

FRUSTRATED BY PAINFUL KNEES?

Give your knees
the cushioning they need.



*Synvisc-One® (hylan G-F 20) lubricates and cushions your knee, and can provide up to six months of osteoarthritis knee pain relief with just one injection.**

* As shown in a medical study comparing Synvisc-One to an injection of salt water.

Synvisc-One® (hylan G-F 20) is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics, e.g., acetaminophen.

Important Safety Information

Before trying Synvisc-One, tell your doctor if you have had an allergic reaction, such as swelling of the face, tongue or throat, respiratory difficulty, rash, itching or hives to SYNVISIC or any hyaluronan-based products.

Please see Important Safety Information on page 10.

Please see Important Patient Information on page 11.



YOU DON'T HAVE TO SETTLE FOR OSTEOARTHRITIS KNEE PAIN

It's time to find the right treatment option for you

Talking to your doctor is the best way to start exploring your treatment options. And when you do, keep in mind:

Osteoarthritis knee pain affects everyone differently

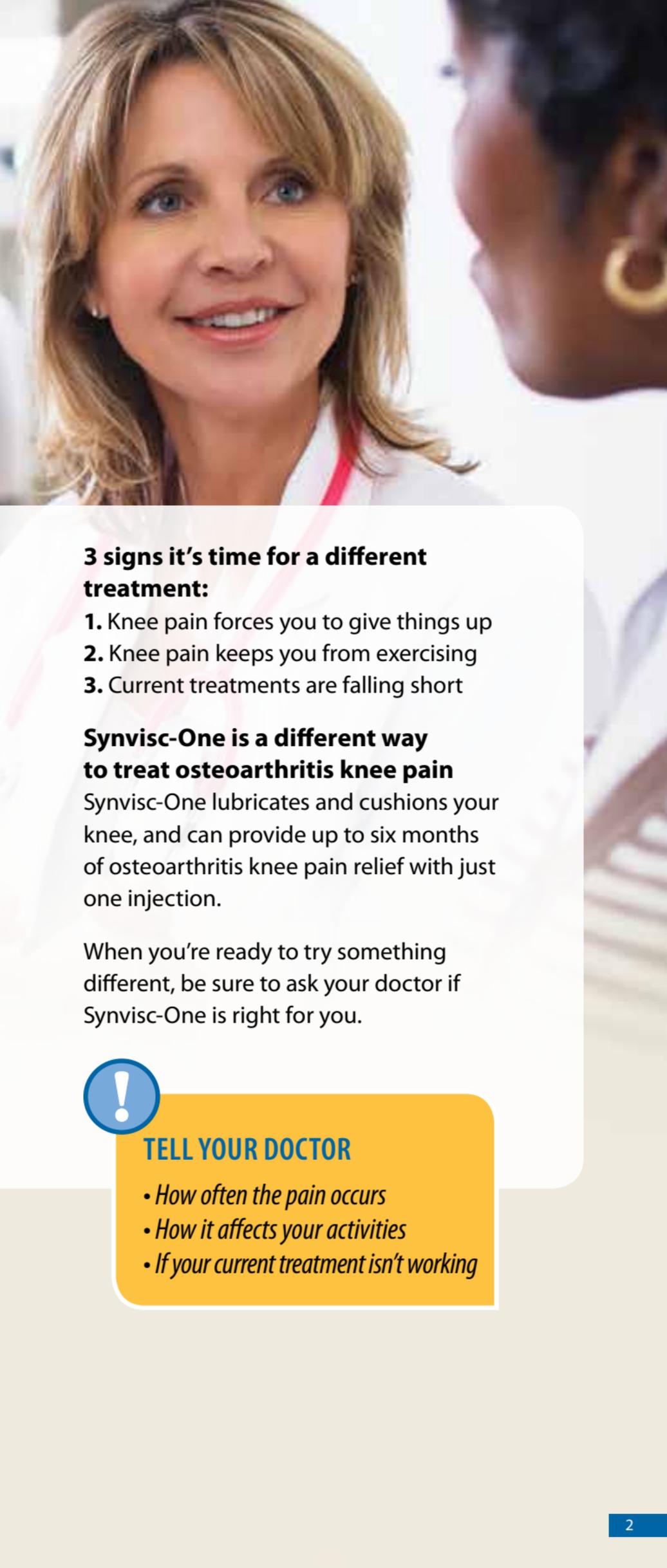
An X-ray can show your grade or stage of osteoarthritis, but your level of pain isn't necessarily connected to it. Your osteoarthritis could be mild with a great deal of pain or severe with little pain. Your doctor is relying on you to give a clear description of how your knee feels.

