GenVisc® 850

(sodium hyaluronate)

Full Prescribing Information

CAUTION

Federal law restricts this device to sale by or on the order of a physician (or a properly licensed practitioner).

DESCRIPTION

GenVisc 850[1] is a sterile, viscoelastic non-pyrogenic solution of purified, high molecular weight sodium hyaluronate (average of 850,000 daltons and a range of 620,000 – 1,170,000 daltons) having a pH of 6.8-7.8. Each 2.5 mL of GenVisc 850 contains 10mg/mL of sodium hyaluronate dissolved in a physiological saline (1.0% solution). The sodium hyaluronate is derived from bacterial fermentation. Sodium hyaluronate is a poly-saccharide containing repeating disaccharide units of glucuronic acid and N-acetylglucosamine.

INDICATIONS AND USAGE

GenVisc 850 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.

CONTRAINDICATIONS

- Do not administer to patients with known hypersensitivity (allergy) to sodium hyaluronate preparations.
- Do not inject this product in the knees of patients with infections or skin diseases in the area of the injection site.

WARNINGS

- Do not concomitantly use disinfectants containing quaternary ammonium salts for skin preparation because sodium hyaluronate can precipitate in their presence.

PRECAUTIONS

- Remove joint effusion, if present, before injecting GenVisc 850.
- Do not use GenVisc 850 if the package is opened or damaged. Store in the original packaging (protected from light) below 86°F (30°C). DO NOT FREEZE. Do not use after expiration date indicated on package. The shelf life of GenVisc 850 is 36 months.
- The effectiveness of a single treatment cycle of less than 3 injections has not been established.
- The effectiveness of repeat treatment cycles of GenVisc 850 has not been established.
- Strict aseptic administration technique must be followed to avoid infections in the injection site.
- The safety and effectiveness of the use of GenVisc 850 in joints other than the knee have not been established.
- The safety and effectiveness of the use of GenVisc 850 concomitantly with other intra-articular injectable products have not been established.

STERILE CONTENTS

The prefilled syringe is intended for single use. The contents of the syringe must be used immediately once the container has been opened. Discard any unused GenVisc 850.

INFORMATION FOR PATIENTS

- Transient pain and/or swelling of the injected joint may occur after intra-articular injection of GenVisc 850.
- As with any invasive joint procedure, it is recommended that the patient avoid any strenuous activities or prolonged (i.e., more than 1 hour) weight-bearing activities such as jogging or tennis within the 48 hours that follow the intra-articular injection.

Use in Specific Populations

- **Pregnancy**: The safety and effectiveness of GenVisc 850 have not been established in pregnant women.
- **Nursing Mothers**: It is not known if GenVisc 850 is excreted in human milk. The safety and effectiveness of GenVisc 850 have not been established in lactating women.
- **Pediatrics**: The safety and effectiveness of GenVisc 850 have not been demonstrated in children (21 years of age or younger).

ADVERSE EVENTS

The primary evidence of safety is provided by the comparison of GenVisc 850 to Phosphate Buffered Saline (PBS) in the AMELIA (Navarro, Spain) study[2]. In this study, four cycles of 5 injections of GenVisc 850 or PBS were administered with an interval of 6 months for the first three cycles and 1 year for the fourth cycle. Patients were followed for 1 year after the last injection. The population of patients evaluated for the safety of GenVisc 850 included 306 subjects (153 GenVisc 850, 153 PBS). In each treatment group, 127 subjects experienced at least one adverse event during the study and 22 patients (11 in each treatment group) experienced at least one adverse event that was reported as possibly, probably or certainly related to the device, Table 1. None of the related adverse events were assessed as severe. For the first cycle of 5 injections in the GenVisc 850 treatment group, the 15 adverse events reported as related were pain at the injection site (6), allergic reaction (3), arthralgia (2), bleeding at the injection site (2), bleeding (1) and heaviness (1). In the first cycle of 5 injections for the PBS treatment group, the 14 adverse events reported as related were bleeding at the injection site (6), allergic reaction (3), pain at the injection site (2), arthralgia (2), and arthritis (1).

