

*Find your osteoarthritis (OA) knee pain*

*Relief*



**SYNVISC<sup>®</sup>** (hylan G-F 20)  
*lubricates and cushions* your knee.

**Indication**

SYNVISC 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, 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.

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

**SYNVISC<sup>®</sup>**  
HYLAN G-F 20

# YOU DON'T HAVE TO SETTLE FOR YOUR OA KNEE PAIN

It's time to explore different treatment options.

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 OA could be mild with a great deal of pain or severe with little pain. Your doctor is relying on you to give them a clear description of how your knee feels.<sup>1</sup>

## **OA is 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 OA knee pain you feel.<sup>2</sup>

## **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

\*Please see page 9 for additional information about the SYNVISIC clinical trials.

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



## **SYNVISC® (hylan G-F 20) is a different way to treat OA knee pain**

SYNVISC lubricates and cushions your knee, and can provide up to 6 months of OA knee pain relief.<sup>a,b,\*</sup>

In a large, observational study assessing tolerability and short-term effectiveness, **81% of patients** rated SYNVISC as a “good” or “very good” therapy at 3 weeks after the first injection.<sup>3,c,\*</sup>

## **SYNVISC provides rapid and long-lasting (up to 6 months) OA knee pain relief<sup>a,b,\*</sup>**

- As early as **1 week**, SYNVISC patients in a medical study experienced reduced OA knee pain compared with the pain patients experienced before treatment
- At **6 months**, SYNVISC still provided significantly greater OA knee pain relief in 52 knees compared with an injection of salt water in 57 knees
- Adverse events observed with SYNVISC were similar to those for the salt water injection

When you're ready to find a solution to your OA knee pain, ask your doctor if SYNVISC is right for you.

### **Important Safety Information (cont'd)**

Serious allergic reactions have been reported. 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.



### **TELL YOUR DOCTOR**

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

# ASK ABOUT SYNVISC® (*hylan G-F 20*)

Designed to mimic young,  
healthy joint fluid

## What is SYNVISIC?

SYNVISC is a series of three injections, given one week apart, that supplement the fluid in your knee to help lubricate and cushion the joint. It has been shown to improve OA knee pain for **up to 6 months**.<sup>a,b,\*</sup>

Patients receiving SYNVISIC injections have also experienced knee pain relief **as early as 1 week**.<sup>a,b,\*</sup>

## What is SYNVISIC 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.

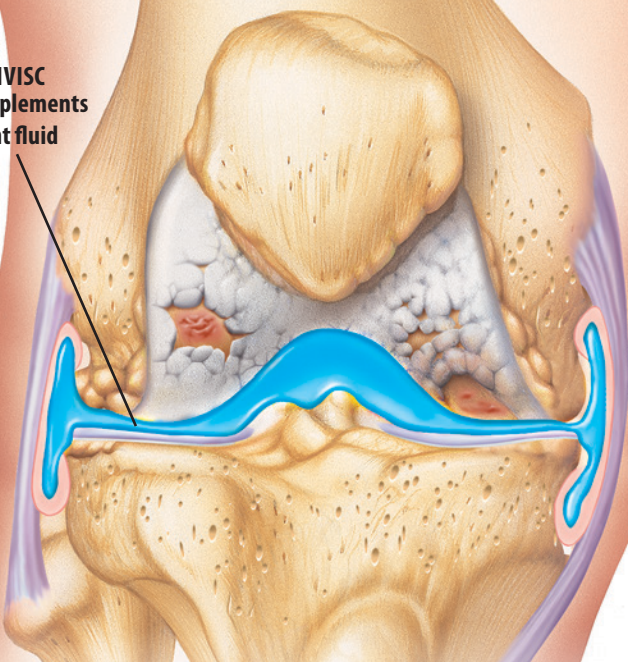
## When should I consider SYNVISIC?

SYNVISC is for people with knee OA who have not received enough pain relief from diet, exercise, and over-the-counter pain medication (such as acetaminophen). If you've tried these options and are still feeling OA knee pain, tell your doctor and ask if SYNVISIC could help.

\*Please see page 9 for additional information about the SYNVISIC clinical trials.