It's caused by more than just cartilage loss

In knees with osteoarthritis, the cartilage protecting the ends of the bones gradually deteriorates, joint fluid loses its shock-absorbing qualities, and bones may begin to rub against each other—all of which may cause the osteoarthritis knee pain you're feeling.

Please see Important Safety Information on page 10.

Please see Important Patient Information on page 11.



3 signs it's time for a different treatment:

1. Knee pain forces you to give things up
2. Knee pain keeps you from exercising
3. Current treatments are falling short

Synvisc-One is a different way to treat osteoarthritis knee pain

Synvisc-One lubricates and cushions your knee, and can provide up to six months of osteoarthritis knee pain relief with just one injection.

When you're ready to try something different, be sure to ask your doctor if Synvisc-One is right for you.



TELL YOUR DOCTOR

- *How often the pain occurs*
- *How it affects your activities*
- *If your current treatment isn't working*

ASK ABOUT SYNVISC-ONE® *(hylan G-F 20)*

A natural way to
treat osteoarthritis knee pain

What is Synvisc-One?

Synvisc-One is a one-injection treatment that supplements the fluid in your knee to help lubricate and cushion the joint. Synvisc-One is the #1 prescribed viscosupplement; it provides up to six months of osteoarthritis knee pain relief with just one injection.

What is Synvisc-One made from?

The injection contains a gel-like mixture made from a substance called hyaluronan (pronounced hy-al-u-ROE-nan) that comes from chicken combs.

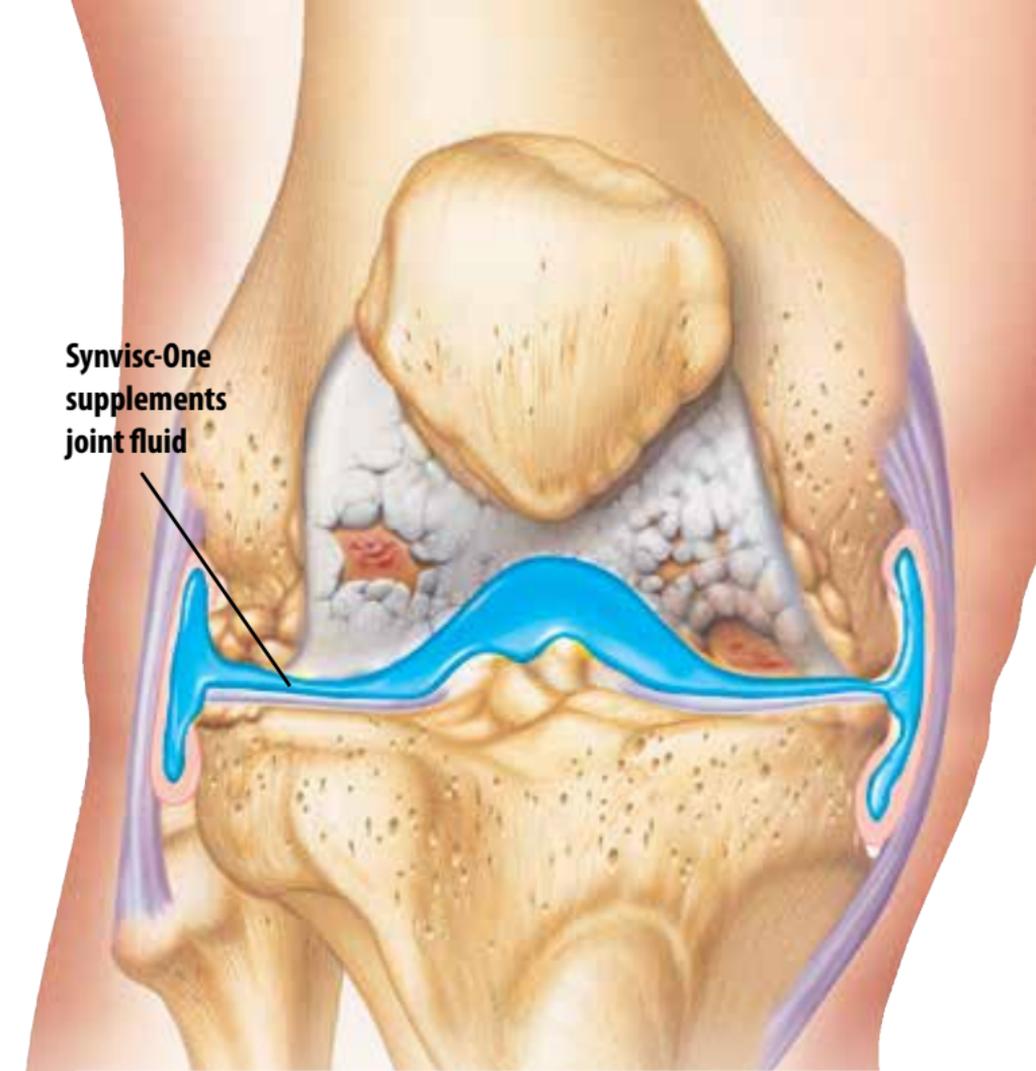
Hyaluronan is a natural substance found in the body and is present in very high amounts in joints. The body's own hyaluronan acts like a lubricant and a shock absorber in the joint and is needed for the joint to work properly.