Table 1: Related Adverse Events by Severity[2]

Related Adverse Events	GenVisc 850			PBS		
	Mild	Moderate	Total	Mild	Moderate	Total
Allergic reaction	2	1	3	3	--	3
Pain injection site	2	4	6	2	--	2
Bleeding	--	1	1	--	--	--
Bleeding injection site	2	--	2	6	--	6
Arthralgia	--	2	2	1	1	2
Arthritis	--	--	--	--	1	1
Heaviness	1	--	1	--	--	--
Total	7	8	15	12	2	14

A total of 513 complete GenVisc 850 treatment cycles and a total of 487 complete PBS treatment cycles were administered in the study. Table 2 provides the number of related adverse events per complete treatment cycle. The rate of adverse events per treatment cycle for GenVisc 850 is 0.029, which is the same as the PBS rate. This low adverse event rate demonstrates the safety of GenVisc 850 following repeat treatments.

Table 2: Related Adverse Events by Treatment Cycles

Treatment	No. Complete Cycles	No. Related Adverse Events	Related AEs per Complete Cycles
GenVisc 850	513	15	0.029
PBS	487	14	0.029

Supporting evidence of safety is provided by the comparison of GenVisc 850 to Supartz®/Supartz FX™ (sodium hyaluronate, Seikagaku Corp.) in the Yong Ping study. The population of patients evaluated for the safety of GenVisc included 229 subjects (116 GenVisc 850, 113 Supartz/Supartz FX). In the Supartz/Supartz FX group, 26 (23.0%) subjects experienced adverse events (AEs) and 6 (5.3%) of them, 4 cases of local pain and 2 cases of swelling, were judged possibly related to the device. In the GenVisc 850 group, 21 (18.1%) subjects experienced AEs and 2 (1.7%) of them, 1 case of local pain and 1 case of rash, were judged possibly related to the device. There were no statistically significant differences in the incidence rates of these adverse events between the GenVisc 850 and Supartz/Supartz FX groups. A summary of AEs is provided in Table 3.

Table 3: Adverse Events Reported in Yong Ping Study

	Category	Supartz/Supartz FX Group/N (%)	GenVisc 850 Group/N (%)	Statistics	P value	Method
AE	Yes	26 (23.0)	21 (18.1)	0.844	0.358	Chi-square
	No	87 (77.0)	95 (81.9)			
	Total	113	116			
Related AE	Yes	6 (5.3)	2 (1.7)	--	0.167	Fisher
	No	107 (94.7)	114 (98.3)			
	Total	113	116			
SAE	Yes	1 (0.9)	0 (0.0)	--	1.000	Fisher
	No	112 (99.1)	116 (100.0)			
	Total	113	116			

Note: AEs that were definitely related, probably related, or possibly related to the device, and abnormal laboratory findings were judged as Related AEs.

GenVisc 850 has been commercially distributed in 40 countries outside of the United States. GenVisc is also approved in 23 other countries but not presently distributed. GenVisc 850 (sold ex-U.S. as Adant) has been on the market in Japan since 1995 and in Europe since 1996. From the time of its first marketing through 2012 over 35 million syringes were distributed with no major safety concerns related to the product.

CLINICAL STUDIES

The results of the Yong Ping study and the Bayesian longitudinal analysis summarized below confirm that the clinical performance of GenVisc 850 was superior to a saline placebo control and similar to that of Supartz/Supartz FX. The Yong Ping study was a randomized controlled, multicenter clinical trial that demonstrated non-inferiority of GenVisc 850 to Supartz/Supartz FX through 6 weeks. The Bayesian longitudinal analysis included data from four randomized controlled trials, two of which included comparisons of GenVisc 850 to saline and two of which included comparisons of Supartz/Supartz FX to saline. The results of this Bayesian longitudinal analysis demonstrated the superiority of GenVisc 850 to a saline placebo control.

