GELSYN-3

3 injection hyaluronic acid treatment™

PRODUCT INFORMATION

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

CONTENT

Each 1 mL of GELSYN-3 contains:

Sodium Hyaluronate:	8.4 mg
Sodium Chloride:	8.5 mg
Sodium Phosphate, Dibasic:	0.16 mg
Sodium Phosphate, Monobasic:	0.045 mg
Water for Injection:	q.s. to 1.0 mL

DESCRIPTION

GELSYN-3 is a sterile, buffered solution of highly purified sodium hyaluronate with a molecular weight of approximately 1100 kDa, obtained through fermentation of Streptococci of Lancefield groups A and C and is not chemically modified.

INDICATION

GELSYN-3 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 GELSYN-3 into the knees of patients that have knee joint infections or skin diseases or infections 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.
- Inject into the synovial space only. Do not inject by intravascular route.
- Do not inject outside the synovial space or into the synovial tissue or capsule. An extra-articular injection of the product can cause local adverse events.

PRECAUTIONS

General

- The safety and effectiveness of GELSYN-3 in locations other than the knee, and for conditions other than osteoarthritis, have not been established.
- Strict aseptic administration technique must be followed.
- STERILE CONTENTS. EXTERIOR OF SYRINGE IS NOT STERILE. The syringe is intended for single use. The contents of the syringe must be used immediately after its packaging is opened. Do not re-sterilize the product.
- Store in original packaging (protected from light) at room temperature < 25°C (77°F). DO NOT FREEZE.
- Do not use GELSYN-3 if package is opened or damaged.
- GELSYN-3 is sensitive to light, and should therefore be used immediately after removal from the carton box.
- Do not use GELSYN-3 in case of severe intra-articular effusion.
- Remove synovial fluid or effusion before each GELSYN-3 injection.
- GELSYN-3 should be used with caution when there is evidence of lymphatic or venous stasis in the leg to be treated.

INSTRUCTION FOR PATIENTS

- Provide patients with a copy of the Patient Labeling prior to use.
- Transient pain, sensation of heat, reddening or swelling may occur at the injection site after intra-articular injection of GELSYN-3.
- As with any invasive joint procedure, it is recommended that the patient avoid any strenuous activities or prolonged weight-bearing activities such as jogging or tennis within 48 hours following the intra-articular injection.

USE IN SPECIFIC POPULATIONS

Pregnancy: The safety and effectiveness of GELSYN-3 have not been established in pregnant women.

Nursing Mothers: It is not known if GELSYN-3 is excreted in human milk. The safety and effectiveness of GELSYN-3 have not been established in lactating women.

Children: The safety and effectiveness of GELSYN-3 have not been established in children.

Table 1: Primary Endpoint (100 mm WOMAC Pain Subscore)* for Intent-To-Treat (ITT) Patients

	GELSYN-3		Commercial Hyaluronan			
Variable	N	Mean ± SE	N	Mean ± SE	Difference*	95% CI
Absolute Values						
Baseline	192	55.2 ± 0.8	188	55.5 ± 0.8	-0.3 ± 1.1	(-2.5, 1.9)
4 Weeks	189	27.0 ± 1.6	183	28.6 ± 1.7	-1.6 ± 1.7	(-4.9, 1.7)
12 Weeks	185	23.6 ± 1.6	178	25.6 ± 1.7	-2.0 ± 1.7	(-5.4, 1.4)
26 Weeks	181	22.2 ± 1.6	175	22.9 ± 1.7	-0.7 ± 1.7	(-4.1, 2.7)
Overall	-	24.3 ± 1.5	-	25.7 ± 1.6	-1.4 ± 1.5	(-4.3, 1.4)
Change from Baseline						
4 Weeks	189	28.1 ± 1.6	183	26.5 ± 1.7	1.6 ± 1.7	(-1.7, 4.9)
12 Weeks	185	31.5 ± 1.6	178	29.5 ± 1.7	2.0 ± 1.7	(-1.4, 5.4)
26 Weeks	181	32.9 ± 1.6	175	32.2 ± 1.7	0.7 ± 1.7	(-2.7, 4.1)
Overall	-	30.8 ± 1.5	-	29.4 ± 1.6	1.4 ± 1.5	(-1.4, 4.3)

* GELSYN-3 minus Commercial Hyaluronan ± SE.
Mixed models include factors for treatment, visit, treatment* visit interaction, center and baseline level.