When should I consider Synvisc-One?

Synvisc-One is for people with knee osteoarthritis who have not received enough pain relief from diet, exercise and over-the-counter pain medication. If you've tried these options and are still feeling osteoarthritis knee pain, tell your doctor and ask if Synvisc-One could help.

Please see Important Safety Information on page 10.

Please see Important Patient Information on page 11.



**Synvisc-One
supplements
joint fluid**

Synvisc-One supplements your joint fluid to relieve pain and improve lubrication and cushioning in your knee.

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What are the side effects?

The most common side effects are pain, swelling, heat, redness and/or fluid build-up around the knee. In a medical study less than 6% of patients experienced these side effects, which were generally mild and did not last long.



ASK YOUR DOCTOR ABOUT A NATURAL SOLUTION

Synvisc-One is a product made from a natural substance that lubricates and cushions your knee joint.

PREPARE FOR YOUR APPOINTMENT

Be informed about a Synvisc-One®
(hylan G-F 20) injection

How is Synvisc-One given?

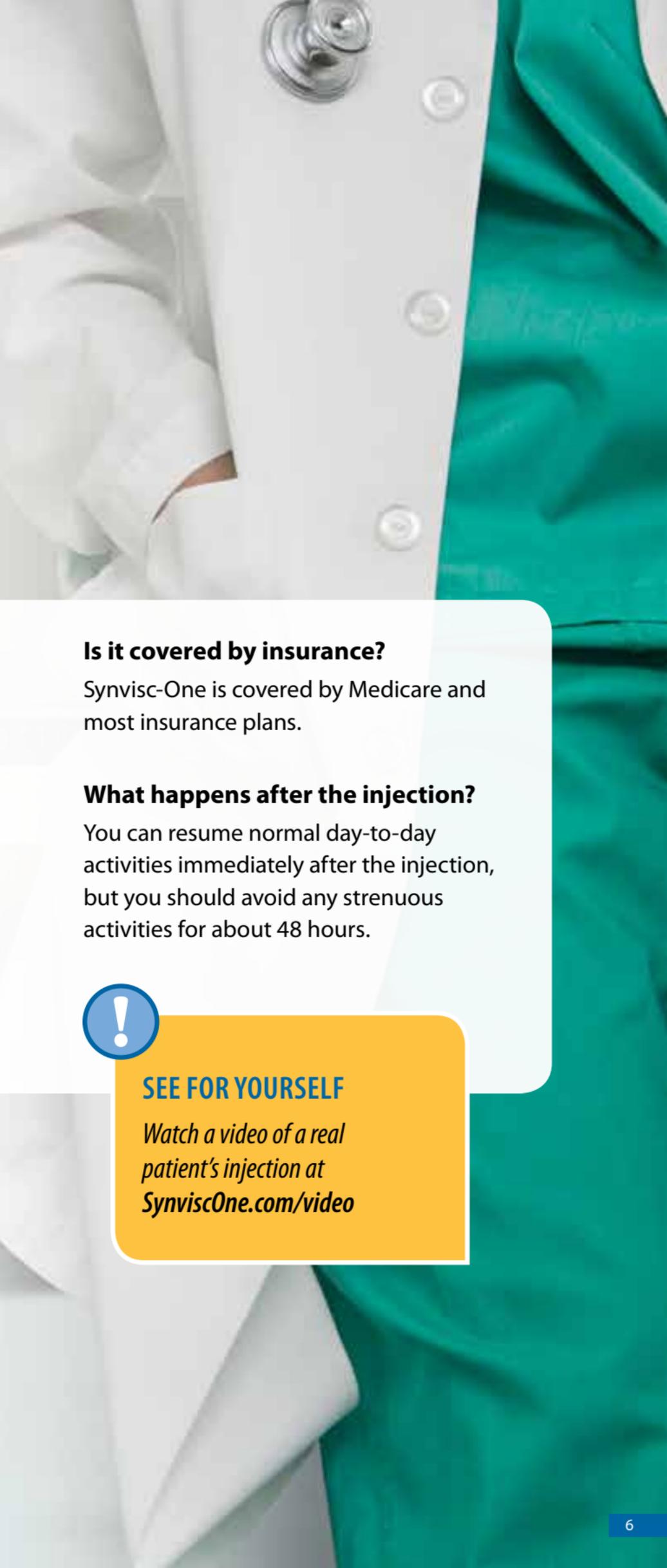
Synvisc-One is a single-dose treatment that's injected directly into your knee.