GenVisc® 850

(sodium hyaluronate)

Patient Information

Product Information

GenVisc 850 (sodium hyaluronate)

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 GenVisc 850. 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, naproxen, ibuprofen, and Celebrex, 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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For more Information, please refer to the Full Prescribing Information for GenVisc 850.

General

WHAT IS GENVISC 850 (SODIUM HYALURONATE)?

GenVisc 850 is a product from the class of products known as hyaluronic acid, sodium hyaluronate, or hyaluronan (HA), and also known as viscosupplementation therapy. It helps supplement the viscous properties of the fluid in your knee joint. It is approved for treatment of pain due to osteoarthritis of the knee in patients who do not get adequate relief from simple painkillers like acetaminophen or from exercise and physical therapy.

WHAT IS GENVISC 850 USED FOR?

GenVisc 850 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 GENVISC 850 GIVEN?

GenVisc 850 is administered by intra-articular injection. Intra-articular means your healthcare professional will insert a needle into the space in your knee joint that contains fluid used for lubrication and cushioning.

HOW DOES GENVISC 850 WORK?

The precise mechanism by which GenVisc 850 works is unknown. The fluid (synovial fluid) in your knee helps to lubricate and cushion the joint during movement. The major component in the synovial fluid is hyaluronic acid, the same active component of GenVisc 850. One of the early effects of OA is to break down this fluid, making it less effective. It is thought that GenVisc 850 injection helps restore the synovial fluid to a more healthy state, thereby reducing the pain of OA.

ARE THERE ANY REASONS WHY I SHOULD NOT RECEIVE GENVISC 850?

Your doctor will determine if you are a candidate for GenVisc 850 treatment, but you should also be aware that GenVisc 850 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:
- GenVisc 850 is only for injection into the knee, performed by a qualified healthcare professional.
- GenVisc 850 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 effectiveness of repeat treatment cycles of GenVisc 850 has not been established.
- Use of GenVisc 850 in joints other than the knee and for conditions other than OA has not been tested.
- GenVisc 850 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.
- GenVisc 850 has not been tested in children (21 years of age or younger).

WHAT ARE THE POSSIBLE SIDE EFFECTS?
- Some side effects (also called reactions) may occur during the use of GenVisc 850, with symptoms such as knee pain, inflammation, reddening, swelling appearing at the injection site, joint pain. If any of these symptoms or signs appears after you are given GenVisc 850 or if you have any other problems, you should call your doctor.
- Because GenVisc is administered through a needle you may experience some local pain or discomfort when it is administered, as may be expected with all injections.

WHAT ARE THE POTENTIAL BENEFITS OF GENVISC 850?

A clinical study was conducted in the People's Republic of China involving 229 patients with knee pain due to degenerative osteoarthritis (OA) of the knee. The result of this study showed that patients treated with GenVisc 850 experienced the same amount of improvement in knee pain over 6 weeks as those treated with Supartz®/Supartz FX™ (sodium hyaluronate, Seikagaku Corp.), a similar product that has been sold in the U.S. since 2001. The overall average reduction of mean pain scores was 49 mm for the GenVisc 850 treatment group and 48 mm for the Supartz/Supartz FX group.

Four additional clinical studies involving 804 patients with knee pain due to OA were performed, three in Europe and one in Australia. Patients received five injections of GenVisc 850, Supartz/Supartz FX, or saline into the knee joint. Pain of the knee joint was measured at various times, 5, 6, 10, 13, 14, 17, 18, 20, 26, and 30 weeks. Analysis of the results of these four studies demonstrated that those patients given five injections of GenVisc 850 achieved greater pain relief up to 30 weeks than those patients given five injections of saline for the same time period. The difference in pain reduction from baseline to 30 weeks was significantly greater for the GenVisc 850 patients versus those receiving saline injections.

Yong Ping (2012): Head-to-Head (GenVisc 850 vs. Supartz/Supartz FX) Randomized Controlled Study

The Yong Ping study was a parallel-controlled, randomized, multi-center clinical conducted at five hospitals. The objective of the trial was to evaluate the comparative efficacy and safety of GenVisc 850 intra-articular injections for the treatment of degenerative osteoarthritis knee pain to Supartz/Supartz FX.