ADVERSE REACTIONS

The most common adverse events related to GELSYN-3 injection reported in the clinical study are the following:

Injection site pain (0.5%)
All adverse events related to GELSYN-3 injection reported in the clinical study are provided in the Adverse Events Summary **(Table 4).**

Post-Marketing Experience
Ten adverse events have been reported since GELSYN-3 was first commercialized in Western Europe in 2002, including knee cooling, metallic taste, skin eruption, inflammatory symptoms, burning and itching sensations, tiredness, fever, psoitis, giant urticaria and edema in both legs, and gouty arthritis. In all the cases, the patients recovered without sequelae.

Potential Adverse Events

The following adverse events are among those that may occur in association with intra-articular injections:

- Arthralgia
- Joint effusion
- Joint warmth
- Arthritis
- Gait disturbance
- Joint stiffness
- Joint swelling
- Injection site pain
- Arthropathy

According to post-marketing experience of other sodium hyaluronate preparations, anaphylactic / anaphylactoid reactions accompanied by transient hypotension (sudden drop in blood pressure), have been rarely reported worldwide, all of which resolved either spontaneously or after conservative treatment.

Pivotal Clinical Trial

Study Design: The safety and efficacy of GELSYN-3 was assessed in a prospective, randomized, double-blind, active control (commercial hyaluronan), non-inferiority study conducted at 23 centers in Europe (Czech Republic, France, Italy, Switzerland, Slovakia, and Germany). A total of 380 patients were enrolled. Patients were given 2 mL intra-articular injections of the randomly assigned GELSYN-3 or commercial hyaluronan once a week for three consecutive weeks, with follow-up visits scheduled for weeks 4, 12 and 26. The primary efficacy variable for this study was the Western Ontario McMaster Universities (WOMAC) pain subscore at week 26 which was required to meet a delta of 8 mm, with secondary efficacy variables including WOMAC total score and stiffness and function subscores, Lequesne Algofunctional Index, global pain assessed by patient, global status assessed by patient and Investigator, paracetamol consumption, patient satisfaction, and overall clinical response based on OMERACT-OARSI criteria. Safety variables included adverse events, pain and local tolerability at the injection site, and global tolerability as assessed by both patient and Investigator.

Patient Population: The average age of the 380 intent-to-treat (ITT) patients, defined as receiving at least one intra-articular injection, was 65.0 years, the majority were female (72.9%), BMI ranged from 19.8 to 34.7 kg/m^2, and the mean duration of osteoarthritis in the target knee was 7.61 years. For 52.6% of the patients, the right knee was the target knee, but 66.1% also had osteoarthritis in the contralateral knee. The anatomical location of target knee osteoarthritis was usually in the medial tibio-femoral region (82.9%), with some degree of joint space narrowing being reported in nearly all patients (95.0%). Patient assessed global pain scores at the screening and baseline visits averaged 65.3 and 65.6, respectively, while the other indices of disease severity at these time-points (i.e. global status, range of motion, WOMAC & Lequesne scoring) were also suggestive of mild to moderate target knee osteoarthritis. The only baseline variable reaching statistical significance with regard to differences between the two treatment groups was venous insufficiency which was more prevalent for commercial hyaluronan patients (5.3% vs 1.0%, p =0.019), with hypercholesterolemia and the requirement for ambulatory assistance also being somewhat (but not statistically significantly) greater (11.7% vs 6.3%, p = 0.073 and 5.9% vs 2.1%, p = 0.069, respectively).