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

**SYNVISC  
supplements  
joint fluid**



**SYNVISC supplements your joint fluid to relieve pain and improve lubrication and cushioning in your knee.**

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## **Is SYNVISc safe?**

SYNVISC has a demonstrated safety profile and adverse reactions observed with SYNVISc in clinical studies were similar to those for placebo.<sup>3,4,a-c,\*</sup>

SYNVISC demonstrated a high level of patient satisfaction based on a large observational study assessing its tolerability and short-term effectiveness. **81% of patients** rated SYNVISc as a “good” or “very good” therapy at 3 weeks after the first injection.<sup>3,c,\*</sup>

## **What are the side effects?**

Side effects from SYNVISc are infrequent. In clinical trials, about 7% of patients experienced pain, swelling, and/or fluid buildup around the knee.

## **Important Safety Information (cont’d)**

SYNVISC is only for injection into the knee, performed by a doctor or other qualified health care professional. SYNVISc 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.

# PREPARE FOR YOUR APPOINTMENTS

Be informed about  
SYNVISC® (hylan G-F 20) injections

## **How is SYNVISIC given?**

SYNVISC is injected directly into your knee over the course of 3 doctor visits, one week apart.

## **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 SYNVISIC injections. You may feel some pressure, but it shouldn't be painful.

## **Is it covered by insurance?**

SYNVISC is covered by Medicare and many insurance plans.

## **What happens after the injections?**

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

Please consult your doctor regarding the appropriate time to resume such activities.





## SYNVISC IS A LOCALIZED TREATMENT FOR YOUR CHRONIC OA KNEE PAIN

*Systemic treatments such as acetaminophen and opioids may have adverse effects throughout the body that a localized treatment like SYNVISIC does not.<sup>5-7</sup>*

*Please be sure to consult with your doctor on any potential side effects for any treatment you consider.*

### **Important Safety Information (cont'd)**

SYNVISC has not been tested in children ( $\leq 21$  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.

# KNOW WHAT TO EXPECT

## What happens after your SYNVISC® (hylan G-F 20) injections

### **In the first 48 hours after your SYNVISC 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 as recommended by your doctor

Please consult with your doctor if you have any concerns and/or have additional side effects.

### **In the months following an injection:**

- Some patients may begin to feel OA knee pain relief after the first injection, but you need to have all 3 injections to get the maximum benefit
- Although everyone responds differently, most patients feel the greatest relief 8 to 12 weeks after the first injection
- SYNVISC can provide up to 6 months of OA knee pain relief<sup>f,a,b,\*</sup>

\*Please see page 9 for additional information about the SYNVISC clinical trials.

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Please see Patient Information on page 11.**





## ASK YOUR DOCTOR ABOUT AN ALTERNATIVE SOLUTION

*SYNVISC is a product made to  
mimic the young, healthy joint  
fluid originally in your knee.*

### **Important Safety Information (cont'd)**

The most commonly occurring side effects reported after SYNVISIC include joint pain, swelling, stiffness, heat, redness, and/or fluid build-up in or around the knee.

**References:** **1.** Gwilym SE, Pollard TC, Carr AJ. Understanding pain in osteoarthritis. *J Bone Joint Surg Br.* 2008;90(3):280-287. **2.** Felson DT. Osteoarthritis. In: Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine.* Chapter 326. 17th ed. New York, NY: McGraw-Hill;2008:2158-2165. **3.** Kemper F, Gebhardt U, Meng T, Murray C. Tolerability and short-term effectiveness of hylan G-F 20 in 4253 patients with osteoarthritis of the knee in clinical practice. *Curr Med Res Opin.* 2005;21(8):1261-1269. **4.** Wobig M, Dickhut A, Maier R, Vetter G. Viscosupplementation with hylan G-F 20: a 26-week controlled trial of efficacy and safety in the osteoarthritic knee. *Clin Ther.* 1998;20(3):410-423. **5.** Makris UE, Abrams RC, Gurland B, Reid MC. Management of persistent pain in the older patient: a clinical review. *JAMA.* 2014;312(8):825-836. **6.** Mader R, Lavi I, Luboshitzky R. Evaluation of the pituitary-adrenal axis function following single intraarticular injection of methylprednisolone. *Arthritis Rheum.* 2005;52(3):924-928. **7.** Jones T, Kelsberg G, Safranek S. FPIN's clinical inquiries: intra-articular corticosteroid injections for osteoarthritis of the knee. *Am Fam Physician.* 2014;90(2):115-116.