A total of 229 subjects were enrolled with 113 in the Supartz/Supartz FX treatment group and 116 in the GenVisc 850 group. Of those, 92.9% and 93.1% in the Supartz/Supartz FX and GenVisc 850 groups, respectively, completed the trial. Each group received 5 injections of the respective product at weekly intervals.

The average age was 62.3 years in the Supartz/Supartz FX group and 74% of the subjects were female. The average age was 61.9 years in the GenVisc 850 group and 80% of the subjects were female. In both groups, the average weight was 66 kg. There were no statistically significant differences in demographic characteristics.

Primary Effectiveness: In the full analysis set (FAS) population, the VAS pain on movement of the Supartz/Supartz FX group at week 6 decreased by 48.0±23.39 mm compared to baseline, and that of the GenVisc 850 group decreased by 49.2±21.50 mm. The difference between the two groups was not statistically or clinically significant (P>0.05). These analyses are shown in Table 4.

Table 4: VAS pain on movement (mm) and baseline variations (Week 6 - Baseline) (FAS)

	Supartz/ Supartz FX group	GenVisc 850 group	Statistics	P value	Method
N	113	116	0.403	0.688	t test
Mean±SD	–48.0±23.39	–49.2±21.50			
95%CI(Lower-Upper)	–52.33-–43.61	–53.12-–45.21			
Min-Max	–95.0-1.00	–90.0-17.00			
Median	–50.00	–50.25			

Meta-Analysis of 4 Studies Using Bayesian Modeling

To further support the clinical similarities between GenVisc 850 and Supartz/Supartz FX, a prospective meta-analysis of the pivotal studies for both products was undertaken using Bayesian longitudinal modeling. The studies analyzed include:

- For GenVisc 850, two saline-controlled studies (AMELIA[2] and Blanco[3]); and
- For Supartz/Supartz FX, two saline-controlled studies conducted in Australia[4] and Sweden[5].

Primary Objectives of the Bayesian Analysis:

- Supartz/Supartz FX is superior to PBS. The null hypothesis is that PBS is superior to Supartz/Supartz FX. Rejection of the null hypothesis will in effect validate the statistical approach and modeling as it duplicates the results of the approved PMA for Supartz/Supartz FX.
- GenVisc 850 is superior to PBS. The non-inferiority margin for addressing this objective is 4 mm.

Supporting Objective of the Bayesian Analysis:

- GenVisc 850 advantage over PBS is non-inferior to Supartz/Supartz FX's advantage over PBS. The non-inferiority margin for addressing this objective is 4 mm.

Results of Meta-Analysis of 4 Studies Using Bayesian Modeling

Primary Analysis: For the primary analysis, which pools all data from post-baseline visits for all treatments in all studies, the estimated between-study variability (T) was examined and found to be acceptable for superiority and non-inferiority assessments.

The Gelman-Rubin convergence statistic was very close to 1, thus indicating convergence of the sampler. Overall the model fits the data well.

Primary Analysis

The posterior probability of superiority of GenVisc 850 vs. PBS is 79% at week 30 (mean 6.88 mm advantage) thus giving confidence that GenVisc 850 is superior to PBS up to 30 weeks.

Secondary Analysis

For the primary and supporting analyses, differences in mean change from baseline between GenVisc 850 and PBS were examined. Paucity of data towards the end of the time interval causes an increase in variance and therefore the posterior probability of non-inferiority does not increase. The posterior mean difference between effect GenVisc 850 and Supartz/Supartz FX was always below the non-inferiority margin with a posterior probability of 50%, but the scarcity of data limits the ability to declare non-inferiority of GenVisc 850 to Supartz/Supartz FX for the interval extending to 30 weeks.

Further details of the primary and secondary analysis assessments are provided below in Table 5 and Figure 1.