Efficacy Data: For the primary outcome measure (change from baseline), the protocol-defined 8 mm non-inferiority margin was met for all time points. In addition, the 95% lower-bound confidence interval of the difference (GELSYN-3 minus commercial hyaluronan) in pain subscore reduction from baseline for the overall 26 week WOMAC pain subscore for the ITT patient population was -1.4 (see Change from Baseline – Overall, **Table 1**). Overall WOMAC pain subscore mean reduction from baseline was 30.8 mm (56%) for the GELSYN-3 treatment group, in contrast to 29.4 mm (53%) for patients receiving commercial hyaluronan.

For the secondary study variables, because this was a non-inferiority study not designed to test superiority, no claims can be made about the statistical significance of any intergroup differences such as those observed at 26 weeks following either three GELSYN-3 or commercial hyaluronan injections (**Table 2**).

Table 2: Secondary Outcome Variables for ITT Patients at 26 Weeks

	GELSYN-3 (N=192)		Commercial Hyaluronan (N=188)		
Variable	**N**	**Mean ± SE or %**	**N**	**Mean ± SE or %**	**p**
1. WOMAC Function	181	28.3 ± 1.7	175	28.0 ± 1.8	0.860
2. WOMAC Stiffness	181	25.9 ± 1.8	175	25.2 ± 1.9	0.735
3. WOMAC Total Score	181	29.0 ± 1.6	175	28.6 ± 1.7	0.811
4. Lequesne Pain	181	2.08 ± 0.16	175	1.79 ± 0.17	0.097
5. Lequesne Walking	181	0.79 ± 0.10	175	0.66 ± 0.11	0.262
6. Lequesne Daily Living	181	1.23 ± 0.12	175	1.10 ± 0.13	0.320
7. Lequesne Total Score	181	4.07 ± 0.32	175	3.53 ± 0.33	0.124
8. Patient Global Pain	181	37.2 ± 2.2	175	33.6 ± 2.3	0.138
9. Patient Global Status	180	25.4 ± 2.0	175	25.7 ± 2.1	0.892
10. Paracetamol Usage	187	46.8 ± 9.7	183	62.8 ± 10.1	0.090
11. Patient Satisfaction	181	82.9%	174	77.0%	0.185
12. Investigator Global Status	181	85.0%	174	76.5%	0.043
13. OMERACT-OARSI	181	89.9%	175	87.7%	0.504
1 to 9: 26-Week Change from Baseline Score (higher=better). Mixed models include factors for treatment, visit, treatment*visit interaction, center and baseline level.					
10: Number of paracetamol rescue medication tablets over the entire 26 Weeks. Mixed model includes factors for treatment and center.					
11: Patients satisfied or very satisfied at 26 Weeks. Generalized Estimating Equation (GEE) logistic regression model includes factors for treatment, visit, treatment*visit interaction and center.					
12: Status good or very good at 26 Weeks. Generalized Estimating Equation (GEE) logistic regression model includes factors for treatment, visit, treatment*visit interaction, center and baseline level.					
13: OMERACT-OARSI Success at 26 Weeks. Generalized Estimating Equation (GEE) logistic regression model includes factors for treatment, visit, treatment*visit interaction and center.					

Safety Data: *Adverse Events* – Of the 380 patients in the intent-to-treat (ITT) patient population, 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 GELSYN-3 treatment group (**Table 3**). 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 (**Table 4**). Overall adverse event rates for the GELSYN-3 treatment group were comparable to those of the commercial hyaluronan treatment group.