## Study parameters for SYNVIS<sup>®</sup> (hylan G-F 20) clinical trials

<sup>a</sup>The following reported adverse events (AEs) are among those that may occur in association with intra-articular injections, including SYNVIS: arthralgia, joint stiffness, joint effusion, joint swelling, joint warmth, injection site pain, arthritis, arthropathy, and gait disturbance.

<sup>b</sup>N=109 (SYNVIS=52, saline=57), three 3-mL injections given at 1-week intervals. Primary endpoints (assessed by patients on a 100-mm visual analog scale [0=no pain and 100=unbearable pain or complete cessation of activity]) represented: Pain during weight-bearing at 26 weeks. Improvements from baseline were 34 mm for SYNVIS and 19.1 mm for saline ( $P=0.005$ ) (48.8% reduction from baseline for SYNVIS vs 25% for saline). There were no reports of local adverse reactions or severe AEs to SYNVIS in the injected knee. In clinical trials, the most commonly reported AEs were transient pain, swelling, and joint effusion in the injected knee.

<sup>c</sup>Tolerability was assessed by the occurrence of AEs, both local and systemic, including their severity and relatedness to treatment, at visits 2, 3, and 4 (3 weeks after the first injection). Treatment-related AEs were reported in 4.2% of patients (2.4% of injections). Most AEs were mild (21.4%) to moderate (40.3%) and included joint effusion, joint swelling, arthralgia, joint warmth, and injection site erythema.

## **Indication**

SYNVISC 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 SYNVISIC, 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. Serious allergic reactions have been reported. 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 is only for injection into the knee, performed by a doctor or other qualified health care professional. SYNVISIC 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 has not been tested in children ( $\leq 21$  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 most commonly occurring side effects reported after SYNVISIC include joint pain, swelling, stiffness, heat, redness, and/or fluid build-up in or around the knee.

Tell your doctor if you experience any side effects after treatment with SYNVISIC.

## IMPORTANT PATIENT INFORMATION

### SYNVISC® (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 only be obtained 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.

#### Table of Contents

- Glossary of Terms
- Table of Contents
- What is the SYNVIS<sup>®</sup> product?
- How is the SYNVIS<sup>®</sup> product used? (Indications)
- How is the SYNVIS<sup>®</sup> product given?
- Are there any reasons why I should not receive SYNVIS<sup>®</sup> injections? (Contraindications)
- What should my doctor warn me about?
- What are the risks of getting SYNVIS<sup>®</sup> injections?
- What are the benefits of getting SYNVIS<sup>®</sup> injections?
- What do I need to do after I get a SYNVIS<sup>®</sup> injection?
- What other treatments are available for OA?
  - Non-drug treatments
  - Drug therapy
- What adverse events were observed in the clinical studies?
- How do I get more information about the SYNVIS<sup>®</sup> product? (User Assistance)

#### What is the SYNVIS<sup>®</sup> product?

SYNVISC is a gel-like mixture that 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. Osteoarthritis (pronounced os-TE-o-ar-THRI-tis) (OA) is a type of arthritis that involves the wearing down of cartilage (the protective covering on the ends of your bones). In OA, there may not be enough hyaluronan, and there may be a decrease in the quality of the hyaluronan in the joint. SYNVIS<sup>®</sup> comes in syringes containing 2 mL (half a teaspoon) of product. SYNVIS<sup>®</sup> is injected directly into your knee.

## **How is the SYNVISIC® product used? (Indications)**

The FDA-approved indication for SYNVISIC is:

SYNVISIC 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.

## **How is the SYNVISIC® product given?**

Your doctor will inject SYNVISIC into your knee.

## **Are there any reasons why I should not receive SYNVISIC® injections? (Contraindications)**

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

- Should not be used in patients who have had any prior allergic reactions to SYNVISIC, 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.

## **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:

- SYNVISIC is only for injection into the knee, performed by a doctor or other qualified health care professional. SYNVISIC has not been tested to show pain relief in joints other than the knee.
- SYNVISIC 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 should be used with caution when there is evidence of lymphatic or venous stasis in the leg to be injected.
- SYNVISIC 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.
- SYNVISIC has not been tested in children ( $\leq 21$  years of age).

