Missing out on what you enjoy?

Are you missing out on doing the things you enjoy because of the pain of knee osteoarthritis? If so, you're not alone. Approximately 10 million people suffer from osteoarthritis of the knee¹ and for many, it means diminished quality of life. Today, thanks to an FDA-approved non-drug therapy—Orthovisc®—you can experience relief and get back to living and enjoying your life.



Is Orthovisc® right for you?

This brochure is designed to help you understand your osteoarthritis of the knee. It provides an overview of this common form of arthritis and its causes, as well as possible treatment with Orthovisc® (High Molecular Weight Hyaluronan) injections. This treatment option can relieve knee pain for up to 6 months.

Review the information in this brochure, visit our Web site (www.orthovisc.com), and talk to your doctor to find out if you're a candidate for Orthovisc® treatment.

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HIGH MOLECULAR WEIGHT HYALURONAN

How did I get knee osteoarthritis?

Osteoarthritis can be caused by many things. Heredity and age do play a role, but it's primarily a result of excess stress on knee joints. This can be from work, sports, or any other regular activity that adds stress on your joints. Being overweight or living a non-active lifestyle may also be a contributing factor. Typically, more women than men develop osteoarthritis. It can affect people earlier in life, but it occurs most often in people over 45 years of age.

How does osteoarthritis progress?

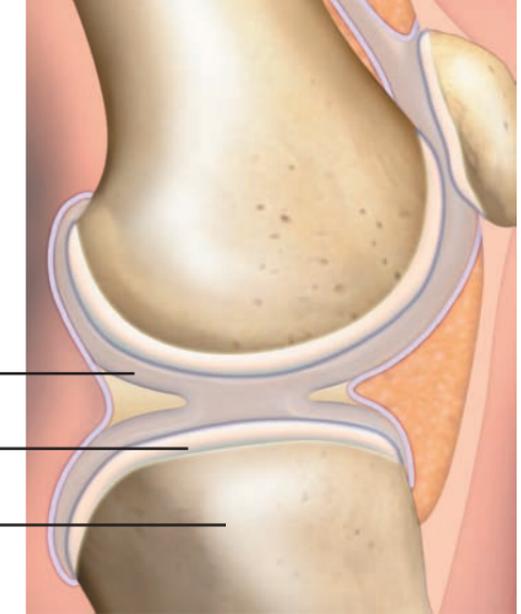
Healthy knee. In the knee joint, the bones work like a hinge. In healthy knees, the space between the bones is filled with a thick and slippery liquid (**joint fluid**).

Joint fluid acts like a shock absorber to help cushion your knee while walking, working, or playing sports. The bones are covered by **cartilage**—a connective tissue found in various parts of the body, such as joints.

Joint
fluid

Cartilage

Bone



Healthy joint fluid cushions and lubricates your knees

A knee with mild to moderate osteoarthritis

At first, your body's joint fluid becomes less healthy and the cartilage begins to break down, leading to irritation and discomfort in the knee.

Next, pieces of bone and cartilage can break off and float in the joint, which may cause pain and swelling.

As time passes, large areas of cartilage can be completely worn away. Growths (bone spurs) may appear on the bone, leading to more irritation.

Unhealthy joint fluid

Eroded cartilage



As osteoarthritis progresses, healthy joint fluid begins to break down

A knee with severe osteoarthritis

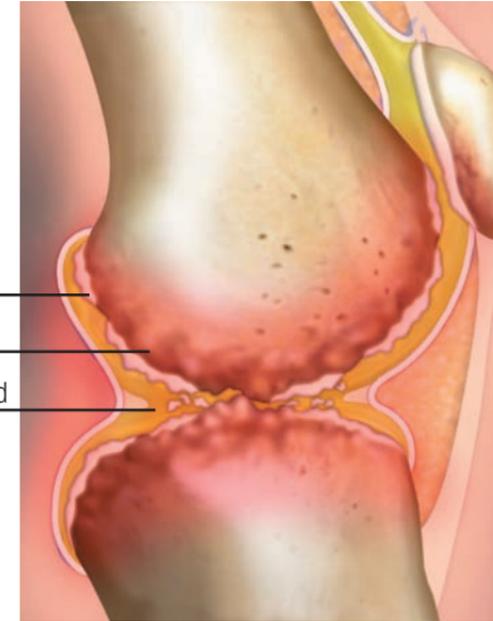
In severe cases of osteoarthritis, your cartilage may be completely worn away. Your bones may actually rub together, which may cause pain and swelling.