Table 3: ITT Patients – Adverse Events*

	GELSYN-3 (N=192)			Commercial Hyaluronan (N=188)			
Variable	**n†**	**n**	**Percent**	**n**	**n**	**Percent**	**p Values‡**
Any Adverse Event	222	83	43.2%	220	77	41.0%	0.679
Gastrointestinal Disorders							
Toothache	8	7	3.6%	3	3	1.6%	0.337
Diarrhea	1	1	0.5%	4	3	1.6%	0.368
Abdominal pain upper	0	0	0.0%	2	2	1.1%	0.244
General Disorders/Administrative Site Conditions							
Pyrexia	6	5	2.6%	7	5	2.7%	1.000
Injection site pain	3	1	0.5%	4	3	1.6%	0.368
Hepatobiliary disorders							
Cholecystitis acute	0	0	0.0%	2	2	1.1%	0.244
Infections and infestations							
Nasopharyngitis	27	19	9.9%	22	15	8.0%	0.591
Respiratory tract infection	4	4	2.1%	3	3	1.6%	1.000
Urinary tract infection	4	4	2.1%	3	3	1.6%	1.000
Influenza	6	3	1.6%	3	3	1.6%	1.000
Cystitis	1	1	0.5%	5	4	2.1%	0.211
Herpes zoster	0	0	0.0%	2	2	1.1%	0.244
Viral infection	1	1	0.5%	2	2	1.1%	0.620
Musculoskeletal/Connective Tissue Disorders							
Back pain	25	19	9.9%	39	26	13.8%	0.268
Arthralgia	29	18	9.4%	28	22	11.7%	0.506
Pain in extremity	9	9	4.7%	4	2	1.1%	0.062
Musculoskeletal pain	6	5	2.6%	2	2	1.1%	0.449
Neck pain	3	1	0.5%	5	4	2.1%	0.211
Joint swelling	2	2	1.0%	5	2	1.1%	1.000
Nervous System Disorders							
Headache	29	13	6.8%	31	18	9.6%	0.353
Respiratory/Thoracic/Mediastinal Disorders							
Oropharyngeal pain	3	3	1.6%	2	2	1.1%	1.000

*Adverse events are included in this table only if the incidence in one of the treatment groups exceeded 1%.
†First n is number of events, and second n is number of patients experiencing an event.
‡Fisher's exact test.

Pain at Injection Site/Local Tolerability – Pain associated with the initial injection of the experimental product or comparator in ITT patients averaged 2.95 on a 10 point scale, declining slightly to 2.80 then 2.65 after the second and third injections, respectively, with local tolerability being judged as good/very good by 91% to 93% of the patients at each of the visits following product administration.

Patient/Investigator Global Tolerability – Patient and investigator assessed global tolerability at the 4, 12 and 26-week follow-up visits were nearly identical and comparable to local tolerability scoring, as good/very good scores were obtained from 93% to 97% of the respondents. There were no statistically significant intergroup differences for any of these variables.

Table 4: ITT Patients – Adverse Events Based on Relationship to Treatment, Severity, Seriousness

	GELSYN-3 (N=192)			Commercial Hyaluronan (N=188)			
Variable	**n***	**n**	**Percent**	**n**	**n**	**Percent**	**p Values†**
Adverse Events Certainly or Probably Related to Treatment							
Any Adverse Event	1	1	0.5%	5	4	2.1%	0.211
General disorders and administration site conditions							
Injection site hematoma	0	0	0.0%	1	1	0.5%	0.495
Injection site pain	1	1	0.5%	1	1	0.5%	1.000
Musculoskeletal and connective tissue disorders							
Arthralgia	0	0	0.0%	1	1	0.5%	0.495
Joint swelling	0	0	0.0%	2	1	0.5%	0.495
Severe Adverse Events							
Any Adverse Event	1	1	0.5%	6	6	3.2%	0.065
Gastrointestinal Disorders							
Diverticulum intestinal	0	0	0.0%	1	1	0.5%	0.495
Hepatobiliary disorders							
Cholecystitis acute	0	0	0.0%	1	1	0.5%	0.495
Infections and infestations							
Influenza	0	0	0.0%	1	1	0.5%	0.495
Injury, poisoning and procedural complications							
Radius fracture	0	0	0.0%	1	1	0.5%	0.495
Musculoskeletal and connective tissue disorders							
Arthritis	0	0	0.0%	1	1	0.5%	0.495
Intervertebral disc protrusion	1	1	0.5%	0	0	0.0%	1.000
Surgical and medical procedures							
Hip arthroplasty	0	0	0.0%	1	1	0.5%	0.495
Serious Adverse Events							
Any Adverse Event	2	2	1.0%	5	4	2.1%	0.445
Gastrointestinal disorders							
Abdominal wall hematoma	1	1	0.5%	0	0	0.0%	1.000
Diverticulum intestinal	0	0	0.0%	1	1	0.5%	0.495
General disorders and administration site conditions							
Pyrexia	0	0	0.0%	1	1	0.5%	0.495
Hepatobiliary disorders							
Cholecystitis acute	0	0	0.0%	1	1	0.5%	0.495
Musculoskeletal and connective tissue disorders							
Arthritis	0	0	0.0%	1	1	0.5%	0.495
Intervertebral disc protrusion	1	1	0.5%	0	0	0.0%	1.000
Surgical and medical procedures							
Hip arthroplasty	0	0	0.0%	1	1	0.5%	0.495