## **What are the risks of getting SYNVISIC® injections?**

The side effects (also called reactions) sometimes seen when SYNVISIC is injected into the knee as a first or repeat set of injections were pain, swelling, heat, redness, and/or fluid build-up around the knee. These reactions were generally mild and did not last long. If you have a reaction where the swelling is extensive and painful you should notify your doctor. The reactions seemed to occur more often when SYNVISIC was injected into the knee as a repeat set of injections than when SYNVISIC was injected as a first set of injections. 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 less common side effects have been: rashes, hives, itching, muscle pain/cramps, flushing and/or swelling of your face, fast heart beat, 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 clot your blood when you are cut or injured). Allergic reactions, some which can be potentially severe, were observed during the use of Synvisc. Before you are given SYNVISC, tell your doctor if something like this has ever happened to you after receiving an injection of SYNVISC or other hyaluronan products. If any of the above symptoms or signs appear after you are given SYNVISC, or if you have any other problems, you should call your doctor. Rare cases of knee joint infection have been reported after SYNVISC injections.

### **What are the benefits of getting SYNVISC® injections?**

As shown in medical studies of patients with osteoarthritis (OA) of the knee, where approximately half received a single injection of SYNVISC and the other half either had fluid removed from the knee and/or received injections of the same volume of salt water (a “Saline Control” injection), the major benefits of SYNVISC 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® injection?**

It is recommended you avoid strenuous activities (for example, high-impact sports such as soccer, 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. 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 nonsteroidal anti-inflammatory drugs (NSAIDs, for example ibuprofen and naproxen)
- Steroids that are injected directly into your knee.



### **What did the clinical studies show?**

Two medical studies involving a total of 132 patients were done in Germany. The patients in these studies were at least 40 years old and had knee pain due to OA. The patients were placed in one of two groups. One group was given an injection of SYNVISIC into one or both knees once a week for three weeks. The second group was given an injection of salt water once a week for three weeks. As part of the study, knee joint pain was measured for 26 weeks. Also, patients and doctors were asked to judge the success of the treatment for 26 weeks. Patients with OA knee pain, who did not get pain relief with other medicines, got pain relief with SYNVISIC. The patients given SYNVISIC had more pain relief than the patients given salt water. Some patients started to feel pain relief after the first week of SYNVISIC treatment. The most pain relief and the greatest amount of treatment success was seen 8 to 12 weeks after SYNVISIC treatment started.

A medical study done in the United States involved 90 patients. The patients were at least 40 years old and had knee pain due to OA. Patients were placed into one of two groups. One group was given SYNVISIC once a week for three weeks. The second group had a needle inserted into the knee to have any fluid removed (this procedure is called arthrocentesis [pronounced AR-thro-sen-TEE-sis]) once a week for three weeks.

Patients improved after SYNVISIC treatment, but not more than patients who had arthrocentesis. This study was different from the German studies because the last time the two groups were compared was only two weeks after the last SYNVISIC injection. The study was also different in other ways, including length of time that patients had to stop taking medicines before they could start treatment. The length of time patients had to stop taking medicines was two weeks in the German studies and four weeks in the U.S. study.

### **What adverse events were observed in the clinical studies?**

The side effects (also called reactions) sometimes seen when SYNVISIC is injected into the knee as a first or repeat set of injections were pain, swelling, heat, redness, and/or fluid build-up around the knee. These reactions were generally mild and did not last long. Allergic reactions, some which can be potentially severe, were observed during the use of Synvisc.

### **How do I get more information about the SYNVISIC® product? (User Assistance)**

If you have any questions or would like to find out more about SYNVISIC, you may call Sanofi at 1-888-3-SYNVISIC (1-888-379-6847) or visit [www.synvisc.com](http://www.synvisc.com).

**Manufactured by Genzyme Corporation,  
a Sanofi Company 1-888-3-SYNVISIC**

# HAVE OSTEOARTHRITIS KNEE PAIN?

*Ask your doctor about*

**SYNVISC®**  
HYLAN G-F 20

## **Indication**

SYNVISC 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 (cont'd)**

Tell your doctor if you experience any side effects after treatment with SYNVISC.

**Please see additional Important Safety Information on page 10.**

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