Table 5. Posterior Probabilities for Main Analysis of GenVisc 850 Superiority

Objective	π	Probability
GenVisc Superiority	π_1	79

The results of the longitudinal analyses are presented in support of the observation that GenVisc 850 is superior to PBS across time. There is a good linear fit of the data to the model demonstrating increasing mean differences between GenVisc 850 and PBS through 30 weeks, Figure 1.

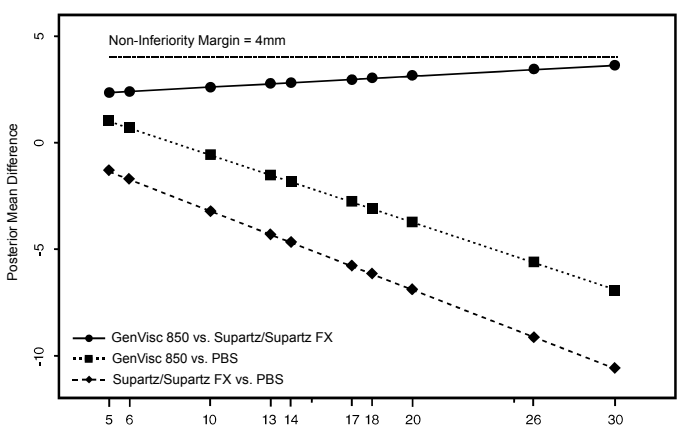

Figure 1. Treatment Difference Estimates Across Time Using a Linear Trend Longitudinal Model.

DETAILED DEVICE DESCRIPTION

Each 3mL prefilled syringe of GenVisc 850 contains:

Sodium Hyaluronate	25.0mg
Sodium Chloride	21.3mg
Disodium Phosphate Dodecahydrate	1.5mg
Sodium Hydroxide	q.s. to adjust pH
Hydrochloric acid	q.s. to adjust pH
Water for Injection	q.s. 2.5mL

HOW SUPPLIED

GenVisc 850 is supplied as a sterile, non-pyrogenic solution in 3mL pre-filled syringe.

DIRECTIONS FOR USE

GenVisc 850 is administered by intra-articular injection. A treatment cycle consists of five injections given at weekly intervals. Some patients may experience benefit with three injections given at weekly intervals. Injection of subcutaneous lidocaine or similar local anesthetic may be recommended prior to injection of GenVisc 850.

Warning: Do not concomitantly use disinfectants containing quaternary ammonium salts for skin preparation because sodium hyaluronate can precipitate in their presence.

Precaution: Do not use GenVisc 850 if the package is opened or damaged. Store in the original packaging (protected from light) below 86°F (30°C). DO NOT FREEZE. Do not use after expiration date indicated on package. The shelf life is 36 months.

Precaution: Strict aseptic administration technique must be followed.

Precaution: Remove joint effusion, if present, before injection GenVisc 850.

To ensure a tight seal and prevent leakage during administration, firmly HOLD the luer lock when removing the tip cap and attaching the needle. Take care not to rotate the luer lock which can lead to loosening of the hub. Inject GenVisc 850 into the knee joint through a 21-23 gauge needle.

Inject the full 2.5mL in one knee only. If treatment is bilateral, a separate syringe should be used for each knee.

Precaution: The prefilled syringe is intended for single use. The content of the syringe must be used immediately once the container has been opened. Discard any unused GenVisc 850.

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1 GenVisc® is a registered trademark of Channel-Markers Medical, LLC. GenVisc 850 is sold outside the U.S. under the branded name Adant®, a registered trademark of Meiji Seika Pharma Co., Ltd.

2 Navarro-Sarabia F, Coronel P, Collantes E, Navarro FJ, de la Serna AR, Naranjo A, Gimeno M, Herrero-Beaumont G; AMELIA study group. A 40-month multicentre, randomised placebo-controlled study to assess the efficacy and carry-over effect of repeated intra-articular injections of hyaluronic acid in knee osteoarthritis: the AMELIA project. Ann Rheum Dis. 2011;70: 1957-62.