* First n is number of events, and second n is number of patients experiencing an event.
† Fisher's exact test.

DETAILED DEVICE DESCRIPTION

GELSYN-3 consists of a buffered physiological solution of 0.84% sodium hyaluronate (**Table 5**).

Table 5: GELSYN-3 Components (per syringe)

Component Name	Unitary Amount
Sodium Hyaluronate	16.8 mg
Sodium Chloride	17.0 mg
Sodium Phosphate Dibasic Anhydrous	0.32 mg
Sodium Phosphate Monobasic Dehydrate	0.090 mg
Water for Injection	q.s to 2 mL

INTERACTIONS

None currently known.

HOW SUPPLIED

GELSYN-3 is supplied as a sterile solution in a pre-filled glass syringe. Only the contents of the syringe are sterile; exterior of the syringe is not sterile. One syringe and a 21 gauge needle in an individually sealed blister are contained within a carton box.

SHELF LIFE

36 months.

STORAGE INSTRUCTIONS

GELSYN-3 should be stored in the original packaging (protected from light) at room temperature < 25°C (77°F). DO NOT FREEZE.

DIRECTIONS FOR USE

1. Using an appropriate gauge needle, remove synovial fluid or effusion before injecting GELSYN-3. A 21-gauge needle of 1½ inch length has been provided with the product for user convenience. Gauges ranging from 18 to 22G may be used according to user preference.
2. To ensure a tight seal and prevent leakage during administration, secure the needle tightly while firmly holding the luer hub.
3. Inject the full 2 mL in one knee only.
4. Do not use if the packaging is opened or damaged.
5. Use the product immediately once opened; product must be protected from light.

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bioventus®
Active Healing Through Orthobiologics

GELSYN-3™

3 injection hyaluronic acid treatment

PATIENT INFORMATION

GELSYN-3™ (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 GELSYN-3. 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.

WHAT IS GELSYN-3?

GELSYN-3 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.

GELSYN-3 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 GELSYN-3 USED FOR?

GELSYN-3 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 GELSYN-3 GIVEN?

Your doctor, or other qualified health professional, will inject GELSYN-3 (2 mL) into your knee for a total of three weekly injections.

ARE THERE ANY REASONS WHY I SHOULD NOT RECEIVE GELSYN-3?

Your doctor will determine if you are a candidate for GELSYN-3 treatment, but you should also be aware that GELSYN-3 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:

- GELSYN-3 is only for injection into the knee, performed by a qualified doctor.
- GELSYN-3 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 GELSYN-3 have not been established.
- Use of GELSYN-3 in joints other than the knee and for conditions other than OA has not been tested.
- GELSYN-3 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.
- GELSYN-3 has not been tested in children (≤ 21 years of age).

WHAT ARE THE POSSIBLE SIDE EFFECTS?

- Extra-articular seepage of GELSYN-3 may cause undesired effects locally.
- Some side effects (also called reactions) may occur during the use of GELSYN-3, 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 GELSYN-3 or if you have any other problems, you should call your doctor.

WHAT ARE THE POTENTIAL BENEFITS OF GELSYN-3?

