

PATIENT INFORMATION

GEL-SYN™ (sodium hyaluronate 0.84%)

Be sure to read the following important information carefully. This information does not take the place of your doctor's advice. Your doctor has determined that the knee pain you are experiencing is caused by osteoarthritis and that you are a candidate for a non-surgical, non-pharmacological, pain-relieving therapy called Gel-Syn. If you do not understand this information or want to know more, ask your doctor.

Glossary of Terms

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

Non-steroidal anti-inflammatory drug: Non-steroidal anti-inflammatory drugs are often abbreviated to "NSAIDs". NSAIDs are drugs, such as aspirin and ibuprofen, for reducing pain, fever and inflammation.

Osteoarthritis (OA): Osteoarthritis is a condition 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 GEL-SYN?

Gel-Syn contains sodium hyaluronate (0.84% sodium hyaluronate), a viscoelastic material made from bacterial fermentation and is the same material as a natural substance found throughout the body, including joints where it functions as lubricant and shock absorber. 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 end of your bones. In OA, there

may not be enough sodium hyaluronate, and there may be a decrease in the quality of the sodium hyaluronate in the joint.

Gel-Syn is provided in a 2.25 mL glass syringe (half a teaspoon) containing 2.1 mL of solution. The content of the syringe is sterile and is injected directly into the knee, with 2.0 mL being delivered.

WHAT IS GEL-SYN USED FOR?

Gel-Syn is used to relieve knee pain due to OA. It is given to patients who do not get enough relief from non-steroidal anti-inflammatory drugs (NSAIDs) or from simple pain medications, such as acetaminophen, or from exercise and physical therapy.

HOW IS GEL-SYN GIVEN?

Your doctor, or other qualified health professional, will inject Gel-Syn (2 mL) into your knee for a total of three weekly injections.

ARE THERE ANY REASONS WHY I SHOULD NOT RECEIVE GEL-SYN?

Your doctor will determine if you are a candidate for Gel-Syn treatment, but you should also be aware that Gel-Syn should not be administered to patients who:

- have ever had an allergic response to hyaluronate-containing products such as a rash, itching, hives, flushing, swelling of the face, tongue or throat, and/or difficulty breathing;
- have a knee joint infection or 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:

- Gel-Syn is only for injection into the knee, performed by a qualified doctor.
- Gel-Syn has not been tested to show better pain relief or safety when combined with other injected medicines.
- Tell your doctor if you are allergic to hyaluronate products.
- For 48 hours after you receive the injection, you should avoid any strenuous activities (such as jogging, tennis, other active sports, heavy lifting) and prolonged weight-bearing activities such as standing on your feet for more than one hour.
- The safety and effectiveness of repeat treatment cycles of Gel-Syn have not been established.
- Use of Gel-Syn in joints other than the knee and for conditions other than OA has not been tested.
- Gel-Syn has not been tested in pregnant or nursing women. You should tell your doctor if you think you are pregnant or if you are nursing a child.
- Gel-Syn has not been tested in children (≤ 21 years of age).

WHAT ARE THE POSSIBLE SIDE EFFECTS?

- Extra articular seepage of Gel-Syn may cause undesired effects locally.

- Some side effects (also called reactions) may occur during the use of Gel-Syn, with symptoms such as knee pain, stiffness, effusion, or swelling, the sensation of heat, reddening, swelling appearing at the injection site, arthritis, or gait disturbance. These secondary reactions can be relieved by applying ice to the treated joint.
- If any of these symptoms or signs appear after you are given Gel-Syn or if you have any other problems, you should call your doctor.

WHAT ARE THE POTENTIAL BENEFITS OF GEL-SYN?

A clinical study involving 380 patients with knee pain due to OA was performed at 23 centers in Europe (Czech Republic, France, Italy, Switzerland, Slovakia, and Germany). The study investigated the safety and effectiveness of Gel-Syn. Patients with osteoarthritic knee joint pain, who had not obtained pain relief with other medications, received either three injections of Gel-Syn or a commercial hyaluronate into the knee joint. Pain of the knee joint was measured at various times over 4, 12 and 26 weeks. The patients given three injections of Gel-Syn had the same pain relief as the patients given three injections of commercial hyaluronate for up to 26 weeks after the first injection.

WHAT DID CLINICAL STUDY SHOW?

The clinical study was conducted at 23 centers in Europe (Czech Republic, France, Italy, Switzerland, Slovakia, and Germany). A total of 380 patients with osteoarthritis were given 2 mL intra-articular injections of either Gel-Syn or commercial hyaluronate, once a week for three consecutive weeks, with follow-up visits scheduled for weeks 4, 12, and 26. A total of 380 patients were treated, with 192 being injected three times with Gel-Syn and the remaining 188 being injected three times with a commercially available hyaluronan. Patients were asked to rate their pain under the following five conditions: walking on a flat surface, walking up or down stairs, at night in bed, sitting or lying down (at rest), and while standing. Patients rated their pain from 0 (no pain) to 100 (bad pain) by marking on a 100 mm line. Pain was evaluated in this manner at 1, 4, 12 and 26 weeks after the three injections. The pain scores were used to compare the effectiveness of the Gel-Syn injections to commercial hyaluronate, and demonstrated that the patients receiving Gel-Syn experienced the same amount of improvement in knee pain over 26 weeks as those who received the commercially available hyaluronan. Overall pain score mean reduction from baseline was 30.8 mm(56%) for the Gel-Syn treatment group, whereas that for the commercial hyaluronan group was 29.4 mm (53%).

WHAT ADVERSE EVENTS WERE OBSERVED IN THE CLINICAL STUDY?

Of the 380 patients in the study, one or more adverse events were recorded for 160 (42.1%) sometime over the course of the study following the first injection of the assigned hyaluronic acid preparation, by far the most common being back pain (11.8%), arthralgia (10.5%), nasopharyngitis (8.9%), and headache (8.2%). Back pain, arthralgia, and headache were more common in the commercial hyaluronan treatment group than in the Gel-Syn treatment group. Adverse events judged to be related to treatment, severe and/or serious were relatively rare (1.6%), and none of the serious adverse events were thought to be treatment-related. Overall adverse event rates for Gel-Syn treated patients were comparable to those of the commercially available hyaluronan group.

WHAT OTHER TREATMENTS ARE AVAILABLE FOR OA?

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

Non-drug treatments

- Avoiding activities that cause knee pain
- Exercise
- Physical therapy
- 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) such as ibuprofen and naproxen
- Steroids injected directly into your knee

THINGS YOU SHOULD KNOW ABOUT GEL-SYN.

- Gel-Syn is only for injection into the knee, performed by a doctor or other qualified health care professional;
- After you receive the injection, you may need to avoid activities such as jogging, tennis, heavy lifting, or standing for a long time for approximately 48 hours.
- If any of the above symptoms or signs appear after you are given Gel-Syn, or if you have any other problems, you should call your doctor.

HOW DO I GET MORE INFORMATION ABOUT GEL-SYN?

If you have any questions or would like to find out more about Gel-Syn, you may call **XX**.

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