3 Blanco FJ, Fernández-Sueiro JL, Pinto-Tasende JA, Fernández-López JC, Ramallal M, Freire A et al. Intra-articular hyaluronan treatment of patients with knee osteoarthritis waiting for replacement surgery. The Open Arthritis Journal 2008; 1: 1-7.

4 Day, R. et al. A double blind, randomized, multicenter, parallel group study of the effectiveness and tolerance of intraarticular hyaluronan on osteoarthritis of the knee. J Rheumatol 2004; 31: 755-782.

5 Lohmander LS, Dalén N, Englund G, Hämäläinen M, Jensen EM, Karlsson K, Odensten M, Ryd L, Sernbo I, Suomalainen O, Tegnander A. Intra-articular hyaluronan injections in the treatment of osteoarthritis of the knee: a randomised, double blind, placebo controlled multicentre trial. Hyaluronan Multicentre Trial Group. Ann Rheum Dis. 1996; 55: 424-31.

WHAT ADVERSE EVENTS WERE OBSERVED IN THE CLINICAL STUDIES?

In the GenVisc 850 treatment group for one of the clinical studies performed in Spain, 15 reported adverse events included pain at the injection site (6), allergic reaction (3), arthralgia (2), bleeding at the injection site (2), bleeding (1) and heaviness (1). In the GenVisc 850 treatment group for the clinical study performed in the People's Republic of China, two adverse events were reported, 1 report of local pain and 1 report of rash. There were no significant differences in the rate of occurrences of adverse events between patients injected with GenVisc 850 and patients injected with Supartz/Supartz FX or saline.

WHAT OTHER TREATMENTS ARE AVAILABLE FOR OA?

If you have OA, there are other things you can do besides getting GenVisc 850. These include:

Non-drug treatments

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

Drug therapy

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

THINGS YOU SHOULD KNOW ABOUT GENVISC 850.

- GenVisc 850 is only for injection into the knee, performed by a doctor or other qualified health care professional.
- If you have pain in both knees, the effects of pain relief on the knee opposite to the one injected have not been evaluated. Your doctor may recommend that both knees be injected.
- After you receive the injection, you may need to avoid strenuous 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 GenVisc 850, or if you have any other problems, you should call your doctor.

WHY IS MY DOCTOR RECOMMENDING I RECEIVE GENVISC 850?

GenVisc 850 is indicated for patients with osteoarthritis knee pain who do not obtain adequate relief from simple painkillers, like acetaminophen (Tylenol®), or from exercise and physical therapy. Ask your doctor for additional information and discuss your treatment options.

IS GENVISC 850 APPROVED FOR USE IN THE U.S.?

GenVisc 850 was approved for use in the United States in September 2015. GenVisc 850 has demonstrated a very favorable safety profile, with over 35 million doses administered worldwide since its first approval, and has been studied in over 30 clinical trials for use in relieving osteoarthritis knee pain.

WHAT IS GENVISC 850 MADE FROM?

Hyaluronic acid is a natural chemical found in almost all species and various parts of your body. It is in high amounts particularly in joint tissues and in the fluid that fills the knee joint space (synovial fluid). GenVisc 850 is made from an extraction and purification of hyaluronic acid from fermentation of bacteria that make hyaluronic acid identical in chemical composition to human hyaluronic acid.

WILL MY INSURANCE COVER GENVISC 850?

Most insurance carriers and Medicare cover GenVisc 850. The process of obtaining reimbursement varies from plan to plan so talk with your doctor's office and your insurance provider before you begin treatment to find out if GenVisc 850 is covered.

Treatment

ARE FIVE INJECTIONS REQUIRED?

Clinical investigations with GenVisc 850 have demonstrated that five injections one week apart provide optimal pain relief. Some patients have derived benefit following the third injection. The effectiveness of less than three injections has not been evaluated. You should discuss this with your doctor. Completion of the full injection treatment course is recommended to achieve the greatest therapeutic benefit.

HOW DO I KNOW IF GENVISC 850 IS RIGHT FOR ME?