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 GELSYN-3. Patients with osteoarthritic knee joint pain, who had not obtained pain relief with other medications, received either three injections of GELSYN-3 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 GELSYN-3 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 GELSYN-3 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 GELSYN-3 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 GELSYN-3 injections to commercial hyaluronate, and demonstrated that the patients receiving GELSYN-3 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 GELSYN-3 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 GELSYN-3 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 GELSYN-3 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 GELSYN-3. 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 GELSYN-3

- GELSYN-3 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 GELSYN-3, or if you have any other problems, you should call your doctor.

HOW DO I GET MORE INFORMATION ABOUT GELSYN-3?

If you have any questions or would like to find out more about GELSYN-3, you may call 1-800-836-4080 (toll free) or 1-919-474-6700.

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GELSYN-3™

3 injection hyaluronic acid treatment

INFORMACIÓN PARA EL PACIENTE

GELSYN-3 (hialuronato de sodio 0,84 %)

Asegúrese de leer atentamente la siguiente información importante. Esta información no reemplaza el consejo de su médico. Su médico determinó que el dolor de rodilla que usted presenta es provocado por una osteoartritis, y que está en condiciones de recibir un tratamiento para aliviar el dolor, no farmacológico y sin cirugías denominado GELSYN-3. Consulte con su médico si no entiende esta información o si quiere obtener más detalles.

Glosario de términos

Hialuronato: el hialuronato es una sustancia natural que se encuentra en el cuerpo humano y está presente en grandes cantidades en las articulaciones. El hialuronato propio del cuerpo actúa como un lubricante y un amortiguador en las articulaciones, y es necesario para que las articulaciones funcionen de manera apropiada.

Medicamento antiinflamatorio no esteroide: a menudo, los medicamentos antiflamatorios no esteroides se abrevian "AINE". Los AINE son medicamentos tales como aspirina e ibuprofeno, que sirven para calmar el dolor, la fiebre y la inflamación.

Osteoartritis (OA): la osteoartritis es una afección que comprende el desgaste del cartílago (el revestimiento que protege los extremos de los huesos) y la pérdida de sustancia de amortiguación en las articulaciones.

¿QUÉ ES GELSYN-3?

GELSYN-3 contiene hialuronato de sodio (0,84 % de hialuronato de sodio), un material viscoelástico que se obtiene a partir de una fermentación bacteriana, y que es el mismo material que la sustancia natural que se encuentra en todo el cuerpo, incluso en las articulaciones, donde actúa como lubricante y amortiguador. La osteoartritis (OA) es un tipo de artritis que implica el desgaste del cartílago, el revestimiento protector que se encuentra en los extremos de los huesos. En los casos de OA, el hialuronato de sodio puede no ser suficiente, y se puede registrar una disminución de la calidad del hialuronato de sodio en las articulaciones.

GELSYN-3 se provee en una jeringa de vidrio de 2,25 mL (media cucharadita) que contiene 2,1 mL de solución. El contenido de la jeringa es estéril y se inyecta directamente en la rodilla, lo que da un total de 2,0 mL inyectados.

¿PARA QUÉ SE UTILIZA GELSYN-3?

GELSYN-3 se utiliza para aliviar el dolor en las rodillas provocado por la OA. Este medicamento se administra a pacientes que no obtienen suficiente alivio del dolor mediante medicamentos antiinflamatorios no esteroides (AINE) o medicamentos típicos para el dolor, como acetaminofén, o ejercicio y tratamiento físico.

¿CÓMO SE ADMINISTRA GELSYN-3?

El médico o cualquier otro profesional de la salud calificado le inyectarán GELSYN-3 (2 mL) en la rodilla, en un total de tres inyecciones semanales.

¿HAY ALGÚN MOTIVO POR EL QUE NO DEBERÍA RECIBIR GELSYN-3?