Pain is not necessarily related to the severity of your disease and, therefore, varies from person to person. Some people with mild osteoarthritis can have a lot of pain while others with severe osteoarthritis have little or no pain. Talk to your doctor about the level of pain you are feeling.

Damaged cartilage

Bone spurs

Scarce synovial fluid



Without healthy joint fluid, your knees become sore and swollen

I don't want to give in to the pain. What can I do to fight it?

Is there a cure?

No. There is no cure for osteoarthritis, but there are treatments to relieve pain and reduce swelling, which may help the knee move better. Physiotherapy and knee exercises can help **keep the knee moving**. Simple pain relievers can also help.

As osteoarthritis progresses, a doctor may recommend medications like steroids or anti-inflammatories to help relieve swelling and inflammation. Some people with severe osteoarthritis may have surgery to replace the knee with an artificial joint.



Orthovisc® injections *Replace What's Missing™* and can give you freedom from knee pain...

What is Orthovisc®?

Orthovisc® (High Molecular Weight Hyaluronan) is an FDA-approved non-drug therapy, also known as hyaluronic acid or viscosupplementation injections. The only injection made from ultra-pure natural hyaluronan, it contains no buffers or preservatives. In fact, Orthovisc® contains the highest concentration of hyaluronan available per injection.²

Hyaluronan is naturally found in healthy joint fluid. In an osteoarthritic knee, there is less hyaluronan in the joint fluid. Orthovisc® injections restore hyaluronic acid, which acts to cushion, protect, and lubricate your knee joint. By helping *Replace What's Missing™* and restoring knee function, Orthovisc® can relieve your knee pain for up to 6 months.³ Although individual results may vary, some people feel pain relief after the first injection.

Questions and Answers About Orthovisc®

1. Why is Orthovisc® being recommended by my doctor?

You may have tried a variety of treatments—over-the-counter and prescription pain relievers, physical therapy, exercise, corticosteroid injections. But nothing seems to work, or it is no longer effective. You're still in pain. And now, it has reached a point where it is interfering with your daily living.

2. How is Orthovisc® given?

A healthcare professional injects Orthovisc® into your knee joint 3 times, 7 days apart, over a 15-day period (days 1, 8, and 15) for 3 consecutive weeks.

3. Can I receive Orthovisc® injections in my doctor's office?

Yes. Orthovisc® is given by a trained healthcare professional and can be injected in a physician's office.

4. What kind of pain relief should I experience with Orthovisc®?

Orthovisc® provides approximately 6 months of symptom relief with just 3 injections. Although individual results may vary, some people may experience pain relief after the first injection. Studies show all 3 injections must be administered for symptom relief that lasts a full 6 months.



5. Are there any special treatment instructions?

If you have any known allergies, you should consult with your healthcare professional to determine if you are able to take Orthovisc®. For the first 48 hours after each injection, it is recommended that you avoid activities such as jogging, tennis, heavy lifting, or standing on your feet for a long time (more than one hour).

6. Are there any side effects?

The most commonly reported adverse events are joint pain, back pain, and headache. Other side effects included temporary pain at the injection site. Orthovisc® should not be injected in patients with infections or skin diseases in the area of the injection site or joint.

7. Will Orthovisc® affect any other medication I am taking related or not related to my osteoarthritis of the knee?

Your doctor is in the best position to evaluate your medication and make that determination. Make sure you share all of your medical information with your doctor so the correct decision can be made regarding Orthovisc® as a therapy for your osteoarthritis of the knee.

8. How often can Orthovisc® be injected in the knee?

The number of courses of therapy/injections is a decision you and your doctor need to make. Studies have shown that retreatment with Orthovisc® is safe following the

initial 6-month treatment period. You should consult your insurance company about when an additional retreatment series will be covered by insurance.