What is the procedure like?

Each injection takes a few minutes and can be done in your doctor's office.

Will the injection hurt?

Your doctor will likely apply a numbing agent before your Synvisc-One injection. You may feel some pressure, but it shouldn't be painful.



Is it covered by insurance?

Synvisc-One is covered by Medicare and most insurance plans.

What happens after the injection?

You can resume normal day-to-day activities immediately after the injection, but you should avoid any strenuous activities for about 48 hours.



SEE FOR YOURSELF

Watch a video of a real patient's injection at SynviscOne.com/video

KNOW WHAT TO EXPECT

What happens after a Synvisc-One® (hylan G-F 20) injection?

In the first 48 hours after a Synvisc-One injection:

- You should be able to resume your normal day-to-day activities
- You should avoid activities that put excessive strain on your knee such as jogging, lifting or prolonged standing
- If you have any mild pain or swelling at the injection site, place an ice pack on your knee for 10 minutes or as recommended by your doctor

Please see Important Safety Information on page 10.
Please see Important Patient Information on page 11.



In the coming months:

- Everyone responds differently, but in a medical study, many patients experienced osteoarthritis knee pain relief starting one month after their injection¹
- Synvisc-One can provide up to six months of osteoarthritis knee pain relief
- Synvisc-One can be repeated safely. In a medical study involving 160 patients, 77 received a second injection of Synvisc-One
- When your osteoarthritis knee pain returns, talk to your doctor to see if Synvisc-One is right for you

1. Chevalier X, Jerosch J, Goupille P, et al. Single, intra-articular treatment with 6 ml hylan G-F 20 in patients with symptomatic primary osteoarthritis of the knee; a randomised, multicentre, double-blind, placebo controlled trial. *Ann Rheum Dis*. 2010;69(1):113-119. doi:10.1136/ard.2008.094623.



JOIN ONTRACK with SYNVISC-ONE

Get timely treatment resources

Sign up to receive the latest information on knee exercises, nutrition and activities.

Join today for your FREE Knee Exercise Program Guide

With step-by-step instructions for exercises designed specifically for patients with knee osteoarthritis.



JOIN **ONTRACK** with SYNVISC-ONE

Two easy ways to enroll

- 1 Call 1-866-480-8912 or
- 2 Visit SynviscOne.com/ontrack

Please see Important Safety Information on page 10.
Please see Important Patient Information on page 11.

Indication

Synvisc-One® (hylan G-F 20) is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics, e.g., acetaminophen.

Important Safety Information

Before trying Synvisc-One, tell your doctor if you have had an allergic reaction, such as swelling of the face, tongue or throat, respiratory difficulty, rash, itching or hives to SYNVISC or any hyaluronan-based products. Should not be used in patients with an infected knee joint, skin disease or infection around the area where the injection will be given, or circulatory problems in the legs.