Su médico determinará si usted está en condiciones de recibir un tratamiento con GELSYN-3 pero, además, usted debe tener en cuenta que GELSYN-3 no debe ser administrado a pacientes que:

- alguna vez hayan tenido una respuesta alérgica a los productos que contienen hialuronato, tales como una erupción, picazón, urticarias, sofocos, inflamación de la cara, lengua o garganta, y/o dificultad para respirar;
- tengan una infección en la articulación de la rodilla o enfermedad de la piel, o infección alrededor del área donde se colocará la inyección, o problemas circulatorios en las piernas.

¿QUÉ ME DEBE ADVERTIR EL MÉDICO?

A continuación, se presentan ciertas consideraciones importantes para que usted las debata con su médico y las entienda, para evitar resultados no satisfactorios y complicaciones:

- GELSYN-3 se utiliza solamente para inyección en la rodilla, y solo lo puede administrar un médico calificado.
- GELSYN-3 no ha sido analizado para demostrar mejor alivio del dolor o seguridad cuando se lo combina con otros medicamentos inyectados.
- Si es alérgico a los productos de hialuronato, comuníqueselo a su médico.
- Después de las 48 horas de haber recibido la inyección, deberá evitar todas las actividades extenuantes (tales como correr, jugar al tenis, otros deportes activos, levantar cosas pesadas), y las actividades en las que se carga con el peso del cuerpo, como permanecer parado por más de una hora.
- No se ha establecido la seguridad y la efectividad de los ciclos de tratamiento repetidos de GELSYN-3.
- No se ha analizado la administración de GELSYN-3 en otras articulaciones además de las de rodilla ni para otras afecciones además de OA.
- No se ha analizado la administración de GELSYN-3 en mujeres embarazadas o lactantes. Debe comentarle a su médico si sospecha que está embarazada o si está amamantando a un niño.
- No se ha analizado la administración de GELSYN-3 en niños (≤ 21 años de edad).

¿CUÁLES SON LOS POSIBLES EFECTOS SECUNDARIOS?

- La administración articular extra de GELSYN-3 puede provocar efectos locales no deseados.
- Algunos efectos secundarios (también denominados reacciones) pueden ocurrir durante la administración de GELSYN-3, con síntomas tales como dolor de rodilla, rigidez, efusión, o hinchazón, sensación de calor, enrojecimiento, inflamación en el área de la administración de la inyección, artritis, o trastorno de la marcha. Estas reacciones secundarias se pueden aliviar aplicando hielo en la zona de la articulación tratada.
- Si alguno de estos síntomas o signos aparece mientras se le administra GELSYN-3, o si presenta algún otro problema, debe llamar a su médico.

¿CUÁLES SON LOS POSIBLES BENEFICIOS DE GELSYN-3?

Se realizó un estudio clínico que involucró a 380 pacientes con dolor de rodilla debido a OA en 23 centros en Europa (República Checa, Francia, Italia, Suiza, Eslovaquia y Alemania). El estudio investigó la seguridad y la efectividad de GELSYN-3. Los pacientes con dolor articular de rodilla provocado por la osteoartritis que no habían obtenido un alivio del dolor con otros medicamentos, recibieron tres inyecciones de GELSYN-3 o un hialuronato comercial en la articulación de la rodilla. Se realizó la medición del dolor de articulación de rodilla en distintos momentos, en las semanas 4, 12 y 26. Los pacientes a los que se les habían administrado tres inyecciones de GELSYN-3 obtuvieron el mismo alivio del dolor que los pacientes a los que se les habían administrado tres inyecciones de hialuronato comercial por hasta 26 semanas después de la primera inyección.

¿QUÉ DEMOSTRÓ EL ESTUDIO CLÍNICO?