A doctor is the best person to advise you on any course of treatment. GenVisc 850 is approved for the treatment of pain due to osteoarthritis of the knee in patients who do not get adequate relief from simple painkillers or from exercise and physical therapy.

AM I TOO OLD FOR GENVISC 850 INJECTIONS?

There are no specific precautions or contraindications regarding the use of GenVisc 850 in older patients.

CAN I TAKE OTHER MEDICATIONS WITH GENVISC 850?

Because GenVisc 850 is injected directly into the joint rather than administered systemically and there are no known drug interactions, you may be able to take other medications with it. It is not known to interfere with other pain relievers and anti-inflammatory drugs. The safety and effectiveness of the use of GenVisc 850 at the same time as other intra-articular injections, such as steroids, have not been established. Because it is administered locally it is unlikely that you will observe any benefit in joints not specifically injected. You should discuss all of your current medications and vitamin supplements with your physician on a periodic basis.

CAN I RECEIVE GENVISC 850 IN BOTH OF MY KNEES?

Yes, if both knees have pain. GenVisc 850 treatment may be given in both knees simultaneously or separately, according to your physician's recommendations. Because GenVisc 850 is only injected locally into the knee joint and not administered systemically, it is not likely that injections into one knee will have an effect on the opposite knee if it is not injected. In addition, it is unknown whether a good response in one knee is a good predictor of an equivalent response in the opposite knee should you decide to have this therapy.

SHOULD I MODIFY MY LEVEL OF PHYSICAL ACTIVITY AFTER RECEIVING GENVISC 850 TREATMENT?

It is recommended that you avoid strenuous activities such as jogging, tennis, and heavy lifting for at least 48 hours after receiving an injection. Your doctor will advise you about the level of activity that is right for you, but in general, patients are able to maintain their normal daily activities after receiving GenVisc 850 treatment.

CAN GENVISC 850 BE USED IN JOINTS OTHER THAN THE KNEE?

The U.S. Food and Drug Administration has only approved GenVisc 850 for use in the treatment of OA of the knee. The FDA has not approved or made an evaluation regarding the safety and effectiveness in other joints.

IS GENVISC 850 A CURE FOR OSTEOARTHRITIS OF THE KNEE?

There is no cure for osteoarthritis. GenVisc 850 is a treatment for the symptoms of knee pain of osteoarthritis.

Benefits

WHEN CAN I EXPECT TO EXPERIENCE PAIN RELIEF?

Each patient's response to GenVisc 850 may vary, depending on severity of your OA, degree of pain, and pre-existing medical conditions. In some patients, successful treatment may reduce pain within the first week after treatment begins. However, based upon clinical trials, most patients experienced pain relief after their third injection of GenVisc 850.

IS GENVISC 850 TREATMENT EFFECTIVE IN KNEES WITH ADVANCED OSTEAOTHRITIS AND LOSS OF CARTILAGE?

Most of the clinical studies with GenVisc 850 have selected patients with mild to moderate OA.

WHAT ARE THE BENEFITS OF RECEIVING GENVISC 850 TREATMENT?

Successful treatment with GenVisc 850 should reduce pain in an osteoarthritic knee. Because it is a local treatment, GenVisc 850 should not interfere with any medicine that the patient may take.

HOW LONG CAN I EXPECT THE BENEFIT OF GENVISC 850 TO LAST?

Each patient reacts differently to GenVisc 850 treatment. Five injections given at weekly intervals can provide most patients up to 30 weeks of pain relief. The duration of pain relief you experience may vary.

Safety

HOW SAFE IS GENVISC 850?

Extensive safety and toxicity tests were performed on GenVisc 850. GenVisc 850 is approved in over 60 countries worldwide. GenVisc 850 has been in use since 1995 in Japan, 1997 in Europe, and 2015 in the U.S., with over 4 million injections given worldwide. In clinical trials, transient local pain or swelling occurred with some patients with injections of GenVisc 850. Since introduction into the global market, GenVisc 850 has not been withdrawn in any market because of safety concerns.

For more Information, please ask your doctor or refer to the Full Prescribing Information for GenVisc 850.