Synvisc-One is only for injection into the knee, performed by a doctor or other qualified health care professional. Synvisc-One has not been tested to show pain relief in joints other than the knee. Tell your doctor if you are allergic to products from birds—such as feathers, eggs or poultry—or if your leg is swollen or infected.

Synvisc-One has not been tested in children (≤ 21 years old), pregnant women or women who are nursing. You should tell your doctor if you think you are pregnant or if you are nursing a child.

Talk to your doctor before resuming strenuous weight-bearing activities after treatment.

The side effects sometimes seen after Synvisc-One include ($< 2\%$ each): pain, swelling, heat, redness, and/or fluid build-up in or around the knee. Tell your doctor if you experience any side effects after treatment with Synvisc-One.



IMPORTANT PATIENT INFORMATION

SYNVISC-ONE® (HYLAN G-F 20)

Be sure to read the following important information carefully. This information does not take the place of your doctor's advice. If you do not understand this information or want to know more, ask your doctor.

Glossary of Terms

Hyaluronan (pronounced hy-al-u-ROE-nan): is a natural substance that is present in very high amounts in joints. It acts like a lubricant and a shock absorber in the joint and is needed for the joint to work properly.

Non-steroidal anti-inflammatory drugs: also known as "NSAIDs"; medication used to treat pain or swelling. There are many examples of NSAIDs, including (but not limited to) aspirin and ibuprofen. Some of these are over-the-counter drugs, and some can be obtained only by prescription.

Osteoarthritis (pronounced OS-te-o-arth-RI-tis): (OA) is a type of arthritis that involves the wearing down of cartilage (the protective covering on the ends of your bones) and loss of cushioning fluid in the joint.

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What is the Synvisc-One® product?

Synvisc-One is a gel-like mixture that comes in a syringe containing 6 mL (1 ½ teaspoon) and is injected into your knee. It is made up of hylan A fluid, hylan B gel, and salt water. Hylan A and hylan B are made from a substance called hyaluronan (pronounced hy-al-u-ROE-nan), also known as sodium hyaluronate that comes from chicken combs. Hyaluronan is a natural substance found in the body and is present in very high amounts in joints. The body's own hyaluronan acts like a lubricant and a shock absorber in the joint and is needed for the joint to work properly.

How is the Synvisc-One® product used? (Indications)

The FDA-approved indication for Synvisc-One is: Synvisc-One is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative nonpharmacologic therapy and simple analgesics, e.g., acetaminophen.

How is the Synvisc-One® product given?

Your doctor will inject Synvisc-One into your knee.

Are there any reasons why I should not receive a Synvisc-One® injection? (Contraindications)

Your doctor will determine if there is any reason why you are not an appropriate candidate for Synvisc-One. You should be aware that Synvisc-One:

- Should not be used in patients who have had any prior allergic reactions to SYNVISC, Synvisc-One or any hyaluronan-based products. Signs of an allergic reaction may include swelling of your face, tongue, or throat; difficulty breathing or swallowing; shortness of breath; wheezing; chest pain; a tightness in your throat; sleepiness; rash; itching; hives; flushing; and/or fever.
- Should not be used in patients with a knee joint infection, skin disease or infection around the area where the injection will be given, or circulatory problems in the legs.

What should my doctor warn me about?

The following are important treatment considerations for you to discuss with your doctor and understand in order to help avoid unsatisfactory results and complications:

- Synvisc-One is only for injection into the knee, performed by a doctor or other qualified health care professional. Synvisc-One has not been tested to show pain relief in joints other than the knee.
- Synvisc-One has not been tested to show better pain relief when combined with other injected medicines.
- Tell your doctor if you are allergic to products from birds such as feathers, eggs, and poultry.
- Tell your doctor if you have significant swelling or blood clots in the leg.
- Synvisc-One has not been tested in pregnant women, or women who are nursing. You should tell your doctor if you think you are pregnant, or if you are nursing a child.
- Synvisc-One has not been tested in children (≤21 years of age).

What are the risks of getting a Synvisc-One® injection?

The side effects (also called reactions) sometimes seen after any injection into the knee, including Synvisc-One, include: pain, swelling, heat, redness, and/or fluid build-up around the knee. These reactions are generally mild and do not last long. Reactions are generally treated by resting and applying ice to the injected knee.