Se realizó un estudio clínico en 23 centros en Europa (República Checa, Francia, Italia, Suiza, Eslovaquia y Alemania). Se administraron inyecciones intraarticulares de 2 mL de GELSYN-3 o de hialuronato comercial a un total de 380 pacientes con osteoartritis una vez por semana durante tres semanas consecutivas, con visitas de seguimiento programadas para las semanas 4, 12 y 26. Se realizó el tratamiento en 380 pacientes, de los cuales 192 fueron inyectados tres veces con GELSYN-3 y los 188 restantes fueron inyectados tres veces con un hialurónico comercial disponible. Se le pidió a los pacientes que calificaran el dolor bajo estas cinco condiciones: caminar en una superficie plana, subir o bajar las escaleras, durante la noche en la cama, sentado o recostado (descansando), y parado. Los pacientes calificaron el dolor de 0 (sin dolor) a 100 (dolor fuerte) marcando en una línea de 100 mm. Se evaluó el dolor de esta manera en las semanas 1, 4, 12 y 26 después de las tres inyecciones. Se usaron las calificaciones de dolor para comparar la efectividad de las inyecciones de GELSYN-3 con el hialuronato comercial, y se demostró que los pacientes que recibieron GELSYN-3 presentaron una mejora en el dolor de rodilla después de las 26 semanas igual que los pacientes que recibieron el hialurónico comercialmente disponible. La reducción media de las calificaciones del dolor de rodilla desde el período inicial fue de 30,8 mm (56 %) para el grupo de tratamiento con GELSYN-3, mientras que para el grupo tratado con el hialurónico comercial fue de 29,4 mm (53 %).

¿QUÉ EVENTOS ADVERSOS SE OBSERVARON EN LOS ESTUDIOS CLÍNICOS?

De los 380 pacientes que participaron en el estudio, se informaron uno o más eventos adversos para 160 pacientes (42,1 %) en algún momento durante el transcurso del estudio, luego de la primera inyección de la preparación de ácido hialurónico asignada. Los eventos adversos más frecuentes fueron dolor de espalda (11,8 %), artralgia (10,5 %), nasofaringitis (8,9 %) y dolor de cabeza (8,2 %). Los eventos de dolor de espalda, artralgia y dolor de cabeza fueron más frecuentes en el grupo de tratamiento con hialurónico comercial que en el grupo de tratamiento con GELSYN-3. Los eventos adversos considerados como relacionados con el tratamiento, ya fueran severos y/o serios, resultaron relativamente raros (1,6 %), y ninguno de los eventos adversos serios estuviera relacionado con el tratamiento. Los índices de eventos adversos generales para los pacientes tratados con GELSYN-3 fueron comparables con los índices del grupo tratado con el hialurónico comercialmente disponible.

¿QUÉ OTROS TRATAMIENTOS EXISTEN PARA LA OSTEOARTRITIS?

Si usted padece OA, puede llevar a cabo otros tratamientos además de aquel con GELSYN-3. Estos incluyen:

Tratamientos sin medicamentos

- Evitar actividades que produzcan dolor de rodilla
- Ejercicio
- Terapia física
- Extracción del líquido extra acumulado en la rodilla

Tratamientos con medicamentos

- Analgésicos, tales como acetaminofén o estupefacientes
- Medicamentos para reducir la inflamación (los signos de inflamación son hinchazón, dolor o enrojecimiento), tales como aspirinas, y otros medicamentos antiinflamatorios no esteroides (AINE), como ibuprofeno y naproxeno
- Medicamentos esteroides inyectados directamente en la rodilla

COSAS QUE DEBE SABER ACERCA DE GELSYN-3

- GELSYN-3 se utiliza solamente para inyección en la rodilla, y solo se lo puede administrar un médico calificado.
- Luego de que reciba la inyección debe evitar realizar ciertas actividades como correr, jugar al tenis o permanecer parado durante mucho tiempo por aproximadamente 48 horas.
- Si alguno de estos síntomas o signos aparece luego de que se le administra GELSYN-3, o si presenta algún otro problema, debe llamar inmediatamente a su médico.

¿DÓNDE SE PUEDE OBTENER MÁS INFORMACIÓN SOBRE GELSYN-3?

Si tiene alguna duda o le gustaría obtener más información acerca de GELSYN-3, llame al 1-800-836-4080 (número gratuito) o al 1-919-474-6700.

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