9. Will my insurance cover Orthovisc®?

Most insurance carriers cover Orthovisc®. For more information, call our reimbursement hotline at 1-866-633-VISC (8472).

10. How can I find out if Orthovisc® can Replace What's Missing™ in my osteoarthritic knee?

Talk to your healthcare provider to see if Orthovisc® is the right choice for your mild to moderate osteoarthritis of the knee. To learn more about Orthovisc®, visit our Web site at www.orthovisc.com.

Patient Information ORTHOVISC® High Molecular Weight Hyaluronan

What is ORTHOVISC®? ORTHOVISC® is a viscous (thick) sterile mixture made from highly purified hyaluronan from bacterial fermentation. Hyaluronan is a natural chemical found in the body. High amounts of hyaluronan are found in the joint tissues and in the fluid that fills the joints. The body's own hyaluronan acts like a lubricant and a shock absorber in the joint. It is needed for the joint to work properly. When you have osteoarthritis, there may not be enough natural hyaluronan in the joint, and the quality of that hyaluronan may be poorer than normal. ORTHOVISC® is given in a shot (injection) directly into the knee joint.

What is ORTHOVISC® used for? ORTHOVISC® is used to relieve knee pain due to osteoarthritis. It is used for patients who do not get adequate pain relief from simple pain relievers like acetaminophen or from exercise and physical therapy.

What are the benefits of ORTHOVISC®? Clinical trials conducted in the U.S. have shown that ORTHOVISC® provides pain relief to patients who have not been able to find pain relief with simple pain medication or exercise compared to saline placebo injections.

What other treatments are available for osteoarthritis? If you have pain due to osteoarthritis of

the knee, there are things you can do that do not involve ORTHOVISC® injections. These include:

Non-drug treatments:

- Avoiding activities that cause pain in your knee
- Exercise
- Physical therapy
- Removal of excess fluid from the knee

Drug therapy:

- Pain medication such as acetaminophen and narcotics
- Drugs that reduce inflammation, such as aspirin and other “nonsteroidal anti-inflammatory” agents (NSAIDs) (such as ibuprofen and naproxen)
- Corticosteroids that are injected directly into the knee joint

Are there any reasons why you should not take ORTHOVISC®?

- You should not take this product if you are allergic to hyaluronate products.
- If you have any known allergies, you should consult with your healthcare professional to determine if you are able to take ORTHOVISC®.
- You should not have an injection into the knee if you have infections or skin diseases around the injection site.

Things you should know about ORTHOVISC®

- ORTHOVISC® should be injected by a qualified physician or properly licensed practitioner.
- Tell your healthcare professional if you have any known allergies before ORTHOVISC® is administered.
- For 48 hours after you receive the injection, you should avoid activities such as jogging, tennis, heavy lifting or standing on your feet for a long time (more than one hour).
- The safety and effectiveness of ORTHOVISC® in joints other than the knee has not been demonstrated in U.S. studies.
- The safety and effectiveness of ORTHOVISC® has not been shown in pregnant or nursing women. You should tell your healthcare professional if you are pregnant or nursing.
- The safety and effectiveness of ORTHOVISC® has not been shown in children.
- The effectiveness of ORTHOVISC® has not been established for more than one course of treatment.

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References: **1.** Parmet S. Osteoarthritis of the knee. *JAMA*. 2003;289(8):1068. **2.** Data on file. Depuy Mitek, Inc. Raynham, MA. **3.** Brandt KD, et al. Efficacy and safety of intraarticular sodium hyaluronate in knee osteoarthritis. ORTHOVISC Study Group. *Clin Orthop Relat Res*. 2001 ;385:130-143.

Possible complications

- Side effects are sometimes seen when ORTHOVISC® is injected into the knee joint. These can include: pain, swelling, heat, rash, itching, bruising and/or redness. You may also feel achy. These reactions are generally mild and do not last long.
- If any of these symptoms or signs appear after you are given ORTHOVISC® or if you have any other problems, you should call your healthcare professional.

How is ORTHOVISC® given?

Your healthcare professional will inject ORTHOVISC® (30 mg/2 mL) into your knee once a week, for a total of 3 or 4 injections.