Sometimes it is necessary to give pain relievers by mouth such as acetaminophen or NSAIDs, or to give injections of steroids, or to remove fluid from the knee joint. Patients rarely undergo arthroscopy (a surgical inspection of the knee joint) or other medical procedures related to these reactions.

Other side effects seen with SYNVISC or Synvisc-One are: rashes, hives, itching, muscle pain/cramps, flushing and/or swelling of your face, fast heartbeat, nausea (or feeling sick to your stomach), dizziness, fever, chills, headache, difficulty breathing, swelling in your arms and/or legs, prickly feeling of your skin,

and in rare cases a low number of platelets in the blood (platelets are a type of blood cell that are needed to help your blood clot when you are cut or injured). Rare cases of knee joint infection have been reported. If any of the above side effects or symptoms appear after you are given Synvisc-One, or if you have any other problems, you should call your doctor.

What are the benefits of getting a Synvisc-One® injection?

As shown in a medical study of 253 patients with osteoarthritis (OA) of the knee, where approximately half received either a single injection of Synvisc-One or an injection of the same volume of salt water (a "Saline Control" injection), the major benefits of Synvisc-One are pain relief and improvement in other symptoms related to OA of the knee.

What do I need to do after I get a Synvisc-One® injection?

It is recommended you avoid strenuous activities (for example, high-impact sports such as tennis or jogging) or prolonged weight-bearing activities for approximately 48 hours following the injection. You should consult your doctor regarding the appropriate time to resume such activities.

What other treatments are available for OA?

If you have OA, there are other things you can do besides getting Synvisc-One. These include:

Non-drug treatments

- Avoiding activities that cause knee pain
- Exercise or physical therapy
- Weight loss
- Removal of excess fluid from your knee

Drug therapy

- Pain relievers such as acetaminophen and narcotics
- Drugs that reduce inflammation (signs of inflammation are swelling, pain or redness), such as aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs, for example ibuprofen and naproxen)
- Steroids that are injected directly into your knee

When should I call my doctor? (Troubleshooting)

If any of the side effects or symptoms described above appear after you are given Synvisc-One, or if you have any other problems, you should call your doctor.

What did the clinical studies show?

A study was conducted in 6 countries outside the United States with 21 physicians. The patients in the study had mild to moderate knee OA, moderate to severe pain, and did not have sufficient relief of their pain and symptoms with medications taken by mouth.

A total of 253 patients in the study were assigned by chance to receive either a single injection of Synvisc-One (n=123 patients), or an injection of the same volume of salt water (a "Saline Control" injection) (n=130 patients). Neither the patients nor the doctors evaluating them knew which treatment they received. Any fluid that was present in the patient's knee was removed before the injection. The patients were seen by their doctor at standard times over 6 months. Information was collected about

how much pain they were experiencing doing various types of activities, how much they were limited in their daily activities by their OA, and on their overall condition. Their doctor also provided an overall rating of their OA.

The main measure of the study was how much pain the subjects had doing five common types of activities over the 6 months duration of the study. Daily activity limitations and overall evaluations were also compared between the group of patients receiving Synvisc-One injection and the group receiving salt water injection. The study showed that patients receiving Synvisc-One had significantly less pain over 6 months, and felt significantly better than the patients who received the salt water injections. The difference in pain score reduction from baseline to 6 months between the Synvisc-One and salt water control injection was 0.15 out of a 5 point scale for the measurement of OA pain in the knee.

What adverse events were observed in the clinical study?

The following are the most common adverse events that occurred during the clinical trial of Synvisc-One:

- Pain in the knee or at the injection site
 - Stiffness, swelling or warmth in or around the knee
 - Changes in the way that you walk (e.g., limping)
- Severe adverse events were not observed in the Synvisc-One trial. Joint infections did not occur in the injected knee in the Synvisc-One clinical trial. The most commonly occurring adverse events outside of the injected knee were headache, back pain, sore throat and the flu. One patient had a single episode of feeling faint.

How do I get more information about the Synvisc-One® product? (User Assistance)

If you have any questions or would like to find out more about Synvisc-One, you may call Genzyme Biosurgery at 1-888-3-SYNVISC (1-888-379-6847) or visit www.synvisc.com.

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